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PREAMBLE

It is important that the medical profession play a significant role in critically evaluating the use of diagnostic procedures and therapies as they are introduced and tested in the detection, management, or prevention of disease states. Rigorous and expert analysis of the available data documenting the absolute and relative benefits and risks of those procedures and therapies can produce helpful guidelines that improve the effectiveness of care, optimize patient outcomes, and favorably affect the overall cost of care by focusing resources on the most effective strategies.

The American College of Cardiology (ACC) Foundation and the American Heart Association (AHA) have jointly engaged in the production of such guidelines in the area of cardiovascular disease since 1980. The ACC/AHA Task Force on Practice Guidelines, whose charge is to develop, update, or revise practice guidelines for important cardiovascular diseases and procedures, directs this effort. Writing committees are charged with the task of performing an assessment of the evidence and acting as an independent group of authors to develop, update, or revise written recommendations for clinical practice.

Experts in the subject under consideration have been selected from both organizations to examine subject-specific data and write guidelines. The process includes additional representatives from other medical practitioner and specialty groups when appropriate. Writing committees are specifically charged to perform a formal literature review, weigh the strength of evidence for or against a particular treatment or procedure, and include estimates of expected health outcomes where data exist. Patient-specific modifiers, comorbidities, and issues of patient preference that might influence the choice of particular tests or therapies are considered, as well as frequency of follow-up and cost-effectiveness. When available, information from studies on cost will be considered; however, review of data on efficacy and clinical outcomes will
Table 1. Applying classification of recommendations and level of evidence.

<table>
<thead>
<tr>
<th>Level A</th>
<th>Level B</th>
<th>Level C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple (3-5) population risk strata evaluated*</td>
<td>Multiple (2-3) population risk strata evaluated*</td>
<td>Very limited (1-2) population risk strata evaluated*</td>
</tr>
<tr>
<td>General consistency of direction and magnitude of effect</td>
<td>Procedure/Treatment SHOULD be performed/administered</td>
<td>Procedure/Treatment SHOULD be performed/administered</td>
</tr>
<tr>
<td>• Recommendation that procedure or treatment is useful/effective</td>
<td>• Recommendation that procedure or treatment is useful/effective</td>
<td>• Recommendation that procedure or treatment is useful/effective</td>
</tr>
<tr>
<td>• Sufficient evidence from multiple randomized trials or meta-analyses</td>
<td>• Limited evidence from single randomized trial or non-randomized studies</td>
<td>• Only expert opinion, case studies, or standard-of-care</td>
</tr>
<tr>
<td>• Recommendation in favor of treatment or procedure being useful/effective</td>
<td>• Recommendation in favor of treatment or procedure being useful/effective</td>
<td>• Recommendation in favor of treatment or procedure being useful/effective</td>
</tr>
<tr>
<td>• Some conflicting evidence from multiple randomized trials or meta-analyses</td>
<td>• Some conflicting evidence from single randomized trial or non-randomized studies</td>
<td>• Only diverging expert opinion, case studies, or standard-of-care</td>
</tr>
<tr>
<td>• Recommendation’s usefulness/efficacy less well established</td>
<td>• Greater conflicting evidence from single randomized trial or non-randomized studies</td>
<td>• Recommendation’s usefulness/efficacy less well established</td>
</tr>
<tr>
<td>• Greater conflicting evidence from multiple randomized trials or meta-analyses</td>
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<td>• Only diverging expert opinion, case studies, or standard-of-care</td>
</tr>
<tr>
<td>• Recommendation that procedure or treatment not useful/effective and may be harmful</td>
<td>• Recommendation that procedure or treatment not useful/effective and may be harmful</td>
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</tr>
</tbody>
</table>

**Suggested phrases for writing recommendations**

<table>
<thead>
<tr>
<th>Class I</th>
<th>Class IIa</th>
<th>Class IIb</th>
<th>Class III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benefit &gt;&gt; Risk</td>
<td>Benefit &gt;&gt; Risk Additional studies with focused objectives needed</td>
<td>Benefit ≥ Risk Additional studies with broad objectives needed; Additional registry data would be helpful</td>
<td>Risk ≥ Benefit No additional studies needed</td>
</tr>
<tr>
<td>Procedure/Treatment SHOULD be performed/administered</td>
<td>IT IS REASONABLE to perform procedure/administer treatment</td>
<td>Procedure/Treatment MAY BE CONSIDERED</td>
<td>Procedure/Treatment should NOT be performed/administered since it is NOT HELPFUL and MAY BE HARMFUL</td>
</tr>
</tbody>
</table>

*Data available from clinical trials or registries about the usefulness/efficacy in different sub-populations, such as gender, age, history of diabetes, history of prior MI, history of heart failure, and prior aspirin use. A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Even though randomized trials are not available, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

In 2003, the ACC/AHA Task Force on Practice Guidelines developed a list of suggested phrases to use when writing recommendations. All recommendations in this guideline have been written in full sentences that express a complete thought, so that a recommendation, even if separated and presented apart from the rest of the document (including headings above sets of recommendations), would still convey the full intent of the recommendation. It is hoped that this will increase readers’ comprehension of the guidelines and will allow queries at the individual recommendation level.
constitute the primary basis for preparing recommendations in these guidelines.

The ACC/AHA Task Force on Practice Guidelines makes every effort to avoid any actual, potential, or perceived conflicts of interest that may arise as a result of an industry relationship or personal interest of the writing committee. Specifically, all members of the writing committee, as well as peer reviewers of the document, were asked to provide disclosure statements of all such relationships that may be perceived as real or potential conflicts of interest. Writing committee members are also strongly encouraged to declare a previous relationship with industry during their tenure, they are required to notify guideline staff in writing. The continued participation of the writing committee member will be reviewed. These statements are reviewed by the parent task force, reported orally to all members of the writing committee at each meeting, and updated and reviewed by the writing committee as changes occur. Please refer to the methodology manual for ACC/AHA guideline writing committees, available on the ACC and AHA World Wide Web sites (http://www.acc.org/qualityandscience/clinical/manual/manual_I.htm and http://circ.ahajournals.org/manual/), for further description of the policy on relationships with industry. Please see Appendix I for author relationships with industry and Appendix II for peer reviewer relationships with industry that are pertinent to these guidelines.

These practice guidelines are intended to assist healthcare providers in clinical decision making by describing a range of generally acceptable approaches for the diagnosis, management, and prevention of specific diseases or conditions. These guidelines attempt to define practices that meet the needs of most patients in most circumstances. Clinical decision making should consider the quality and availability of expertise in the area where care is provided. These guideline recommendations reflect a consensus of expert opinion after a thorough review of the available, current scientific evidence and are intended to improve patient care.

Patient adherence to prescribed and agreed on medical regimens and lifestyles is an important aspect of treatment. Prescribed courses of treatment in accordance with these recommendations will only be effective if they are followed. Because lack of patient understanding and adherence may adversely affect treatment outcomes, physicians and other healthcare providers should make every effort to engage the patient in active participation with prescribed medical regimens and lifestyles.

If these guidelines are used as the basis for regulatory or payer decisions, the ultimate goal is quality of care and serving the patient’s best interests. The ultimate judgment regarding care of a particular patient must be made by the healthcare provider and the patient in light of all of the circumstances presented by that patient. There are circumstances in which deviations from these guidelines are appropriate.

The guidelines will be reviewed annually by the ACC/AHA Task Force on Practice Guidelines and will be considered current unless they are updated, revised, or sunsetting and withdrawn from distribution. The executive summary and recommendations are published in the October 23, 2007, issue of the Journal of the American College of Cardiology and October 23, 2007, issue of Circulation. The full text-guidelines are e-published in the same issue of the journals noted above, as well as posted on the ACC (www.acc.org) and AHA (www.americanheart.org) Web sites. Copies of the full text and the executive summary are available from both organizations.

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Alice K. Jacobs, MD, FACC, FAHA, Vice Chair, ACC/AHA Task Force on Practice Guidelines

I. DEFINITION OF THE PROBLEM
A. Purpose of These Guidelines

These guidelines represent an update to those published in 2002 and are intended for physicians and nonphysician caregivers who are involved in the preoperative, operative, and postoperative care of patients undergoing noncardiac surgery. They provide a framework for considering cardiac risk of noncardiac surgery in a variety of patient and surgical situations. The writing committee that prepared these guidelines strove to incorporate what is currently known about perioperative risk and how this knowledge can be used in the individual patient.

The tables and algorithms provide quick references for decision making. The overriding theme of this document is that intervention is rarely necessary to simply lower the risk of surgery unless such intervention is indicated irrespective of the preoperative context. The purpose of preoperative evaluation is not to give medical clearance but rather to perform an evaluation of the patient’s current medical status; make recommendations concerning the evaluation, management, and risk of cardiac problems over the entire perioperative period; and provide a clinical risk profile that the patient, primary physician and nonphysician caregivers, anesthesiologist, and surgeon can use in making treatment decisions that may influence short- and long-term cardiac outcomes. No test should be performed unless it is likely to influence patient treatment. The goal of the consultation is the optimal care of the patient.
B. Methodology and Evidence

The ACC/AHA Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery conducted a comprehensive review of the literature relevant to perioperative cardiac evaluation published since the last publication of these guidelines in 2002. Literature searches were conducted in the following databases: PubMed, MEDLINE, and the Cochrane Library (including the Cochrane Database of Systematic Reviews and the Cochrane Controlled Trials Register). Searches were limited to the English language, the years 2002 through 2007, and human subjects. Related-article searches were conducted in MEDLINE to find additional relevant articles. Finally, committee members recommended applicable articles outside the scope of the formal searches.

All of the recommendations in this guideline update were converted from the tabular format used in the 2002 guidelines to a listing of recommendations that has been written in full sentences to express a complete thought, such that a recommendation, even if separated and presented apart from the rest of the document, would still convey the full intent of the recommendation. It is hoped that this will increase the reader’s comprehension of the guidelines. Also, the level of evidence, either an A, B, or C, for each recommendation is now provided (Table 1).

Recommendations

Recommendations for Preoperative Noninvasive Evaluation of Left Ventricular Function

Class IIa

1. It is reasonable for patients with dyspnea of unknown origin to undergo preoperative evaluation of left ventricular (LV) function. (Level of Evidence: C)

2. It is reasonable for patients with current or prior heart failure with worsening dyspnea or other change in clinical status to undergo preoperative evaluation of LV function if not performed within 12 months. (Level of Evidence: C)

Class IIb

1. Reassessment of LV function in clinically stable patients with previously documented cardiomyopathy is not well established. (Level of Evidence: C)

Class III

1. Routine perioperative evaluation of LV function in patients is not recommended. (Level of Evidence: B)

Recommendations for Preoperative Resting 12-Lead ECG

Class I

1. Preoperative resting 12-lead ECG is recommended for patients with at least 1 clinical risk factor* who are undergoing vascular surgical procedures. (Level of Evidence: B)

2. Preoperative resting 12-lead ECG is recommended for patients with known coronary heart disease, peripheral arterial disease, or cerebrovascular disease who are undergoing intermediate-risk surgical procedures. (Level of Evidence: C)

Class IIa

1. Preoperative resting 12-lead ECG is reasonable in persons with no clinical risk factors who are undergoing vascular surgical procedures. (Level of Evidence: B)

Class IIb

1. Preoperative resting 12-lead ECG may be reasonable in patients with at least 1 clinical risk factor who are undergoing intermediate-risk operative procedures. (Level of Evidence: B)

Class III

1. Preoperative and postoperative resting 12-lead ECGs are not indicated in asymptomatic persons undergoing low-risk surgical procedures. (Level of Evidence: B)

Recommendations for Noninvasive Stress Testing Before Noncardiac Surgery

Class I

1. Patients with active cardiac conditions (Table 2) in whom noncardiac surgery is planned should be evaluated and treated per ACC/AHA guidelines† before noncardiac surgery. (Level of Evidence: B)

Class IIa

1. Noninvasive stress testing of patients with 3 or more clinical risk factors and poor functional capacity (less than 4 metabolic equivalents [METs]) who require vascular surgery‡ is reasonable if it will change management. (Level of Evidence: B)

Class IIb

1. Noninvasive stress testing may be considered for patients with at least 1 to 2 clinical risk factors and poor functional capacity (less than 4 METs) who require vascular surgery.
Class III

1. Noninvasive testing is not useful for patients with no clinical risk factors undergoing intermediate-risk noncardiac surgery. (Level of Evidence: C)
2. Noninvasive testing is not useful for patients undergoing low-risk noncardiac surgery. (Level of Evidence: C)

Recommendations for Preoperative Coronary Revascularization With Coronary Artery Bypass Grafting or Percutaneous Coronary Intervention

(All of the Class I indications below are consistent with the ACC/AHA 2004 Guideline Update for Coronary Artery Bypass Graft Surgery.)

Class I

1. Coronary revascularization before noncardiac surgery is useful in patients with stable angina who have significant left main coronary artery stenosis. (Level of Evidence: A)
2. Coronary revascularization before noncardiac surgery is useful in patients with stable angina who have 3-vessel disease. (Survival benefit is greater when left ventricular ejection fraction is less than 0.50.) (Level of Evidence: A)
3. Coronary revascularization before noncardiac surgery is useful in patients with stable angina who have 2-vessel disease with significant proximal left anterior descending stenosis and either ejection fraction less than 0.50 or demonstrable ischemia on noninvasive testing. (Level of Evidence: A)
4. Coronary revascularization before noncardiac surgery is recommended for patients with high-risk unstable angina or non–ST-segment elevation myocardial infarction (MI). (Level of Evidence: A)
5. Coronary revascularization before noncardiac surgery is recommended in patients with acute ST-elevation MI. (Level of Evidence: A)

Class IIa

1. In patients in whom coronary revascularization with percutaneous coronary intervention (PCI) is appropriate for mitigation of cardiac symptoms and who need elective noncardiac surgery in the subsequent 12 months, a strategy of balloon angioplasty or bare-metal stent placement followed by 4 to 6 weeks of dual-antiplatelet therapy is probably indicated. (Level of Evidence: B)
2. In patients who have received drug-eluting coronary stents and who must undergo urgent surgical procedures that mandate the discontinuation of thienopyridine therapy, it is reasonable to continue aspirin if at all possible and restart the thienopyridine as soon as possible. (Level of Evidence: C)

Class IIb

1. The usefulness of preoperative coronary revascularization is not well established in high-risk ischemic patients (eg, abnormal dobutamine stress echocardiogram with at least 5 segments of wall-motion abnormalities). (Level of Evidence: C)
2. The usefulness of preoperative coronary revascularization is not well established for low-risk ischemic patients with an abnormal dobutamine stress echocardiogram (segments 1 to 4). (Level of Evidence: B)

Class III

1. It is not recommended that routine prophylactic coronary revascularization be performed in patients with stable coronary artery disease (CAD) before noncardiac surgery. (Level of Evidence: B)
2. Elective noncardiac surgery is not recommended within 4 to 6 weeks of bare-metal coronary stent implantation or within 12 months of drug-eluting coronary stent implantation in patients in whom thienopyridine therapy or aspirin and thienopyridine therapy will need to be discontinued perioperatively. (Level of Evidence: B)
3. Elective noncardiac surgery is not recommended within 4 weeks of coronary revascularization with balloon angioplasty. (Level of Evidence: B)

Recommendations for Beta-Blocker Medical Therapy

Class I

1. Beta blockers should be continued in patients undergoing surgery who are receiving beta blockers to treat angina, symptomatic arrhythmias, hypertension, or other ACC/AHA Class I guideline indications. (Level of Evidence: C)
2. Beta blockers should be given to patients undergoing vascular surgery who are at high risk for postoperative cardiac events. (Level of Evidence: B)

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4 METs who require intermediate-risk noncardiac surgery if it will change management. (Level of Evidence: B)

2. Noninvasive stress testing may be considered for patients with at least 1 to 2 clinical risk factors and good functional capacity (greater than or equal to 4 METs) who are undergoing vascular surgery. (Level of Evidence: B)

Class III

1. Noninvasive testing is not useful for patients with no clinical risk factors undergoing intermediate-risk noncardiac surgery. (Level of Evidence: C)
2. Noninvasive testing is not useful for patients undergoing low-risk noncardiac surgery. (Level of Evidence: C)

Recommendations for Preoperative Coronary Revascularization With Coronary Artery Bypass Grafting or Percutaneous Coronary Intervention

(All of the Class I indications below are consistent with the ACC/AHA 2004 Guideline Update for Coronary Artery Bypass Graft Surgery.)

Class I

1. Coronary revascularization before noncardiac surgery is useful in patients with stable angina who have significant left main coronary artery stenosis. (Level of Evidence: A)
2. Coronary revascularization before noncardiac surgery is useful in patients with stable angina who have 3-vessel disease. (Survival benefit is greater when left ventricular ejection fraction is less than 0.50.) (Level of Evidence: A)
3. Coronary revascularization before noncardiac surgery is useful in patients with stable angina who have 2-vessel disease with significant proximal left anterior descending stenosis and either ejection fraction less than 0.50 or demonstrable ischemia on noninvasive testing. (Level of Evidence: A)
4. Coronary revascularization before noncardiac surgery is recommended for patients with high-risk unstable angina or non–ST-segment elevation myocardial infarction (MI). (Level of Evidence: A)
5. Coronary revascularization before noncardiac surgery is recommended in patients with acute ST-elevation MI. (Level of Evidence: A)

Class IIa

1. In patients in whom coronary revascularization with percutaneous coronary intervention (PCI) is appropriate for mitigation of cardiac symptoms and who need elective noncardiac surgery in the subsequent 12 months, a strategy of balloon angioplasty or bare-metal stent placement followed by 4 to 6 weeks of dual-antiplatelet therapy is probably indicated. (Level of Evidence: B)
2. In patients who have received drug-eluting coronary stents and who must undergo urgent surgical procedures that mandate the discontinuation of thienopyridine therapy, it is reasonable to continue aspirin if at all possible and restart the thienopyridine as soon as possible. (Level of Evidence: C)

Class IIb

1. The usefulness of preoperative coronary revascularization is not well established in high-risk ischemic patients (eg, abnormal dobutamine stress echocardiogram with at least 5 segments of wall-motion abnormalities). (Level of Evidence: C)
2. The usefulness of preoperative coronary revascularization is not well established for low-risk ischemic patients with an abnormal dobutamine stress echocardiogram (segments 1 to 4). (Level of Evidence: B)

Class III

1. It is not recommended that routine prophylactic coronary revascularization be performed in patients with stable coronary artery disease (CAD) before noncardiac surgery. (Level of Evidence: B)
2. Elective noncardiac surgery is not recommended within 4 to 6 weeks of bare-metal coronary stent implantation or within 12 months of drug-eluting coronary stent implantation in patients in whom thienopyridine therapy or aspirin and thienopyridine therapy will need to be discontinued perioperatively. (Level of Evidence: B)
3. Elective noncardiac surgery is not recommended within 4 weeks of coronary revascularization with balloon angioplasty. (Level of Evidence: B)

Recommendations for Beta-Blocker Medical Therapy

Class I

1. Beta blockers should be continued in patients undergoing surgery who are receiving beta blockers to treat angina, symptomatic arrhythmias, hypertension, or other ACC/AHA Class I guideline indications. (Level of Evidence: C)
2. Beta blockers should be given to patients undergoing vascular surgery who are at high risk for postoperative cardiac events. (Level of Evidence: B)

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High-risk unstable angina/non–ST-elevation MI patients were identified as those with age greater than 75 years, accelerating tempo of ischemic symptoms in the preceding 48 hours, ongoing rest pain greater than 20 minutes in duration, pulmonary edema, angina with S3 gallop or rales, new or worsening mitral regurgitation murmur, hypotension, bradycardia, tachycardia, dynamic ST-segment change greater than or equal to 1 mm, new or presumed new bundle-branch block on ECG, or elevated cardiac biomarkers, such as troponin.

Care should be taken in applying recommendations on beta-blocker therapy to patients with decompensated heart failure, nonischemic cardiomyopathy, or severe valvular heart disease in the absence of coronary heart disease.
cardiac risk owing to the finding of ischemia on preoperative testing. (Level of Evidence: B)

Class IIa

1. Beta blockers are probably recommended for patients undergoing vascular surgery in whom preoperative assessment identifies coronary heart disease. (Level of Evidence: B)

2. Beta blockers are probably recommended for patients in whom preoperative assessment for vascular surgery identifies high cardiac risk, as defined by the presence of more than 1 clinical risk factor.* (Level of Evidence: B)

3. Beta blockers are probably recommended for patients in whom preoperative assessment identifies coronary heart disease or high cardiac risk, as defined by the presence of more than 1 clinical risk factor,* who are undergoing intermediate-risk or vascular surgery. (Level of Evidence: B)

Class IIb

1. The usefulness of beta blockers is uncertain for patients who are undergoing either intermediate-risk procedures or vascular surgery, in whom preoperative assessment identifies a single clinical risk factor.* (Level of Evidence: C)

2. The usefulness of beta blockers is uncertain in patients undergoing vascular surgery with no clinical risk factors who are not currently taking beta blockers. (Level of Evidence: B)

Class III

1. Beta blockers should not be given to patients undergoing surgery who have absolute contraindications to beta blockade. (Level of Evidence: C)

Recommendations for Statin Therapy

Class I

1. For patients currently taking statins and scheduled for noncardiac surgery, statins should be continued. (Level of Evidence: B)

Class IIa

1. For patients undergoing vascular surgery with or without clinical risk factors, statin use is reasonable. (Level of Evidence: B)

Class IIb

1. For patients with at least 1 clinical risk factor who are undergoing intermediate-risk procedures, statins may be considered. (Level of Evidence: C)

Recommendations for Alpha-2 Agonists

Class IIa

1. Alpha-2 agonists for perioperative control of hypertension may be considered for patients with known CAD or at least 1 clinical risk factor who are undergoing surgery. (Level of Evidence: B)

Class III

1. Alpha-2 agonists should not be given to patients undergoing surgery who have contraindications to this medication. (Level of Evidence: C)

Recommendation for Preoperative Intensive Care Monitoring

Class IIb

1. Preoperative intensive care monitoring with a pulmonary artery catheter for optimization of hemodynamic status might be considered; however, it is rarely required and should be restricted to a very small number of highly selected patients whose presentation is unstable and who have multiple comorbid conditions. (Level of Evidence: B)

Recommendations for Use of Volatile Anesthetic Agents

Class IIa

1. It can be beneficial to use volatile anesthetic agents during noncardiac surgery for the maintenance of general anesthesia in hemodynamically stable patients at risk for myocardial ischemia. (Level of Evidence: B)

Recommendation for Prophylactic Intraoperative Nitroglycerin

Class IIb

1. The usefulness of intraoperative nitroglycerin as a prophylactic agent to prevent myocardial ischemia and cardiac morbidity is unclear for high-risk patients undergoing noncardiac surgery, particularly those who have required nitrate therapy to control angina. The recommendation for prophylactic use of nitroglycerin must take into account the anesthetic plan and patient hemodynamics and must recognize that vasodilation and hypovolemia can readily occur during anesthesia and surgery. (Level of Evidence: C)

Recommendation for Use of Transesophageal Echocardiography

Class IIa

1. The emergency use of intraoperative or perioperative transesophageal echocardiography is reasonable to determine the cause of an acute, persistent, and life-threatening hemodynamic abnormality. (Level of Evidence: C)

Recommendation for Maintenance of Body Temperature

Class I

1. Maintenance of body temperature in a normothermic range is recommended for most procedures other than during periods in which mild
hypothermia is intended to provide organ protection (eg, during high aortic cross-clamping). (Level of Evidence: B)

Recommendations for Perioperative Control of Blood Glucose Concentration

Class IIa

1. It is reasonable that blood glucose concentration be controlled during the perioperative period in patients with diabetes mellitus or acute hyperglycemia who are at high risk for myocardial ischemia or who are undergoing vascular and major noncardiac surgical procedures with planned intensive care unit admission. (Level of Evidence: B)

Class IIb

1. The usefulness of strict control of blood glucose concentration during the perioperative period is uncertain in patients with diabetes mellitus or acute hyperglycemia who are undergoing noncardiac surgical procedures without planned intensive care unit admission. (Level of Evidence: C)

Recommendations for Perioperative Use of Pulmonary Artery Catheters

Class IIb

1. Use of a pulmonary artery catheter may be reasonable in patients at risk for major hemodynamic disturbances that are easily detected by a pulmonary artery catheter; however, the decision must be based on 3 parameters: patient disease, surgical procedure (ie, intraoperative and postoperative fluid shifts), and practice setting (experience in pulmonary artery catheter use and interpretation of results), because incorrect interpretation of the data from a pulmonary artery catheter may cause harm. (Level of Evidence: B)

Class III

1. Routine use of a pulmonary artery catheter perioperatively, especially in patients at low risk of developing hemodynamic disturbances, is not recommended. (Level of Evidence: A)

Recommendations for Intraoperative and Postoperative Use of ST-Segment Monitoring

Class IIa

1. Intraoperative and postoperative ST-segment monitoring can be useful to monitor patients with known CAD or those undergoing vascular surgery, with computerized ST-segment analysis, when available, used to detect myocardial ischemia during the perioperative period. (Level of Evidence: B)

Class IIIb

1. Intraoperative and postoperative ST-segment monitoring may be considered in patients with single or multiple risk factors for CAD who are undergoing noncardiac surgery. (Level of Evidence: B)

Recommendations for Surveillance for Perioperative MI

Class I

1. Postoperative troponin measurement is recommended in patients with ECG changes or chest pain typical of acute coronary syndrome. (Level of Evidence: C)

Class IIIb

1. The use of postoperative troponin measurement is not well established in patients who are clinically stable and have undergone vascular and intermediate-risk surgery. (Level of Evidence: C)

Class III

1. Postoperative troponin measurement is not recommended in asymptomatic stable patients who have undergone low-risk surgery. (Level of Evidence: C)

II. GENERAL APPROACH TO THE PATIENT

This guideline focuses on the evaluation of the patient undergoing noncardiac surgery who is at risk for perioperative cardiac morbidity or mortality. In patients with known CAD or the new onset of signs or symptoms suggestive of CAD, baseline cardiac assessment should be performed. In the asymptomatic patient, a more extensive assessment of history and physical examination is warranted in those individuals 50 years of age or older, because the evidence related to the determination of cardiac risk factors and derivation of a revised cardiac risk index occurred in this population. Preoperative cardiac evaluation must therefore be carefully tailored to the circumstances that have prompted the evaluation and to the nature of the surgical illness. In patients in whom coronary revascularization is not an option, it is often not necessary to perform a noninvasive stress test. Under other, less urgent circumstances, the preoperative cardiac evaluation may lead to a variety of responses, including cancellation of an elective procedure.

If a consultation is requested, then it is important to identify the key questions and ensure that all of the perioperative caregivers are considered when providing a response. Once a consultation has been obtained, the consultant should review available patient data, obtain a history, and perform a physical examination that includes a comprehensive cardiovascular examination and elements pertinent to the patient’s problem and the proposed surgery. A critical role of the consultant is to determine the stability of the patient’s cardiovascular status and whether the patient is in optimal medical condition within the context of the hospital and surgical environment.
surgical illness. The consultant may recommend changes in medication, suggest preoperative tests or procedures, or propose higher levels of care postoperatively. In general, preoperative tests are recommended only if the information obtained will result in a change in the surgical procedure performed, a change in medical therapy or monitoring during or after surgery, or a postponement of surgery until the cardiac condition can be corrected or stabilized.

The consultant must also bear in mind that the perioperative evaluation may be the ideal opportunity to effect the long-term treatment of a patient with significant cardiac disease or risk of such disease. The referring physician and patient should be informed of the results of the evaluation and implications for the patient’s prognosis. It is the cardiovascular consultant’s responsibility to ensure clarity of communication so that findings and impressions will be incorporated effectively into the patient’s overall plan of care. This ideally would include direct communication with the surgeon, anesthesiologist, and other physicians, as well as frank discussion directly with the patient and, if appropriate, the family. The consultant should not use phrases such as “clear for surgery.”

A. History

A careful history is crucial to the discovery of cardiac and/or comorbid diseases that would place the patient in a high surgical risk category. The history should seek to identify serious cardiac conditions such as unstable coronary syndromes, prior angina, recent or past MI, decompensated heart failure, significant arrhythmias, and severe valvular disease (Table 2). It should also determine whether the patient has a prior history of a pacemaker or implantable cardioverter defibrillator (ICD) or a history of orthostatic intolerance and should identify risk factors associated with increased perioperative cardiovascular risk. In patients with established cardiac disease, any recent change in symptoms must be ascertained. Accurate recording of current medications used, including herbal and other nutritional supplements, and dosages is essential. Use of alcohol, tobacco, and over-the-counter and illicit drugs should be documented.

The history should also seek to determine the patient’s functional capacity (Table 3). An assessment of an individual’s capacity to perform a spectrum of common daily tasks has been shown to correlate well with maximum oxygen uptake by treadmill testing. A patient classified as high risk owing to age or known CAD but who is asymptomatic and runs for 30 minutes daily may need no further evaluation. In contrast, a sedentary patient without a history of cardiovascular disease but with clinical factors that suggest increased perioperative risk may benefit from a more extensive preoperative evaluation.

B. Physical Examination and Routine Laboratory Tests

A careful cardiovascular examination should include an assessment of vital signs (including measurement of blood pressure in both arms), carotid pulse contour and bruits, jugular venous pressure and pulsations, auscultation of the lungs, precordial palpation and auscultation, abdominal palpation, and examination of the extremities for edema and vascular integrity.

Anemia imposes a stress on the cardiovascular system that may exacerbate myocardial ischemia and aggravate heart failure. Hematocrits of less than 28% are associated with an increased incidence of perioperative ischemia and postoperative complications in patients undergoing prostate and vascular surgery. 

Table 2. Active Cardiac Conditions for Which the Patient Should Undergo Evaluation and Treatment Before Noncardiac Surgery (Class I, Level of Evidence: B)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unstable coronary syndromes</td>
<td>Unstable or severe angina* (CCS class III or IV)† Recent MI‡</td>
</tr>
<tr>
<td>Decompenated HF (NYHA functional class IV; worsening or new-onset HF)</td>
<td>High-grade atrioventricular block Mobitz II atrioventricular block Third-degree atrioventricular heart block Symptomatic ventricular arrhythmias Supraventricular arrhythmias (including atrial fibrillation) with uncontrolled ventricular rate (HR greater than 100 beats per minute at rest) Symptomatic bradycardia Newly recognized ventricular tachycardia Severe aortic stenosis (mean pressure gradient greater than 40 mm Hg, aortic valve area less than 1.0 cm², or symptomatic) Symptomatic mitral stenosis (progressive dyspnea on exertion, exertional presyncope, or HF)</td>
</tr>
<tr>
<td>Severe valvular disease</td>
<td></td>
</tr>
</tbody>
</table>

* According to Campeau.† May include “stable” angina in patients who are unusually sedentary.‡ The American College of Cardiology National Database Library defines recent MI as more than 7 days but less than or equal to 1 month (within 30 days). CCS indicates Canadian Cardiovascular Society; HF, heart failure; HR, heart rate; MI, myocardial infarction; NYHA, New York Heart Association.
C. Multivariable Indices to Predict Preoperative Cardiac Morbidity

The basic clinical evaluation obtained by history, physical examination, and review of the ECG usually provides the consultant with sufficient data to estimate cardiac risk. Lee et al. derived and validated a “simple index” for the prediction of cardiac risk for stable patients undergoing nonurgent major noncardiac surgery. Six independent risk correlates were identified: ischemic heart disease (defined as history of MI, history of positive treadmill test, use of nitroglycerin, current complaints of chest pain thought to be secondary to coronary ischemia, or ECG with abnormal Q waves); congestive heart failure (defined as history of heart failure, pulmonary edema, paroxysmal nocturnal dyspnea, peripheral edema, bilateral rales, S₃, or chest radiograph with pulmonary vascular redistribution); cerebral vascular disease (history of transient ischemic attack or stroke); high-risk surgery (abdominal aortic aneurysm or other vascular, thoracic, abdominal, or orthopedic surgery); preoperative insulin treatment for diabetes mellitus; and preoperative creatinine greater than 2 mg per dL. Increasing numbers of risk factors correlated with increased risk, yet the risk was substantially lower than described in many of the original indices. The Revised Cardiac Risk Index has become one of the most widely used risk indices.

D. Clinical Assessment

In the original guidelines, the committee chose to segregate clinical risk factors into major, intermediate, and minor risk factors. There continues to be a group of active cardiac conditions that when present indicate major clinical risk. The presence of 1 or more of these conditions mandates intensive management and may result in delay or cancellation of surgery unless the surgery is emergent (Table 2). These include

- Unstable coronary syndromes,
  - Unstable or severe angina,
  - Recent MI,
- Decompensated heart failure,
- Significant arrhythmias,
- Severe valvular disease.

Given the increasing use of the Revised Cardiac Risk Index, the committee chose to replace the intermediate-risk category with the clinical risk factors from the index, with the exclusion of the type of surgery, which is incorporated elsewhere in the approach to the patient. Clinical risk factors include

- history of ischemic heart disease,
- history of compensated or prior heart failure,
- history of cerebrovascular disease,
- diabetes mellitus, and
- renal insufficiency.

A history of MI or abnormal Q waves by ECG is listed as a clinical risk factor, whereas an acute MI (defined as at least 1 documented MI 7 days or less before the examination) or recent MI (more than 7 days but less than or equal to 1 month before the examination) with evidence of important ischemic risk by clinical symptoms or noninvasive study is an active cardiac condition. This definition reflects the consensus of the ACC Cardiovascular Database Committee. Minor predictors are recognized markers for cardiovascular disease that have not been proven to independently increase perioperative risk. For example, advanced age (greater than 70 years), abnormal ECG (LV hypertrophy, left bundle-branch block, ST-T abnormalities), rhythm other than sinus, and uncontrolled systemic hypertension. The presence of multiple minor predictors might lead to a

Table 3. Estimated Energy Requirements for Various Activities

<table>
<thead>
<tr>
<th>METs</th>
<th>Can you...</th>
<th>Can you...</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 MET</td>
<td>Take care of yourself?</td>
<td>Climb a flight of stairs or walk up a hill?</td>
</tr>
<tr>
<td></td>
<td>Eat, dress, or use the toilet?</td>
<td>Walk on level ground at 4 mph (6.4 kph)?</td>
</tr>
<tr>
<td></td>
<td>Walk indoors around the house?</td>
<td>Run a short distance?</td>
</tr>
<tr>
<td></td>
<td>Walk a block or 2 on level ground at 2 to 3 mph (3.2 to 4.8 kph)?</td>
<td>Do heavy work around the house like scrubbing floors or lifting or moving heavy furniture?</td>
</tr>
<tr>
<td>4 METs</td>
<td>Do light work around the house like dusting or washing dishes?</td>
<td>Participate in moderate recreational activities like golf, bowling, dancing, doubles tennis, or throwing a baseball or football?</td>
</tr>
<tr>
<td></td>
<td>Greater than 10 METs</td>
<td>Participate in strenuous sports like swimming, singles tennis, football, basketball, or skiing?</td>
</tr>
</tbody>
</table>

kph indicates kilometers per hour; MET, metabolic equivalent; and mph, miles per hour.
* Modified from Hlatky et al., copyright 1989, with permission from Elsevier, and adapted from Fletcher et al.

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higher suspicion of CAD but is not incorporated into the recommendations for treatment.

1. **Stepwise Approach to Perioperative Cardiac Assessment**

   Figure 1 presents in algorithmic form a framework for determining which patients are candidates for cardiac testing. Since publication of the perioperative cardiovascular evaluation guidelines in 2002, several new randomized trials and cohort studies have led to modification of the original algorithm. Given the availability of this evidence, the Writing Committee chose to include the level of the recommendations and strength of evidence for many of the pathways.

   Step 1: The consultant should determine the urgency of noncardiac surgery. In many instances, patient- or surgery-specific factors dictate an obvious strategy (eg, emergent surgery) that may not allow for further cardiac assessment or treatment. In such cases, the consultant may function best by providing recommendations for perioperative medical management and surveillance.

   Step 2: Does the patient have 1 of the active cardiac conditions or clinical risk factors listed in Table 2? If not, proceed to Step 3. In patients being considered for elective noncardiac surgery, the presence of unstable coronary disease, decompensated heart failure, or severe arrhythmia or valvular heart disease usually leads to cancellation or delay of surgery until the cardiac problem has been clarified and treated appropriately. Examples of unstable coronary syndromes include previous MI with evidence of important ischemic risk by clinical symptoms or noninvasive study, unstable or severe angina, and new or poorly controlled ischemia-mediated heart failure. Many patients in these circumstances are referred for coronary angiography to assess further therapeutic options. Depending on the results of the test or interventions and the risk of delaying surgery, it may be appropriate to proceed to the planned surgery with maximal medical therapy.

   Step 3: Is the patient undergoing low-risk surgery? In these patients, interventions based on cardiovascular testing in stable patients would rarely result in a change in management, and it would be appropriate to proceed with the planned surgical procedure.

   Step 4: Does the patient have good functional capacity without symptoms? In highly functional...
### III. DISEASE-SPECIFIC APPROACHES

#### A. Coronary Artery Disease

1. **Patients With Known CAD**

   In patients with known CAD, as well as those with previously occult coronary disease, the questions become 1) What is the amount of myocardium in jeopardy? 2) What is the ischemic threshold, that is, the amount of stress required to produce ischemia? 3) What is the patient’s ventricular function? and 4) Is the patient on his or her optimal medical regimen? Clarification of these questions is an important goal of the preoperative history and physical examination, and selected noninvasive testing is used to determine the patient’s prognostic gradient of ischemic response during stress testing.

#### B. Hypertension

For stage 3 hypertension (systolic blood pressure greater than or equal to 180 mm Hg and diastolic blood pressure greater than or equal to 110 mm Hg), the potential benefits of delaying surgery to optimize the effects of antihypertensive medications should be weighed against the risk of delaying the surgical procedure. With rapidly acting intravenous agents, blood pressure can usually be controlled within a matter of several hours. One randomized trial was unable to demonstrate a benefit to delaying surgery in chronically treated hypertensive patients who presented for noncardiac surgery with diastolic blood pressure between 110 and 130 mm Hg and who had no previous MI, unstable or severe angina pectoris, renal failure, pregnancy-induced hypertension, LV hypertrophy, previous coronary revascularization, aortic stenosis, preoperative dysrhythmias, conduction defects, or stroke.

Several authors have suggested withholding angiotensin-converting enzyme inhibitors and angiotensin receptor antagonists the morning of surgery. Consideration should be given to restarting angiotensin-converting enzyme inhibitors in the postoperative period only after the patient is euvolemic, to decrease the risk of perioperative renal dysfunction.

#### C. Valvular Heart Disease

In symptomatic aortic stenosis, elective noncardiac surgery should generally be postponed or canceled. Such patients require aortic valve replacement before management. Other types of surgery may be associated with similar risk to vascular surgery but have not been studied extensively. In nonvascular surgery in which the perioperative morbidity related to the procedures ranges from 1% to 5% (intermediate-risk surgery), there are insufficient data to determine the best strategy (proceeding with the planned surgery with tight heart rate control with beta blockade or further cardiovascular testing if it will change management).
elective but necessary noncardiac surgery. If the aortic stenosis is severe but asymptomatic, the surgery should be postponed or canceled if the valve has not been evaluated within the year. On the other hand, in patients with severe aortic stenosis who refuse cardiac surgery or are otherwise not candidates for aortic valve replacement, noncardiac surgery can be performed with a mortality risk of approximately 10%. If a patient is not a candidate for valve replacement, percutaneous balloon aortic valvuloplasty may be reasonable as a bridge to surgery in hemodynamically unstable adult patients with aortic stenosis who are at high risk for aortic valve replacement surgery and may be reasonable in adult patients with aortic stenosis in whom aortic valve replacement cannot be performed because of serious comorbid conditions.

Significant mitral stenosis increases the risk of heart failure. However, preoperative surgical correction of mitral valve disease is not indicated before noncardiac surgery, unless the valvular condition should be corrected to prolong survival and prevent complications unrelated to the proposed noncardiac surgery. When the stenosis is severe, the patient may benefit from balloon mitral valvuloplasty or open surgical repair before high-risk surgery.

In patients with persistent or permanent atrial fibrillation who are at high risk for thromboembolism, preoperative and postoperative therapy with intravenous heparin or subcutaneous low-molecular-weight heparin may be considered to cover periods of subtherapeutic anticoagulation. When they undergo surgery that may result in bacteremia and the need for careful anticoagulation management. The Seventh American College of Chest Physicians Consensus Conference on Antithrombotic and Thrombolytic Therapy recommends the following: for patients who require minimally invasive procedures (dental work, superficial biopsies), the recommendation is to briefly reduce the international normalized ratio to the low or subtherapeutic range and resume the normal dose of oral anticoagulation immediately after the procedure. Perioperative heparin therapy is recommended for patients in whom the risk of bleeding with oral anticoagulation is high and the risk of thromboembolism without anticoagulation is also high (mechanical valve in the mitral position; Bjork-Shiley valve; recent [ie, less than 1 year] thrombosis or embolus; or 3 or more of the following risk factors: atrial fibrillation, previous embolus at any time, hypercoagulable condition, mechanical prosthesis, and LV ejection fraction less than 30%). For patients between these 2 extremes, physicians must assess the risk and benefit of reduced anticoagulation versus perioperative heparin therapy.

### IV. SURGERY-SPECIFIC ISSUES

Although different operations are associated with different cardiac risks, these differences are most often a reflection of the context in which the patient under- goes surgery (stability or opportunity for adequate preoperative preparation), surgery-specific factors (eg, fluid shifts, stress levels, duration of procedure, or blood loss), or patient-specific factors (the incidence of CAD associated with the condition for which the patient is undergoing surgery). The surgical procedures have been classified as low risk, high risk, and vascular. Although coronary disease is the overwhelming risk factor for perioperative morbidity, procedures with different levels of stress are associated with different levels of morbidity and mortality. Superficial and ophthalmologic procedures represent the lowest risk and are rarely associated with excess morbidity and mortality. Major vascular procedures represent the highest-risk procedures and are now considered distinctly in the decision to perform further evaluation because of the large body of evidence regarding the value of perioperative interventions in this population (Figure 1). Both endovascular aortic aneurysm repair and carotid endarterectomy should be considered within the intermediate-risk category, distinct from the open vascular surgery procedures, on the basis of their preoperative morbidity and mortality rates, but clinicians should incorporate the similarly poor long-term survival rates that accompany these procedures into their decision-making processes. Within the intermediate-risk category, morbidity and mortality vary depending on the surgical location and extent of the procedure. Some procedures may be short, with minimal fluid shifts, whereas others may be associated with prolonged duration, large fluid shifts, and greater potential for postoperative myocardial ischemia and respiratory depression. Therefore, the physician must exercise judgment to correctly assess perioperative surgical risks and the need for further evaluation.

### V. SUPPLEMENTAL PREOPERATIVE EVALUATION

#### A. Assessment of LV Function

Resting LV function has been evaluated preoperatively before noncardiac surgery by radionuclide angiography, echocardiography, and contrast ventriculography. It is noteworthy that resting LV function was not found to be a consistent predictor of perioperative ischemic events.

#### B. Assessment of Risk for CAD and Assessment of Functional Capacity

1. **The 12-Lead ECG**

Although the optimal time interval between obtaining a 12-lead ECG and elective surgery is unknown, general consensus suggests that an ECG within 30 days
of surgery is adequate for those with stable disease in whom a preoperative ECG is indicated.

2. Exercise Stress Testing for Myocardial Ischemia and Functional Capacity

The aim of supplemental preoperative testing is to provide an objective measure of functional capacity, to identify the presence of important preoperative myocardial ischemia or cardiac arrhythmias, and to estimate perioperative cardiac risk and long-term prognosis.

3. Noninvasive Stress Testing

Pharmacological stress with vasodilators or adrenergic stimulation in conjunction with radionuclide or echocardiographic cardiac imaging has been shown to predict perioperative cardiac events in patients scheduled for noncardiac surgery who are unable to exercise. Importantly, perioperative cardiac risk is directly related to the extent of jeopardized viable myocardium identified by stress cardiac imaging.

The expertise of the practitioner’s available stress laboratory resources in identifying severe coronary disease is as important as the particular type of stress test ordered. For patients with unstable myocardial ischemia, who are at high risk for noncardiac surgery, it is usually appropriate to proceed with coronary angiography or to attempt to stabilize them with aggressive medical treatment rather than to perform a stress test.

VI. PERIOPERATIVE THERAPY

A. Preoperative Coronary Revascularization With Coronary Artery Bypass Grafting or PCI

1. Preoperative Coronary Artery Bypass Grafting

Until recently, all of the evidence regarding the value of surgical coronary revascularization was derived from cohort studies in patients who presented for noncardiac surgery after successful cardiac surgery. There are now several randomized trials that have assessed the overall benefit of prophylactic coronary bypass surgery to lower the perioperative cardiac risk of noncardiac surgery, the results of which can be applied to specific subsets of patients and will be discussed later.

The first large, randomized trial (Coronary Artery Revascularization Prophylaxis [CARP]) was published by McFalls and colleagues, who randomly assigned 510 patients with significant coronary artery stenosis from among 5899 patients scheduled for vascular operations to either coronary artery revascularization before surgery or no revascularization before surgery. The authors concluded that routine coronary revascularization in patients with stable cardiac symptoms before elective vascular surgery does not significantly alter the long-term outcome or short-term risk of death or MI.

The DECREASE (Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography) II trial was designed to evaluate the utility of cardiac testing in patients undergoing major vascular surgery with intermediate cardiac risk factors and adequate beta-blocker therapy. A composite end point of death and nonfatal MI was assessed at 30 days after vascular surgery. This study confirms that extensive cardiac ischemia is a risk factor for perioperative cardiac events, but it was too small to assess the effect of revascularization.

The DECREASE-V pilot study identified a high-risk cohort of patients scheduled for vascular surgery who were randomized to best medical therapy and revascularization or best medical therapy alone before vascular surgery. There was no difference in the combined outcomes of death or MI at 30 days or 1 year between the revascularization and medical therapy groups, although there was a high incidence of cardiac events in this high-risk cohort. This study was not sized to definitively answer the question as to the value of preoperative coronary revascularization in high-risk patients; however, the findings are consistent with the previously published literature suggesting a lack of benefit of preoperative coronary revascularization in preventing death or MI. The indications for preoperative surgical coronary revascularization, therefore, are essentially identical to those recommended by the ACC/AHA 2004 Guideline Update for Coronary Artery Bypass Graft Surgery and the accumulated data on which those conclusions were based.

2. Preoperative PCI

Review of the literature suggests that PCI before noncardiac surgery is of no value in preventing perioperative cardiac events, except in those patients in whom PCI is independently indicated for an acute coronary syndrome. However, unscheduled noncardiac surgery in a patient who has undergone a prior PCI presents special challenges, particularly with regard to management of dual-antiplatelet agents required in those who receive coronary stents.

3. PCI Without Stents: Coronary Balloon Angioplasty

Several retrospective series of coronary balloon angioplasty before noncardiac surgery have been reported. On the basis of the available literature, delaying noncardiac surgery for more than 8 weeks after balloon angioplasty increases the chance that restenosis at the angioplasty site will have occurred and theoretically increases the chances of perioperative ischemia or MI. However, performing the surgical procedure too soon after the PCI procedure might also be hazardous. Delaying surgery for at least 2 to 4 weeks after balloon angioplasty to allow for healing of the vessel injury at the balloon treatment site is supported by a study by Brilakis et al. Daily aspirin antiplatelet therapy should be continued perioperatively. The risk of stopping the aspirin should be
weighed against the benefit of reduction in bleeding complications from the planned surgery.

4. PCI: Bare-Metal Coronary Stents

If a coronary stent is used in the revascularization procedure, as in the majority of percutaneous revascularization procedures, further delay of noncardiac surgery may be beneficial. Bare-metal stent thrombosis is most common in the first 2 weeks after stent placement and is exceedingly rare (less than 0.1% of most case series) more than 4 weeks after stent placement. Given that stent thrombosis will result in Q-wave MI or death in the majority of patients in whom it occurs, and given that the risk of bare-metal stent thrombosis diminishes after endothelialization of the stent has occurred (which generally takes 4 to 6 weeks), it appears reasonable to delay elective noncardiac surgery for 4 to 6 weeks to allow for at least partial endothelialization of the stent, but not for more than 12 weeks, when restenosis may begin to occur.

A thienopyridine (ticlopidine or clopidogrel) is generally administered with aspirin for 4 weeks after bare-metal stent placement. The thienopyridines and aspirin inhibit platelet aggregation and reduce stent thrombosis but increase the risk of bleeding. Rapid endothelialization of bare-metal stents makes late thrombosis rare, and thienopyridines are rarely needed for more than 4 weeks after implantation of bare-metal stents. For this reason, delaying surgery 4 to 6 weeks after bare-metal stent placement allows proper thienopyridine use to reduce the risk of coronary stent thrombosis; then, after the thienopyridine has been discontinued, the noncardiac surgery can be performed. However, once the thienopyridine is stopped, its effects do not diminish immediately. It is for this reason that some surgical teams request a 1-week delay after thienopyridines are discontinued before the patient proceeds to surgery. In patients with bare-metal stents, daily aspirin antiplatelet therapy should be continued perioperatively. The risk of stopping the aspirin should be weighed against the benefit of reduction in bleeding complications from the planned surgery. In the setting of noncardiac surgery in patients who have recently received a bare-metal stent, the risk of stopping dual-antiplatelet agents prematurely (within 4 weeks of implantation) is significant compared with the risk of major bleeding from most commonly performed surgeries.

5. PCI: Drug-Eluting Stents

Thrombosis of drug-eluting stents may occur late and has been reported up to 1.5 years after implantation, particularly in the context of discontinuation of antiplatelet agents before noncardiac surgery. In January 2007, an AHA/ACC/Society for Cardiovascular Angiography and Interventions (SCAI)/American College of Surgeons (ACS)/American Diabetes Association (ADA) science advisory was issued regarding the prevention of premature discontinuation of dual-antiplatelet therapy in patients with coronary artery stents. This advisory report concluded that premature discontinuation of dual-antiplatelet therapy markedly increases the risk of catastrophic stent thrombosis and death and/or MI. To eliminate the premature discontinuation of thienopyridine therapy, the advisory group recommended the following:

- Elective procedures for which there is a significant risk of perioperative or postoperative bleeding should be deferred until patients have completed an appropriate course of thienopyridine therapy (12 months after drug-eluting stent implantation if they are not at high risk of bleeding and a minimum of 1 month for bare-metal stent implantation).
- For patients treated with drug-eluting stents who are to undergo subsequent procedures that mandate discontinuation of thienopyridine therapy, aspirin should be continued if at all possible and the thienopyridine restarted as soon as possible after the procedure because of concerns about late-stent thrombosis.

Given the above reports and recommendations, the use of drug-eluting stents for coronary revascularization before imminent or planned noncardiac surgery that will necessitate the discontinuation of dual-antiplatelet agents is not recommended.

In patients with stable CAD, the indications for PCI in the preoperative setting should be identical to those developed by the joint ACC/AHA Task Force that provided guidelines for the use of PCI in patients with stable angina and asymptomatic ischemia. There is no evidence to support prophylactic preoperative percutaneous revascularization in patients with asymptomatic ischemia or stable angina, particularly with drug-eluting stents. Similarly, there is little evidence to show how long a more distant PCI (ie, months to years before noncardiac surgery) protects against perioperative MI or death. Because additional coronary restenosis is unlikely to occur more than 8 to 12 months after PCI (whether or not a stent is used), it is reasonable to expect ongoing protection against untoward perioperative ischemic complications in currently asymptomatic, active patients who had been symptomatic before complete percutaneous coronary revascularization more than 8 to 12 months previously.

6. Perioperative Management of Patients With Prior PCI Undergoing Noncardiac Surgery

For patients who have undergone successful coronary intervention with or without stent placement before planned or unplanned noncardiac surgery, there is uncertainty regarding how much time should pass before the noncardiac procedure is performed. One approach is outlined in Figure 2, which is based...
on expert opinion. Given the reports of late drug-eluting stent thrombosis and the current recommendations discussed above, clinicians should remain vigilant even beyond 365 days after drug-eluting stent placement. The times of 14, 30 to 45, and 365 days for balloon angioplasty, bare-metal stent, and drug-eluting stent, respectively, recommended in Figure 2 are somewhat arbitrary because of a lack of high-quality evidence.

Consideration should be given to continuing dual-antiplatelet therapy in the perioperative period for any patient needing noncardiac surgery that falls within the time frame that requires dual-antiplatelet therapy, particularly those who have received drug-eluting stents. In addition, consideration should be given to continuing dual-antiplatelet therapy perioperatively beyond the recommended time frame in any patient at high risk for the consequences of stent thrombosis, such as patients in whom previous stent thrombosis has occurred, after left main stenting, after multivessel stenting, and after stent placement in the only remaining coronary artery or graft conduit. Even after thienopyridines have been discontinued, serious consideration should be given to continuation of aspirin antiplatelet therapy perioperatively in any patient with previous placement of a drug-eluting stent. The risk of stopping antiplatelet therapy should be weighed against the benefit of reduction in bleeding complications from the planned surgery. If thienopyridines must be discontinued before major surgery, aspirin should be continued and the thienopyridine restarted as soon as possible. There is no evidence that warfarin, antithrombotics, or glycoprotein IIb/IIIa agents will reduce the risk of stent thrombosis after discontinuation of oral antiplatelet agents.54

7. Perioperative Management in Patients Who Have Received Intracoronary Brachytherapy

Intracoronary radiation with gamma or beta brachytherapy has been used in the past to treat recurrent in-stent restenosis. Antiplatelet therapy should be continued as per the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention, with a class IIa recommendation.55

Serious consideration should be given to continuing dual-antiplatelet therapy in the perioperative period for any patient who has received brachytherapy for restenosis or in-stent restenosis, particularly those in whom additional stents (bare-metal or drug-eluting) were placed at the time of or subsequent to the administration of brachytherapy. The risk of stopping antiplatelet therapy should be weighed against the benefit of reduction in bleeding complications from the planned surgery.

8. Strategy of Percutaneous Revascularization in Patients Needing Urgent Noncardiac Surgery

Patients who require percutaneous coronary revascularization in whom near-term noncardiac surgery is necessary require special consideration.54,56 A potential strategy is outlined in Figure 3. Percutaneous coronary revascularization should not be routinely performed in patients who need noncardiac surgery unless clearly indicated for high-risk coronary anatomy, unstable angina, MI, or hemodynamically or rhythmically unstable active CAD amenable to percutaneous intervention. If PCI is necessary, then the urgency of the noncardiac surgery and the risk of bleeding associated with the surgery in a patient taking dual-antiplatelet agents need to be considered. If there is little risk of bleeding or if the noncardiac surgery can be delayed 12 months or more, then PCI with drug-eluting stents and prolonged aspirin and thienopyridine therapy could be considered if the patient meets the criteria outlined in the AHA/ACC/SCAI/ACS/ADA Science Advisory Group recommendations discussed above.54 If the noncardiac surgery is likely to occur within 1 to 12 months, then a strategy of bare-metal stenting and 4 to 6 weeks of aspirin and thienopyridine therapy with continuation of aspirin perioperatively should be considered. Although the risk of restenosis with this strategy is higher than with drug-eluting stents, restenotic lesions are usually not life-threatening, even though they may present as an
acute coronary syndrome, and they can usually be dealt with by repeat PCI if necessary. If the noncardiac surgery is imminent (within 2 to 6 weeks) and the risk of bleeding is high, then consideration should be given to balloon angioplasty and provisional bare-metal stenting plus continued aspirin antiplatelet monotherapy, with restenosis dealt with by repeat PCI if necessary. If the noncardiac surgery is urgent or emergent, then cardiac risks, the risk of bleeding, and the long-term benefit of coronary revascularization must be weighed, and if coronary revascularization is absolutely necessary, coronary artery bypass grafting combined with the noncardiac surgery could be considered.

B. Perioperative Medical Therapy

1. Perioperative Beta-Blocker Therapy

Since publication of the ACC/AHA focused update on perioperative beta-blocker therapy, several randomized trials have been published that have not demonstrated the efficacy of these agents, in contrast to the earlier studies that demonstrated efficacy. Although many of the randomized controlled trials of beta blocker therapy are small, the weight of evidence—especially in aggregate—suggests a benefit to perioperative beta-blockade during noncardiac surgery in high-risk patients (Table 5). Current studies suggest that beta blockers reduce perioperative ischemia and may reduce the risk of MI and death in patients with known CAD. Available evidence strongly suggests but does not definitively prove that when possible, beta blockers should be started days to weeks before elective surgery. Additionally, data suggest that long-acting beta blockade may be superior to short-acting beta blockade.

B. Perioperative Medical Therapy

1. Perioperative Beta-Blocker Therapy

Since publication of the ACC/AHA focused update on perioperative beta-blocker therapy, several randomized trials have been published that have not demonstrated the efficacy of these agents, in contrast to the earlier studies that demonstrated efficacy. Although many of the randomized controlled trials of beta blocker therapy are small, the weight of evidence—especially in aggregate—suggests a benefit to perioperative beta-blockade during noncardiac surgery in high-risk patients (Table 5). Current studies suggest that beta blockers reduce perioperative ischemia and may reduce the risk of MI and death in patients with known CAD. Available evidence strongly suggests but does not definitively prove that when possible, beta blockers should be started days to weeks before elective surgery. Additionally, data suggest that long-acting beta blockade may be superior to short-acting beta blockade.

### Table 5. Recommendations for Perioperative Beta-Blocker Therapy Based on Published Randomized Clinical Trials

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<th>CHD or High Cardiac Risk</th>
<th>Patients Currently Taking Beta Blockers</th>
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<td>Class IIa, Level of Evidence: B</td>
<td>Patients found to have myocardial ischemia on preoperative testing; Class I, Level of Evidence: B*</td>
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* Applies to patients found to have coronary ischemia on preoperative testing.
† Applies to patients found to have coronary heart disease.

Figure 3. Treatment for patients requiring percutaneous coronary intervention who need subsequent surgery. ACS indicates acute coronary syndrome; COR, class of recommendation; LOE, level of evidence; and MI, myocardial infarction.
come. Poldermans and colleagues\textsuperscript{39} randomly assigned 770 intermediate-risk patients to cardiac stress testing (n = 386) or no testing (n = 384). The authors concluded that cardiac testing can safely be omitted in intermediate-risk patients, provided that beta blockers aimed at tight heart rate control are prescribed. Accumulating evidence suggests that effective heart rate control with beta blockers should be targeted at less than 65 beats per minute.

\textbf{b. Withdrawal of Beta Blockers}

Concerns regarding the discontinuation of beta-blocker therapy in the perioperative period have existed for several decades.\textsuperscript{62–64} As noted in the recommendations, continuation of beta-blocker therapy in the perioperative period is a Class I indication, and accumulating evidence suggests that titration to maintain tight heart rate control should be the goal.

\textbf{2. Perioperative Statin Therapy}

The evidence accumulated thus far suggests a protective effect of perioperative statin use on cardiac complications during noncardiac surgery. Hindler and colleagues\textsuperscript{65} conducted a meta-analysis to evaluate the overall effect of preoperative statin therapy, and a 44% reduction in mortality was observed. Le Manach and colleagues\textsuperscript{66} demonstrated that postoperative statin withdrawal (more than 4 days) was an independent predictor of postoperative myonecrosis. Most of these data are observational and identify patients in whom time of initiation of statin therapy and duration of statin therapy are unclear.

\textbf{3. Alpha-2 Agonists}

Wijeysundera and colleagues\textsuperscript{67} performed a meta-analysis of perioperative alpha-2 agonist administration through 2002 comprising 23 trials enrolling 3395 patients. Alpha-2 agonists reduced mortality (relative risk 0.76, 95\% CI 0.63 to 0.91) and MI (relative risk 0.66, 95\% CI 0.46 to 0.94) during vascular surgery.

More recently, Wallace et al.\textsuperscript{68} conducted a prospective, double-blinded, clinical trial on patients with or at risk for CAD and determined that administration of clonidine had minimal hemodynamic effects and reduced postoperative mortality for up to 2 years.

\textbf{4. Perioperative Calcium Channel Blockers}

A meta-analysis of perioperative calcium channel blockers in noncardiac surgery that was published in 2003 identified 11 studies involving 1007 patients.\textsuperscript{69} Calcium channel blockers significantly reduced ischemia (relative risk 0.49, 95\% confidence interval 0.30 to 0.80, \(P=0.004\)) and supraventricular tachycardia (relative risk 0.52, 95\% confidence interval 0.37 to 0.72, \(P\) less than 0.0001) and were associated with trends toward reduced death and MI.

\textbf{C. Intraoperative Electromagnetic Interference With Implanted Pacemakers and Cardioverter Defibrillators}

It is important to be aware of the potential for adverse interactions between electrical/magnetic activity and pacemaker or ICD function that may occur during the operative period. A practice advisory on this topic has been published recently by the American Society of Anesthesiology.\textsuperscript{70} Patients with permanent pacemakers, who are pacemaker dependent, should have their device evaluated within 3 to 6 months before significant surgical procedures, as well as after surgery. Significant surgical procedures include major abdominal or thoracic surgery, particularly when the surgery involves large amounts of electrocautery. If a patient is pacemaker dependent, the device should be reprogrammed to an asynchronous mode during surgery (VOO or DOO), or a magnet should be placed over the device during surgery. Implantable cardioverter defibrillator devices should have their tachyarrhythmia treatment algorithms programmed off before surgery and turned on after surgery to prevent unwanted shocks due to spurious signals that the device might interpret as ventricular tachycardia or fibrillation. If emergent cardioversion is required, the paddles should be placed as far from the implanted device as possible and in an orientation likely to be perpendicular to the orientation of the device leads (anterior-posterior paddle position is preferred). After the surgery, the function of the implanted device should be assessed and in some cases formally evaluated. In the case of an ICD, an interrogated programmer printout should be produced to verify that its antitachycardia function has been restored to its active status.

Placement of a magnet over an implanted device has variable effects depending on the type of device, its manufacturer, and its model. If a magnet will be used during surgery in a patient with a pacemaker who is pacemaker dependent, it should be applied before surgery to be certain that appropriate asynchronous pacing is triggered by the magnet. Magnet application will affect only the antitachycardia function of an ICD. With some models of ICDs, the magnet will first suspend the antitachycardia (shocking) function and then actually turn the therapy off. With other ICD models, the magnet will only temporarily disable the shock function (while the magnet is in place), and the therapy will then become active again on its removal (either intentional or unintentional). Programming the shock function off with an ICD programmer (and turning it back on after the surgery) is the preferred method of addressing these issues. Because some patients with ICDs are also pacemaker dependent, the pacing function of the ICD may need to be programmed to an asynchronous mode (eg, VOO or DOO) during surgery to prevent electromagnetic interference–induced inhibition.
VII. ANESTHETIC CONSIDERATIONS AND INTRAOPERATIVE MANAGEMENT

There are many different approaches to the details of the anesthetic care of the cardiac patient, including the use of specific anesthetic agents or anesthetic techniques (eg, general, regional, or monitored anesthetic care). Each has implications regarding anesthetic and intraoperative monitoring. In addition, no study has clearly demonstrated a change in outcome from the routine use of the following techniques: a pulmonary artery catheter, ST-segment monitor, transesophageal echocardiography, or intravenous nitroglycerin. Therefore, the choice of anesthetic technique and intraoperative monitors is best left to the discretion of the anesthesia care team. Intraoperative management may be influenced by the perioperative plan, including the need for postoperative monitoring, ventilation, analgesia, and the perioperative use of anticoagulants or antiplatelet agents. Therefore, a discussion of these issues before the planned surgery will allow for a smooth transition through the perioperative period.

B. Perioperative Pain Management

From the cardiac perspective, pain management may be a crucial aspect of perioperative care. Although no randomized controlled study specifically addressing analgesic regimens has demonstrated improvement in outcome, patient-controlled analgesia techniques are associated with greater patient satisfaction and lower pain scores. An effective analgesic regimen must be included in the perioperative plan and should be based on issues unique to a given patient undergoing a specific procedure at a specific institution.

VIII. PERIOPERATIVE SURVEILLANCE

A. Intraoperative and Postoperative Use of Pulmonary Artery Catheters

Use of a pulmonary artery catheter may provide significant information critical to the care of the cardiac patient; however, the potential risk of complications and the cost associated with catheter insertion and use must be considered. Practice guidelines for pulmonary artery catheterization, as well as methods of performing perioperative optimization of the high-risk surgical patient, have been developed and reported elsewhere.71,72 Evidence of benefit of pulmonary artery catheter use from controlled trials is equivocal, and a large-scale cohort study demonstrated potential harm.73

B. Surveillance for Perioperative MI

Perioperative MI can be documented by assessing clinical symptoms, serial ECGs, cardiac-specific biomarkers, comparative ventriculographic studies before and after surgery, radioisotopic or magnetic resonance studies specific for myocardial necrosis, and autopsy studies. Over the last decade, the diagnosis of myocardial damage has become more sensitive with the application of cardiac biomarkers. Measurement of troponin T or I facilitates the recognition of myocardial damage with much smaller amounts of injury. Because of the augmentation of sensitivity, the threshold to diagnosis of an MI is lower and the frequency greater.74 On the basis of current evidence, in patients without documented CAD, surveillance should be restricted to those patients who develop perioperative signs of cardiovascular dysfunction. The diagnosis of a perioperative MI has both short- and long-term prognostic value.

On the basis of the available literature, routine measurement of troponin after surgery is more likely to identify patients without acute MI than with MI. Moreover, studies of troponin elevations neither consistently show associations with adverse cardiovascular outcomes at any time point nor provide insight into the effect of treatment on outcomes in patients with an elevated troponin level. Although it is known that elevations in troponin are more likely to occur in patients with more extensive CAD, the role of revascularization in patients with an elevated troponin level but no other manifestation of MI remains unclear. Until each of these issues has been addressed, routine troponin measurement cannot be recommended. Perioperative surveillance for acute coronary syndromes with routine ECG and cardiac serum biomarkers is unnecessary in clinically low-risk patients undergoing low-risk operative procedures.

IX. POSTOPERATIVE AND LONG-TERM MANAGEMENT

Advances in preoperative risk assessment, surgical and anesthetic techniques, and better implementation of medical therapy have served to decrease the frequency of cardiovascular complications associated with noncardiac surgery. Despite these advances, cardiovascular complications represent the most common and most treatable adverse consequences of noncardiac surgery. Those patients who have a symptomatic MI after surgery have a marked increase in the risk of death, reaching as high as 40% to 70%.75 Because the consequences of infarction are so severe, management of patients must continue after risk assessment to the postoperative setting.

A. Myocardial Infarction: Surveillance and Treatment

In contrast to clinically silent elevations in troponin, the development of coronary artery plaque rupture that results in thrombotic coronary artery occlusion requires rapid intervention. Although fibrinolytic therapy has been administered to patients for life-threatening pulmonary embolus shortly after noncardiac surgery, the fibrinolytic dosage has generally been less and has been administered over a longer time interval than is standard for the treatment of acute MI.76,77 Only a single small
study has evaluated the role of immediate angiography and angioplasty among 48 patients who were believed able to take aspirin and intravenous heparin and to undergo immediate angiography and PCI; this study demonstrated that such a strategy is feasible and may be beneficial. These reperfusion procedures should not be performed routinely on an emergency basis in postoperative patients in whom MI is not related to an acute coronary occlusion. Moreover, because of the requirements for periprocedural anticoagulation and postrevascularization antiplatelet therapy, the benefits of revascularization must be weighed against the risk of postoperative bleeding, individualizing the decision for referral.

Therapy with aspirin, a beta blocker, and an angiotensin-converting enzyme inhibitor, particularly for patients with low ejection fractions or anterior infarctions, may be beneficial, whether or not the patients are rapidly taken to the catheterization laboratory. An extensive evidence-based review of therapy for acute MI can be found in the ACC/AHA Guidelines for the Management of Patients With Acute Myocardial Infarction. Similarly, the “ACC/AHA Guidelines for Unstable Angina/Non–ST-Segment Elevation Myocardial Infarction” represent an important template for management of this condition in the postoperative setting.

In the approach to the long-term postoperative management of noncardiac surgery patients, one should first appreciate that the occurrence of an intraoperative nonfatal MI carries a high risk for future cardiac events that are often dominated by cardiovascular death. Patients who sustain a perioperative MI should have evaluation of LV function performed before hospital discharge, and standard postinfarction therapeutic medical therapy should be prescribed as defined in the ACC/AHA acute MI guidelines. The ACC/AHA guidelines for post-MI evaluation in these types of patients should be followed as soon as possible after surgical recovery.

B. Long-Term Management

Although the occasion of noncardiac surgery brings a period of increased cardiovascular risk, physicians should also use the opportunity to ensure appropriate cardiovascular medical therapy. In the recently released ACC/AHA 2005 Guidelines for the Management of Patients With Peripheral Arterial Disease, treatment with a statin to achieve a low-density lipoprotein level of less than 100 mg/dL, control of blood pressure to less than 140/90 mm Hg, smoking cessation, and antiplatelet therapy all received Class I indications. It is important that the care team responsible for the long-term care of the patient be provided with complete information about any cardiovascular abnormalities or risk factors for CAD identified during the perioperative period.

X. CONCLUSIONS

Successful perioperative evaluation and management of high-risk cardiac patients undergoing noncardiac surgery requires careful teamwork and communication between surgeon, anesthesiologist, the patient’s primary caregiver, and the consultant. In general, indications for further cardiac testing and treatments are the same as in the nonoperative setting, but their timing is dependent on several factors, including the urgency of noncardiac surgery, patient-specific risk factors, and surgery-specific considerations. The use of both noninvasive and invasive preoperative testing should be limited to those circumstances in which the results of such tests will clearly affect patient management. Finally, for many patients, noncardiac surgery represents their first opportunity to receive an appropriate assessment of both short- and long-term cardiac risk. Thus, the consultant best serves the patient by making recommendations aimed at lowering the immediate perioperative cardiac risk, as well as assessing the need for subsequent postoperative risk stratification and interventions directed at modifying coronary risk factors. Future research should be directed at determining the value of routine prophylactic medical therapy versus more extensive diagnostic testing and interventions.

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Appendix I. Author Relationships With Industry: ACC/AHA Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery

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This table represents the actual or potential relationships with industry that were reported as of May 11, 2007. This table was updated in conjunction with all meetings and conference calls of the writing committee. QI/CME indicates quality improvement/continuing medical education.

*Significant relationship (greater than $10,000).

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<td>N.A. Mark Estes III</td>
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<td>Bradley Knight</td>
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<td>M. Sean McMurtry</td>
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<th>Ownership/Partnership/Principal</th>
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<th>Salary</th>
<th>Institutional or Other Financial Benefit</th>
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<td>Rick Nishimura</td>
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<td>Don Poldermans</td>
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<td>Robert Safford</td>
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<td>Jay Silverstein</td>
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<td>Kim Williams</td>
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<td>Janet Wyman</td>
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This table represents the relationships of peer reviewers with industry that were disclosed at the time of peer review of this guideline. It does not necessarily reflect relationships with industry at the time of publication. Names are listed in alphabetical order within each category of review. Participation in the peer review process does not imply endorsement of this document. ACC indicates American College of Cardiology; ACCF, American College of Cardiology Foundation; and AHA, American Heart Association.

*Significant relationship (greater than $10,000).
†Spousal relationship.
Appendix III. Abbreviations List

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<tr>
<th>Abbreviation</th>
<th>Definition</th>
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<tr>
<td>ACC</td>
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<td>ACS</td>
<td>American College of Surgeons</td>
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<tr>
<td>ADA</td>
<td>American Diabetes Association</td>
</tr>
<tr>
<td>AHA</td>
<td>American Heart Association</td>
</tr>
<tr>
<td>CAD</td>
<td>coronary artery disease</td>
</tr>
<tr>
<td>CARP</td>
<td>Coronary Artery Revascularization Prophylaxis</td>
</tr>
<tr>
<td>DECREASE</td>
<td>Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography</td>
</tr>
<tr>
<td>ECG</td>
<td>electrocardiogram</td>
</tr>
<tr>
<td>ICD</td>
<td>implantable cardioverter-defibrillator</td>
</tr>
<tr>
<td>LV</td>
<td>left ventricle/left ventricular</td>
</tr>
<tr>
<td>MET</td>
<td>metabolic equivalent</td>
</tr>
<tr>
<td>MI</td>
<td>myocardial infarction</td>
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<tr>
<td>PCI</td>
<td>percutaneous coronary intervention</td>
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<tr>
<td>SCAI</td>
<td>Society for Cardiovascular Angiography and Interventions</td>
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REFERENCES


An erratum has been published regarding this article. Please see the attached page or:
http://circ.ahajournals.org/cgi/content/full/circulationaha;117/6/e161
PCI Focused Update

2007 Focused Update of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

2007 Writing Group to Review New Evidence and Update the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention, Writing on Behalf of the 2005 Writing Committee

Spencer B. King III, MD, MACC, FAHA, FSCAI, Co-Chair*†; Sidney C. Smith, Jr, MD, FACC, FAHA, Co-Chair*‡; John W. Hirshfeld, Jr, MD, FACC, FAHA, FSCAI§; Alice K. Jacobs, MD, FACC, FAHA, FSCAI; Douglass A. Morrison, MD, PhD, FACC, FSCAI; David O. Williams, MD, FACC, FAHA, FSCAI§

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*Chair of 2005 Writing Committee.
†Recused from voting on Section 7: Antiplatelet Therapy.
‡Society for Cardiovascular Angiography and Interventions Representative.
§Recused from voting on Section 8: Bare-Metal and Drug-Eluting Stents.
∥Former Task Force member during this writing effort.


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Appendix 2

focused update). It is important to note that this focused population and of other new data deemed to have an impact based vetting process as important to the relevant patient family of late-breaking clinical trials identified through a broad-consensus of expert opinion following a thorough review primarily during their more than 20 years of partnership.

methodology that the ACC and AHA have developed basis as quickly as possible while maintaining the rigorous and quality of care. Evidence will be reviewed at least trends that could have a major impact on patient outcomes efficiently respond to important science and treatment evidence will be reviewed in an ongoing fashion to more acquired up to 3 years to complete. Now, however, new periods for PCI may not be available, there may be a very clear clinical consensus that a particular test or therapy is useful and effective. Both the class of recommendation and level of evidence listed in the focused updates are based on consideration of the evidence reviewed in previous iterations of the guidelines as well as the focused update. Of note, the implications of older studies that have informed recommendations but have not been repeated in contemporary settings are carefully considered.

The ACC/AHA practice guidelines are intended to assist practice community, key stakeholders, regulatory agencies, and other sources free of relationships with industry or other potential bias.

Number of previous trials showing consistent results

Need for consistency with other new guidelines or guideline revisions

In analyzing the data and developing updated recommendations and supporting text, the focused update writing group used evidence-based methodologies developed by the ACC/AHA Task Force on Practice Guidelines, which are described elsewhere.

The schema for class of recommendation and level of evidence is summarized in Table 1, which also illustrates how the grading system provides estimates of the size of the treatment effect and the certainty of the treatment effect. Note that a recommendation with Level of Evidence B or C does not imply that the recommendation is weak.

Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although randomized trials may not be available, there may be a very clear clinical consensus that a particular test or therapy is useful and effective. Both the class of recommendation and level of evidence listed in the focused updates are based on consideration of the evidence reviewed in previous iterations of the guidelines as well as the focused update. Of note, the implications of older studies that have informed recommendations but have not been repeated in contemporary settings are carefully considered.

The ACC/AHA practice guidelines address patient populations (and health care providers) residing in North America. As such, drugs that are not currently available in North America are discussed in the text without a specific class of recommendation. For studies performed in large numbers of subjects outside of North America, each writing committee reviews the potential impact of different practice patterns and patient populations on the treatment effect and on the relevance to the ACC/AHA target population to determine whether the findings should form the basis of a specific recommendation.

The ACC/AHA practice guidelines are intended to assist health care providers in clinical decision making by describing a range of generally acceptable approaches for the diagnosis, management, and prevention of specific diseases or conditions. The guidelines attempt to define practices that meet the needs of most patients in most
circumstances. The ultimate judgment regarding care of a particular patient must be made by the health care provider and patient in light of all the circumstances presented by that patient. Thus, there are circumstances in which deviations from these guidelines may be appropriate. Clinical decision making should consider the quality and availability of expertise in the area where care is provided. These guidelines may be used as the basis for regulatory or payer decisions, but the ultimate goal is quality of care and serving the patient’s best interests.

Prescribed courses of treatment in accordance with these recommendations are only effective if they are followed by the patient. Because lack of patient adherence may adversely affect treatment outcomes, health care providers should make every effort to engage the patient in active participation with prescribed treatment.

The ACC/AHA Task Force on Practice Guidelines makes every effort to avoid any actual, potential, or perceived conflict of interest arising from industry relationships or personal interests of a writing committee member. All writing committee members and peer reviewers were required to provide disclosure statements of all such relationships pertaining to the trials and other evidence under consideration (see Appendixes 1 and 2). Final recommendations were balloted to all writing committee members. Writing committee members with significant (greater than $10,000) relevant relationships with industry (RWI) were required to recuse themselves from voting on that recommendation. Writing committee members who did not participate are not listed as authors of this focused update.

With the exception of the recommendations presented in this statement, the full guidelines remain current. Only the

---

### Table 1. Applying Classification of Recommendations and Level of Evidence†

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<th>CLASS I</th>
<th>Benefit &gt;&gt; Risk</th>
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<tr>
<td>CLASS IIa</td>
<td>Benefit &gt;&gt; Risk</td>
<td>Additional studies with focused objectives needed IT IS REASONABLE to perform procedure/administer treatment</td>
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<td>CLASS IIb</td>
<td>Benefit ≥ Risk</td>
<td>Additional studies with broad objectives needed; additional registry data would be helpful Procedure/Treatment MAY BE CONSIDERED</td>
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<td>CLASS III</td>
<td>Risk ≥ Benefit</td>
<td>No additional studies needed Procedure/Treatment should NOT be performed/administered SINCE IT IS NOT HELP-FUL AND MAY BE HARMFUL</td>
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†Data available from clinical trials or registries about the usefulness/efficacy in different subpopulations, such as gender, age, history of diabetes, history of prior myocardial infarction, history of heart failure, and prior aspirin use. A recommendation with Level of Evidence B or C does not imply that the recommendation is weak. Many important clinical questions addressed in the guidelines do not lend themselves to clinical trials. Even though randomized trials are not available, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

*In 2003, the ACC/AHA Task Force on Practice Guidelines developed a list of suggested phrases to use when writing recommendations. All guideline recommendations have been written in full sentences that express a complete thought, such that a recommendation, even if separated and presented apart from the rest of the document (including headings above sets of recommendations), would still convey the full intent of the recommendation. It is hoped that this will increase readers’ comprehension of the guidelines and will allow queries at the individual recommendation level.

---

Suggested phrases for writing recommendations:
- should is reasonable
- is recommended can be useful/effective/beneficial
- is indicated is probably recommended or indicated
- is useful/effective/beneficial may/might be considered
- usefulness/effectiveness is unknown/unclear/uncertain or not well established
- may/might be reasonable

---

For example:

- Suggested phrases for writing recommendations:
  - should be...
  - is reasonable...
  - is indicated...
  - is useful/effective/beneficial...
  - may/might be considered...
  - usefulness/effectiveness is unknown/unclear/uncertain or not well established...
  - may/might be reasonable...

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recommendations from the affected section(s) of the full guidelines are included in this focused update. For easy reference, all recommendations from any section of guidelines impacted by a change are presented with a notation as to whether they remain current, are new, or have been modified. When evidence impacts recommendations in more than one set of guidelines, those guidelines are updated concurrently.

The recommendations in this focused update will be considered current until they are superseded by another focused update or the full-text guidelines are revised. This focused update is published in the January 15, 2008, issue of the Journal of the American College of Cardiology, the January 15, 2008, issue of Circulation, and e-published in Catheterization and Cardiovascular Interventions as an update to the full-text guidelines and is posted on the ACC (www.acc.org), AHA (my.americanheart.org), and Society for Angiography and Interventions (SCAI) (www.scai.org) Web sites. Copies of the focused update are available from all organizations.

Sidney C. Smith, Jr., MD, FACC, FAHA
Chair, ACC/AHA Task Force on Practice Guidelines
Alice K. Jacobs, MD, FACC, FAHA
Vice-Chair, ACC/AHA Task Force on Practice Guidelines

1. Introduction

1.1. Evidence Review

Selected late-breaking clinical trials presented at the 2005 and 2006 annual scientific meetings of the ACC, AHA, and European Society of Cardiology, as well as selected other data, were reviewed by the standing guideline writing committee along with the parent Task Force and other experts to identify those trials and other key data that might impact guideline recommendations. On the basis of the criteria/concerns noted above, recent trial data and other clinical information were considered important enough to prompt a focused update of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention.3–13

To provide clinicians with a comprehensive set of data, whenever possible, the exact event rates in various treatment arms of clinical trials are presented to permit calculation of the absolute risk difference (ARD) and number needed to treat (NNT) or harm (NNH); the relative treatment effects are described either as odds ratio (OR), relative risk (RR), or hazard ratio (HR), depending on the format in the original publication.

Consult the full-text version or executive summary of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention for policy on clinical areas not covered by the focused update.5,14 Individual recommendations updated in this focused update will be incorporated into future revisions and/or updates of the full-text guidelines.

1.2. Organization of Committee and Relationships With Industry

For this focused update, all members of the 2005 PCI writing committee were invited to participate; those who agreed (referred to as the 2007 focused update writing group) were required to disclose all RWI relevant to the data under consideration.2 Focused update writing group members who had no significant relevant RWI wrote the first draft of the focused update; the draft was then reviewed and revised by the full writing group. Each recommendation required a confidential vote by the writing group members before external review of the document. Any writing committee member with a significant (greater than $10 000) RWI relevant to the recommendation was recused from voting on that recommendation.

1.3. Review and Approval

This document was reviewed by 2 outside reviewers nominated by each cosponsoring organization (ACC, AHA, and SCAI) and 24 individual content reviewers. All reviewer RWI information was collected and distributed to the writing committee and is published in this document (see Appendix 2 for details).

This document was approved for publication by the governing bodies of the American College of Cardiology Foundation, AHA, and SCAI.

2. Patients With Unstable Angina/Non–ST-Elevation Myocardial Infarction

This 2007 PCI Focused Update section regarding patients with unstable angina (UA)/non–ST-elevation myocardial infarction (NSTEMI) is based on recommendations from the ACC/AHA 2007 Guidelines for the Management of Patients With Unstable Angina/Non–ST-Elevation Myocardial Infarction,14 which emphasize the importance of assessing risk of cardiovascular events as a guide to therapeutic decision making and the need for interventional therapy (see Table 2).

Because of the importance of several new changes in the ACC/AHA 2007 UA/NSTEMI Guidelines, selected text from the guidelines is included in the following paragraphs and summarized in Table 2.

A number of risk-assessment tools have been developed to assist in assessing risk of death and ischemic events in patients with UA/NSTEMI, thereby providing a basis for therapeutic decision making. It should be recognized that the predictive ability of these commonly used risk assessment scores for risk of nonfatal coronary heart disease (CHD) is only moderate.

The Thrombolysis in Myocardial Infarction (TIMI) risk score15 is a simple tool composed of 7 (1-point) risk indicators rated on presentation (Table 4). The composite end points (all-cause mortality, new or recurrent myocardial infarction [MI], or severe recurrent ischemia prompting urgent revascularization within 14 days) increase as the TIMI risk score increases. The TIMI risk score has been validated internally within the TIMI IIb trial and 2 separate cohorts of patients from the ESSENCE (Efficacy and Safety of Subcutaneous Enoxaparin in Unstable Angina and Non–Q-Wave Myocardial Infarction) trial.16 The model remained a significant predictor of events and appeared relatively insensitive to missing information, such as knowledge of previously documented coronary stenosis of 50% or greater. The model’s
predictive ability remained intact, with a cutoff of 65 years of age. The TIMI risk score was recently studied in an unselected emergency department population with chest pain syndrome; its performance was similar to that in the acute coronary syndrome (ACS) population from which it was derived and validated.\textsuperscript{17} The TIMI risk calculator is available at \textit{www.timi.org}. The TIMI risk index, a modification of the TIMI risk score that uses the variables age, systolic blood pressure, and heart rate, has not only been shown to predict short-term mortality in ST-elevation myocardial infarction (STEMI) but also has been useful in prediction of 30-day and 1-year mortality rates across the spectrum of patients with ACS, including UA/NSTEMI.\textsuperscript{18}

The PURSUIT (Platelet Glycoprotein IIb-IIIa in Unstable Angina: Receptor Suppression Using Integrilin Therapy) trial risk model,\textsuperscript{19} based on patients enrolled in the PURSUIT trial, is another useful tool to guide the clinical decision-making process when the patient is admitted to the hospital. In the PURSUIT risk model, critical clinical features associated with an increased 30-day incidence of death and the composite of death or myocardial (re)infarction were (in order of strength) age, heart rate, systolic blood pressure, ST-segment depression, signs of heart failure (HF), and cardiac enzymes.\textsuperscript{19}

The GRACE (Global Registry of Acute Coronary Events) study risk model, which predicts in-hospital mortality (and death or MI), can be useful to clinicians to guide treatment type and intensity.\textsuperscript{20,21} The GRACE risk tool was developed on the basis of 11,389 patients in GRACE and validated in subsequent GRACE and GUSTO (Global Utilization of Streptokinase and TPA for Occluded Coronary Arteries) IIb cohorts and predicts in-hospital death in patients with STEMI, NSTEMI, or UA (C statistic = 0.83). The 8 variables used in the GRACE risk model are older age (OR 1.7 per 10 years), Killip class (OR 2.0 per class), systolic blood pressure (OR 1.4 per 20 mm Hg decrease), ST-segment deviation (OR 2.4), cardiac arrest during presentation (OR 4.3), serum creatinine level (OR 1.2 per 1 mg per dL increase), positive initial cardiac markers (OR 1.6), and heart rate (OR 1.3 per 30-bpm increase). The sum of scores is applied to a reference nomogram to determine the corresponding all-cause mortality from hospital discharge to 6 months. The GRACE clinical application tool can be downloaded to a handheld PDA (personal digital

Table 2. Updates to Section 5.3: Initial Conservative Versus Initial Invasive Strategies (Patients With UA/NSTEMI)

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<th>2005 PCI Guideline Update Recommendation</th>
<th>2007 PCI Focused Update Recommendation</th>
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</tr>
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<td>An early invasive PCI strategy is indicated for patients with UA/NSTEMI who have no serious comorbidity and coronary lesions amenable to PCI. Patients must have any of the following high-risk features:</td>
<td>1. An early invasive PCI strategy is indicated for patients with UA/NSTEMI who have no serious comorbidity and who have coronary lesions amenable to PCI and who have characteristics for invasive therapy (see Table 3 and Section 3.3 of the ACC/AHA 2007 UA/NSTEMI Guidelines).\textsuperscript{19} (Level of Evidence: A)</td>
<td>Modified recommendation*</td>
</tr>
<tr>
<td>a. Recurrent ischemia despite intensive anti-ischemic therapy. (Level of Evidence: A)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Elevated troponin level. (Level of Evidence: A)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. New ST-segment depression. (Level of Evidence: A)</td>
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<td></td>
</tr>
<tr>
<td>d. HF symptoms or new or worsening MR. (Level of Evidence: A)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>e. Depressed LV systolic function. (Level of Evidence: A)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>f. Hemodynamic instability. (Level of Evidence: A)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>g. Sustained ventricular tachycardia. (Level of Evidence: A)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>h. PCI within 6 months. (Level of Evidence: A)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>i. Prior CABG. (Level of Evidence: A)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>j. High risk score (e.g., TIMI, GRACE). (Level of Evidence: A)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>k. High risk findings from non-invasive testing. (Level of Evidence: A)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Percutaneous coronary intervention (or CABG) is recommended for UA/NSTEMI patients with 1- or 2-vessel CAD with or without significant proximal left anterior descending CAD but with a large area of viable myocardium and high-risk criteria on noninvasive testing. (Level of Evidence: B)</td>
<td></td>
<td>New recommendation*</td>
</tr>
<tr>
<td>3. Percutaneous coronary intervention (or CABG) is recommended for UA/NSTEMI patients with multivessel coronary disease with suitable coronary anatomy, with normal LV function, and without diabetes mellitus. (Level of Evidence: A)</td>
<td></td>
<td>New recommendation*</td>
</tr>
<tr>
<td>4. An intravenous platelet GP IIb/IIIa inhibitor is useful in UA/NSTEMI patients undergoing PCI. (Level of Evidence: A) See Section 3.2.3 and Table 13 of the 2007 ACC/AHA 2007 UA/NSTEMI Guidelines.\textsuperscript{14}</td>
<td></td>
<td>New recommendation*</td>
</tr>
<tr>
<td>5. An early invasive strategy (i.e., diagnostic angiography with intent to perform revascularization) is indicated in UA/NSTEMI patients who have refractory angina or hemodynamic or electrical instability (without serious comorbidities or contraindications to such procedures). (Level of Evidence: B)</td>
<td></td>
<td>New recommendation*</td>
</tr>
</tbody>
</table>
Table 2. Continued

<table>
<thead>
<tr>
<th>2005 PCI Guideline Update Recommendation</th>
<th>2007 PCI Focused Update Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>It is reasonable that PCI be performed in patients with UA/NSTEMI and single-vessel or multivessel CAD who are undergoing medical therapy with focal saphenous vein graft lesions or multiple stenoses who are poor candidates for reoperative surgery. (Level of Evidence: C)</td>
<td>1. Percutaneous coronary intervention is reasonable for focal saphenous vein graft lesions or multiple stenoses in UA/NSTEMI patients who are undergoing medical therapy and who are poor candidates for reoperative surgery. (Level of Evidence: C)</td>
<td>Modified recommendation*</td>
</tr>
<tr>
<td>In the absence of high-risk features associated with UA/NSTEMI, it is reasonable to perform PCI in patients with either an early invasive or early conservative strategy. (Level of Evidence: B)</td>
<td>2. Percutaneous coronary intervention (or CABG) is reasonable for UA/NSTEMI patients with 1- or 2-vessel CAD with or without significant proximal left anterior descending CAD but with a moderate area of viable myocardium and ischemia on noninvasive testing. (Level of Evidence: B)</td>
<td>New recommendation*</td>
</tr>
<tr>
<td>Use of PCI is reasonable in patients with UA/NSTEMI with significant left main CAD (greater than 50% diameter stenosis) who are candidates for revascularization but are not eligible for CABG. (Level of Evidence: B)</td>
<td>3. Percutaneous coronary intervention (or CABG) can be beneficial compared with medical therapy for UA/NSTEMI patients with 1-vessel disease with significant proximal left anterior descending CAD. (Level of Evidence: B)</td>
<td>New recommendation*</td>
</tr>
<tr>
<td>In the absence of high-risk features associated with UA/NSTEMI, PCI may be considered in patients with single-vessel or multivessel CAD who are undergoing medical therapy and who have 1 or more lesions to be dilated with a less than optimal likelihood of success. (Level of Evidence: B)</td>
<td>4. Use of PCI is reasonable in patients with UA/NSTEMI with significant left main CAD (greater than 50% diameter stenosis) who are candidates for revascularization but are not eligible for CABG or who require emergency intervention at angiography for hemodynamic instability. (Level of Evidence: B)</td>
<td>2005 recommendation remains current in 2007 PCI Update but receives additional wording.</td>
</tr>
<tr>
<td>PCI may be considered in patients with UA/NSTEMI who are undergoing medical therapy who have 2- or 3-vessel disease, significant proximal LAD CAD, and treated diabetes or abnormal LV function. (Level of Evidence: B)</td>
<td>1. In the absence of high-risk features associated with UA/NSTEMI, PCI may be considered in patients with single-vessel or multivessel CAD who are undergoing medical therapy and who have 1 or more lesions to be dilated with a reduced likelihood of success. (Level of Evidence: B)</td>
<td>Modified recommendation*</td>
</tr>
<tr>
<td>2. PCI may be considered in patients with UA/NSTEMI who are undergoing medical therapy who have 2- or 3-vessel disease, significant proximal left anterior descending CAD, and treated diabetes or abnormal LV function, with anatomy suitable for catheter-based therapy. (Level of Evidence: B)</td>
<td>3. In initially stabilized patients, an initially conservative (i.e., a selectively invasive) strategy may be considered as a treatment strategy for UA/NSTEMI patients (without serious comorbidities or contraindications to such procedures) who have an elevated risk for clinical events (see Table 3) including those who are troponin positive. (Level of Evidence: B). The decision to implement an initial conservative (versus initial invasive) strategy in these patients may be made by considering physician and patient preference. (Level of Evidence: C)</td>
<td>New recommendation*</td>
</tr>
<tr>
<td>4. An invasive strategy may be reasonable in patients with chronic renal insufficiency. (Level of Evidence: C)</td>
<td>1. Percutaneous coronary intervention (or CABG) is not recommended for patients with 1- or 2-vessel CAD without significant proximal left anterior descending CAD with no current symptoms or symptoms that are unlikely to be due to myocardial ischemia and who have no ischemia on noninvasive testing. (Level of Evidence: C)</td>
<td>New recommendation*</td>
</tr>
</tbody>
</table>
In the absence of high-risk features associated with UA/NSTEMI, PCI is not recommended for patients with UA/NSTEMI who have single-vessel or multivessel CAD and no trial of medical therapy, or who have 1 or more of the following:

a. Only a small area of myocardium at risk. (Level of Evidence: C)
b. All lesions or the culprit lesion to be dilated with morphology that conveys a low likelihood of success. (Level of Evidence: C)
c. A high risk of procedure-related morbidity or mortality. (Level of Evidence: C)
d. Insignificant disease (less than 50% coronary stenosis). (Level of Evidence: C)
e. Significant left main CAD and candidacy for CABG. (Level of Evidence: B)

2. In the absence of high-risk features associated with UA/NSTEMI, PCI is not recommended for patients with UA/NSTEMI who have single-vessel or multivessel CAD and no trial of medical therapy, or who have 1 or more of the following:

a. Only a small area of myocardium at risk. (Level of Evidence: C)
b. All lesions or the culprit lesion to be dilated with morphology that conveys a low likelihood of success. (Level of Evidence: C)
c. A high risk of procedure-related morbidity or mortality. (Level of Evidence: C)
d. Insignificant disease (less than 50% coronary stenosis). (Level of Evidence: C)
e. Significant left main CAD and candidacy for CABG. (Level of Evidence: B)

3. A PCI strategy in stable patients (see Table 12 Class III No. 1 for specific recommendations) with persistently occluded infarct related coronary arteries after STEMI/NSTEMI is not indicated. (Level of Evidence: B)

**Table 3. Selection of Initial Treatment Strategy: Invasive Versus Conservative Strategy**

<table>
<thead>
<tr>
<th>Preferred Strategy</th>
<th>Patient Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invasive</td>
<td>Recurrent angina or ischemia at rest or with low-level activities despite intensive medical therapy</td>
</tr>
<tr>
<td></td>
<td>Elevated cardiac biomarkers (TnT or TnI)</td>
</tr>
<tr>
<td></td>
<td>New or presumably new ST-segment depression</td>
</tr>
<tr>
<td></td>
<td>Signs or symptoms of HF or new or worsening mitral regurgitation</td>
</tr>
<tr>
<td></td>
<td>High-risk findings from noninvasive testing</td>
</tr>
<tr>
<td></td>
<td>Hemodynamic instability</td>
</tr>
<tr>
<td></td>
<td>Sustained ventricular tachycardia</td>
</tr>
<tr>
<td></td>
<td>PCI within 6 months</td>
</tr>
<tr>
<td></td>
<td>Prior CABG</td>
</tr>
<tr>
<td></td>
<td>High-risk score (e.g., TIMI, GRACE)</td>
</tr>
<tr>
<td></td>
<td>Reduced LV function (LVEF less than 40%)</td>
</tr>
<tr>
<td>Conservative</td>
<td>Low-risk score (e.g., TIMI, GRACE)</td>
</tr>
<tr>
<td></td>
<td>Patient or physician preference in absence of high-risk features</td>
</tr>
</tbody>
</table>

The electrocardiogram (ECG) provides unique and important diagnostic and prognostic information (see also Section 2.1 below). Accordingly, ECG changes have been incorporated into quantitative decision aids for the triage of patients who present with chest discomfort. Although ST elevation carries the highest early risk of death, ST depression on the presenting ECG portends the highest risk of death, MI, or cardiac arrest. The TIMI risk score (Table 4) is used for specific recommendations (see also Section 2.1 below). It is based on data from the Thrombolysis in Myocardial Infarction (TIMI) trial (1986–1988) and has been validated using other large datasets (1991–2000). The TIMI risk score is determined by the sum of the presence of 7 variables at admission; 1 point is given for each of the following variables: age 65 years or older; at least 3 risk factors for CAD; prior coronary stenosis of 50% or more; ST-segment deviation on ECG presentation; at least 2 anginal events in prior 24 hours; use of aspirin in prior 7 days; and elevated serum cardiac biomarkers. Prior coronary stenosis of 50% or more remained relatively insensitive to missing information and remained a significant predictor of events. Reprinted with permission from Antman EM, Cohen M, Bernink PJ, et al. The TIMI risk score for unstable angina/non-ST elevation MI: a method for prognostication and therapeutic decision making. JAMA. 2000;284:835–42. Copyright © 2000 American Medical Association.

Table 4. TIMI Risk Score for Unstable Angina/Non–ST-Elevation Myocardial Infarction

<table>
<thead>
<tr>
<th>TIMI Risk Score</th>
<th>14 Days After Randomization, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–1</td>
<td>4.7</td>
</tr>
<tr>
<td>2</td>
<td>8.3</td>
</tr>
<tr>
<td>3</td>
<td>13.2</td>
</tr>
<tr>
<td>4</td>
<td>19.9</td>
</tr>
<tr>
<td>5</td>
<td>26.2</td>
</tr>
<tr>
<td>6–7</td>
<td>40.9</td>
</tr>
</tbody>
</table>

The TIMI risk score is determined by the sum of the presence of 7 variables at admission; 1 point is given for each of the following variables: age 65 years or older; at least 3 risk factors for CAD; prior coronary stenosis of 50% or more; ST-segment deviation on ECG presentation; at least 2 anginal events in prior 24 hours; use of aspirin in prior 7 days; and elevated serum cardiac biomarkers.

CABG indicates coronary artery bypass graft surgery; GRACE, Global Registry of Acute Coronary Events; HF, heart failure; LV, left ventricular; LVEF, left ventricular ejection fraction; PCI, percutaneous coronary intervention; TIMI, Thrombolysis In Myocardial Infarction; TnI, troponin I; and TnT, troponin T.
of death at 6 months, with the degree of ST-segment depression showing a strong relationship to outcome. 24

The recommendations in the ACC/AHA 2007 UA/NSTEMI Guidelines 14 recognize recent data from the ACUITY (Acute Catheterization and Urgent Intervention Triage strategY) trial, which showed that in patients with ACS who were undergoing invasive treatment, bivalirudin alone was associated with rates of ischemia similar to those treated with glycoprotein (GP) IIb/IIIa inhibitors plus heparin and significantly less bleeding. 25

The ACC/AHA 2007 UA/NSTEMI Guidelines cite a progressively greater benefit from newer, more aggressive therapies such as low-molecular-weight heparin (LMWH), 16,26 platelet GP IIb/IIIa inhibition, 27 and an invasive strategy 28 with increasing risk score.

2.1. Electrocardiogram
The ECG lies at the center of the decision pathway for the evaluation and management of patients with acute ischemic discomfort (Table 5). The diagnosis of MI is confirmed with serial cardiac biomarkers in more than 90% of patients who present with ST-segment elevation greater than or equal to 1 mm (0.1 mV) in at least 2 contiguous leads, and such patients should be considered candidates for acute reperfusion therapy. Patients who present with ST-segment depression are initially considered to have either UA or NSTEMI; the distinction between the 2 diagnoses is ultimately based on the detection of markers of myocardial necrosis in the blood. 29–31

Up to 25% of patients with NSTEMI and elevated CK-MB go on to develop Q-wave MI during their hospital stay, whereas the remaining 75% have non–Q-wave MI. Acute fibrinolytic therapy is contraindicated for ACS patients without ST-segment elevation, except for those with electrocardiographic true posterior MI manifested as ST-segment depression in 2 contiguous anterior precordial leads and/or isolated ST-segment elevation in posterior chest lead. 32–34 Inverted T waves may also indicate UA/NSTEMI. In patients suspected of having ACS on clinical Figure 1. GRACE Prediction Score Card and Nomogram for All-Cause Mortality From Discharge to 6 Months. Reprinted with permission. 20 Copyright © 2004 American Medical Association.
occurred in the setting of both STEMI and NSTEMI, and there is high mortality and morbidity in each. The SHOCK (SHould we emergently revascularize Occluded Coronaries for cardiogenic shock) study\textsuperscript{43} found that approximately 20\% of all cardiogenic shock complicating MI was associated with NSTEMI. The GUSTO-II\textsuperscript{44} and PURSUIT\textsuperscript{45} trials found that cardiogenic shock occurs in up to 5\% of patients with NSTEMI and that mortality rates are greater than 60\%. Thus, hypotension and evidence of organ hypoperfusion can occur and constitute a medical emergency in NSTEMI.

### 2.1.1. Comparison of Early Invasive and Initial Conservative Strategies for UA/NSTEMI

Prior meta-analyses concluded that routine invasive therapy (the “invasive” or “early” strategy) triages patients to undergo an invasive diagnostic evaluation without first getting a noninvasive stress test or without failing medical treatment [i.e., an initial conservative diagnostic strategy or sometimes now known as the “selective invasive strategy”\textsuperscript{14}] is better than an initial conservative or selectively invasive approach (the “initial conservative strategy” [also referred to as “selective invasive management”] calls for proceeding with an invasive evaluation only for those patients who fail medical therapy [refractory angina or angina at rest or with minimal activity despite rigorous medical therapy] or in whom objective evidence of ischemia [dynamic ECG changes, high-risk stress test] is identified\textsuperscript{14}). Mehta et al\textsuperscript{47} concluded that the routine invasive strategy resulted in an 18\% relative reduction in death or MI, including a significant reduction in MI alone. The routine invasive arm was associated with higher in-hospital mortality (1.8\% versus 1.1\%), but this disadvantage was more than compensated for by a significant reduction in mortality between discharge and the end of follow-up (3.8\% versus 4.9\%). In those analyses, the invasive strategy was associated with less angina and fewer rehospitalizations than the conservative pathway. Patients undergoing routine invasive treatment also had improved quality of life.

In contrast to these findings, other studies, most recently ICTUS (Invasive versus Conservative Treatment in Unstable
coronary Syndromes), have favorably highlighted a strategy of selective invasive therapy. In ICTUS, 1200 high-risk ACS patients without ST-segment elevation were randomized to receive routine invasive versus selective invasive management and followed up for 1 year with respect to the combined incidence of death, MI, and ischemic rehospitalization. All patients were treated with optimal medical therapy that included aspirin, clopidogrel, LMWH, and lipid-lowering therapy; abciximab was given to those undergoing revascularization. At the end of 1 year, there was no significant difference in the composite end point between groups. This study suggests that a selective invasive strategy could be reasonable for ACS patients. A possible explanation for the lack of benefit of the invasive approach in this trial (and other trials) could be related to the relatively high rate of revascularization actually performed in patients treated in the selective invasive arm (47%), thereby reducing observed differences between treatment strategies, and to the lower event rate (lower-risk population) than in other studies. Results were unchanged during longer-term follow-up. Nevertheless, ICTUS required troponin positivity for entry. Thus, troponin alone might no longer be an adequate criterion for strategy selection, especially with increasingly sensitive troponin assays. The degree of troponin elevation and other high-risk clinical factors taken together should be considered in selecting a treatment strategy. The ICTUS trial was relatively underpowered for hard end points, and it used a controversial definition for post procedural MI (i.e., even minimal asymptomatic CK-MB elevation).

Additionally, 1-year follow-up may be inadequate to fully realize the long-term impact and benefit of the routine invasive strategy. In the RITA-3 trial (Third Randomized Intervention Trial of Angina), 5-year but not 1-year event rates favored the early invasive arm (see Figure 2 and text below). In ICTUS, however, results were maintained during a 3-year follow-up.

Thus, the 2007 UA/NSTEMI Guidelines recommend that in initially stabilized UA/NSTEMI patients, an initial conservative (selective invasive) strategy may be considered as an alternative treatment option. The writing committee also believes that additional comparative trials of the selective invasive with the routine initial invasive strategies are indicated, using aggressive contemporary medical therapies in both arms, including routine dual antiplatelet therapy (DAT) in medically treated patients as well as aggressive lipid lowering and other updated secondary prevention measures.

Nevertheless, a meta-analysis of contemporary randomized trials in NSTEMI, including ICTUS, currently support long-term mortality and morbidity benefits of an early invasive compared with an initial conservative strategy. Nonfatal MI at 2 years (7.6% vs. 9.1%, respectively; RR 0.83 [95% CI 0.72 to 0.96]; p = 0.012) and hospitalization (at 13 months; RR = 0.69 [95% CI 0.65 to 0.74]; p less than 0.0001) also were reduced by an early invasive strategy (Figure 3). A separate review of contemporary randomized trials in the stent era using the Cochrane Database arrived at similar conclusions. Details of selected contemporary trials of invasive versus conservative strategies may be found in the ACC/AHA 2007 UA/NSTEMI Guidelines.

Thus, the FRISC-II (Fragmin and Fast Revascularisation during InStability in Coronary artery disease) and TACTICS (Treat Angina with Aggrastat and Determine Cost of Therapy with an Invasive or Conservative Strategy)-TIMI 18 trials showed a benefit in patients assigned to invasive strategy. In contrast to earlier trials, a large majority of patients undergoing percutaneous coronary intervention (PCI) in these 2 trials received coronary stenting as opposed to balloon angioplasty alone. Also, there was a differential rate of thienopyridine use between the 2 arms; only stented patients were treated. In FRISC-II, the invasive strategy involved treatment with LMWH, aspirin, nitrates, and beta blockers for an average of 6 days in the hospital before coronary angiography, an approach that would be difficult to adopt in US hospitals. In TACTICS-TIMI 18, treatment included the GP IIb/IIIa antagonist tirofiban, which was administered for an average of 22 hours before coronary angiography. The routine use of the GP IIb/IIIa inhibitor in this trial may have eliminated the excess risk of early (within 7 days) MI in the invasive arm, a risk that was observed in FRISC-II and other trials in which there was no routine “upstream” use of a GP IIb/IIIa blocker. Therefore, an invasive strategy is associated with a better outcome in UA/NSTEMI patients at high risk as defined in Table 3 and as demonstrated in TACTICS-TIMI 18 when a GP IIb/IIIa inhibitor is used. Although the benefit of intravenous GP...
IIb/IIIa inhibitors is established for UA/NSTEMI patients undergoing PCI, the optimal time to start these drugs before the procedure has not been established. In the PURSUIT trial, in patients with UA/NSTEMI who were admitted to community hospitals, the administration of eptifibatide was associated with a reduced need for transfer to tertiary referral centers and improved outcomes.

The RITA-3 trial compared early and conservative therapy in 1810 moderate-risk patients with ACS. Patients with positive cardiac biomarkers (CK-MB greater than 2 times the upper limit of normal at randomization) were excluded from randomization, as were those with new Q waves, MI within 1 month, PCI within 1 year, and any prior coronary artery bypass graft (CABG). The combined end point of death, nonfatal MI, and refractory angina was reduced from 14.5% to 9.6% by early invasive treatment. The benefit was driven primarily by a reduction in refractory angina. There was a late divergence of the curves, with reduced 5-year death and MI in the early invasive arm.

In the VINO trial (Value of first day angiography/angioplasty In evolving Non-ST segment elevation myocardial infarction: Open multicenter randomized trial), 131 patients with NSTEMI were randomized to cardiac catheterization on the day of admission versus conservative therapy. Despite the fact that 40% of the conservatively treated patients crossed over to revascularization by the 6-month follow-up, there was a significant reduction in death or reinfarction for patients assigned to early angiography and revascularization (6% versus 22%).

The ISAR-COOL (Intracoronary Stenting with Antithrombotic Regimen COOLing-off) trial randomized 410 intermediate- to high-risk patients to early angiography and revascularization versus a delayed invasive strategy. All patients were treated with intensive medical therapy that included aspirin, heparin, clopidogrel (600-mg loading dose), and the intravenous GP IIb/IIIa receptor inhibitor tirofiban. In the very early arm, patients underwent cardiac catheterization at a mean time of 2.4 hours versus 86 hours in the delayed invasive arm. The very early invasive strategy was associated with significantly better outcome at 30 days, as measured by reduction in death and large MI (5.9% versus 11.6%). More importantly, the benefit seen was attributable to a reduction in events before cardiac catheterization, which raises the possibility that there is a hazard associated with a “cooling-down” period.

2.1.2. Selection for Coronary Angiography

In contrast to the noninvasive tests, coronary angiography provides detailed structural information to allow assessment of prognosis and provide direction for appropriate management. When combined with left ventricular (LV) angiography, it also allows an assessment of global and regional LV function. Indications for coronary angiography are interwoven with indications for possible therapeutic plans, such as PCI or CABG.
Coronary angiography is usually indicated in patients with UA/NSTEMI who either have recurrent symptoms or ischaemia despite adequate medical therapy or are at high risk as categorized by clinical findings (HF, serious ventricular arrhythmias) or noninvasive test findings (significant LV dysfunction: ejection fraction less than 0.35, large anterior or multiple perfusion defects) (Tables 6, 7, and 8). Patients with UA/NSTEMI who have had previous PCI or CABG also should generally be considered for early coronary angiography unless prior coronary angiography data indicate that further revascularization is not likely to be possible. The placement of an intra-aortic balloon pump (IABP) may allow coronary angiography and revascularization in those with hemodynamic instability. Patients with suspected Prinzmetal’s variant angina also are candidates for coronary angiography.

In all cases, the general indications for coronary angiography and revascularization are tempered by individual patient characteristics and preferences. Patient and physician judgments regarding risks and benefits are particularly important for patients who might not be candidates for coronary revascularization, such as very frail older adults and those with serious comorbid conditions (i.e., severe hepatic, pulmonary, or renal failure or active or inoperable cancer).

### 2.1.3. Chronic Kidney Disease

The following recommendations have been added to the PCI Focused Update in accordance with new recommendations appearing in the 2007 UA/NSTEMI Guidelines (Table 9). Supporting text from that guidelines statement is presented in the following paragraphs.

Chronic kidney disease (CKD) is not only a coronary risk equivalent for ascertainment of coronary risk but also a risk factor for the development and progression of cardiovascular disease (CVD).63 CKD constitutes a risk factor for adverse outcomes after MI,64 including NSTEMI and other coronary patient subsets. In the highly validated GRACE risk score, serum creatinine is 1 of 8 independent predictors of death.20,65 In 1 recent study, even early CKD constituted a significant risk factor for cardiovascular events and death.64,66 CKD also predicts an increase in recurrent cardiovascular events.67 Cardiovascular

<table>
<thead>
<tr>
<th>Table 6. Noninvasive Risk Stratification</th>
</tr>
</thead>
<tbody>
<tr>
<td>High risk (greater than 3% annual mortality rate)</td>
</tr>
<tr>
<td>Severe resting LV dysfunction (LVEF less than 0.35)</td>
</tr>
<tr>
<td>High-risk treadmill score (score –11 or less)</td>
</tr>
<tr>
<td>Severe exercise LV dysfunction (exercise LVEF less than 0.35)</td>
</tr>
<tr>
<td>Stress-induced large perfusion defect (particularly if anterior)</td>
</tr>
<tr>
<td>Stress-induced multiple perfusion defects of moderate size</td>
</tr>
<tr>
<td>Large, fixed perfusion defect with LV dilation or increased lung uptake (thallium-201)</td>
</tr>
<tr>
<td>Stress-induced moderate perfusion defect with LV dilation or increased lung uptake (thallium-201)</td>
</tr>
<tr>
<td>Echocardiographic wall-motion abnormality (involving more than 2 segments) developing with low dose of dobutamine (10 mg/kg per min or less) or at a low heart rate (less than 120 bpm)</td>
</tr>
<tr>
<td>Stress echocardiographic evidence of extensive ischemia</td>
</tr>
<tr>
<td>Intermediate risk (1% to 3% annual mortality rate)</td>
</tr>
<tr>
<td>Mild/moderate resting LV dysfunction (LVEF 0.35 to 0.49)</td>
</tr>
<tr>
<td>Intermediate-risk treadmill score (–11 to 5)</td>
</tr>
<tr>
<td>Stress-induced moderate perfusion defect without LV dilation or increased lung intake (thallium-201)</td>
</tr>
<tr>
<td>Limited stress echocardiographic ischemia with a wall-motion abnormality only at higher doses of dobutamine involving less than or equal to 2 segments</td>
</tr>
<tr>
<td>Low risk (less than 1% annual mortality rate)</td>
</tr>
<tr>
<td>Low-risk treadmill score (score 5 or greater)</td>
</tr>
<tr>
<td>Normal or small myocardial perfusion defect at rest or with stress*</td>
</tr>
<tr>
<td>Normal stress echocardiographic wall motion or no change of limited resting wall-motion abnormalities during stress*</td>
</tr>
</tbody>
</table>

*Although published data are limited, patients with these findings will probably not be at low risk in the presence of either a high-risk treadmill score or severe resting LV dysfunction (LVEF less than 0.35). Reprinted from reference 60.

LV indicates left ventricular, and LVEF, left ventricular ejection fraction.

<table>
<thead>
<tr>
<th>Table 7. Noninvasive Test Results That Predict High Risk for Adverse Outcome (Left Ventricular Imaging)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress Radionuclide Ventriculography Stress Echocardiography</td>
</tr>
<tr>
<td>Exercise EF 0.50 or less</td>
</tr>
<tr>
<td>Rest EF 0.35 or less</td>
</tr>
<tr>
<td>Fall in EF 0.10 or greater</td>
</tr>
</tbody>
</table>

Modified from references 61 and 62. EF indicates ejection fraction.

<table>
<thead>
<tr>
<th>Table 8. Noninvasive Test Results That Predict High Risk for Adverse Outcome on Stress Radionuclide Myocardial Perfusion Imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal myocardial tracer distribution in more than 1 coronary artery region at rest or with stress or a large anterior defect that reperfuses</td>
</tr>
<tr>
<td>Abnormal myocardial distribution with increased lung uptake</td>
</tr>
<tr>
<td>Cardiac enlargement</td>
</tr>
</tbody>
</table>

Modified from reference 61.
Table 9. Indications for Chronic Kidney Disease

<table>
<thead>
<tr>
<th>2005 PCI Guideline Update Recommendation</th>
<th>2007 PCI Focused Update Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Class I</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Creatinine clearance should be estimated in UA/NSTEMI patients, and the doses of renally cleared drugs should be adjusted appropriately. (Level of Evidence: B)</td>
<td>New recommendation*</td>
<td></td>
</tr>
<tr>
<td>2. In chronic kidney disease patients undergoing angiography, isosmolar contrast agents are indicated and are preferred. (Level of Evidence: A)</td>
<td>New recommendation*</td>
<td></td>
</tr>
</tbody>
</table>

*Based on the ACC/AHA 2007 UA/NSTEMI Guidelines.14
CKD indicates chronic kidney disease; PCI, percutaneous coronary intervention; and UA/NSTEMI, unstable angina/non–ST-elevation myocardial infarction.

death is 10 to 30 times higher in dialysis patients than in the general population. The underrepresentation of patients with renal disease in randomized controlled trials of CVD is a concern.68 Current opinion and most of the limited evidence available suggest that when appropriately monitored, cardiovascular medications and interventional strategies can be applied safely in those with renal impairment and provide therapeutic benefit.64 However, not all recent evidence is consistent with this premise: atorvastatin did not significantly reduce the primary end point of cardiovascular death, nonfatal MI, or stroke in a prospective randomized trial of patients with diabetes and end-stage CKD who were undergoing hemodialysis.69 The preference for primary PCI has also been questioned.70

Particularly in the setting of ACS, bleeding complications are higher in this patient subgroup because of platelet dysfunction and dosing errors; benefits of fibrinolytic therapy, antiplatelet agents, and anticoagulants can be negated or outweighed by bleeding complications; and renin-angiotensin-aldosterone inhibitors can impose a greater risk because of the complications of hyperkalemia and worsening renal function in the patient with CKD. Angiography carries an increased risk of contrast-induced nephropathy; the usual benefits of PCI can be lessened or abolished; and PCI in patients with CKD is associated with a higher rate of early and late complications of bleeding, restenosis, and death.68 Thus, identification of CKD is important in that it represents an ACS subgroup with a far more adverse prognosis but for whom interventions have less certain benefit.

Coronary arteriography is a frequent component of the care of ACS patients. As such, contrast-induced nephropathy can constitute a serious complication of diagnostic and interventional procedures. In patients with CKD or CKD and diabetes, isosmolar contrast material lessens the rise in creatinine and is associated with lower rates of contrast-induced nephropathy than low-osmolar contrast media. This has been documented in a randomized clinical trial (RECOVERY [Renal Toxicity Evaluation and Comparison Between Visipaque (Iodixanol) and Hexabrix (Ioxaglate) in Patients With Renal Insufficiency Undergoing Coronary Angiography]) comparing iodixanol with ioxaglate71 and in a meta-analysis of 2727 patients from 16 randomized clinical trials.72

Identification of patients with CKD as recommended in the AHA Science Advisory on Detection of CKD in patients with or at increased risk of CVD should guide the use of isosmolar contrast agents.63 The advisory, which was developed in collaboration with the National Kidney Foundation, recommends that all patients with CVD be screened for evidence of kidney disease by estimating glomerular filtration rate, testing for microalbuminuria, and measuring the albumin-to-creatinine ratio. A glomerular filtration rate of less than 60 ml per min per 1.73 square meters of body surface should be regarded as abnormal. Furthermore, the albumin-to-creatinine ratio should be used to screen for the presence of kidney damage in adult patients with CVD, with values greater than 30 mg of albumin per 1 g of creatinine considered abnormal.

A diagnosis of renal dysfunction is critical to proper medical therapy for UA/NSTEMI. Many cardiovascular drugs used in patients with UA/NSTEMI are renally cleared; their doses should be adjusted for estimated creatinine clearance [see also Section 3 of the 2007 UA/NSTEMI Guidelines14]. In a large community-based registry study, 42% of patients with UA/NSTEMI received excessive initial dosing of at least 1 antiplatelet or antithrombin agent (fractionated heparin [UFH], LMWH, or GP IIb/IIIa inhibitor).73 Renal insufficiency was an independent predictor of excessive dosing. Dosing errors predicted an increased risk of major bleeding. Clinical studies and labeling that defines adjustments for several of these drugs have been based on the Cockcroft-Gault formula for estimating creatinine clearance, which is not identical to the Modification of Diet and Renal Disease (MDRD) formula. Use of the Cockcroft-Gault formula to generate dose adjustments is recommended. The impact of renal dysfunction on biomarkers of necrosis (i.e., troponin) is discussed in Section 2.2.8.2.1 of the 2007 UA/NSTEMI Guidelines.14

To increase the meager evidence base and to optimize care for this growing high-risk population, the recognition of CKD patients with or at risk of CVD and the inclusion and reporting of renal disease in large CVD trials must be increased in the future.

3. Facilitated PCI

Facilitated PCI refers to a strategy of planned immediate PCI after administration of an initial pharmacological regimen intended to improve coronary patency before the procedure. These regimens have included high-dose heparin, platelet GP IIb/IIIa inhibitors, full-dose or reduced-dose fibrinolytic therapy, and the combination of a GP IIb/IIIa inhibitor with a reduced-dose fibrinolytic agent (e.g., fibrinolytic dose typically reduced 50%). Facilitated PCI should be differentiated from primary PCI without fibrinolytic therapy, from primary PCI with a GP IIb/IIIa inhibitor started at the time of PCI,
from early or delayed PCI after successful fibrinolytic therapy, and from rescue PCI after unsuccessful fibrinolytic therapy. Potential advantages of facilitated PCI include earlier time to reperfusion, smaller infarct size, improved patient stability, lower infarct artery thrombus burden, greater procedural success rates, higher TIMI flow rates, and improved survival rates. Potential risks include increased bleeding complications, especially in older patients; potential limitations include added cost.

Despite the potential advantages, clinical trials of facilitated PCI have not demonstrated any benefit in reducing infarct size or improving outcomes. The largest of these was the ASSENT-4 (Assessment of the Safety and Efficacy of a New Treatment Strategy with Percutaneous Coronary Intervention) PCI trial,\(^5\) in which 1667 patients were randomized to full-dose tenecteplase and PCI versus primary PCI. The trial was terminated prematurely because of a higher in-hospital mortality rate in the facilitated PCI group (6% vs. 3%, \(p = 0.01\)). The primary end point, a composite of death, shock, and congestive heart failure within 90 days, was significantly higher with facilitated PCI than with primary PCI (18.6% vs. 13.4%; \(p = 0.0045\)), and there was a trend toward higher 90-day mortality (6.7% vs. 4.9%; \(p = 0.14\)).

Defenders of the facilitated PCI strategy point out that the absence of an infusion of heparin after bolus administration and of a loading dose of clopidogrel, plus prohibition of GP IIb/IIIa inhibitors except in bail-out situations, made adjunctive antithrombotic therapy suboptimal for the facilitated PCI group. Moreover, the median treatment delay between tenecteplase and PCI was only 104 minutes, and mortality rates with facilitated PCI were higher in PCI centers. Whether earlier (prehospital) administration of fibrinolytic therapy, better antithrombotic therapy, longer delays to PCI, or selective use of PCI as a rescue strategy would make the facilitated PCI strategy beneficial is unclear and requires further study. On the basis of these data, however, facilitated PCI offered no clinical benefit.

Keeley and coworkers performed a quantitative review of 17 trials that compared facilitated PCI and primary PCI\(^74\) (Figure 4). Included were 9 trials with GP IIb/IIIa inhibitors alone (\(n = 1148\)), 6 trials with fibrinolytic therapy (including ASSENT-4 PCI) (\(n = 2953\)), and 2 trials with a fibrinolytic agent plus a GP IIb/IIIa inhibitor (\(n = 399\)). Facilitated PCI with fibrinolytic therapy had significantly higher rates of mortality, nonfatal infarction, urgent target vessel revascularization, total and hemorrhagic stroke, and major bleeding compared with primary PCI. There were no differences in efficacy or safety when facilitated PCI with a GP IIb/IIIa inhibitor was compared with primary PCI.

A planned reperfusion strategy using full-dose fibrinolytic therapy followed by immediate PCI may be harmful (Table 10). Nevertheless, selective use of the facilitated strategy with regimens other than full-dose fibrinolytic therapy in high-risk subgroups of patients (large MI or hemodynamic or electrical instability) with low bleeding risk who present to hospitals without PCI capability might be performed when transfer delays for primary PCI are anticipated. Although the quantitative analysis showed no advantage for pretreatment with a GP IIb/IIIa inhibitor, neither did it document any major disadvantage. The use of GP IIb/IIIa inhibitors, particularly abciximab, during primary PCI is well established. Further trials of reduced-dose fibrinolytic therapy, with or without GP IIb/IIIa inhibitors, are in progress and may yield different efficacy and/or safety results.

Pharmacological reperfusion with full-dose fibrinolysis is not uniformly successful in restoring antegrade flow in the infarct artery. In such situations, a strategy of prompt coronary angiography with intent to perform PCI is frequently contemplated. In certain patients, such as those with cardiogenic shock (especially in those less than 75 years of age), severe congestive heart failure/pulmonary edema, or hemodynamically compromising ventricular arrhythmias (regardless of age), a strategy of coronary angiography with intent to perform PCI is a useful approach regardless of the time since initiation of fibrinolytic therapy, provided further invasive management is not considered futile or unsuitable given the clinical circumstances (Table 11).

### Table 10. Updates to Section 5.4.3: PCI for STEMI in Conjunction With Concomitant Fibrinolytic Therapy

<table>
<thead>
<tr>
<th>2005 PCI Guideline Update Recommendation</th>
<th>2007 PCI Focused Update Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Class IIb</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Facilitated PCI might be performed as a reperfusion strategy in higher-risk patients when PCI is not immediately available and bleeding risk is low. (Level of Evidence: B)</td>
<td>1. Facilitated PCI using regimens other than full-dose fibrinolytic therapy might be considered as a reperfusion strategy when all of the following are present: a. Patients are at high risk, b. PCI is not immediately available within 90 minutes, and c. Bleeding risk is low (younger age, absence of poorly controlled hypertension, normal body weight). (Level of Evidence: C)</td>
<td>Modified recommendation (changed LOE and text)</td>
</tr>
<tr>
<td><strong>Class III</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. A planned reperfusion strategy using full-dose fibrinolytic therapy followed by immediate PCI may be harmful. (Level of Evidence: B)</td>
<td>New recommendation</td>
<td></td>
</tr>
</tbody>
</table>

LOE indicates level of evidence; PCI, percutaneous coronary intervention; and STEMI, ST-elevation myocardial infarction.
management of such patients may be found in Section 5.4.4 (which has been updated in this document) of the 2005 PCI Guideline Update.13a

4. Rescue PCI

In other patients who do not exhibit the clinical instability noted above, PCI may also be reasonable if there is clinical suspicion of failure of fibrinolysis. This is referred to as rescue PCI. Critical to the success of rescue PCI is the initial clinical identification of patients who are suspected of having failed reperfusion with full-dose fibrinolysis. Because the presence or absence of ischemic discomfort may be unreliable for identifying failed reperfusion, clinicians should search for evidence of inadequate ST-segment resolution on the 12-lead ECG. Operationally, the 12-lead ECG should be scrutinized after adequate time has elapsed before making the judgment that fibrinolytic therapy has not been effective. Although earlier periods have been used in some studies, the writing committee felt that 90 minutes after initiation of fibrinolysis provided the best time for evaluating the need for rescue PCI: hence, if there is less than 50% ST resolution in the lead showing the greatest degree of ST-segment elevation at presentation, fibrinolytic therapy has likely failed to produce reperfusion.

The 2005 PCI Guideline Update13a recommendations for rescue PCI were based on observational data and 2 small randomized clinical trials (n/H11005179) from the early 1990s.94,95 More recently, MERLIN (Middlesbrough Early Revascularization to Limit Infarction) (n = 307) and REACT (Rescue Angioplasty versus Conservative Treatment or Repeat Thrombolysis) (n = 427) and 3 meta-analyses have refocused attention on rescue PCI.96–100 This subject has been studied with fewer than 1000 patients enrolled in randomized trials. In the period between trials studying rescue PCI, there was a transition between angiographic and electrocardiographic diagnosis to detect failed reperfusion. Importantly, in the earlier studies, rescue PCI was performed in infarct arteries with TIMI 0/1 flow, often after a protocol-mandated 90-minute angiogram.

In MERLIN and REACT, however, patients were randomized if they had less than 50% ST-segment elevation resolution at 60 or 90 minutes, respectively. Many patients had patent infarct arteries at angiography; only 54% of patients in MERLIN and 74% of patients in REACT (which required less than TIMI grade 3 flow for PCI) actually underwent PCI. From a procedural standpoint, stents have replaced balloon angioplasty, antiplatelet therapy has improved with the addition of a thienopyridine agent and often a GP IIb/IIIa receptor antagonist, and procedural success rates are higher.

Despite these historical differences, recent data support the initial observation that rescue PCI decreases adverse clinical events compared with medical therapy. In the Wijesundera meta-analysis100 (Figure 5, there was a trend toward reduced mortality rates with rescue PCI from 10.4% to 7.3% (RR 0.69 [95% CI 0.46 to 1.05]; p = 0.09), reduced reinfarction rates from 10.7% to 6.1% (RR 0.58 [95% CI 0.35 to 0.97]; p = 0.04), and reduced HF rates from 17.8% to 12.7% (RR 0.73 [95% CI 0.54 to 1.00]; p = 0.05). These event rates suggest that high-risk patients were selected for enrollment, so these data do not define the role of rescue PCI in lower-risk patients. Also, the benefits of rescue PCI need to be balanced against the risk. There was an excess occurrence of stroke in 2 trials (10 events versus 2 events), but the majority were thromboembolic rather than hemorrhagic, and the sample size was small, so more data are required to define this risk. There was also an increase of 13% in absolute risk of bleeding, suggesting that adjustments in antithrombotic medication dosing are needed to improve safety. It should be noted that the majority of patients who underwent rescue PCI received streptokinase as fibrinolytic therapy.

Given the association between bleeding events and subsequent ischemic events,103 it might be reasonable to select moderate- and high-risk patients for PCI after fibrinolysis and to treat low-risk patients with medical therapy. As noted above, patients with cardiogenic shock,
severe HF, or hemodynamically compromising ventricular arrhythmias are excellent candidates. An electrocardiographic estimate of potential infarct size in patients with persistent ST-segment elevation (less than 50% resolution at 90 minutes after initiation of fibrinolytic therapy in the lead showing the worst initial elevation) and ongoing ischemic pain is useful in selecting other patients for rescue PCI. Anterior MI or inferior MI with right ventricular involvement or precordial ST-segment depression usually predicts increased risk. Conversely, patients

<table>
<thead>
<tr>
<th>2005 PCI Guideline Update Recommendation</th>
<th>2007 PCI Focused Update Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td>1. A strategy of coronary angiography with intent to perform PCI (or emergency CABG) is recommended for patients who have received fibrinolytic therapy and have any of the following:</td>
<td>Modified recommendation (changed LOE and text)</td>
</tr>
<tr>
<td>Rescue PCI should be performed in patients less than 75 years old with ST elevation or left bundle-branch block who develop shock within 36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock unless further support is futile because of the patient’s wishes or contraindications/unsuitability for further invasive care. (Level of Evidence: B)</td>
<td>a. Cardiogenic shock in patients less than 75 years who are suitable candidates for revascularization. (Level of Evidence: B)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b. Severe congestive heart failure and/or pulmonary edema (Killip class III). (Level of Evidence: B)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>c. Hemodynamically compromising ventricular arrhythmias. (Level of Evidence: C)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Deleted recommendation</td>
<td></td>
</tr>
<tr>
<td>Class Ila</td>
<td>1. A strategy of coronary angiography with intent to perform PCI (or emergency CABG) is reasonable in patients 75 years of age or older who have received fibrinolytic therapy and are in cardiogenic shock, provided that they are suitable candidates for revascularization. (Level of Evidence: B)</td>
<td>Modified recommendation (changed text)</td>
</tr>
<tr>
<td>Rescue PCI is reasonable for selected patients 75 years or older with ST elevation or left bundle-branch block or who develop shock within 36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock. Patients with good prior functional status who are suitable for revascularization and agree to invasive care may be selected for such an invasive strategy. (Level of Evidence: B)</td>
<td>a. Hemodynamic or electrical instability. (Level of Evidence: C)</td>
<td></td>
</tr>
<tr>
<td>It is reasonable to perform rescue PCI for patients with 1 or more of the following:</td>
<td>b. Persistent ischemic symptoms. (Level of Evidence: C)</td>
<td></td>
</tr>
<tr>
<td>a. Hemodynamic or electrical instability. (Level of Evidence: C)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Class IIb</td>
<td>1. A strategy of coronary angiography with intent to perform rescue PCI is reasonable for patients in whom fibrinolytic therapy has failed (ST-segment elevation less than 50% resolved after 90 minutes following initiation of fibrinolytic therapy in the lead showing the worst initial elevation) and a moderate or large area of myocardium at risk (anterior MI, inferior MI with right ventricular involvement or precordial ST-segment depression). (Level of Evidence: B)</td>
<td>New recommendation</td>
</tr>
<tr>
<td>Rescue PCI in the absence of 1 or more of the above Class I or IIa indications is not recommended. (Level of Evidence: C)</td>
<td>a. Hemodynamic or electrical instability. (Level of Evidence: C)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>b. Persistent ischemic symptoms. (Level of Evidence: C)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3. A strategy of coronary angiography with intent to perform rescue PCI is reasonable for patients with good prior functional status who are suitable for revascularization and agree to invasive care may be selected for such an invasive strategy. (Level of Evidence: B)</td>
<td></td>
</tr>
<tr>
<td>Class III</td>
<td>1. A strategy of coronary angiography with intent to perform PCI (or emergency CABG) is not recommended in patients who have received fibrinolytic therapy if further invasive management is contraindicated or the patient or designee does not wish further invasive care. (Level of Evidence: C)</td>
<td>New recommendation</td>
</tr>
<tr>
<td>1. A strategy of coronary angiography with intent to</td>
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<td></td>
</tr>
<tr>
<td>perform PCI (or emergency CABG) is not recommended in patients who have received fibrinolytic therapy if further invasive management is contraindicated or the patient or designee does not wish further invasive care. (Level of Evidence: C)</td>
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</table>

CABG indicates coronary artery bypass graft; COR, class of recommendation; HF, heart failure; LOE, level of evidence; MI, myocardial infarction; PCI, percutaneous coronary intervention; and STEMI, ST-elevation myocardial infarction.
with symptom resolution, improving ST-segment elevation (less than 50% resolution), or inferior MI localized to 3 ECG leads probably should not be referred for angiography. Likewise, it is doubtful that PCI of a branch artery (diagonal or obtuse marginal branch) will change prognosis in the absence of the high-risk criteria noted above.

5. PCI After Fibrinolysis or for Patients Not Undergoing Primary Reperfusion

The open artery hypothesis suggests that late patency of an infarct artery is associated with improved LV function, increased electrical stability, and provision of collateral vessels to other coronary beds for protection against future events (see Table 12). The OAT ( Occluded Artery Trial)\textsuperscript{12} tested the hypothesis that routine PCI for total occlusion 3 to 28 days after MI would reduce the composite of death, reinfarction, or Class IV heart failure. Stable patients (n\textsubscript{11005} 2166) with an occluded infarct artery after MI (about 20% of whom received fibrinolytic therapy for the index event) were randomized to optimal medical therapy and PCI with stenting or optimal medical therapy alone. The qualifying period of 3 to 28 days was based on calendar days; thus, the minimal time from symptom onset to angiography was just over 24 hours. Inclusion criteria included total occlusion of the infarct-related artery with TIMI grade 0 or 1 antegrade flow and LV ejection fraction (LVEF) less than 50% or proximal occlusion of a major epicardial artery with a large risk region. Exclusion criteria included NYHA Class III or IV heart failure, serum creatinine greater than 2.5 mg per dL, left main or 3-vessel disease, clinical instability, or severe inducible ischemia on stress testing if the infarct zone was not akinetic or dyskinetic.

The 4-year cumulative end point was 17.2% in the PCI group and 15.6% in the medical therapy group (HR 1.16 [95% CI 0.92 to 1.45] p = 0.2). Reinfarction rates tended to be higher in the PCI group, which may have attenuated any benefit in LV remodeling. There was no interaction between treatment effect and any subgroup variable.

Preclinical studies have suggested that late opening of an occluded infarct artery may reduce adverse LV remodeling and preserve LV volumes. However, 5 previous clinical studies in 363 patients have demonstrated inconsistent improvement in LVEF or LV end-systolic and end-diastolic volumes after PCI. The largest of these, the DECOPI (DEsobstruction COronaire en Post-Infarctus) trial, found a higher LVEF at 6 months with PCI.\textsuperscript{105} TOSCA-2 (Total Occlusion Study of Canada)\textsuperscript{13} enrolled 381 stable patients in a mechanistic ancillary study of OAT and had the same eligibility criteria.\textsuperscript{12} The PCI procedure success rate was 92% and the complication rate was 3%, although 9% had periprocedural MI as measured by biomarkers. At 1 year, patency rates (n\textsubscript{11005} 332) were higher with PCI (83% vs. 25%; p less than 0.0001), but each group (n\textsubscript{11005} 286) had equivalent improvement in LVEF (4.2% vs. 3.5%; p = 0.47). There was modest benefit of PCI on preventing LV dilation over 1 year in a multivariate model, but only 42% had paired volume determinations, so it is unclear whether this finding extends to the whole cohort. The potential benefit of PCI in attenuating remodeling may have been decreased by periprocedural MI and the high rate of use of beta blockers and ACE inhibitors. There was no significant interaction between treatment effect and time, infarct artery, or infarct size.
Table 12. Updates to Section 5.4.5: PCI After Successful Fibrinolysis or for Patients Not Undergoing Primary Reperfusion

<table>
<thead>
<tr>
<th>2005 PCI Guideline Update Recommendation</th>
<th>2007 PCI Focused Update Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
<td></td>
<td></td>
</tr>
<tr>
<td>In patients whose anatomy is suitable, PCI should be performed when there is objective evidence of recurrent MI. (Level of Evidence: C)</td>
<td>1. In patients whose anatomy is suitable, PCI should be performed when there is objective evidence of recurrent MI. (Level of Evidence: C)</td>
<td>2005 recommendation remains current in 2007 PCI Update</td>
</tr>
<tr>
<td>In patients whose anatomy is suitable, PCI should be performed for moderate or severe spontaneous or provokable myocardial ischemia during recovery from STEMI. (Level of Evidence: B)</td>
<td>2. In patients whose anatomy is suitable, PCI should be performed for moderate or severe spontaneous or provokable myocardial ischemia during recovery from STEMI. (Level of Evidence: B)</td>
<td>2005 recommendation remains current in 2007 PCI Update</td>
</tr>
<tr>
<td>In patients whose anatomy is suitable, PCI should be performed for cardiogenic shock or hemodynamic instability. (Level of Evidence: B)</td>
<td>3. In patients whose anatomy is suitable, PCI should be performed for cardiogenic shock or hemodynamic instability. (Level of Evidence: B)</td>
<td>2005 recommendation remains current in 2007 PCI Update</td>
</tr>
<tr>
<td>Class IIa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>It is reasonable to perform routine PCI in patients with LV ejection fraction less than or equal to 0.40, HF, or serious ventricular arrhythmias. (Level of Evidence: C)</td>
<td>1. It is reasonable to perform routine PCI in patients with LV ejection fraction less than or equal to 0.40, HF, or serious ventricular arrhythmias. (Level of Evidence: C)</td>
<td>2005 recommendation remains current in 2007 PCI Update</td>
</tr>
<tr>
<td>It is reasonable to perform PCI when there is documented clinical heart failure during the acute episode, even though subsequent evaluation shows preserved LV function (LV ejection fraction greater than 0.40). (Level of Evidence: C)</td>
<td>2. It is reasonable to perform PCI when there is documented clinical heart failure during the acute episode, even though subsequent evaluation shows preserved LV function (LV ejection fraction greater than 0.40). (Level of Evidence: C)</td>
<td>2005 recommendation remains current in 2007 PCI Update</td>
</tr>
<tr>
<td>Class IIb</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCI might be considered as part of an invasive strategy after fibrinolytic therapy. (Level of Evidence: C)</td>
<td>1. PCI of a hemodynamically significant stenosis in a patent infarct artery greater than 24 hours after STEMI may be considered as part of an invasive strategy. (Level of Evidence: B)</td>
<td>Modified recommendation (changed COR/LOE and text)</td>
</tr>
<tr>
<td>Class III</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. PCI of a totally occluded infarct artery greater than 24 hours after STEMI is not recommended in asymptomatic patients with 1- or 2-vessel disease if they are hemodynamically and electrically stable and do not have evidence of severe ischemia. (Level of Evidence: B)</td>
<td>1</td>
<td>New recommendation</td>
</tr>
</tbody>
</table>

COR/LOE indicates class of recommendation/level of evidence; HF, heart failure; LV, left ventricular; PCI, percutaneous coronary intervention; and STEMI, ST-elevation myocardial infarction.

6. Ancillary Therapy for Patients Undergoing PCI for STEMI

The 2007 STEMI Guidelines Focused Update\textsuperscript{106} includes a new section on the use of anticoagulant therapy for patients undergoing PCI to establish reperfusion for STEMI. The recommendations associated with PCI are summarized in Table 13.

Full discussion of the background and basis of these recommendations may be found in the 2007 STEMI Guidelines Focused Update. When moving to PCI after fibrinolytic therapy, those patients who received upstream UFH or enoxaparin can continue to receive those anticoagulants in a seamless fashion (i.e., without crossover to another agent) under the dosing regimens listed in the recommendations.\textsuperscript{106,107} On the basis of reports of catheter thrombosis with fondaparinux alone during primary PCI in OASIS-6 (Organization for Assessment of Strategies for Ischemic Syndromes)\textsuperscript{7} and the experience with fondaparinux in the OASIS-5 trial,\textsuperscript{108} the STEMI focused update writing group recommended that fondaparinux should not be used as the sole anticoagulant during PCI but should be coupled with an additional agent that has anti-IIa activity to ameliorate the risk of catheter complications. Although bivalirudin or UFH are potential options for supplemental anticoagulation with fondaparinux, the available experience, albeit limited, is largely with UFH. The only available data from the CREATE (Clinical Trial of Reviparin and Metabolic Modulation in Acute Myocardial Infarction Treatment) trial that bear on this point are with UFH.\textsuperscript{109}

Given the complexities of the characteristics of the individual agents and their actions on the coagulation cascade, clinicians are cautioned about extrapolating any of the observations with agents discussed in this update to other anticoagulant regimens. In particular, as noted by the Food and Drug Administration (FDA), the LMWHs are sufficiently distinct that they should be evaluated individually rather than considered as a class of interchangeable agents.\textsuperscript{110}

7. Antiplatelet Therapy

The 2005 PCI Guideline Update\textsuperscript{13a} recommended aspirin antplatelet therapy of 325 mg, which was based primarily on results from the TAXUS IV and SIRIUS trials.\textsuperscript{111–128} Since that time, experience has been gained with doses of aspirin ranging from 75 mg to 325 mg (see Table 14 for further information and Table 15 for a list of the trials). No significant trials have been reported comparing lower-dose...
aspirin (75 mg to 100 mg) with higher-dose aspirin (162 mg to 325 mg) in subacute or late stent thrombosis with the incidence of bleeding as the initial course of therapy after placement of drug-eluting stents (DES). Two major trials involving patients not undergoing placement of DES report an increase in risk of bleeding on higher-dose aspirin. No conclusive data are available regarding higher-dose aspirin and subacute stent thrombosis among patients who are considered aspirin resistant.

Continued treatment with the combination of aspirin and clopidogrel after PCI appears to reduce rates of cardiovascular ischemic events. On the basis of randomized clinical trial protocols, aspirin 162 mg to 325 mg daily should be given for at least 1 month after implantation of a bare-metal stent (BMS), 3 months after implantation of a sirolimus-eluting stent (SES), and 6 months after implantation of a paclitaxel-eluting stent (PES), after which daily long-term use of aspirin should be continued indefinitely at a dose of 75 mg to 162 mg. In patients for whom there is concern about bleeding, the opinion of the writing group is that lower doses of aspirin—75 mg to 162 mg—can be used.

Likewise, clopidogrel 75 mg daily should be given for a minimum of 1 month after implantation of a BMS [minimum 2 weeks for patients at significant increased risk of bleeding] and for 12 months after implantation of a SES or PES and ideally in all patients post PCI who are not at high risk of bleeding. Under urgent circumstances that prevent the use of clopidogrel for 1 year, the duration studied for FDA approvals was 3 months for an SES and 6 months for a PES. The optimal duration of clopidogrel therapy after 1 year has not been established and should depend on the judgment of the risk—benefit ratio for the individual patient. Predictors of late stent thrombosis have included stenting of small vessels, multiple lesions, long stents, overlapping stents, ostial or bifurcation lesions, prior brachytherapy, suboptimal stent result, low ejection fraction, advanced age, diabetes mellitus, renal failure, ACS, and premature discontinuation of antiplatelet agents. Patients should be counseled on the need for and risks of DAT before placement of intracoronary stents, especially a DES, and alternative therapies to pursue if they are unwilling or unable to comply with the recommended duration of DAT. To reduce the incidence of bleeding complications associated with DAT, lower-dose aspirin (75 mg to 162 mg daily) is reasonable for long-term therapy. Given the importance of a 1-year course of DAT, it is recommended that elective surgery be postponed for 1 year, and among those patients for whom surgery cannot be deferred, aspirin therapy should be considered during the perioperative period in high-risk patients with DES.

Several investigations have explored various loading doses of clopidogrel before or during PCI. Consistent findings are that compared with a 300-mg loading dose, doses of either 600 or 900 mg achieve greater degrees of platelet inhibition with less variability among patients. Fewer patients may demonstrate “resistance” or nonresponsiveness to clopidogrel following the 600-mg dose. There appears to be no significant additive value of the 900-mg dose over the 600-mg dose.

The 600-mg dose appears to achieve maximum inhibition more rapidly than the 300-mg dose. Superior clinical outcomes at 30 days, primarily reduction in evidence of MI, have been reported after the 600-mg dose given 2 hours before the procedure, although this salutary
### Table 14. Updates to Section 6.2.1: Oral Antiplatelet Therapy

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>2005 PCI Guideline Update Recommendation</th>
<th>2007 PCI Focused Update Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1</td>
<td>Patients already taking daily chronic aspirin therapy should take 75 to 325 mg of aspirin before the PCI procedure is performed. (Level of Evidence: A)</td>
<td>1. Patients already taking daily long-term aspirin therapy should take 75 mg to 325 mg of aspirin before PCI is performed. (Level of Evidence: A)</td>
<td>2005 recommendation remains current in 2007 PCI Update</td>
</tr>
<tr>
<td>#2</td>
<td>Patients not already taking daily chronic aspirin therapy should be given 300 to 325 mg of aspirin at least 2 hours and preferably 24 hours before the PCI procedure is performed. (Level of Evidence: C)</td>
<td>2. Patients not already taking daily long-term aspirin therapy should be given 300 mg to 325 mg of aspirin at least 2 hours and preferably 24 hours before PCI is performed. (Level of Evidence: C)</td>
<td>2005 recommendation remains current in 2007 PCI Update</td>
</tr>
<tr>
<td>#3</td>
<td>A loading dose of clopidogrel should be administered before PCI is performed. (Level of Evidence: A) An oral loading dose of 300 mg, administered at least 6 hours before the procedure, has the best established evidence of efficacy. (Level of Evidence: B)</td>
<td>3. After PCI, in patients without allergy or resistance, an increased risk of bleeding, aspirin 325 mg daily should be given for at least 1 month after bare-metal stent implantation, 3 months after sirolimus-eluting stent implantation, and 6 months after paclitaxel-eluting stent implantation, after which daily chronic aspirin use should be continued indefinitely at a dose of 75 to 162 mg. (Level of Evidence: B)</td>
<td>Modified recommendation (changed text)</td>
</tr>
<tr>
<td>#4</td>
<td>In patients who have undergone PCI, clopidogrel 75 mg daily should be given for at least 1 month after bare-metal stent implantation (unless the patient is at increased risk of bleeding; then it should be given for a minimum of 2 weeks), 3 months after sirolimus stent implantation, and 6 months after paclitaxel-eluting stent implantation, and ideally up to 12 months in patients who are not at high risk of bleeding. (Level of Evidence: B)</td>
<td>4. A loading dose of clopidogrel,* generally 600 mg, should be administered before or when PCI is performed. (Level of Evidence: C) In patients undergoing PCI within 12 to 24 hours of receiving fibrinolytic therapy, a clopidogrel oral loading dose of 300 mg may be considered. (Level of Evidence: C)</td>
<td>Modified recommendation (changed LOE and text)</td>
</tr>
<tr>
<td>#5</td>
<td>If clopidogrel is given at the time of procedure, supplementation with GP IIb/IIIa receptor antagonists can be beneficial to facilitate earlier platelet inhibition than with clopidogrel alone. (Level of Evidence: B)</td>
<td>5. For all post-PCI stented patients receiving a DES, clopidogrel 75 mg daily should be given for at least 12 months if patients are not at high risk of bleeding. For post-PCI patients receiving a BMS, clopidogrel should be given for a minimum of 1 month and ideally up to 12 months (unless the patient is at increased risk of bleeding; then it should be given for a minimum of 2 weeks). (Level of Evidence: B)</td>
<td>Modified recommendation (changed text)</td>
</tr>
</tbody>
</table>

*Some uncertainty exists about optimal loading dose of clopidogrel. Randomized trials establishing its efficacy and providing data on bleeding risks used a loading dose of 300 mg orally followed by a daily oral dose of 75 mg. Higher oral loading doses such as 600 mg or 900 mg of clopidogrel more rapidly inhibit platelet aggregation and achieve a higher absolute level of inhibition of platelet aggregation, but the additive clinical efficacy and safety of higher oral loading doses have not been rigorously established.

BMS indicates bare-metal stent; DES, drug-eluting stent; GP, glycoprotein; IV, intravenous; LOE, level of evidence; PCI, percutaneous coronary intervention; and STEMI, ST-elevation myocardial infarction.
With the 600-mg dose, 2 hours may be the minimum time. With the 300-mg dose, 6 hours is the desirable therapeutic effect. Evidence from the CREDO trial suggests that with a 300-mg dose, 6 hours is the time when the loading dose must be given to achieve the optimal treatment strategy.

Clopidogrel and will provide further evidence about the optimal treatment strategy.

Long-term clopidogrel therapy alone may not achieve the desired therapeutic effect. Evidence from the CREDO (Clopidogrel for the Reduction of Events During Observation) trial suggests that with a 300-mg dose, 6 hours is the minimum time. With the 600-mg dose, 2 hours may be sufficient, although maximal platelet inhibition may not be achieved until 3 to 4 hours.

Long-term clopidogrel therapy alone may not achieve adequate inhibition for PCI. Patients on long-term therapy with clopidogrel experience significant additional incremental inhibition of platelet aggregation when given a loading dose. In patients treated with fibrinolytic therapy, however, loading doses of greater than 300 mg have not been studied.

8. Bare-Metal and Drug-Eluting Stents

8.1. Selection of a Bare-Metal or Drug-Eluting Stent

Observational studies indicate that physicians routinely implant stents when performing coronary interventions. Two types of stents are available: BMS and DES. Drug-eluting stents have become increasingly popular as standard therapy. In 2005, a sampling of 140 US hospitals indicated that 94% of patients treated with a stent received at least 1 DES. More recently, however, because of concerns about stent thrombosis and the mandate that each DES-treated patient take prolonged DAT, the proportion of DES use has declined to 60% to 70%.

The results of the clinical trials that led to FDA approval of the DES provide support for its use in suitable patients. Extended follow-up of the initial investigated patient cohorts to 4 years confirms the sustained benefit of DES in decreasing the need for repeat revascularization but without differences in death or MI.

<table>
<thead>
<tr>
<th>Trial Name</th>
<th>Stents Compared</th>
<th>Total Patients</th>
<th>Duration of Treatment</th>
<th>Aspirin Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAVEL</td>
<td>SES versus BMS</td>
<td>238</td>
<td>Indefinite</td>
<td>100 mg once a day</td>
</tr>
<tr>
<td>E-SIRIUS</td>
<td>SES versus BMS</td>
<td>352</td>
<td>Indefinite</td>
<td>100 mg once a day</td>
</tr>
<tr>
<td>TAXUS I</td>
<td>PES versus BMS</td>
<td>61</td>
<td>Greater than or equal to 12 months</td>
<td>Greater than 80 mg once a day</td>
</tr>
<tr>
<td>TAXUS II</td>
<td>PES versus BMS</td>
<td>536</td>
<td>Indefinite</td>
<td>75 mg once a day</td>
</tr>
<tr>
<td>TAXUS III</td>
<td>PES for ISR only</td>
<td>28</td>
<td>Not stated</td>
<td>Greater than or equal to 75 mg</td>
</tr>
<tr>
<td>C-SIRIUS</td>
<td>SES versus BMS</td>
<td>100</td>
<td>Indefinite</td>
<td>81 to 325 mg once a day</td>
</tr>
<tr>
<td>DELIVER</td>
<td>ACHIEVE versus ML PENTA</td>
<td>1043</td>
<td>1 year</td>
<td>325 mg once a day</td>
</tr>
<tr>
<td>ELUTES</td>
<td>PES versus BMS</td>
<td>190</td>
<td>3 months</td>
<td>Not stated</td>
</tr>
<tr>
<td>SIRIUS</td>
<td>SES versus BMS</td>
<td>1058</td>
<td>Indefinite</td>
<td>325 mg once a day</td>
</tr>
<tr>
<td>TAXUS IV</td>
<td>PES versus BMS EXPRESS</td>
<td>1314</td>
<td>Indefinite</td>
<td>325 mg once a day</td>
</tr>
<tr>
<td>ISAR-DESIRE</td>
<td>SES versus PES versus balloon angioplasty</td>
<td>300</td>
<td>Indefinite</td>
<td>500 mg IV during; 100 mg bid after</td>
</tr>
<tr>
<td>ISAR-DIABETES</td>
<td>SES versus PES</td>
<td>250</td>
<td>Indefinite</td>
<td>100 mg twice a day</td>
</tr>
<tr>
<td>SIRTA</td>
<td>SES versus PES</td>
<td>1012</td>
<td>Indefinite</td>
<td>100 mg once a day</td>
</tr>
<tr>
<td>TAXI</td>
<td>SES versus PES</td>
<td>202</td>
<td>“Long term&quot;</td>
<td>100 mg once a day</td>
</tr>
<tr>
<td>TAXUS V</td>
<td>PES versus BMS</td>
<td>1172</td>
<td>Indefinite</td>
<td>325 mg once a day</td>
</tr>
<tr>
<td>TAXUS VI</td>
<td>PES versus BMS</td>
<td>448</td>
<td>Greater than or equal to 6 months</td>
<td>75 mg at least 2 hours prior; greater than or equal to 75 mg after</td>
</tr>
<tr>
<td>REALITY</td>
<td>SES versus PES</td>
<td>1353</td>
<td>Indefinite</td>
<td>100 mg once a day</td>
</tr>
<tr>
<td>TAXUS V ISR</td>
<td>PES versus VBT for ISR</td>
<td>396</td>
<td>Indefinite (9-month minimum, indefinite recommended)</td>
<td>325 mg once a day</td>
</tr>
</tbody>
</table>

ACHIEVE indicates a brand-name paclitaxel-coated stent; BMS, bare-metal stent; C-SIRIUS, Canadian Sirolimus-Eluting Stent in Coronary Lesions; ELUTES, European evaluation of paclitaxel stent; E-SIRIUS, European Sirolimus-Eluting Stent in Coronary Lesions; h, hour; ISAR-DESIRE, Drug-Eluting Stents for in-stent Restenosis; ISAR-DIABETES, Paclitaxel-Eluting Stent Versus Sirolimus-Eluting Stent for the Prevention of Restenosis in Diabetic Patients With Coronary Artery Disease; ISR, in-stent restenosis; IV, intravenous; ML PENTA, multilink stainless steel bare metal stent; PCI, percutaneous coronary intervention; PES, paclitaxel-eluting stent; RAVEL, A Randomized Comparison of a Sirolimus-Eluting Stent With a Standard Stent for Coronary Revascularization; REALITY, Prospective Randomized Multi-Center Head-to-Head Comparison of the Sirolimus-Eluting Stent (Cypher) and the Paclitaxel-Eluting Stent (TAXUS); SES, sirolimus-eluting stent; SIRIUS, Sirolimus-Eluting Stent in Coronary Lesions; SIRTA, Sirolimus-Eluting Stent Compared With Paclitaxel-Eluting Stent for Coronary Revascularization; TAXI, Paclitaxel and sirolimus stents in the real world of interventional cardiology; TAXUS V ISR, Paclitaxel-Eluting Stents versus Brachytherapy for In-Stent Restenosis; and VBT, vascular brachytherapy.
A drug-eluting stent (DES) should be considered as an alternative to the bare-metal stent in subsets of patients in whom trial data suggest efficacy. (Level of Evidence: A)

1. A DES should be considered as an alternative to a BMS in those patients for whom clinical trials indicate a favorable effectiveness/safety profile. (Level of Evidence: A)

2. Before implanting a DES, the interventional cardiologist should discuss with the patient the need for and duration of DAT and confirm the patient’s ability to comply with the recommended therapy for DES. (Level of Evidence: B)

3. In patients who are undergoing preparation for PCI and are likely to require invasive or surgical procedures for which DAT must be interrupted during the next 12 months, consideration should be given to implantation of a BMS or performance of balloon angioplasty with a provisional stent implantation instead of the routine use of a DES. (Level of Evidence: C)

A DES may be considered for use in anatomic settings in which the usefulness, effectiveness, and safety have not been fully documented in published trials. (Level of Evidence: C)

1. A DES may be considered for clinical and anatomic settings in which the effectiveness/safety profile appears favorable but has not been fully confirmed by clinical trials. (Level of Evidence: C)

BMS indicates bare-metal stent; DAT, dual antiplatelet therapy; DES, drug-eluting stent; and PCI, percutaneous coronary intervention.

trials in selected clinical subsets such as BMS in-stent restenosis, total occlusions, diabetes mellitus, and small-diameter arteries have also demonstrated the value of DES and have prompted physicians to extend the application of DES beyond the narrow patient populations included in the initial approval trials.122,126,149–154 The duration of follow-up of these “off-label” studies and the small number of patients enrolled, however, limit the detection of subtle differences in important end points such as stent thrombosis, death, or MI.

It is important to recognize certain differences between the BMS and DES when selecting a stent for an individual patient or lesion. First, in general, a DES may be more difficult to implant than a BMS. The DES has a polymer coating that stiffens the stent and makes it less conformable. Accordingly, one reason for using a BMS is that it can be used in patients in whom a DES cannot be implanted successfully. Second, the DES is substantially more expensive than the BMS. When financial resources are limited, use of the DES may be rationed, with implantation only in those patients at greatest risk for restenosis.

A third but very important difference relates to the inhibition of endothelial coverage of the DES and the need for extended DAT (Table 16). After introduction of the BMS, it was associated with a disturbingly high incidence of stent thrombosis.141 Stent thrombosis often presented as MI or even death and usually occurred in the first 30 days after implantation. Changes in technique such as high inflation pressure and intravascular ultrasound (IVUS)-guided deployment and use of concomitant combined aspirin and thienopyridine therapy substantially reduced the incidence of stent thrombosis to a clinically acceptable level.155 Importantly, the requisite duration of DAT was only 4 weeks, and some advocated only 2 weeks. The importance of DAT in preventing stent thrombosis was further strengthened by the outcome of patients for whom DAT was discontinued prematurely because of the need for those patients to undergo surgical procedures. These patients experienced a disturbingly high incidence of stent thrombosis.156 The critical role of DAT in preventing stent thrombosis was also noted among patients with BMS who had received brachytherapy for in-stent restenosis. Presumably these patients were less likely to develop subsequent neointimal coverage of the endoluminal stent surface and were accordingly then more susceptible to stent thrombosis.

In the initial randomized trials that compared the DES with BMS, DAT was administered for 30 days to 6 months. The most recent guidelines update describes a minimum duration of 3 months of DAT for an SES and 6 months for a PES. On the basis of results from other trials that suggest a sustained benefit of DAT, these guidelines further state that ideally DAT should be extended to 12 months. Although these recommendations were to some extent arbitrary, subsequent studies have confirmed that premature discontinuation of DAT, that is, at a time less than “minimal duration” (3 months for the SES and 6 months for the PES) was highly associated with stent thrombosis.157

The tight relationship between DAT and stent thrombosis for patients treated with DES warrants emphasis and has
implications for selecting the type of stent deployed at the time of PCI. For example, the clinician should not select a DES for a patient who does not have access to DAT for financial reasons or who is unlikely to be compliant in taking DAT. One study revealed that 14% of patients had stopped DAT 1 month after implantation of the DES.\textsuperscript{158} Also, implantation of a BMS may be more appropriate in a patient with a known increased risk of bleeding. In situations such as these, the consequences of developing restenosis are considered less untoward than those of stent thrombosis or significant bleeding.

Furthermore, prescribed premature discontinuation of DAT in patients treated with a DES should not be done casually. For example, routine dental procedures should not justify cessation of DAT even though it is anticipated DAT will be subsequently resumed.\textsuperscript{133} Consideration should be given to delay scheduling of elective procedures that normally warrant discontinuation of antiplatelet agents. The benefit of DES in reducing the need for target vessel revascularization (TVR) also should be taken into account. Some registries have shown 1-digit TVR rates with the BMS, and the absolute reduction in these events using the DES depends on patient and lesion characteristics.

There are also concerns related to the appropriate duration of DAT. More recently, the occurrence of late (up to 1 year) or very late (beyond 1 year) stent thrombosis among DES-treated patients has been described.\textsuperscript{159} One database analysis suggests that extended use of DAT may have value in preventing late stent thrombosis, whereas others disagree.\textsuperscript{160}

Outcomes of patients in the initial FDA-approval trials to 4 years provides reassurance that, at least for those types of patients, despite a small excess of stent thrombosis, there appears to be no increase in death or MI when comparing DES-treated groups with BMS-treated groups. As noted, protocol-recommended DAT in these patients was not more than 6 months, although extended DAT was not prohibited. (These results are observed despite a significant excess occurrence of stent thrombosis among patients who received a paclitaxel stent.) Some have postulated that the substantial additional revascularization procedures experienced by BMS patients were associated with a small but significant excess rate of death and MI that offset any deaths or MIs that may have occurred in the DES group related to stent thrombosis.

Less data are available regarding the outcomes of patients who receive a DES for an “off-label” indication. Such patients have characteristics of their coronary disease, for example, a lesion in an artery less than 2.5 mm in diameter, very long lesions, bifurcation lesions, or a clinical syndrome such as acute MI, that were excluded in the FDA-approval trials. Reports from large observational studies indicate that “off-label” patients may experience higher rates of repeat revascularization and death and MI at 1 year than DES patients with “on-label” features. Importantly, a similar relationship is observed for patients treated with a BMS. In addition, there appears to be a significant association between “off-label” use and stent thrombosis. Accordingly, the appropriate selection for DAT among “off-label” DES patients may be different than for “on-label” patients.

At this point in time, 12 months of DAT is recommended for all patients who receive a DES\textsuperscript{120} (see Section 6.2.1) unless there is a high risk of bleeding. The benefits and indications for treatment with DAT beyond 1 year in patients with DES are the subject of ongoing studies. Low-dose aspirin should be continued indefinitely. For patients with clinical features associated with stent thrombosis, such as renal insufficiency, diabetes, or procedural characteristics such as multiple stents or treatment of a bifurcation lesion, extended DAT beyond 1 year may be reasonable. The risk of stent thrombosis needs to be balanced with other medical conditions and nonmedical factors that might affect the risk-benefit ratio of DAT versus other therapies. Finally, certain DES-treated patients have already discontinued DAT 1 year after stent implantation. No information yet supports restarting DAT in these patients.

9. Secondary Prevention

Table 17 presents revised recommendations based on the 2006 AHA/ACC Secondary Prevention Guidelines for Patients with Coronary and Other Atherosclerotic Vascular Diseases.\textsuperscript{11} This table replaces Table 26 from the 2005 PCI Guideline Update.\textsuperscript{13a} Classes of recommendation and a corresponding level of evidence have been added for all recommendations. There is a new recommendation for annual influenza vaccination, and the section on antiplatelet agents/anticoagulants has been modified slightly to reflect the recent evidence on aspirin dosage in patients who have undergone PCI with stent placement. Other changes since publication of the 2006 ACC/AHA Secondary Prevention Guidelines include the addition of recommended daily physical activity and a Class IIA recommendation for lowered low-density lipoprotein cholesterol.
### Smoking

**Goal:** Complete cessation, no exposure to environmental tobacco smoke

<table>
<thead>
<tr>
<th>2005 PCI Recommendations</th>
<th>2007 PCI Recommendations</th>
<th>2007 COR and LOE</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ask about tobacco status at every visit.</td>
<td>1. Status of tobacco use should be asked about at every visit.</td>
<td>/ (B)</td>
<td>Modified recommendation (changed text)</td>
</tr>
<tr>
<td>Strongly encourage patient and family to stop smoking and avoid secondhand smoke.</td>
<td>2. Every tobacco user and family members who smoke should be advised to quit at every visit.</td>
<td>/ (B)</td>
<td>No content change</td>
</tr>
<tr>
<td>Assess the tobacco user’s willingness to quit.</td>
<td>3. The tobacco user’s willingness to quit should be assessed.</td>
<td>/ (B)</td>
<td>No content change</td>
</tr>
<tr>
<td>Assist by counseling and developing a plan for quitting.</td>
<td>4. The tobacco user should be assisted by counseling and developing a plan for quitting.</td>
<td>/ (B)</td>
<td>No content change</td>
</tr>
<tr>
<td>Arrange follow-up, referral to special programs, or pharmacological therapy (including nicotine replacement and bupropion).</td>
<td>5. Follow-up, referral to special programs, or pharmacotherapy (including nicotine replacement and pharmacological treatment) should be arranged.</td>
<td>/ (B)</td>
<td>No content change</td>
</tr>
<tr>
<td>Urge avoidance of exposure to environmental tobacco smoke at work and home.</td>
<td>6. Exposure to environmental tobacco smoke at work and home should be avoided.</td>
<td>/ (B)</td>
<td>No content change</td>
</tr>
</tbody>
</table>

### Blood Pressure Control

**Goal:** Less than 140/90 mm Hg or less than 130/80 mm Hg if patient has diabetes or chronic kidney disease

<table>
<thead>
<tr>
<th>2005 PCI Recommendations</th>
<th>2007 PCI Recommendations</th>
<th>2007 COR and LOE</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiate or maintain lifestyle modification (weight control, increased physical activity, alcohol moderation, moderate sodium restriction, and emphasis on fruits, vegetables, and low-fat dairy products) in all patients.</td>
<td>1. For patients with blood pressure greater than or equal to 140/90 mm Hg (or greater than or equal to 130/80 mm Hg for patients with diabetes or chronic kidney disease), it is recommended to initiate or maintain lifestyle modification—weight control, increased physical activity, alcohol moderation, sodium reduction, and emphasis on increased consumption of fresh fruits, vegetables, and low-fat dairy products.</td>
<td>/ (B)</td>
<td>No content change</td>
</tr>
<tr>
<td>Add blood pressure medication,* emphasizing the use of beta blockers and inhibitors of the renin-angiotensin-aldosterone system.</td>
<td>2. For patients with blood pressure greater than or equal to 140/90 mm Hg (or greater than or equal to 130/80 mm Hg for patients with diabetes or chronic kidney disease), it is useful as tolerated, to add blood pressure medication, treating initially with beta blockers and/or ACE inhibitors, with the addition of other drugs such as thiazides as needed to achieve goal blood pressure.</td>
<td>/ (A)</td>
<td>Modified recommendation (changed text)</td>
</tr>
</tbody>
</table>

### Lipid Management

**Goal:** LDL-C substantially less than 100 mg per dL

<table>
<thead>
<tr>
<th>2005 PCI Recommendations</th>
<th>2007 PCI Recommendations</th>
<th>2007 COR and LOE</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start dietary therapy in all patients (less than 7% of total calories as saturated fat and less than 200 mg/d cholesterol).</td>
<td>1. Starting dietary therapy is recommended. Reduce intake of saturated fats (to less than 7% of total calories), trans fatty acids, and cholesterol (to less than 200 mg per day).</td>
<td>/ (B)</td>
<td>Modified recommendation (changed text)</td>
</tr>
<tr>
<td>Promote physical activity and weight management.</td>
<td>2. Adding plant stanol/sterols (2 g per day) and/or viscous fiber (greater than 10 g per day) is reasonable to further lower LDL-C.</td>
<td>Ila (A)</td>
<td>New recommendation</td>
</tr>
<tr>
<td>Encourage increased consumption of omega-3 fatty acids in fish‡ or 1 g/d omega-3 fatty acids from supplements for risk reduction (for treatment of elevated triglycerides, higher doses are usually necessary for risk reduction).</td>
<td>3. Promotion of daily physical activity and weight management is recommended.</td>
<td>/ (B)</td>
<td>Modified recommendation (changed text)</td>
</tr>
<tr>
<td>Assess fasting lipid profile in all patients, preferably within 24 hours of an acute event. For hospitalized patients, initiate lipid-lowering medication as recommended below before discharge according to the following guide:</td>
<td>4. It may be reasonable to encourage increased consumption of omega-3 fatty acids in the form of fish‡ or in capsules (1 g per day) for risk reduction. For treatment of elevated triglycerides, higher doses are usually necessary for risk reduction.</td>
<td>/b (B)</td>
<td>No content change</td>
</tr>
<tr>
<td></td>
<td>5. A fasting lipid profile should be assessed in all patients and within 24 hours of hospitalization for those with an acute cardiovascular or coronary event. For hospitalized patients, initiation of lipid-lowering medication is indicated as recommended below before discharge according to the following schedule:</td>
<td>/ (A)</td>
<td>Modified recommendation (changed text)</td>
</tr>
</tbody>
</table>
Table 17. Continued

<table>
<thead>
<tr>
<th>2005 PCI Recommendations</th>
<th>2007 PCI Recommendations</th>
<th>2007 COR and LOE</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-C less than 100 mg/dL (baseline or on treatment): Statins preferred to lower LDL-C.</td>
<td>LDL-C should be less than 100 mg per dL.</td>
<td>I (A)</td>
<td>Modified recommendation (changed text)</td>
</tr>
<tr>
<td></td>
<td>Further reduction of LDL-C to less than 70 mg per dL is reasonable.</td>
<td>IIa (A)</td>
<td>New recommendation</td>
</tr>
<tr>
<td>If LDL-C is greater than or equal to 100 mg/dL (baseline or on treatment), initiate or intensify LDL-C-lowering therapy with drug treatment. May require combination therapy with standard-dose ezetimide, bile acid sequestrant, or niacin.</td>
<td>If baseline LDL-C is greater than or equal to 100 mg per dL, LDL-lowering drug therapy§ should be initiated.</td>
<td>I (A)</td>
<td>Modified recommendation (changed text)</td>
</tr>
<tr>
<td></td>
<td>If on-treatment LDL-C is greater than or equal to 100 mg per dL, intensity LDL-lowering drug therapy (may require LDL-lowering drug combination¶) is recommended.</td>
<td>I (A)</td>
<td>New recommendation</td>
</tr>
<tr>
<td>If triglycerides are greater than or equal to 150 mg/dL or HDL-C is less than 40 mg/dL, emphasize weight management and physical activity. Advise smoking cessation.</td>
<td>If triglycerides are greater than or equal to 150 mg per dL or HDL-C is less than 40 mg per dL, weight management, physical activity, and smoking cessation should be emphasized.</td>
<td>I (B)</td>
<td>Modified recommendation (changed text)</td>
</tr>
<tr>
<td>If triglycerides are 200 to 499 mg/dL:</td>
<td>If triglycerides are 200 to 499 mg per dL††, non–HDL-C target should be less than 130 mg per dL.</td>
<td>I (B)</td>
<td>Modified recommendation (changed text)</td>
</tr>
<tr>
<td></td>
<td>If triglycerides are 200 to 499 mg per dL††, further reduction of non–HDL-C to less than 100 mg per dL is reasonable.</td>
<td>IIa (B)</td>
<td>New recommendation</td>
</tr>
<tr>
<td>6. Therapeutic options to reduce non–HDL-C include:</td>
<td>More intense LDL-C-lowering therapy is indicated.</td>
<td>I (B)</td>
<td>New recommendation</td>
</tr>
<tr>
<td></td>
<td>After LDL-C-lowering therapy,”*** consider adding fibrate or niacin¶</td>
<td>Ila (B)</td>
<td>Modified recommendation (changed text)</td>
</tr>
<tr>
<td></td>
<td>Fibrate therapy¶¶ (after LDL-C-lowering therapy) can be beneficial.</td>
<td>Ila (B)</td>
<td>Modified recommendation (changed text)</td>
</tr>
<tr>
<td>If triglycerides are greater than or equal to 500 mg/dL:</td>
<td>Consider fibrate or niacin§ before LDL-C-lowering therapy.¶††</td>
<td>I (C)</td>
<td>Modified recommendation (changed text)</td>
</tr>
<tr>
<td></td>
<td>Consider omega-3 fatty acids as an adjunct for high triglycerides.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Physical Activity**

**Goal:** 30 minutes 5 days per week; optimal daily

|  | 1. Advising medically supervised programs (cardiac rehabilitation) for high-risk patients (e.g., recent acute coronary syndrome or revascularization, heart failure) is recommended. | I (B) | Modified recommendation (changed text) |
|  | Assess risk, preferably with exercise testing, to guide prescription. |  |  |
|  | Encourage a minimum of 30 to 60 minutes of activity, preferably daily or at least 5 days per week (brisk walking, jogging, cycling, or other aerobic activity) supplemented by an increase in daily lifestyle activities (e.g., walking breaks at work, gardening, and household work). |  |  |
|  | Encourage resistance training 2 days per week. |  |  |
|  | Cardiac rehabilitation programs are recommended, particularly for patients with multiple modifiable risk factors and/or moderate-to high-risk patients for whom supervised exercise training is warranted. |  |  |
|  | For all patients, it is recommended that risk be assessed with a physical activity history and/or an exercise test to guide prescription. | I (B) | Modified recommendation (changed text) |
|  | For all patients, encouraging 30 to 60 minutes of moderate-intensity aerobic activity is recommended, such as brisk walking on most—preferably all—days of the week, supplemented by an increase in daily lifestyle activities (e.g., walking breaks at work, gardening, and household work). | I (B) | Modified recommendation (changed text) |
|  | For all patients, encouraging resistance training 2 days per week may be reasonable. | IIb (C) | No content change |
Table 17. Continued

<table>
<thead>
<tr>
<th>Weight Management</th>
<th>2005 PCI Recommendations</th>
<th>2007 PCI Recommendations</th>
<th>2007 COR and LOE</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goal: BMI: 18.5 to 24.9 kg/m²</td>
<td>1. It is useful to assess BMI and/or waist circumference on each visit and consistently encourage weight maintenance/reduction through an appropriate balance of physical activity, caloric intake, and formal behavioral programs when indicated to maintain/achieve a BMI between 18.5 and 24.9 kg/m².</td>
<td>I (B)</td>
<td>Modified recommendation (changed text)</td>
<td></td>
</tr>
<tr>
<td>Waist circumference: men less than 40 inches (102 cm), women less than 35 inches (89 cm)</td>
<td>2. The initial goal of weight-loss therapy should be to reduce body weight by approximately 10% from baseline. With success, further weight loss can be attempted if indicated through further assessment.</td>
<td>I (B)</td>
<td>Modified recommendation (changed text)</td>
<td></td>
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<tr>
<td>Calculate BMI and measure waist circumference as part of evaluation. Monitor response of BMI and waist circumference to therapy.</td>
<td>3. If waist circumference (measured horizontally at the iliac crest) is 35 inches (89 cm) or greater in women and 40 inches (102 cm) or greater in men, it is useful to initiate lifestyle changes and consider treatment strategies for metabolic syndrome.</td>
<td>I (B)</td>
<td>Modified recommendation (changed text)</td>
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Diabetes Management
Goal: HbA₁c less than 7%

| 1. It is recommended to initiate lifestyle and pharmacotherapy to achieve near-normal HbA₁c. | I (B) | Modified recommendation (changed text) |
| 2. Beginning vigorous modification of other risk factors (e.g., physical activity, weight management, blood pressure control, and cholesterol management as recommended above) is beneficial. | I (B) | Modified recommendation (changed text) |
| 3. Coordination of diabetic care with the patient’s primary care physician or endocrinologist is beneficial. | I (C) | New recommendation |

Antiplatelet Agents/Anticoagulants: Aspirin

For all post-PCI stented patients, aspirin 325 mg daily should be given for at least 1 month after BMS implantation, 3 months after sirolimus stent implantation, and 6 months after paclitaxel stent implantation, after which daily long-term aspirin use should be continued indefinitely in all patients if not contraindicated.  

1. For all post-PCI stented patients without allergy or increased risk of bleeding, aspirin 162 mg to 325 mg daily should be given for at least 1 month after BMS implantation, 3 months after sirolimus-eluting stent implantation, and 6 months after paclitaxel-eluting stent implantation, after which long-term aspirin use should be continued indefinitely at a dose of 75 mg to 162 mg daily.  

2. In patients for whom the physician is concerned about risk of bleeding, lower-dose 75 mg to 162 mg of aspirin is reasonable during the initial period after stent implantation.  

Antiplatelet Agents/Anticoagulants: Clopidogrel

For all post-PCI stented patients, clopidogrel 75 mg per day should be given for at least 1 month after BMS implantation, 3 months after sirolimus stent implantation, and 6 months after paclitaxel stent implantation, after which clopidogrel should ideally be continued for up to 12 months in all stented patients who are not at high risk of bleeding.  

1. For all post-PCI patients who receive a DES, clopidogrel 75 mg daily should be given for at least 12 months if patients are not at high risk of bleeding. For post-PCI patients receiving a BMS, clopidogrel should be given for a minimum of 1 month and ideally up to 12 months (unless the patient is at increased risk of bleeding; then it should be given for a minimum of 2 weeks).  

2. For all post-PCI non-stented STEMI patients, treatment with clopidogrel should continue for at least 14 days.  

3. Long-term maintenance therapy (e.g., 1 year) with clopidogrel (75 mg per day orally) is reasonable in STEMI and non-STEMI patients who undergo PCI without reperfusion therapy.
Table 17. Continued

<table>
<thead>
<tr>
<th>2005 PCI Recommendations</th>
<th>2007 PCI Recommendations</th>
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<td><strong>Antiplatelet Agents/Anticoagulants: Warfarin</strong></td>
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<tr>
<td>Manage warfarin to an INR of 2.5 to 3.5 for post-MI patients when clinically indicated or for those not able to take aspirin or clopidogrel.</td>
<td>1. Managing warfarin to an INR equal to 2.0 to 3.0 for paroxysmal or chronic atrial fibrillation or flutter is recommended, and in post-MI patients when clinically indicated (e.g., atrial fibrillation, left ventricular thrombus).</td>
<td>I (A)</td>
<td>Modified recommendation (changed text)</td>
</tr>
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<td></td>
<td>2. Use of warfarin in conjunction with aspirin and/or clopidogrel is associated with an increased risk of bleeding and should be monitored closely.</td>
<td>I (B)</td>
<td>New Recommendation</td>
</tr>
<tr>
<td></td>
<td>3. In patients requiring warfarin, clopidogrel, and aspirin therapy after PCI, an INR of 2.0 to 2.5 is recommended with low dose aspirin (75 mg to 81 mg) and a 75-mg dose of clopidogrel.</td>
<td>I (C)</td>
<td>New recommendation</td>
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<td><strong>Renin-Angiotensin-Aldosterone System Blockers: ACE Inhibitors</strong></td>
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<tr>
<td>Consider use of ACE inhibitors for all CHD patients indefinitely; start early after MI in stable high-risk patients (anterior MI, previous MI, Killip class greater than or equal to II [S3 gallop, rales, radiographic HF]).</td>
<td>1. ACE inhibitors should be started and continued indefinitely in all patients with LVEF less than or equal to 40% and for those with hypertension, diabetes, or chronic kidney disease, unless contraindicated.</td>
<td>I (A)</td>
<td>Modified recommendation (changed text)</td>
</tr>
<tr>
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<td>2. ACE inhibitors should be started and continued indefinitely in patients who are not lower risk (lower risk defined as those with normal LVEF in whom cardiovascular risk factors are well controlled and revascularization has been performed), unless contraindicated.</td>
<td>I (B)</td>
<td>Modified recommendation (changed text)</td>
</tr>
<tr>
<td></td>
<td>3. Among lower risk patients (i.e., those with normal LVEF in whom cardiovascular risk factors are well controlled and revascularization has been performed) use of ACE inhibitors is reasonable.</td>
<td>IIa (B)</td>
<td>Modified recommendation (changed text)</td>
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<td><strong>Renin-Angiotensin-Aldosterone System Blockers: Angiotensin Receptor Blockers</strong></td>
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<td>Use angiotensin receptor blockers in post-STEMI patients who are intolerant of ACE inhibitors and who have either clinical or radiological signs of heart failure or LVEF less than 0.40.</td>
<td>1. Use of angiotensin receptor blockers is recommended in patients who are intolerant of ACE inhibitors and have HF or have had an MI with LVEF less than or equal to 40%.</td>
<td>I (A)</td>
<td>Modified recommendation (changed text)</td>
</tr>
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<td></td>
<td>2. Angiotensin receptor blockers are useful in other patients who are ACE-inhibitor intolerant and have hypertension.</td>
<td>I (B)</td>
<td>New recommendation</td>
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<tr>
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<td>3. Considering use in combination with ACE inhibitors in systolic dysfunction HF may be reasonable.</td>
<td>IIb (B)</td>
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<tr>
<td><strong>Renin-Angiotensin-Aldosterone System Blockers: Aldosterone Blockade</strong></td>
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<tr>
<td>Aldosterone blockade in post-STEMI patients without significant renal dysfunction¶¶ or hyperkalemia*** who are already receiving therapeutic doses of an ACE inhibitor, have an LVEF less than or equal to 0.40, and have either diabetes or heart failure.</td>
<td>1. Use of aldosterone blockade in post-MI patients without significant renal dysfunction¶¶ or hyperkalemia*** is recommended in patients who are already receiving therapeutic doses of an ACE inhibitor and beta blocker, have an LVEF of less than or equal to 40%, and have either diabetes or HF.</td>
<td>I (A)</td>
<td>Modified recommendation (changed text)</td>
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Recommendations in bold type are those the writing committee felt deserved extra emphasis. The 2007 PCI recommendations are written in complete sentences, in accordance with ACC/AHA Guidelines methodology.

“No content change” indicates the updated recommendation now includes a LOE and COR and a verb consistent with that LOE and COR as outlined in the ACC/AHA LOE/COR table (Table 1).

For compelling indications for individual drug classes in specific vascular diseases, see the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) (161).

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<th>Beta Blockers</th>
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<td>Start in all post-MI and acute patients (arrhythmia, LV dysfunction, inducible ischemia). Continue for a minimum of 6 months; continue indefinitely in patients with STEMI. Observe usual contraindications. Use as needed to manage angina, rhythm, or blood pressure in all other patients.</td>
<td>1. It is beneficial to start and continue beta-blocker therapy indefinitely in all patients who have had MI, acute coronary syndrome, or LV dysfunction with or without HF symptoms, unless contraindicated. 2. It is reasonable to consider long-term therapy for all other patients with coronary or other vascular disease or diabetes unless contraindicated.</td>
<td>I (A)</td>
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<tr>
<td>1. Patients with cardiovascular disease should have an annual influenza vaccination.</td>
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</table>

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### Appendix 1. Author Relationships With Industry—Writing Group to Develop the 2007 Percutaneous Coronary Intervention Focused Update of the ACC/AHA/SCAI 2005 Guidelines for Percutaneous Coronary Intervention

<table>
<thead>
<tr>
<th>Committee Member</th>
<th>Research Grant</th>
<th>Speakers’ Bureau/Honoraria</th>
<th>Stock Ownership</th>
<th>Board of Directors</th>
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<td>Dr. John W. Hirshfeld, Jr.</td>
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<td>None</td>
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<tr>
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<td>Dr. Douglass A. Morrison</td>
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<td>None</td>
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<td>• Abbott • Boston Scientific • Cordis</td>
<td>None</td>
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This table represents the actual or potential relationships with industry that were reported as of September 24, 2007. This table was updated in conjunction with all conference calls of this writing committee. A person is deemed to have a significant interest in a business if the interest represents ownership of 5% or more of the voting stock or share of the business entity, or ownership of $10,000 or more of the fair market value of the business entity; or if funds received by the person from the business entity exceed 5% of the person’s gross income for the previous year. A relationship is considered to be modest if it is less than significant under the preceding definition. Relationships in this table are modest unless otherwise noted.

*Recused from voting on Section 7: Antiplatelet Therapy.
†Significant (greater than $10,000) relationship.
‡Recused from voting on Section 8: Bare-Metal and Drug-Eluting Stents.


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<td>Dr. Vincent F. Carr</td>
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<td>Dr. Ik-Kyung Jang</td>
<td>• Content Reviewer—AHA Acute Cardiac Care Committee</td>
<td>Mitsubishi-Tokyo Pharma</td>
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<td>None</td>
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*Names are listed in alphabetical order with each category of review.
†Significant (greater than $10,000) relationship.
ACC indicates American College of Cardiology; ACCF, American College of Cardiology Foundation; ACS, American College of Surgeons; AHA, American Heart Association; and SCAI, Society for Cardiovascular Angiography and Interventions.
In the article by King et al., “2007 Focused Update of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines” that appeared in the January 15, 2008, issue of the journal, folio information for Circulation was incomplete in the footnote. The complete citation is Circulation. 2008;117:261–295. The current online version of the article has been corrected.

The publisher regrets this error.

DOI: 10.1161/CIRCULATIONAHA.107.188911
PRACTICE guidelines are systematically developed recommendations that assist the practitioner and patient in making decisions about health care. These recommendations may be adopted, modified, or rejected according to clinical needs and constraints. Practice guidelines are not intended as standards or absolute requirements. The use of practice guidelines cannot guarantee any specific outcome. Practice guidelines are subject to revision as warranted by the evolution of medical knowledge, technology, and practice. They provide basic recommendations that are supported by analysis of the current literature and by a synthesis of expert opinion, open forum commentary, and clinical feasibility data.

Methodology

A. Definition of Obstructive Sleep Apnea

Obstructive sleep apnea (OSA) is a syndrome characterized by periodic, partial, or complete obstruction of the upper airway during sleep. This, in turn, causes repetitive arousal from sleep to restore airway patency, which may result in daytime hypsomnolence or other daytime manifestations of disrupted sleep such as aggressive or distractible behavior in children. The airway obstruction may also cause episodic sleep-associated oxygen desaturation, episodic hypercarbia, and cardiovascular dysfunction. It is estimated that the adult prevalence of sleep disordered breathing, as measured in a sleep laboratory, is 9% in women and 24% in men, whereas the prevalence of overt OSA has been estimated to be 2% in women and 4% in men. These figures are likely to increase as the population becomes older and more obese. In the perioperative period, both pediatric and adult patients with OSA, even if asymptomatic, present special challenges that must be systematically addressed to minimize the risk of perioperative morbidity or mortality. It is the opinion of the Task Force that the perioperative risk to patients increases in proportion to the severity of sleep apnea.

Because procedures differ among laboratories, it is not possible to use specific values of indices (such as the apnea-hypopnea index [AHI]) to define the severity of sleep apnea. Therefore, for the purposes of these Guidelines, patients will be stratified using the terms mild, moderate, and severe as defined by the laboratory where the sleep study was performed.

B. Purpose of the Guidelines

The purpose of these Guidelines is to improve the perioperative care and reduce the risk of adverse outcomes in patients with OSA who receive sedation, analgesia, or anesthesia for diagnostic or therapeutic procedures under the care of an anesthesiologist. The Task Force recognizes that it is not possible to determine with 100% accuracy whether a given patient will develop perioperative complications related to OSA. Therefore, these Guidelines should be implemented with the goal of reducing the likelihood of adverse outcomes in patients who are judged to be at the
greatest risk, with the understanding that it may be impractical to eliminate OSA-related perioperative morbidity and mortality completely. However, it is hoped that the implementation of these Guidelines will reduce the likelihood of adverse perioperative outcomes in patients with OSA.

C. Focus
These Guidelines focus on the perioperative management of patients with OSA who may be at increased risk for perioperative morbidity and mortality because of potential difficulty in maintaining a patent airway. This population includes but is not limited to patients who have sleep apnea resulting from obesity, pregnancy, and other skeletal, cartilaginous, or soft tissue abnormalities causing upper airway obstruction. Excluded from the focus of these Guidelines are patients with the following: (1) pure central sleep apnea, (2) abnormalities of the upper or lower airway not associated with sleep apnea (e.g., deviated nasal septum), (3) daytime hypersomnolence from other causes, (4) patients younger than 1 yr, and (5) obesity in the absence of sleep apnea.

D. Application
These Guidelines apply to both inpatient and outpatient settings, and to procedures performed in an operating room, as well as in other locations where sedation or anesthesia is administered. They are directly applicable to care administered by anesthesiologists and individuals who deliver care under the medical direction or supervision of an anesthesiologist. They are also intended to serve as a resource for other physicians and patient care personnel who are involved in the care of these patients. In addition, these Guidelines may serve as a resource to provide an environment for safe patient care.

E. Task Force Members and Consultants
The American Society of Anesthesiologists appointed a Task Force of 12 members to (1) review the published evidence, (2) obtain the opinion of a panel of consultants including anesthesiologists and nonanesthesiologist physicians and researchers who regularly care for patients with OSA, and (3) build consensus within the community of practitioners likely to be affected by the Guidelines. The Task Force included anesthesiologists in both private and academic practices from various geographic areas of the United States, a bariatric surgeon, an otolaryngologist, and two methodologists from the American Society of Anesthesiologists Committee on Practice Parameters.

The Task Force developed the Guidelines by means of a six-step process. First, they reached consensus on the criteria for evidence of effective perioperative management of patients with OSA. Second, original published research studies from peer-reviewed journals relevant to the perioperative management of patients with OSA were evaluated. Third, the panel of expert consultants was asked to (1) participate in opinion surveys on the effectiveness of various perioperative management strategies for patients with OSA and (2) review and comment on a draft of the Guidelines developed by the Task Force. Fourth, the Task Force held open forums at two major national meetings to solicit input on its draft recommendations. National organizations representing most of the specialties whose members typically care for patients with OSA were invited to participate in the open forums. Fifth, the consultants were surveyed to assess their opinions on the feasibility and financial implications of implementing the Guidelines. Sixth, all available information was used to build consensus within the Task Force to finalize the Guidelines.

Tables 1 and 2 are meant to serve as examples of how patients with OSA might be identified and stratified with respect to their perioperative risk. While they were developed by the Task Force with input from the consultants and open forum participants, these tables are not evidence based and have not been clinically validated.

F. Availability and Strength of Evidence
Preparation of these Guidelines followed a rigorous methodologic process (appendix). To convey the findings in a concise fashion, these Guidelines use several descriptive terms that are easier to understand than the technical terms used in the actual analyses.

When sufficient numbers of studies are available for evaluation, the following terms describe the strength of the findings.

**Supportive:** Meta-analyses of a sufficient number of adequately designed studies indicate a statistically significant relationship \((P < 0.01)\) between a clinical intervention and a clinical outcome.

**Suggestive:** Information from case reports and descriptive studies permits inference of a relationship between an intervention and an outcome. This type of qualitative information does not permit a statistical assessment of significance.

**Equivocal:** Qualitative data are not adequate to permit inference of a relationship between an intervention and an outcome. This type of qualitative information does not permit a statistical assessment of significance.

**Silent:** No identified studies address the specified relationship between an intervention and outcome.

**Insufficient:** There are too few published studies to investigate a relationship between an intervention and an outcome.

**Inadequate:** The available studies cannot be used to assess the relationship between an intervention and an outcome. These studies either do not meet the criteria for content as defined in the Focus of these Guide-
If a patient has signs or symptoms in two or more of the above categories, there is a significant probability that he or she has OSA. The severity of OSA may be determined by sleep study (see below). If a sleep study is not available, such patients should be treated as though they have moderate sleep apnea unless one or more of the signs or symptoms above is severely abnormal (e.g., markedly increased BMI or neck circumference, respiratory pauses that are frightening to the observer, patient regularly falls asleep within minutes after being left unstimulated), in which case they should be treated as though they have severe sleep apnea.

If a patient has signs or symptoms in two or more of the above categories, there is a significant probability that he or she has OSA. The severity of OSA may be determined by sleep study (see below). If a sleep study is not available, such patients should be treated as though they have moderate sleep apnea unless one or more of the signs or symptoms above is severely abnormal (e.g., markedly increased BMI or neck circumference, respiratory pauses that are frightening to the observer, patient regularly falls asleep within minutes after being left unstimulated), in which case they should be treated as though they have severe sleep apnea.

B. If a sleep study has been done, the results should be used to determine the perioperative anesthetic management of a patient. However, because sleep laboratories differ in their criteria for detecting episodes of apnea and hypopnea, the Task Force believes that the sleep laboratory’s assessment (none, mild, moderate, or severe) should take precedence over the actual AHI (the number of episodes of sleep-disordered breathing per hour). If the overall severity is not indicated, it may be determined by using the table below:

### Table 1. Identification and Assessment of OSA: Example

<table>
<thead>
<tr>
<th>Severity of OSA</th>
<th>Adult AHI</th>
<th>Pediatric AHI</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>0–5</td>
<td>0</td>
</tr>
<tr>
<td>Mild OSA</td>
<td>6–20</td>
<td>1–5</td>
</tr>
<tr>
<td>Moderate OSA</td>
<td>21–40</td>
<td>6–10</td>
</tr>
<tr>
<td>Severe OSA</td>
<td>&gt; 40</td>
<td>&gt; 10</td>
</tr>
</tbody>
</table>

* Items in brackets refer to pediatric patients.

AHI = apnea-hypopnea index; BMI = body mass index; OSA = obstructive sleep apnea; TV = television.

A scoring system similar to this table may be used to estimate whether a patient is at increased perioperative risk of complications from obstructive sleep apnea (OSA). This example, which has not been clinically validated, is meant only as a guide, and clinical judgment should be used to assess the risk of an individual patient.

* One point may be subtracted if a patient has been on continuous positive airway pressure (CPAP) or noninvasive positive-pressure ventilation (NIPPV) before surgery and will be using his or her appliance consistently during the postoperative period. † One point should be added if a patient with mild or moderate OSA also has a resting arterial carbon dioxide tension (Paco2) greater than 50 mmHg. ‡ Patients with a score of 4 may be at increased perioperative risk from OSA; patients with a score of 5 or 6 may be at significantly increased perioperative risk from OSA.

### Table 2. OSA Scoring System: Example

<table>
<thead>
<tr>
<th>A. Severity of sleep apnea based on sleep study (or clinical indicators if sleep study not available).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Point score (0–3)‡</td>
</tr>
<tr>
<td>Severity of OSA (table 1)</td>
</tr>
<tr>
<td>None</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B. Invasiveness of surgery and anesthesia. Point score (0–3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of surgery and anesthesia</td>
</tr>
<tr>
<td>Superficial surgery under local or peripheral nerve block anesthesia without sedation</td>
</tr>
<tr>
<td>Superficial surgery with moderate sedation or general anesthesia</td>
</tr>
<tr>
<td>Peripheral surgery with spinal or epidural anesthesia (with no more than moderate sedation)</td>
</tr>
<tr>
<td>Peripheral surgery with general anesthesia</td>
</tr>
<tr>
<td>Airway surgery with moderate sedation</td>
</tr>
<tr>
<td>Major surgery, general anesthesia</td>
</tr>
<tr>
<td>Airway surgery, general anesthesia</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>C. Requirement for postoperative opioids. Point score (0–3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid requirement</td>
</tr>
<tr>
<td>None</td>
</tr>
<tr>
<td>Low-dose oral opioids</td>
</tr>
<tr>
<td>High-dose oral opioids, parenteral or neuraxial opioids</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>D. Estimation of perioperative risk. Overall score = the score for A plus the greater of the score for either B or C. Point score (0–6)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>A scoring system similar to this table may be used to estimate whether a patient is at increased perioperative risk of complications from obstructive sleep apnea (OSA). This example, which has not been clinically validated, is meant only as a guide, and clinical judgment should be used to assess the risk of an individual patient.</td>
</tr>
</tbody>
</table>

**Guidelines**

1. **Preoperative Evaluation**

   Preoperative evaluation of a patient for potential identification of OSA includes (1) medical record review, (2)
patient or family interview, (3) physical examination, (4) sleep studies, and (5) preoperative x-rays for cephalometric measurement in selected cases. Although the comparative literature is insufficient to evaluate the impact of preprocedure identification of OSA status, it suggests that OSA is associated with airway characteristics that may predispose patients to difficulties in perioperative airway management. The literature identified certain patient characteristics that are associated with OSA. These characteristics include such features as a higher body mass index, hypertension, and abnormal cephalometric measurements. Additional literature, although insufficient for statistical analysis, suggests that an association may exist between OSA and a larger neck circumference, a history of snoring or respiratory pauses, lower oxygen saturation values during sleep, clinical signs of difficult airway management, and certain congenital conditions (e.g., Down syndrome, craniofacial abnormality, muscular dystrophy) or disease states (e.g., diabetes mellitus, cerebral palsy).

The consultants agree that, in the absence of a sleep study, a presumptive diagnosis of OSA may be made based on consideration of the following criteria: increased body mass index, a weight or body mass index greater than 95th percentile for age (pediatric patients), increased neck circumference, snoring, congenital airway abnormalities, daytime hypersomnolence, inability to visualize the soft palate, and tonsillar hypertrophy. They strongly agree that observed apnea during sleep is an additional criterion. The consultants agree that preprocedure identification of a patient’s OSA status improves perioperative outcomes, and they are equivocal regarding whether overall costs are decreased. The consultants agree that a patient’s perioperative risk depends on both the severity of the OSA and the invasiveness of the surgical procedure.

**Recommendations.** Anesthesiologists should work with surgeons to develop a protocol whereby patients in whom the possibility of OSA is suspected on clinical grounds are evaluated long enough before the day of surgery to allow preparation of a perioperative management plan. This evaluation may be initiated in a preanesthesia clinic (if available) or by direct consultation from the operating surgeon to the anesthesiologist. A preoperative evaluation should include a comprehensive review of previous medical records (if available), an interview with the patient and/or family, and conducting a physical examination. Medical records review should include (but not be limited to) checking for a history of airway difficulty with previous anesthetics, hypertension or other cardiovascular problems, and other congenital or acquired medical conditions. Review of sleep studies is encouraged. The patient and family interview should include focused questions related to snoring, apneic episodes, frequent arousals during sleep (vocalization, shifting position, extremity movements), morning headaches, and daytime somnolence. A physical examination should include an evaluation of the airway, nasopharyngeal characteristics, neck circumference, tonsil size, and tongue volume. If any of these characteristics suggest that the patient has OSA, the anesthesiologist and surgeon should jointly decide whether to (1) manage the patient perioperatively based on clinical criteria alone or (2) obtain sleep studies, conduct a more extensive airway examination, and initiate indicated OSA treatment in advance of surgery. If this evaluation does not occur until the day of surgery, the surgeon and anesthesiologist together may elect for presumptive management based on clinical criteria or a last-minute delay of surgery. For safety, clinical criteria (table 1) should be designed to have a high degree of sensitivity (despite the resulting low specificity), meaning that some patients may be treated more aggressively than would be necessary if a sleep study were available.

The severity of the patient’s OSA, the invasiveness of the diagnostic or therapeutic procedure, and the requirement for postoperative analgesics should be taken into account in determining whether a patient is at increased perioperative risk from OSA (table 2). The patient and his or her family as well as the surgeon should be informed of the potential implications of OSA on the patient’s perioperative course.

**II. Preoperative Preparation**

Preoperative preparation is intended to improve or optimize an OSA patient’s perioperative physical status and includes (1) preoperative continuous positive airway pressure (CPAP) or noninvasive positive-pressure ventilation (NIPPV) or bilevel positive airway pressure (BiPAP®; Respironics, Murrysville, PA), (2) preoperative use of mandibular advancement or oral appliances, (3) preoperative medications, or (4) preoperative weight loss. There is insufficient literature to evaluate the impact of the preoperative use of CPAP, NIPPV, or mandibular advancement devices on perioperative outcomes. Similarly, there is insufficient literature to evaluate the efficacy of preoperative medications or weight loss. However, the literature supports the efficacy of CPAP in improving AHI, respiratory disturbance index scores, and oxygen saturation levels in nonperioperative settings. Similarly, the literature supports the efficacy of mandibular advancement devices in reducing AHI scores in nonperioperative settings.

The consultants agree that preoperative use of positive airway pressure (CPAP or NIPPV) may improve the preoperative condition of patients who they believe are at increased perioperative risk from OSA, and they are equivocal regarding the efficacy of mandibular advancement devices for these patients. The consultants agree that a

* Refer to the appendix for details of the literature review and data analyses.
preoperative determination should be made regarding whether surgery in patients at increased perioperative risk from OSA should be performed on an inpatient basis.

**Recommendations.** Preoperative initiation of CPAP should be considered, particularly if OSA is severe. For patients who do not respond adequately to CPAP, NIPPV should be considered. In addition, the preoperative use of mandibular advancement devices or oral appliances and preoperative weight loss should be considered when feasible. A patient who has had corrective airway surgery (e.g., uvulopalatopharyngoplasty, surgical mandibular advancement) should be assumed to remain at risk for OSA complications unless a normal sleep study has been obtained and symptoms have not returned. Patients with known or suspected OSA may have difficult airways and therefore should be managed according to the “Practice Guidelines for Management of the Difficult Airway.” In patients at risk for perioperative complications from OSA, a preoperative determination must be made regarding whether surgery should be performed on an inpatient or outpatient basis (see section V below).

### III. Intraoperative Management

Intraoperative concerns in patients at increased perioperative risk from OSA include (1) choice of anesthetic technique, (2) airway management, and (3) patient monitoring. The literature is insufficient to evaluate the effects of various anesthetic techniques on patients with OSA. Similarly, the literature is insufficient to evaluate the impact of specific intraoperative airway management (e.g., awake extubation) or patient monitoring techniques for patients with OSA.

The consultants agree that the use of local anesthesia or peripheral nerve blocks rather than general anesthesia improves outcomes in patients undergoing peripheral surgery. The consultants agree that the use of major conduction anesthesia (i.e., spinal or epidural) rather than general anesthesia improves outcomes for peripheral surgery. The consultants are equivocal regarding the utility of major conduction anesthesia rather than general anesthesia for intraabdominal surgery. The consultants are equivocal regarding whether the use of combined regional and general anesthesia improves outcomes.

The consultants agree that patients at increased perioperative risk from OSA should be extubated when fully awake, and they strongly agree that full reversal of neuromuscular blockade should be verified before extubation. They agree that these patients should be placed in the semiupright position for extubation and recovery.

The consultants agree that respiratory carbon dioxide monitoring should be used during moderate or deep sedation in these patients. The consultants agree that general anesthesia with a secured airway is preferable to deep sedation for superficial procedures, and they are equivocal regarding whether general anesthesia with a secured airway is preferable to moderate sedation for superficial procedures. The consultants agree that general anesthesia with a secured airway is preferable to moderate or deep sedation for patients with OSA undergoing procedures involving the upper airway (e.g., upper endoscopy, bronchoscopy, uvulopalatopharyngoplasty).

**Recommendations.** Because of their propensity for airway collapse and sleep deprivation, patients at increased perioperative risk from OSA are especially susceptible to the respiratory depressant and airway effects of sedatives, opioids, and inhaled anesthetics; therefore, in selecting intraoperative medications, the potential for postoperative respiratory compromise should be considered. For superficial procedures, one should consider the use of local anesthesia or peripheral nerve blocks, with or without moderate sedation. If moderate sedation is used, ventilation should be continuously monitored by capnography or another automated method if feasible because of the increased risk of undetected airway obstruction in these patients. One should consider administering CPAP or using an oral appliance during sedation to patients previously treated with these modalities. General anesthesia with a secure airway is preferable to deep sedation without a secure airway, particularly for procedures that may mechanically compromise the airway. Major conduction anesthesia (spinal/epidural) should be considered for peripheral procedures. Unless there is a medical or surgical contraindication, patients at increased perioperative risk from OSA should be extubated while awake. Full reversal of neuromuscular block should be verified before extubation. When possible, extubation and recovery should be carried out in the lateral, semiupright, or other nonsupine position.

### IV. Postoperative Management

Postoperative concerns in the management of patients with OSA include (1) analgesia, (2) oxygenation, (3) patient positioning, and (4) monitoring. Risk factors for respiratory depression include the systemic and neuraxial administration of opioids, administration of sedatives, site and invasiveness of surgical procedure, and the underlying severity of the sleep apnea. In addition, exacerbation of respiratory depression may occur on the third or fourth postoperative day as sleep patterns are reestablished and “REM rebound” occurs.

**Postoperative Analgesia.** The literature is insufficient to evaluate the effects of various postoperative analgesic techniques on patients with OSA. However, the literature is equivocal regarding the use of epidural opioids compared with intramuscular or intravenous opioids in reducing respiratory depression among unselected surgical patients. The literature is insufficient to

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evaluate the effect of adding a basal infusion to systemic patient-controlled opioids on the oxygenation of patients with OSA. However, the literature supports the observation that adding a basal infusion results in an increased incidence of hypoxemia in unselected surgical patients.

The consultants agree that regional analgesic techniques rather than systemic opioids reduce the likelihood of adverse outcomes in patients at increased perioperative risk from OSA. The consultants agree that the exclusion of opioids from neuraxial postoperative analgesia reduces risks as compared with neuraxial techniques which include opioids. The consultants agree that the use of nonsteroidal antiinflammatory agents, when acceptable, reduces adverse outcomes through their opioid-sparing effect. The consultants are equivocal regarding whether patient-controlled analgesia with systemic opioids reduces risks as compared with nurse-administered intramuscular or intravenous opioids. In addition, the consultants are equivocal regarding whether avoiding a basal infusion of opioids in patients at increased perioperative risk from OSA reduces the likelihood of adverse outcomes.

**Oxygenation.** Although the literature is insufficient to evaluate the effects of postoperative supplemental oxygen administration in patients with OSA, it supports the use of postextubation supplemental oxygen to improve the oxygen saturation levels of unselected surgical patients. There is insufficient literature to evaluate the effect of CPAP or NIPPV on the postoperative respiratory status of patients with OSA. However, the literature supports the efficacy of CPAP in nonperioperative settings.

The consultants agree that supplemental oxygen should be administered as needed to maintain acceptable arterial oxygen saturation and that supplemental oxygen may be discontinued when patients are able to maintain their baseline oxygen saturation while breathing room air. The consultants strongly agree that CPAP or NIPPV should be administered as soon as feasible after surgery to patients with OSA who were receiving it preoperatively, but they are equivocal regarding the utility of instituting CPAP or NIPPV in patients who were not previously treated with these modalities. The consultants are equivocal regarding whether patients receiving postoperative CPAP or NIPPV should have the appliance in place whenever the patients are not ambulating.

**Patient Positioning.** The literature supports an improvement in AHI scores when adult patients with OSA sleep in the lateral, prone, or sitting positions rather than the supine position in nonperioperative settings, but the literature is insufficient to provide guidance for the postoperative setting. The literature is insufficient to provide guidance for optimal positioning of pediatric patients with OSA. The consultants agree that the supine position should be avoided when possible during the recovery of adult and pediatric patients who they believe are at increased perioperative risk from OSA.

**Monitoring.** The literature is insufficient to evaluate the efficacy of telemetry monitoring systems (e.g., for pulse oximetry, electrocardiogram, or ventilation) in minimizing the risk of adverse perioperative events in patients with OSA. Similarly, the literature is insufficient to examine the impact of monitored postoperative settings (e.g., stepdown or intensive care unit) versus routine hospital wards for patients with known or suspected OSA. The literature is insufficient to offer guidance regarding the appropriate duration of postoperative respiratory monitoring in patients with OSA.

The consultants agree that continuous oximetry in a stepdown unit or by telemetry reduces the likelihood of perioperative complications among patients who they believe are at increased perioperative risk from OSA. They are equivocal regarding whether pulse oximetry should be continuously monitored until these patients are no longer receiving parenteral narcotics. They agree that pulse oximetry should be applied until room air oxygen saturation remains above 90% during sleep.

**Recommendations.** Regional analgesic techniques should be considered to reduce or eliminate the requirement for systemic opioids in patients at increased perioperative risk from OSA. If neuraxial analgesia is planned, weigh the benefits (improved analgesia, decreased need for systemic opioids) and risks (respiratory depression from rostral spread) of using an opioid or opioid-local anesthetic mixture as compared with a local anesthetic alone. If patient-controlled systemic opioids are used, continuous background infusions should be used with extreme caution or avoided entirely. Nonsteroidal antiinflammatory agents and other modalities (e.g., ice, transcutaneous electrical nerve stimulation) should be considered if appropriate to reduce opioid requirements. Clinicians are cautioned that the concurrent administration of sedative agents (e.g., benzodiazepines, barbiturates) increases the risk of respiratory depression and airway obstruction.

Supplemental oxygen should be administered continuously to all patients who are at increased perioperative risk from OSA until they are able to maintain their baseline oxygen saturation while breathing room air. The Task Force cautions that supplemental oxygen may increase the duration of apneic episodes and may hinder detection of atelectasis, transient apnea, and hypoventilation by pulse oximetry. CPAP or NIPPV, with or without supplemental oxygen, should be continuously ad-
ministered when feasible (e.g., when patients are not ambulating) to patients who were using these modalities preoperatively, unless contraindicated by the surgical procedure. Compliance with CPAP or NIPPV may be improved if patients bring their own equipment to the hospital.

If possible, patients at increased perioperative risk from OSA should be placed in nonsupine positions throughout the recovery process. Hospitalized patients who are at increased risk of respiratory compromise from OSA should have continuous pulse oximetry monitoring after discharge from the recovery room. Continuous monitoring may be provided in a critical care or stepdown unit, by telemetry on a hospital ward, or by a dedicated, appropriately trained professional observer in the patient’s room. Continuous monitoring should be maintained as long as patients remain at increased risk. Intermitent pulse oximetry or continuous bedside oximetry without continuous observation does not provide the same level of safety. If frequent or severe airway obstruction or hypoxemia occurs during postoperative monitoring, initiation of nasal CPAP or NIPPV should be considered.

V. Inpatient versus Outpatient Surgery and Criteria for Discharge to Unmonitored Settings

The literature is insufficient to offer guidance regarding which patients with OSA can be safely managed on an outpatient as opposed to an inpatient basis, and the appropriate time for discharge of these patients from the surgical facility.

The consultants agree that procedures typically performed on an outpatient basis in non-OSA patients may also be safely performed on an outpatient basis in patients who believe they are at increased perioperative risk from OSA when local or regional anesthesia is administered (table 3). The consultants are equivocal regarding whether superficial procedures may be safely performed during general anesthesia in outpatients at increased perioperative risk from OSA, but they disagree that airway surgery (e.g., uvulopalatopharyngoplasty) should be performed on an outpatient basis in adults with OSA. They also disagree that tonsillectomy in children younger than 3 yr with OSA should be performed on an outpatient basis, and they are equivocal regarding outpatient tonsillectomy in older children. The consultants strongly agree that when patients at increased perioperative risk from OSA are anesthetized as outpatients, the facility should have emergency difficult airway equipment, and they agree on the availability of respiratory care equipment (nebulizers, CPAP equipment, ventilators), radiology facilities (for portable chest x-ray), clinical laboratory facilities (blood gases, electrolytes). They strongly agree that a transfer arrangement with an inpatient facility should be in place. The Task Force believes that patients who are at significantly increased risk of perioperative complications (score of 5 or greater on table 2) are generally not good candidates for surgery in a freestanding outpatient facility.

In addition to standard outpatient discharge criteria, the consultants agree that room air oxygen saturation should return to its baseline, and they strongly agree that patients should not become hypoxemic or have development of clinical airway obstruction when left undisturbed in the recovery area. The consultants indicated that patients with OSA should be monitored for a median of 3 h longer than their non-OSA counterparts before discharge from the facility. They also indicated that monitoring of patients with OSA should continue for a median of 7 h after the last episode of airway obstruction or hypoxemia while breathing room air in an unstimulating environment.

Recommendations. Before patients at increased perioperative risk from OSA are scheduled to undergo surgery, a determination should be made regarding whether a given surgical procedure is most appropriately performed on a given patient on an inpatient or outpatient basis. Factors to be considered in determining whether outpatient care is appropriate include (1) sleep apnea status, (2) anatomical and physiologic abnormalities, (3) status of coexisting diseases, (4) nature of surgery, (5) type of anesthesia, (6) need for postoperative opioids, (7) patient age, (8) adequacy of postdischarge observation, and (9) capabilities of the outpatient facility. The availability of emergency difficult airway equipment, respiratory care equipment, radiology facilities, clinical laboratory facilities, and a transfer agreement with an inpatient facility should be considered in making this determination.

These patients should not be discharged from the recovery area to an unmonitored setting (i.e., home or unmonitored hospital bed) until they are no longer at risk for postoperative respiratory depression. Because of their propensity to develop airway obstruction or central respiratory depression, this may require a longer stay as compared

Table 3. Consultant Opinions Regarding Procedures That May Be Performed Safely on an Outpatient Basis for Patients at Increased Perioperative Risk from OSA

<table>
<thead>
<tr>
<th>Type of Surgery/Anesthesia</th>
<th>Consultant Opinion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial surgery/local or regional anesthesia</td>
<td>Agree</td>
</tr>
<tr>
<td>Superficial surgery/general anesthesia</td>
<td>Equivocal</td>
</tr>
<tr>
<td>Airway surgery (adult, e.g., UPPP)</td>
<td>Disagree</td>
</tr>
<tr>
<td>Tonsillectomy in children less than 3 years old</td>
<td>Disagree</td>
</tr>
<tr>
<td>Tonsillectomy in children greater than 3 years old</td>
<td>Equivocal</td>
</tr>
<tr>
<td>Minor orthopedic surgery/local or regional anesthesia</td>
<td>Agree</td>
</tr>
<tr>
<td>Minor orthopedic surgery/general anesthesia</td>
<td>Equivocal</td>
</tr>
<tr>
<td>Gynecologic laparoscopy</td>
<td>Equivocal</td>
</tr>
<tr>
<td>Laparoscopic surgery, upper abdomen</td>
<td>Disagree</td>
</tr>
<tr>
<td>Lithotripsy</td>
<td>Agree</td>
</tr>
</tbody>
</table>

OSA = obstructive sleep apnea; UPPP = uvulopalatopharyngoplasty.

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with non-OSA patients undergoing similar procedures. Ade-
cquacy of postoperative respiratory function may be doc-
umented by observing patients in an unstimulated environ-
ment, preferably while they seem to be asleep, to establish
that they are able to maintain their baseline oxygen satu-
ration while breathing room air.

References
328:1230–5
2. American Society of Anesthesiologists Task Force on Management of the
Difficult Airway: Practice guidelines for management of the difficult airway: An
updated report by the American Society of Anesthesiologists Task Force on
3. American Society of Anesthesiologists Task Force on Acute Pain Manage-
ment: Practice guidelines for acute pain management in the perioperative set-
ing. An updated report by the American Society of Anesthesiologists Task Force on
Acute Pain Management. Anesthesiology 2004; 100:1573–81

Appendix: Methods and Analyses
The scientific assessment of these Guidelines was based on evidence
linkages or statements regarding potential relationships between clin-
ical interventions and outcomes. The interventions listed below were
examined to assess their relationship to a variety of outcomes related to
the management of patients with OSA in the perioperative setting.

1. Preoperative evaluation
   a. Medical records review
   b. Patient and family interview
   c. Screening questionnaire
   d. Focused physical examination
   e. Sleep study

2. Preoperative preparation
   a. Preoperative treatment/optimization for OSA (e.g., CPAP, NIPPV,
mandibular appliances, medical treatment)
   b. Consult the American Society of Anesthesiologists “Practice
Guidelines for Management of the Difficult Airway”
   c. Limit procedures to facilities with full hospital services

3. Intraoperative management
   a. Anesthetic technique
      (i) Local or regional anesthesia versus general anesthesia
      (ii) Combined regional and general anesthesia versus general
anesthesia
      (iii) Sedation versus general anesthesia
   b. Monitoring
      (i) Continuously monitor the respiratory depressant effects of
sedatives and/or opioids (e.g., level of consciousness, pulmo-
nary ventilation, oxygenation, automated apnea monitoring)
      (ii) Special intraoperative monitoring techniques (arterial line,
pulmonary artery catheter)
   c. Exubation
      (i) Verify the full reversal of neuromuscular block before ex-
tubation
      (ii) Extubate patients after they are fully awake (vs. asleep or
partially awake)
      (iii) Extubate patients in the semuprignalt, lateral, or prone po-
sitions (vs. supine)

4. Postoperative management
   a. Analgesic use
      (i) Regional analgesic techniques without neuraxial opioids
versus systemic opioids
      (ii) Neuraxial opioids versus systemic opioids
      (iii) Oral analgesics versus parenteral opioids
(iv) PCA without a background infusion versus PCA with a
background infusion
(v) Titration or lower dosage levels of systemic opioids
b. Oxygenation
   (i) Supplemental oxygen versus no supplemental oxygen
   (ii) CPAP versus no CPAP (oxygen or room air)
   (iii) CPAP for patients who had previously been on CPAP versus
CPAP for patients not previously on CPAP
   (iv) NIPPV versus no NIPPV (CPAP, oxygen, or room air)
c. Positioning patients in the lateral, prone, or tonsil position versus
the supine position
d. Monitoring
   (i) Telemetry monitoring systems versus no telemetry monitor-
ing systems
   (ii) Monitored settings versus routine hospital wards
e. Duration of stay
   (i) Extended stay in PACU versus no extended stay in PACU
   (ii) Hospital admission versus discharge home

Scientific evidence was derived from aggregated research literature,
and opinion-based evidence was obtained from surveys, open presen-
tations, and other consensus-oriented activities (e.g., Internet posting).
For purposes of literature aggregation, potentially relevant clinical
studies were identified via electronic and manual searches of the
literature. The electronic and manual searches covered a 53-yr period
from 1953 through 2005. More than 2000 citations were initially
identified, yielding a total of 622 nonoverlapping articles that ad-
tressed topics related to the evidence linkages. After review of the
articles, 332 studies did not provide direct evidence and were subse-
quently eliminated. A total of 290 articles contained direct linkage-
related evidence.

Initially, each pertinent outcome reported in a study was classified as
supporting an evidence linkage; refuting a linkage, or equivocal.
The results were then summarized to obtain a directional assessment for
each evidence linkage before conducting a formal meta-analysis. Liter-
ature pertaining to six evidence linkages contained enough studies
with well-defined experimental designs and statistical information suf-
ficient for meta-analyses. These linkages were (1) medical records
review (OSA and body mass index; OSA and hypertension); (2) focused
physical examination (OSA associated with neck circumference and
various cephalometric measurements); (3) preoperative treatment/op-
timization for OSA (CPAP [nonperoperative patients] and AHI scores,
respiratory depression index scores, and oxygen saturation levels;
nonperoperative mandibular appliance and AHI scores); (4) postop-
erative analgesic use (neuraxial opioids vs. systemic opioids [in non-
OSA patients] and oxygen saturation levels), postoperative analgesic
use (neuraxial opioids vs. systemic opioids [in non-OSA patients] and
respiratory depression), and postoperative PCA opioids (background
infusion vs. no background infusion [in non-OSA patients] and hypox-
emia); (5) postoperative oxygenation (supplemental oxygen vs. no
supplemental oxygen [in non-OSA patients] and hypoxemia); and (6)
postoperative positioning of patients (lateral, prone, or tonsil versus
supine [nonperoperative patients] and AHI scores).

General variance-based effect-size estimates or combined probability
tests were obtained for continuous outcome measures, and Mantel-
Haenszel odds ratios were obtained for dichotomous outcome mea-
sures. Two combined probability tests were used as follows: (1) The
Fisher combined test, producing chi-square values based on logarith-
ic transformations of the reported P values from the independent
studies, and (2) the Stouffer combined test, providing weighted rep-
resentation of the studies by weighting each of the standard normal
deviates by the size of the sample. An odds ratio procedure based on
the Mantel-Haenszel method for combining study results using 2 x 2
tables was used with outcome frequency information. An acceptable
significance level was set at P < 0.01 (one tailed). Tests for heteroge-
neity of the independent studies were conducted to assure consistency
among the study results. DerSimonian-Laird random effects odds ratios

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were considered when significant heterogeneity was found ($P < 0.01$).
To control for potential publishing bias, a “fail-safe n” value was calculated. No search for unpublished studies was conducted, and no reliability tests for locating research results were done.

Meta-analytic results are reported in Table 4. To be accepted as significant findings, Mantel-Haenszel odds ratios must agree with combined test results whenever both types of data are assessed. In the absence of Mantel-Haenszel odds ratios, findings from both the Fisher and weighted Stouffer combined tests must agree with each other to be acceptable as significant.

Interobserver agreement among Task Force members and two methodologists was established by interrater reliability testing. Agreement levels using a kappa ($\kappa$) statistic for two-rater agreement pairs were as follows: (1) type of study design, $\kappa = 0.50\text{–}0.69$; (2) type of analysis, $\kappa = 0.43\text{–}0.60$; (3) evidence linkage assignment, $\kappa = 0.88\text{–}1.00$; and (4) literature inclusion for database, $\kappa = 0.44\text{–}0.87$. Three-rater chance-corrected agreement values were (1) study design, $\kappa = 0.56$, $\kappa = 0.58$; (2) type of analysis, $\kappa = 0.54$, $\kappa = 0.56$, $\kappa = 0.58$; and (4) literature database inclusion, $\kappa = 0.58$, $\kappa = 0.58$, $\kappa = 0.78$. These values represent moderate to high levels of agreement.

Consensus was obtained from multiple sources, including (1) survey opinion from consultants who were selected based on their knowledge or expertise in perioperative management of patients with OSA, (2) testimony from attendees of two publicly held open forums at two national anesthesia meetings,‡ and (3) Task Force opinion and interpretation. An initial survey obtained consultant opinions regarding the management of patients with known or suspected OSA. The survey rate of return was 65% ($n = 69$ of 106). Results of this survey are reported in Table 5 and in the text of the Guidelines.

A second survey obtained consultant opinions regarding the feasibility of implementing the Guidelines in relation to their clinical practices. Results of this survey are reported below and in Table 6. The rate of return was 42% (n = 45 of 106). Responses by specialty were as follows: anesthesiology, 46.7%; otolaryngology, 20.0%; sleep medicine, 20.0%; pediatrics, 6.7%; general or bariatric surgery, 4.4%; and pulmonology, 2.2%. The median percentage of the respondents’ patients who have OSA is 20%, and they manage a median of 150 patients with OSA per year. They obtain a sleep study for a median number of 25 patients per year. They would need to obtain a sleep study for a median of an additional 10 patients per year to adhere to these Guideline recommendations. The median cost of a sleep study conducted at their facilities is $1,500. They initiate CPAP or NIPPV in preparation for surgery a median of five times a year, and they indicate that an additional median of 10 patients per year would require CPAP or NIPPV to adhere to these Guidelines. They report that a median of 30 additional patients would require postoperative respiratory monitoring at their hospital if the Guidelines were implemented, and they indicate that the median number of days for which such monitoring would be necessary is 1.5. A median of 10% of the consultants’ outpatients with OSA would need to be reclassified as inpatients if the Guidelines were implemented. They report a median of 3 additional hours of recovery room stay that would be required for a typical OSA patient before discharge from their outpatient facility if the Guidelines were implemented. Seventy-three percent of the consultants indicate that the sensitivity of the criteria in section A of Table 1 to detect patients with previously undiagnosed OSA is “about right,” whereas 13% indicate that they are not sensitive enough, and 11% indicate that they are too sensitive. Eighty-two percent of the consultants indicated that the scoring system for assessment of perioperative risk described in Table 2 is “about right,” whereas 11% indicate that it is not stringent enough, and 4% indicate that it is too stringent.

Table 5. Consultant Survey Responses

<table>
<thead>
<tr>
<th>Percent Responding to Each Item</th>
<th></th>
<th>Strongly Agree</th>
<th>Agree</th>
<th>Uncertain</th>
<th>Disagree</th>
<th>Strongly Disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Preoperative evaluation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presumptive diagnosis of OSA:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Elevated body mass index</td>
<td>66</td>
<td>30.3</td>
<td>50.0*</td>
<td>10.6</td>
<td>9.1</td>
<td>0.0</td>
</tr>
<tr>
<td>Weight &gt; 95th percentile (pediatric)</td>
<td>65</td>
<td>20.0</td>
<td>46.2*</td>
<td>21.5</td>
<td>10.8</td>
<td>1.5</td>
</tr>
<tr>
<td>Increased neck circumference</td>
<td>69</td>
<td>30.4</td>
<td>46.4*</td>
<td>14.5</td>
<td>7.2</td>
<td>1.4</td>
</tr>
<tr>
<td>Observed apnea</td>
<td>69</td>
<td>66.7*</td>
<td>29.0</td>
<td>1.4</td>
<td>2.9</td>
<td>0.0</td>
</tr>
<tr>
<td>Snoring</td>
<td>68</td>
<td>26.5</td>
<td>50.0*</td>
<td>13.2</td>
<td>7.4</td>
<td>2.9</td>
</tr>
<tr>
<td>Congenital airway abnormalities</td>
<td>66</td>
<td>21.2</td>
<td>47.0*</td>
<td>28.8</td>
<td>3.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Daytime hypersomnolence</td>
<td>69</td>
<td>30.4</td>
<td>53.6*</td>
<td>8.9</td>
<td>7.2</td>
<td>0.0</td>
</tr>
<tr>
<td>Inability to visualize soft palate</td>
<td>69</td>
<td>11.6</td>
<td>55.1*</td>
<td>23.2</td>
<td>7.2</td>
<td>2.9</td>
</tr>
<tr>
<td>Tonsillar hypertrophy</td>
<td>67</td>
<td>10.4</td>
<td>56.7*</td>
<td>23.9</td>
<td>6.0</td>
<td>3.0</td>
</tr>
<tr>
<td>Tests if OSA is suspected:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Overnight oximetry (no polysomnography)</td>
<td>66</td>
<td>10.6</td>
<td>42.2*</td>
<td>12.1</td>
<td>19.7</td>
<td>15.2</td>
</tr>
<tr>
<td>Polysomnography</td>
<td>68</td>
<td>69.1*</td>
<td>25.0</td>
<td>2.9</td>
<td>2.9</td>
<td>0.0</td>
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<tr>
<td>Indirect laryngoscopy</td>
<td>66</td>
<td>10.6</td>
<td>15.2</td>
<td>27.3*</td>
<td>27.3</td>
<td>19.7</td>
</tr>
<tr>
<td>Radiographic cephalography</td>
<td>66</td>
<td>1.5</td>
<td>15.2</td>
<td>30.3</td>
<td>33.3*</td>
<td>19.7</td>
</tr>
<tr>
<td>Resting pulse oximetry</td>
<td>65</td>
<td>7.7</td>
<td>21.5</td>
<td>12.3</td>
<td>36.9*</td>
<td>21.5</td>
</tr>
<tr>
<td>Arterial blood gases</td>
<td>66</td>
<td>3.0</td>
<td>18.2</td>
<td>16.7</td>
<td>37.9*</td>
<td>24.2</td>
</tr>
<tr>
<td>2. Preprocedure evaluation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep study (improves outcomes)</td>
<td>68</td>
<td>26.5</td>
<td>47.1*</td>
<td>20.6</td>
<td>4.4</td>
<td>1.5</td>
</tr>
<tr>
<td>Sleep study (reduces costs)</td>
<td>68</td>
<td>11.8</td>
<td>29.4</td>
<td>42.6*</td>
<td>14.7</td>
<td>1.5</td>
</tr>
<tr>
<td>Risk depends on both the severity of OSA and invasiveness of procedure</td>
<td>68</td>
<td>44.1</td>
<td>51.5*</td>
<td>2.9</td>
<td>1.5</td>
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<tr>
<td>Delay surgery with incomplete preprocedure evaluation of OSA status if planned procedure is:</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Superficial surgery</td>
<td>67</td>
<td>3.0</td>
<td>13.4</td>
<td>20.9</td>
<td>55.2*</td>
<td>7.5</td>
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<td>Airway surgery</td>
<td>68</td>
<td>52.9*</td>
<td>23.5</td>
<td>8.8</td>
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<td>2.9</td>
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<tr>
<td>Minor laparoscopic surgery</td>
<td>68</td>
<td>4.4</td>
<td>26.5</td>
<td>33.8*</td>
<td>30.9</td>
<td>4.4</td>
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<tr>
<td>Major laparoscopic surgery</td>
<td>69</td>
<td>20.6</td>
<td>41.2*</td>
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<tr>
<td>Open abdominal surgery</td>
<td>68</td>
<td>33.8</td>
<td>44.1*</td>
<td>10.3</td>
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<tr>
<td>Peripheral orthopedic surgery</td>
<td>68</td>
<td>4.4</td>
<td>20.6</td>
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<td>Major orthopedic surgery</td>
<td>68</td>
<td>25.0</td>
<td>48.5*</td>
<td>13.2</td>
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<td>3. Preoperative preparation</td>
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<td>Preoperative interventions:</td>
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<td>CPAP or NIPPV</td>
<td>68</td>
<td>39.7</td>
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<td>Mandibular appliance</td>
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<td>1.5</td>
<td>19.1</td>
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<td>Weight loss</td>
<td>67</td>
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<td>58.2*</td>
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<tr>
<td>Limit procedure to facility with outpatient capability</td>
<td>68</td>
<td>41.2</td>
<td>36.8*</td>
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<td>Determine whether procedure should be performed on an inpatient basis</td>
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<td>26.5</td>
<td>58.8*</td>
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### Table 5. Continued

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<td>32.4</td>
<td>27.9</td>
<td>2.9</td>
<td>0.0</td>
</tr>
</tbody>
</table>

### 4. Intraoperative management

Intraoperative interventions to improve outcomes:

- ASA difficult airway algorithm
- Nerve blocks rather than GA for peripheral surgery
- Major conduction anesthesia rather than GA for peripheral surgery
- Major conduction anesthesia rather than GA for abdominal surgery
- Combined regional and GA (regardless of surgical site)
- GA with secured airway rather than moderate or conscious sedation for superficial procedures
- GA with secured airway rather than deep sedation for superficial procedures
- GA with secured airway rather than moderate or deep sedation for procedures involving the upper airway
- CO₂ respiratory monitoring during moderate or deep sedation

### 5. Extubation

Intraoperative interventions to improve outcomes during extubations:

- Verify full reversal of neuromuscular block before extubation
- Extubate patients when they are fully awake
- Extubate patients in the semiupright position rather than supine

### 6. Postoperative analgesia

Regional techniques rather than systemic opioids
Regional techniques with local anesthetics rather than regional techniques with opioids
Nonsteroidal antiinflammatory agents rather than systemic opioids
Systemic patient-controlled analgesia with opioids rather than nurse-administered i.m. or i.v. opioids
Systemic patient-controlled analgesia without a background infusion rather than patient-controlled analgesia with a background infusion

### 7. Postoperative oxygenation

Supplemental oxygen to maintain acceptable arterial oxygen saturation
Supplemental oxygen may be discontinued when patients can maintain their baseline oxygen saturation level on room air
Resume treatment as soon as feasible for patients previously treated with CPAP or NIPPV
Initiate CPAP or NIPPV after surgery to patients not previously treated with CPAP or NIPPV
When patient is not ambulating, the CPAP or NIPPV appliance should be in place at all times

### 8. Postoperative positioning

Avoid supine position (adult patients)
Avoid supine position (pediatric patients)

### 9. Postoperative inpatient monitoring

Full monitoring in intensive care unit
Oximetry in a stepdown unit

(continued)
Table 5. Continued

<table>
<thead>
<tr>
<th>Percent Responding to Each Item</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
</tr>
<tr>
<td>----</td>
</tr>
<tr>
<td>Oximetry with telemetry on a standard hospital ward</td>
</tr>
<tr>
<td>Oximetry with a dedicated observer in patient’s room or hospital ward</td>
</tr>
<tr>
<td>Oximetry at patient bedside with intermittent monitoring by staff</td>
</tr>
<tr>
<td>Continuous ventilatory monitoring following discharge from the PACU</td>
</tr>
<tr>
<td>Continuous pulse oximetry may be discontinued once patients are no longer receiving parenteral opioid analgesics</td>
</tr>
<tr>
<td>Continuous pulse oximetry may be discontinued if oxygen saturations during sleep remain above 90% while breathing room air</td>
</tr>
</tbody>
</table>

10. Outpatient vs. Inpatient Management
Operations that may be safely performed on an outpatient basis:
- Superficial surgery (local/regional anesthesia)
  - 67 | 19.4 | 74.5* | 6.0 | 0.0 | 0.0 |
- Superficial surgery (GA)
  - 65 | 7.7 | 35.4 | 21.5* | 32.3 | 3.1 |
- Airway surgery (adult)
  - 67 | 0.0 | 7.5 | 11.9 | 41.8* | 38.8 |
- Tonsillectomy in children less than 3 years of age
  - 66 | 0.0 | 9.1 | 16.7 | 36.4* | 37.9 |
- Tonsillectomy in children greater than 3 years of age
  - 66 | 0.0 | 25.8 | 27.3* | 30.3 | 16.7 |
- Minor orthopedic surgery (local/regional anesthesia)
  - 67 | 7.5 | 79.1* | 9.0 | 3.0 | 1.5 |
- Minor orthopedic surgery (GA)
  - 67 | 4.5 | 32.8 | 25.4* | 31.3 | 6.0 |
- Gynecologic laparoscopy
  - 67 | 1.5 | 35.8 | 40.3* | 20.9 | 1.5 |
- Laparoscopic surgery, upper abdomen
  - 67 | 1.5 | 10.4 | 19.4 | 53.7* | 14.9 |
- Lithotripsy
  - 67 | 4.5 | 47.8* | 34.3 | 11.9 | 1.5 |

Equipment that should be available in an outpatient facility:
- Difficult airway equipment
  - 67 | 80.6* | 17.9 | 1.5 | 0.0 | 0.0 |
- Radiology facilities (chest x-ray)
  - 67 | 17.9 | 49.3* | 22.4 | 10.4 | 0.0 |
- Respiratory therapy
  - 67 | 20.9 | 53.7* | 13.4 | 11.9 | 0.0 |
- Clinical laboratory (blood gases, electrolytes)
  - 67 | 28.4 | 52.2* | 10.4 | 9.0 | 0.0 |
- Transfer arrangement with inpatient facility that should be met before patients are discharged from an outpatient facility:
  - 67 | 73.1* | 23.9 | 3.0 | 0.0 | 0.0 |
- Return of room air oxygen saturation to baseline value
  - 67 | 46.3 | 44.8* | 6.0 | 1.5 | 1.5 |
- Documentation that patient does not become hypoxicem when left undisturbed in PACU or observation unit while breathing room air
  - 67 | 55.2* | 35.8 | 4.5 | 3.0 | 1.5 |
- Documentation that patient does not develop clinical airway obstruction when left undisturbed in PACU or observation unit
  - 66 | 65.2* | 31.8 | 1.5 | 0.0 | 1.5 |

* Median.
ASA = American Society of Anesthesiologists; CO₂ = carbon dioxide; CPAP = continuous positive airway pressure; GA = general anesthesia; i.m. = intramuscular; i.v. = intravenous; n = number of consultants who responded to each item; NIPPV = nasal intermittent positive-pressure ventilation; OSA = obstructive sleep apnea; PACU = postanesthesia care unit.
Table 6. Feasibility Survey Responses

<table>
<thead>
<tr>
<th>Preoperative evaluation</th>
<th>Percent “Yes”</th>
</tr>
</thead>
<tbody>
<tr>
<td>Which of the following would you need to initiate or upgrade in order to comply with the recommendations?</td>
<td></td>
</tr>
<tr>
<td>Preoperative protocol for management of OSA patients</td>
<td>64.4</td>
</tr>
<tr>
<td>Improved communication between surgeons and anesthesiologists</td>
<td>68.9</td>
</tr>
<tr>
<td>More careful questioning of patients and family</td>
<td>46.7</td>
</tr>
<tr>
<td>Increased ordering of preoperative sleep studies</td>
<td>46.7</td>
</tr>
<tr>
<td>For a patient who does not have a previous sleep study, based on these Guidelines, would you:</td>
<td></td>
</tr>
<tr>
<td>(1) order a sleep study, or</td>
<td>37.8</td>
</tr>
<tr>
<td>(2) treat the patient as if he or she has OSA</td>
<td>60.0</td>
</tr>
</tbody>
</table>

| Intraoperative management | |
| Would implementation of the Guidelines require the purchase of additional equipment? | 15.6 |

| Postoperative management | |
| Which of the following would you need to initiate or upgrade in order to comply with the recommendations regarding postoperative care of OSA patients? | |
| Caring for patients in nonsupine positions | 35.6 |
| Administration of supplemental oxygen | 11.1 |
| Use of CPAP or NIPPV by patients who were using it preoperatively | 31.1 |
| Continuously monitored pulse oximetry (or other respiratory monitoring) until patients are no longer at risk for postoperative airway obstruction | 40.0 |

<table>
<thead>
<tr>
<th>Cost estimates for consultants’ hospitals or surgicenters</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total annual cost of implementing the Preoperative Evaluation recommendations</td>
<td>$30,000</td>
</tr>
<tr>
<td>Total annual cost of implementing the Preoperative Preparation recommendations</td>
<td>$15,000</td>
</tr>
<tr>
<td>Cost of obtaining the necessary equipment for implementing the Intraoperative Management recommendations</td>
<td>$0</td>
</tr>
<tr>
<td>Total annual cost of implementing the Postoperative Management recommendations including personnel and equipment for postoperative respiratory monitoring</td>
<td>$25,000</td>
</tr>
<tr>
<td>Cost to outfit an outpatient facility to safely care for OSA patients in accordance with the Guidelines</td>
<td>$0</td>
</tr>
<tr>
<td>Annual increase in cost for an outpatient facility to implement the Outpatient Surgery/Discharge recommendations</td>
<td>$50,000</td>
</tr>
</tbody>
</table>

CPAP = continuous positive airway pressure; NIPPV = nasal intermittent positive-pressure ventilation; OSA = obstructive sleep apnea.
STATE-OF-THE-ART PAPER

Perioperative Management of Patients With Coronary Stents

Emmanouil S. Brilakis, MD, PhD, FACC,* Subhash Banerjee, MD, FACC,* Peter B. Berger, MD, FACC†

Dallas, Texas; and Danville, Pennsylvania

Perioperative coronary stent thrombosis is a catastrophic complication that can occur in patients receiving both bare-metal and drug-eluting stents. Noncardiac surgery appears to increase the risk that recently-placed stents thrombose, especially when surgery is performed early after stenting, and particularly if dual antiplatelet therapy is discontinued. We reviewed the existing data about the frequency of stent thrombosis after noncardiac surgery and explored the impact of delay from surgery and discontinuation of antiplatelet therapy. We also reviewed the data about the impact of preoperative revascularization in patients known to require noncardiac surgery. Based on these published data, we offer recommendations that can be used to guide the treatment of patients who require noncardiac surgery after having received a stent. (J Am Coll Cardiol 2007;49:2145–50) © 2007 by the American College of Cardiology Foundation

Coronary revascularization before noncardiac surgery may decrease the perioperative and postoperative risk in selected patients (1). The number of percutaneous coronary interventions (PCIs) now exceeds the number of coronary artery bypass surgeries performed each year, and the difference continues to grow. Stents currently are used in the majority of PCIs because they increase procedural success and decrease restenosis (2). A rare but severe complication after coronary stent implantation is stent thrombosis (3). Stent thrombosis is associated with a suboptimal angiographic result (4–6), specific high-risk lesion characteristics (such as small vessels [7–9] and bifurcation lesions [3]), high-risk patients such as those with diabetes and renal failure (3), and, importantly, early cessation of dual antiplatelet therapy with aspirin and a thienopyridine (3,10). Obtaining a good angiographic result and administering dual antiplatelet therapy (11) (currently aspirin and clopidogrel) are the cornerstones of stent thrombosis prevention.

Noncardiac surgery and most invasive procedures increase the risk of stent thrombosis, especially when the procedure is performed early after stent implantation, likely because stents are not yet endothelialized early after placement, because antiplatelet therapy is often discontinued in the periprocedural period, and because surgery creates a prothrombotic state (12); this may be particularly true when done under general anesthesia compared with regional anesthesia (13). Perioperative stent thrombosis has been studied primarily in patients who received bare-metal stents (BMS). There are limited data about the risk of perioperative thrombosis of drug-eluting stents (DES), even though DES currently are used in 70% to 80% of PCI procedures in the U.S. Clinicians caring for patients with coronary stents who need surgery often have difficulty choosing a treatment strategy that allows the surgery to be as safe as possible while minimizing the risk of perioperative stent thrombosis. The goal of this review is to offer guidance to clinicians by summarizing the available data on the incidence, risk factors, prevention, and treatment of perioperative coronary stent thrombosis.

Risk of Surgery After Stent Implantation

BMS. The high risk of surgery early after coronary stenting was first described in 2000 (14): 8 of the 25 patients undergoing noncardiac surgery within 2 weeks of BMS placement died (32%, 95% confidence interval (CI) 15 to 54). In contrast, none of the 15 patients who underwent surgery 15 to 39 days after stenting died. Six of the 8 deaths were caused by acute myocardial infarction (AMI) and 2 were caused by bleeding (14). A total of 7 patents had AMI that was probably or definitely caused by stent thrombosis, and 6 of them died. Three of the 5 patients who underwent operations while taking ticlopidine died, 1 from bleeding and 2 from AMI and bleeding.

In a much larger population of patients undergoing surgery within 2 months after receiving a BMS at the Mayo Clinic, only 8 of the 207 patients (3.9%, 95% CI 1.7 to 7.5)
died or suffered an AMI or stent thrombosis (15). In contrast to the study by Kaluza et al. (14), the risk of death, MI, or stent thrombosis was elevated for 6 weeks, not just 2 weeks, and to a much lesser degree, with the risk during each of the first 6 weeks ranging from 3.8% to 7.1%; no events occurred among the 39 patients who underwent surgery in the 6th through 8th weeks after stent placement.

Another study analyzed the outcome of 27 patients who underwent noncardiac surgery within 3 weeks after BMS implantation (16). Six of 7 patients (86%), in whom the thienopyridine was stopped for >5 days died (only 1 patient had angiographically documented stent thrombosis) compared with only 1 of the 20 patients (5%) who underwent noncardiac surgery within 3 weeks from stent implantation and continued to take a thienopyridine (p < 0.001). Among 20 patients undergoing surgery 3 weeks to 3 months after stenting (70% of whom continued taking a thienopyridine), only 1 patient died (5%), and 2 suffered a non–ST-segment elevation AMI.

In another series, thrombotic events or major bleeding occurred in 8 of 16 patients (50%) undergoing noncardiac surgery within 42 days after receiving a BMS, and in none of 40 patients who underwent surgery >42 days after receiving a BMS (17). Vicenzi et al. (18) reported a 43% frequency of adverse cardiac events in 103 patients undergoing surgery after stent deployment, but those events were poorly characterized.

These studies have appropriately increased attention to the potential risks of surgery early after stent implantation, and highlighted the importance of delaying surgery when possible and continuing dual antiplatelet therapy in the perioperative period when surgery is not delayed.

DES. There are limited data about the risk of noncardiac surgery after DES placement. McFadden et al. (19) reported DES thrombosis in 3 patients undergoing surgery (bladder polyp resection, colon cancer resection, and colonoscopy with polypectomy) late (343 to 442 days) after implantation. Nasser et al. (20) reported sirolimus-eluting stent (SES) thrombosis in 2 patients after surgery performed 4 and 21 months after SES implantation.

Compton et al. (21) reported a single-center series of 38 patients who underwent 41 major and 18 minor noncardiac surgeries a median of 9 months from successful DES implantation: no major adverse cardiac events or deaths occurred during or after the 41 major (0%, 95% CI 0 to 9%), and 18 minor noncardiac surgical procedures (0%, 95% CI 0 to 19%). Schouten et al. (22) reported that stent thrombosis occurred in 3 of 99 (3%) patients undergoing surgery within 2 years after DES implantation. Bakhru et al. (23) reported no stent thrombosis among 114 patients undergoing noncardiac surgery after a median of 9 days from balloon angioplasty.

Prevention of Perioperative Stent Thrombosis

Perioperative stent thrombosis could be prevented by: 1) avoiding preoperative revascularization; 2) revascularizing patients without using stents; 3) appropriate selection of the type of stent to be implanted; 4) delaying surgery after stent implantation; 5) continuing antiplatelet therapy throughout the perioperative period or only discontinuing it briefly; and 6) improving awareness of this catastrophic complication among all physicians involved in the care of these patients (Fig. 1).

Avoiding preoperative revascularization. Many patients with coronary disease who require noncardiac surgery do not benefit from preoperative revascularization. The CARP (Coronary Artery Revascularization Prophylaxis) trial enrolled 510 stable patients with angiographic coronary artery disease (one-third had 3-vessel disease) undergoing major vascular surgery (33% abdominal aortic aneurysm repair and 67% lower extremity revascularization) (25). Patients with significant left main disease, unstable coronary syndromes, and severe cardiomyopathy were excluded. Patients were randomized to revascularization versus no revascularization before surgery. Revascularization was accomplished with coronary bypass surgery in 41% and with PCI in 59%. Patients who did or did not undergo revascularization had a similar incidence of postoperative AMI (8.4% vs. 8.4%, p = 0.99) and survival after a median of 27 months from randomization (78% vs. 77%, p = 0.98).

Therefore, if a patient with coronary disease is known to require surgery, the first question to ask is whether the patient really needs revascularization. The CARP study results suggest that revascularization may not be necessary for a large number of patients without an unstable coronary syndrome or other very high-risk features. This is further supported by the findings of a recent pilot study of 103 patients with extensive ischemia undergoing vascular surgery, in whom preoperative revascularization did not improve postoperative outcomes (26).

Revascularization without stents (balloon only). Despite the CARP study, many patients are believed to require revascularization before noncardiac surgery, such as patients with acute coronary syndromes or with profound ischemia on noninvasive testing at a heart rate and blood pressure likely to be exceeded in the perioperative period. Although stents are currently used in the vast majority of PCIs, coronary revascularization may be more safely performed in such patients without stents, either with coronary artery bypass grafting or percutaneously with balloon angioplasty.

In an early study of 50 patients undergoing noncardiac surgery after a median of 9 days from balloon angioplasty,
the postoperative mortality and MI rates were 1.9% and 5.6%, respectively (27). In a study of 194 patients undergoing aortic abdominal surgery, carotid endarterectomy or peripheral vascular surgery after a median time of 11 days from balloon angioplasty, only 1 patient died (0.5%) and 1 patient suffered an AMI (0.5%) (28). In the largest study, in which 350 patients underwent noncardiac surgery in the 2 months after a successful balloon angioplasty procedure, only 3 of the 350 patients (0.9%, 95% CI 0.2% to 2.5%) died in the perioperative period (n=1) or suffered a myocardial infarction (n=2) (29).

Therefore, revascularization with balloon angioplasty may be safer than stent placement before planned noncardiac surgery, especially if a good angiographic result can be achieved, and particularly if the noncardiac surgery is planned early (within 4 to 6 weeks) after revascularization.

According to the 2002 American College of Cardiology/American Heart Association guidelines on perioperative cardiovascular care, “there is uncertainty regarding how much time should pass before noncardiac surgery is performed” for patients undergoing preoperative balloon angioplasty (1). Delaying noncardiac surgery for >6 to 8 weeks was discouraged because restenosis could have occurred, leading to perioperative ischemia or MI. However, performing noncardiac surgery too early after the PCI also may be risky because acute or subacute closure after balloon angioplasty usually occurs within hours to days after the procedure. Accordingly, the guidelines emphasize that delaying surgery “for at least a week after balloon angioplasty to allow for healing of the vessel injury at the balloon treatment site has theoretical benefits.”

**Stent selection before surgery.** Sometimes stenting cannot be avoided during PCI, either because of the complexity of the lesion or because of the inability to achieve an optimal result with balloon angioplasty. The type of stent selected should be heavily influenced by the timing of surgery.

If surgery needs to be performed within 12 months from revascularization, then BMS implantation is likely preferable to DES, because BMS endothelialize more rapidly and may therefore carry a lower risk of stent thrombosis. This is particularly likely if dual antiplatelet therapy cannot be continued through the perioperative period. If restenosis, which is more likely to occur after BMS than DES, does develop, it almost always does so more than 2 to 3 months after stent placement, at which point the patient already will have undergone the surgical procedure. At that time, a DES could be used to treat the in-stent restenosis.

If surgery can be delayed for more than 12 months, then placement of a DES may not be inappropriate, although there are data suggesting that DES may have a greater risk of late stent thrombosis than BMS beyond 12 months after implantation, particularly in the perioperative period (19). If placement of a DES is planned, it may be preferable to use a sirolimus-eluting stent, which requires a minimum of 3 months of clopidogrel after placement (30), than a paclitaxel-eluting stent (PES), which requires at least 6 months of clopidogrel (31). However, little is known about the safety of surgery performed 6 to 12 months from DES implantation. An alternative approach would be placement of a heparin-coated stent (which is not considered a DES because the heparin does not elute off of the stent); such an approach is logical but unproven, because heparin-coated stents have not been shown to reduce the frequency of stent thrombosis in any situation with any medical regimen, let alone in the perioperative period. In the future, new stent types, such as bioresorbable stents or antibody-coated stents that can attract endothelial progenitor cells and re-
endothelialize more rapidly, may minimize the risk of stent thrombosis.

Regardless of the type of stent used, every effort should be made to optimally deploy the stent, which reduces the risk of stent thrombosis (4,6). Overlap of DES should be avoided because overlapping may delay their endothelialization significantly (32,33).

**Delay of surgery.** The earlier the surgery is performed after stenting, the higher the risk for stent thrombosis (14–17). According to the American College of Cardiology/American Heart Association guidelines, noncardiac surgery should be “delayed for at least 2 and ideally 4 weeks after BMS implantation to allow for at least partial endothelialization of the stent” (1). The best data suggest that delaying surgery for 6 weeks may be even better than 4 weeks (15). The optimal delay after implantation of a DES before surgery remains unknown but is likely to be more than 12 months (Fig. 1), particularly if antiplatelet therapy must be discontinued for the surgical procedure.

**Antiplatelet therapy in the perioperative period.** Dual antiplatelet therapy is the cornerstone of stent thrombosis prevention (11). The current recommendations that clopidogrel be administered for 3 months after placement of an SES and 6 months after placement of a PES are based on the duration of time that a thienopyridine was required in the pivotal trials of these stents that led to their approval; those durations were largely chosen empirically. Although an observational study showed reduced risk of death or MI when clopidogrel was continued up to 2 years after DES implantation (34), the optimal duration of clopidogrel required to prevent late DES thrombosis is unknown.

Antiplatelet treatment strategies to minimize perioperative stent thrombosis include:

- **Continue dual antiplatelet therapy during and after surgery**
- **Discontinue clopidogrel but “bridge” the patient to surgery using a short-acting antiplatelet agent with a glycoprotein IIb/IIIa inhibitor or an antithrombin, and restart clopidogrel as soon as possible after surgery**
- **Discontinue clopidogrel before surgery and restart it as soon as possible after surgery**

**CONTINUE DUAL ANTIPLATELET THERAPY DURING SURGERY.** This option would likely be associated with the lowest frequency of stent thrombosis, especially in patients undergoing surgery early after stent implantation. Surgeons who are concerned about the risk of perioperative bleeding may need help weighing the risk of bleeding with the particular operation planned against the benefits of continuing dual antiplatelet therapy throughout the perioperative period. In some procedures, such as dental extractions (35), cataract surgery (36), or routine dermatologic surgery (37), bleeding almost always can be controlled with local measures, and discontinuation of antiplatelet therapy is not necessary (38). Even in procedures with higher bleeding risk, when surgeons are informed that stent thrombosis leads to death or a large MI in the majority of patients (39), and that the best available data suggest a greatly increased risk of stent thrombosis in patients undergoing surgery shortly after stent placement when dual antiplatelet therapy is discontinued, they often can be persuaded that the risk of thrombosis outweighs the risk of bleeding. This strategy would not be appropriate for patients in whom any excess bleeding could have catastrophic consequences, such as neurosurgery patients.

**STOP CLOPIDOGREL AND “BRIDGE” THE PATIENT WITH A SHORT-ACTING ANTIPLATELET OR ANTITHROMBOTIC AGENT.** Thienopyridines cause irreversible platelet inhibition, and need to be discontinued for 5 to 10 days to allow the production and release into the circulation of new platelets to replace the inhibited platelets and restore normal hemostasis. If surgery is needed early after stent placement and clopidogrel needs to be stopped, some clinicians “bridge” the patient to surgery using a short-acting antiplatelet agent or an anticoagulant. Because stent thrombosis is primarily a platelet-mediated phenomenon, platelet inhibitors might be a more logical choice if such a strategy is pursued. Furthermore, the cessation of heparin in a patient not on aspirin or other antiplatelet agents has been shown to cause platelet activation and a rebound phenomenon which may actually increase the likelihood of perioperative stent thrombosis compared to if no heparin bridging had been performed. However, it must be emphasized that admitting a patient to a hospital before surgery to bridge them to surgery does not offer complete protection because the greatest risk of stent thrombosis is actually during or after surgery. More data are needed that indicate that such a strategy improves outcome because this strategy is expensive, is logistically difficult, and exposes the patient to the risks associated with a prolonged hospitalization.

**STOP CLOPIDOGREL AND RESTART IT AFTER SURGERY.** This strategy may be sufficient when the stent is believed to be fully endothelialized and the risk of stent thrombosis is very low. It also should be used whenever clopidogrel cannot be continued throughout the perioperative period, such as in patients undergoing neurosurgery, in whom bleeding would likely be catastrophic. There is variability in the rate at which DES are re-endothelialized, and the risk of stent thrombosis may persist in some patients for many months or longer, especially in the prothrombotic state induced by surgery (19). Once the surgeon permits the re-initiation of clopidogrel, it might be wisest to administer a 600-mg loading, which not only reduces the time required to achieve maximal inhibition of platelet aggregation to 2 to 4 h, but also reduces the frequency of hyporesponsiveness to clopidogrel, particularly among patients with activated platelets as is uniformly the case among patients who have just undergone surgery.

The aforementioned recommendations are largely empiric and are based on indirect data, but they are mechanis-
tically sound and logical, and the consequences of perioperative stent thrombosis are severe.

**Education and a team approach.** Given the morbidity and mortality associated with stent thrombosis, there is a need for continuing education of physicians, particularly noncardiologists, about the perioperative risks of patients with coronary stents. The need to delay elective surgery whenever possible after stent implantation cannot be overemphasized. In a survey of anesthesiologists, 63% were not aware of recommendations about the appropriate length of time between stent placement and a subsequent surgical procedure, and one-third recommended no delay or a delay of only 1 to 2 weeks, which is insufficient for BMS, and even more so for DES (40).

Anesthesiologists and surgeons should be alerted to the high risk of stent thrombosis in patients who have received coronary stents (41). They should:

- Determine the type (BMS, SES, PES) and location in the coronary circulation of stents placed in their patient, and the date of implantation
-Consult with an interventional cardiologist and, whenever possible, with the patient’s cardiologist
- Arrive at a joint decision with input from anesthesiologists, cardiologists, and surgeons about the timing of surgery and the most appropriate management of the patient’s antiplatelet regimen
- Ideally, perform surgery in centers with 24-h interventional cardiology coverage so that stent thrombosis, if it occurs, could be treated with immediate PCI

**Treatment of Perioperative Stent Thrombosis**

Stent thrombosis is most often manifest as an ST-segment elevation acute myocardial infarction, and is best treated with early reperfusion. Thrombolytic therapy is less effective at restoring reperfusion than primary PCI among all patients and—although unproven—may be even less effective among patients with stent thrombosis, which is a platelet-mediated phenomenon. Moreover, thrombolytic therapy often carries a prohibitive risk of bleeding in the perioperative period. Primary PCI is, therefore, the treatment of choice for perioperative stent thrombosis, although it also carries increased risk of bleeding when performed early after surgery because antithrombin and antiplatelet agents need to be administered during the procedure. Yet, all that is required in patients with an acute coronary occlusion caused by stent thrombosis or any other cause who are at increased risk of bleeding is aspirin and 1 dose of an anticoagulant such as heparin or bivalirudin. In a retrospective analysis of 48 patients with acute myocardial infarction occurring within 1 week from surgery in whom aspirin and heparin were administered, survival with an early invasive strategy was 65%, which is encouraging given the high frequency of cardiogenic shock and cardiac arrest in the study population (42). Only 1 patient had significant bleeding at the operative site, a patient who had undergone knee replacement. Patients who had recently had brain and thoracic surgery were included in this series.

**Conclusions**

Perioperative coronary stent thrombosis is a catastrophic occurrence. The risk of stent thrombosis seems to be low when surgery is delayed for at least 4 to 6 weeks after implantation of a BMS. The risk of stent thrombosis after DES implantation remains poorly studied, but may occur even in patients who have completed the recommended duration of antiplatelet therapy (3 months for SES and 6 months for PES) and subsequently undergo surgery, in most cases after stopping aspirin and clopidogrel.

If major noncardiac surgery is planned within 1 month and certainly within 2 weeks, stent implantation generally should be avoided. If revascularization is required, then balloon angioplasty or coronary bypass surgery might well be preferred options. If surgery is planned between 1 and 12 months, particularly if complex anatomy is present, then BMS implantation may be preferable. If surgery is planned after 12 months, DES implantation may be an acceptable option. Awareness, prevention, and early treatment of perioperative stent thrombosis are best achieved by collaboration between surgeons, anesthesiologists, and cardiologists.

**Acknowledgment**

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**REFERENCES**

Practice Advisory for the Perioperative Management of Patients with Cardiac Rhythm Management Devices: Pacemakers and Implantable Cardioverter–Defibrillators

A Report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Cardiac Rhythm Management Devices

**PRACTICE advisories** are systematically developed reports that are intended to assist decision making in areas of patient care. Advisories provide a synthesis and analysis of expert opinion, clinical feasibility data, open forum commentary, and consensus surveys. Advisories are not intended as standards, guidelines, or absolute requirements. They may be adopted, modified, or rejected according to clinical needs and constraints.

The use of practice advisories cannot guarantee any specific outcome. Practice advisories summarize the state of the literature and report opinions derived from a synthesis of task force members, expert consultants, open forums, and public commentary. Practice advisories are not supported by scientific literature to the same degree as standards or guidelines because of the lack of sufficient numbers of adequately controlled studies. Practice advisories are subject to periodic revision as warranted by the evolution of medical knowledge, technology, and practice.

**Methodology**

A. Definition of Cardiac Rhythm Management Devices

For this Advisory, a **cardiac rhythm management device** (CRMD) refers to any permanently implanted cardiac pacemaker or any implantable cardioverter–defibrillator (ICD). The term **CRMD** also refers to any cardiac resynchronization device. The term **CRT** refers to a CRMD that provides cardiac resynchronization therapy using biventricular pacing techniques. Generic pacemaker and defibrillator codes are provided in appendix 1.

B. Purposes of the Advisory

The purposes of this Advisory are to (1) facilitate safe and effective perioperative management of the patient with a CRMD and (2) reduce the incidence of adverse outcomes. **Perioperative management** refers to the preoperative, intraoperative, postoperative or recovery period in any setting where an anesthesia provider delivers anesthesia care. Adverse outcomes associated with a CRMD include (but are not limited to) damage to the device, inability of the device to deliver pacing or shocks, lead–tissue interface damage, changes in pacing behavior, electrical reset to the backup pacing mode, or inappropriate ICD therapies.* Adverse clinical outcomes include (but are not limited to) hypotension, tachyarrhythmia or bradyarrhythmia, myocardial tissue damage, and myocardial ischemia or infarction. Other related outcomes may include extended hospital stay, delay or cancellation of surgery, readmission to manage device malfunction, or additional hospital resource utilization and cost.

C. Focus

This Advisory focuses on the perioperative management of patients who have a preexisting, permanently implanted CRMD for treatment of bradyarrhythmia, tachyarrhythmia, or heart failure. Both inpatient and outpatient procedures are addressed by this Advisory. This Advisory does not address the perioperative management of any patient undergoing CRMD implantation or revision. It is not applicable to any patient (1) without...
a permanently implanted pacemaker or ICD, (2) with a temporary CRMD, (3) with a noncardiac implantable device (e.g., neurologic or spinal cord stimulator), or (4) with an implantable mechanical cardiac assist device (e.g., ventricular assist device). This Advisory does not address any procedure where there are no known perioperative CRMD concerns, such as diagnostic radiation (e.g., x-ray studies, fluoroscopy, or mammograms), computed tomography scans, or ultrasound.

**D. Application**

This Advisory is intended for use by anesthesiologists and all other individuals who deliver or who are responsible for anesthesia care. The Advisory may also serve as a resource for other physicians and healthcare professionals who treat patients with CRMDs.

**E. Task Force Members and Consultants**

The American Society of Anesthesiologists (ASA) appointed a Task Force of 12 members to (1) review and assess currently available scientific literature, (2) obtain expert consensus and public opinion, and (3) develop a practice advisory. The Task Force members consisted of anesthesiologists and cardiologists in private and academic practices from various geographic areas of the United States and two methodologists from the ASA Committee on Practice Parameters.

The Task Force used a six-step process. First, they reached consensus on the criteria for evidence of effective perioperative management of cardiac rhythm management devices. Second, original published articles from peer-reviewed journals relevant to these issues were evaluated. Third, consultants who had expertise or interest in CRMDs and who practiced or worked in various settings (e.g., academic and private practice) were asked to (1) participate in opinion surveys on the effectiveness of various perioperative management strategies and (2) review and comment on a draft of the Advisory developed by the Task Force. Fourth, additional opinions were solicited from random samples of active members of both the ASA and the Heart Rhythm Society (HRS).† Fifth, the Task Force held an open forum at a national anesthesia meeting and at a major cardiology meeting to solicit input on the key concepts of this Advisory. Sixth, all available information was used to build consensus within the Task Force on the Advisory.

The draft document was made available for review on the ASA Web site, and input was invited via e-mail announcement to all ASA members. All submitted comments were considered by the Task Force in preparing the final draft.

**F. Availability and Strength of Evidence**

Practice advisories are developed by a protocol similar to that of an ASA evidence-based practice guideline, including a systematic search and evaluation of the literature. However, practice advisories lack the support of a sufficient number of adequately controlled studies to permit aggregate analyses of data with rigorous statistical techniques such as meta-analysis. Nonetheless, literature-based evidence from case reports and other descriptive studies is reported. This literature often permits the identification of recurring patterns of clinical practice.

As with a practice guideline, formal survey information was collected from Consultants and members of the ASA. For this Advisory, surveys were also sent to members of the HRS. Additional information was obtained from open forum presentations and other invited and public sources. The advisory statements contained in this document represent a consensus of the current spectrum of clinical opinion and literature-based findings.‡

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† Formerly North American Society of Pacing and Electrophysiology (NASPE).
‡ Refer to appendix 2 for a summary of the advisories.
§ Refer to appendix 3 for results of the Consultant, ASA membership, and HRS membership surveys.

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Defining the type of device is accomplished by (1) obtaining the manufacturer’s identification card from the patient or other source, (2) ordering chest x-ray studies if no other data are available,† or (3) referring to supplemental resources (e.g., manufacturer’s databases, pacemaker clinic records, consultation with a cardiologist).

Cardiac rhythm management device dependency for pacemaking function may be determined by one or more of the following: (1) a verbal history or an indication in the medical record that the patient has experienced a bradyarrhythmia that has caused syncope or other symptoms requiring CRMD implantation, (2) a history of successful atioventricular nodal ablation that resulted in CRMD placement, or (3) a CRMD evaluation that shows no evidence of spontaneous ventricular activity when the pacemaking function of the CRMD is programmed to VVI pacing mode at the lowest programmable rate.

Cardiac rhythm management device function is ideally assessed by a comprehensive evaluation of the device.³ If a comprehensive evaluation is not possible, then, at a minimum, confirm whether pacing impulses are present and create a paced beat. Consultation with a cardiologist or CRMD service may be necessary. Contacting the manufacturer for perioperative recommendations may be a consideration.

II. Preoperative Preparation
Preparation for patient safety and proper maintenance of the device during a procedure includes (1) determining whether electromagnetic interference (EMI) is likely to occur during the planned procedure; (2) determining whether reprogramming the CRMD pacemaking function to an asynchronous pacing mode for disabling any special algorithms, including rate adaptive functions, is needed; (3) suspending antitachyarrhythmia functions if present; (4) advising the individual performing the procedure to consider use of a bipolar electrocautery system or ultrasonic (harmonic) scalpel to minimize potential adverse effects of EMI on the pulse generator or leads; (5) assuring the availability of temporary pacing and defibrillation equipment; and (6) evaluating the possible effects of anesthetic techniques on CRMD function and patient-CRMD interactions.

Numerous descriptive studies and case reports suggest that the following procedures are likely to be associated with EMI: (1) electrocautery,⁵⁻¹¹ (2) radio frequency ablation,¹²⁻²⁰ (3) magnetic resonance imaging (MRI),²¹⁻³¹ and (4) radiation therapy.³²⁻³⁴ No studies were found that reported EMI during electroconvulsive therapy (ECT). Some descriptive studies report the occurrence of EMI during lithotripsy,³⁵,³⁶ whereas other descriptive studies and case reports indicate no apparent EMI effects.³⁷⁻³⁹ No controlled trials of the clinical impact of programming the pacemaking function to an asynchronous mode for a procedure were found. Although some case reports suggest that such reprogramming is beneficial during electrocautery,⁴⁰⁻⁴² other reports indicate that EMI may continue to affect reprogrammed pacemakers.⁴³,⁴⁴ The literature lacks sufficient guidance regarding the potential perioperative impact of anesthetic techniques on CRMD function. The majority of Consultants as well as the samples of ASA and HRS members agree that it should be determined whether EMI is likely to occur before a planned procedure. The majority of Consultants agree that a CRMD’s rate-adaptive therapy should be turned off before a procedure, whereas the ASA and HRS members are equivocal. The majority of Consultants and HRS members believe that patients’ CRMDs should be programmed to an asynchronous mode before surgery, whereas the ASA members are equivocal. In addition, the majority of Consultants and HRS members agree that pacemaker-dependent patients’ CRMDs should be programmed to an asynchronous mode before surgery, whereas the ASA members are again equivocal. The majority of Consultants and ASA and HRS members agree that (1) suspending antitachyarrhythmia functions if present, (2) advising the individual performing the procedure to consider use of a bipolar electrocautery system to minimize potential adverse effects of EMI on the pulse generator or leads, (3) assuring the availability of temporary pacing and defibrillation equipment, and (4) evaluating the possible effects of anesthetic techniques on CRMD function and patient-CRMD interactions are important steps in promoting patient safety and successfully treating patients with CRMDs. The Consultants and ASA members and the HRS members are equivocal regarding the consideration of using an ultrasonic scalpel.

Advisory. The Task Force agrees that planned procedures should include a determination as to whether EMI is likely to occur for either conventional pacemakers or ICDs. If EMI is likely to occur, the conventional pacing function of a CRMD should be altered by changing to an asynchronous pacing mode# in pacemaker-dependent patients and suspending special algorithms, including rate-adaptive functions. These alterations may be accomplished by programming or applying a magnet when applicable.** However, the Task Force cautions against the use of the magnet over an ICD.†† In addition, an

† Most current CRMDs have an x-ray code that can be used to identify the manufacturer of the device.

‡ The VVT mode (with attention to the upper rate limit) might also be considered for a patient with ventricular ectopy where concern exists regarding R-on-T pacing during an asynchronous pacing mode. However, the upper pacing rate during VVT mode is manufacturer- and possibly generator-specific and can approach 200 beats/min for many devices. Generally, VVT mode pacing would not be a consideration except in very rare circumstances. Before using the VVT mode, a cardiologist and the generator manufacturer should be consulted to determine the suitability of the upper pacing rate for any patient.

** A magnet correctly applied to a pacemaker often results in asynchronous pacemaker function at a predetermined rate without rate responsiveness. The magnet rate and response varies by manufacturer. Magnet response can be affected by programming and remaining battery life. The magnet rate may be excessive for some patients. Some pacemakers may have no magnet response.

†† Magnet application to an ICD rarely alters bradycardia pacing rate and function. A magnet correctly applied to an ICD often results in suspension of tachyarrhythmia therapy. For most ICDs, there is no reliable means to detect appropriate magnet placement. Some ICDs may have no magnet response. Some ICDs can be permanently disabled by magnet application.
or pulse plethysmography or oximetry. Although no recent studies were found examining the impact of electrocardiography or peripheral pulse monitoring, anesthesia-induced physiologic changes (i.e., cardiac rate, rhythm, or ischemia) in the patient may induce unexpected CRMD responses or adversely affect the CRMD–patient interaction.

III. Intraoperative Management

The primary activities associated with intraoperative management of a CRMD include (1) monitoring the operation of the device; (2) preventing potential CRMD dysfunction; and (3) performing emergency defibrillation, cardioversion, or heart rate support.

1. Monitoring. Intraoperative monitoring includes continuous electrocardiography as well as monitoring of the peripheral pulse (e.g., palpation of the pulse, auscultation of heart sounds, monitoring of a tracing of intravascular pressure, ultrasound peripheral pulse monitoring, or pulse plethysmography or oximetry). Although no controlled trials were found that examined the clinical impact of electrocardiography or peripheral pulse monitoring for CRMD patients, case reports note the importance of intraoperative electrocardiographic monitoring in the detection of pacemaker or cardiac dysfunction for these patients. The majority of Consultants and ASA and HRS members agree that (1) continuous electrocardiographic monitoring should be conducted for CRMD patients and (2) continuous peripheral pulse monitoring should be conducted.

Advisory. Electrocardiography and peripheral pulse monitoring are important components of perioperative treatment of patients with CRMDs. The Task Force agrees that a patient’s electrocardiogram should be continuously displayed, as required by ASA standards, from the beginning of anesthesia until the patient is transferred out of the anesthetizing location, with additional electrocardiographic monitoring in the postoperative period as indicated by the patient’s medical condition. The Task Force believes that these standards should apply to all CRMD patients receiving general or regional anesthesia, sedation, or monitored anesthesia care. Continuous peripheral pulse monitoring should be performed for all CRMD patients receiving general or regional anesthesia, sedation, or monitored anesthesia care. If unanticipated device interactions are found, consider discontinuation of the procedure until the source of interference can be eliminated or managed.

2. Managing Potential Sources of EMI. Procedures using electrocautery, radiofrequency ablation, lithotripsy, MRI, or radiation therapy may damage CRMDs or interfere with CRMD function, potentially resulting in severe adverse outcomes. Sources of EMI are often unique to specific procedures, and the management of each of these potential EMI sources is reported separately below.

A. Electrocautery. Management of potential sources of EMI associated with electrocautery includes (1) assuring that the cautery tool and current return pad are positioned so that the current pathway does not pass through or near the CRMD pulse generator and leads; (2) avoiding proximity of the cautery’s electrical field to the pulse generator or leads; (3) using short, intermittent, and irregular bursts at the lowest feasible energy levels; and (4) using a bipolar electrocautery system or an ultrasonic (harmonic) scalpel, if possible.

Two case reports and one observational study suggest that EMI may occur despite positioning the current return pad as far as possible away from the generator and leads. However, the majority of Consultants and ASA and HRS members agree that the current return pad should be positioned so that the electrosurgical current pathway does not pass through or near the CRMD pulse generator or leads.

One case report suggested that application of unipolar electrocautery on the sternum resulted in complete pacemaker inhibition. Although some manufacturers suggest substituting bipolar for monopolar electrocautery to minimize CRMD interactions, no clinical literature was found to support this recommendation. The majority of Consultants and ASA and HRS members agree that direct contact between the electrocautery system and the CRMD pulse generator or its leads should be avoided.

Although no recent studies were found examining the benefit of using short, intermittent bursts at the lowest feasible energy levels, earlier literature suggests that short, intermittent bursts may be useful in completing procedures without notable EMI interference. The majority of Consultants and ASA and HRS members agree that short, intermittent bursts should be performed.

Finally, case reports suggest that surgery for pacemaker patients may proceed uneventfully when bipolar electrocautery systems or harmonic scalpels are used. The majority of Consultants and ASA and HRS members agree that bipolar electrocautery systems should be
used when possible. The majority of Consultants and ASA members agree that harmonic scalpels should be used when possible, and HRS members are equivocal.

**B. Radiofrequency Ablation.** Management of potential sources of EMI associated with radiofrequency ablation primarily involves keeping the radiofrequency current path (electrode tip to current return pad) as far away from the pulse generator and lead system as possible. One observational study reports 3 of 12 cases that resulted in a significant decrease in resistance on the pacemaker leads when radiofrequency ablation was used in proximity to the leads.65 One case report suggests that positioning of the radiofrequency ablation cluster electrode no closer than 5 cm from the pacer leads allowed the procedure to continue uneventfully.40 The majority of Consultants and ASA and HRS members agree that the individual performing the procedure should avoid direct contact between the ablation catheter and the CRMD and leads and should keep the radiofrequency ablation current path as far away from the pulse generator and lead system as possible.

**C. Lithotripsy.** Management of potential sources of EMI associated with lithotripsy includes (1) avoiding focus of the lithotripsy beam near the pulse generator and (2) disabling atrial pacing if the lithotripsy system triggers on the R wave. The literature is silent regarding the benefits of focusing the lithotripsy beam away from the pulse generator as well as the benefits of disabling atrial pacing during lithotripsy. The majority of Consultants and ASA and HRS members agree that focusing the lithotripsy beam near the pulse generator should be avoided, and all three groups are equivocal regarding whether atrial pacing should be disabled before a procedure if the lithotripsy system triggers on the R wave.

**D. Magnetic Resonance Imaging.** The literature is not sufficiently rigorous to examine the effects of specific management activities related to CRMD patients receiving MRI. Some descriptive studies and case reports suggest that MRI may be completed without notable EMI from the pulse generator and lead system as possible.21–29 The majority of Consultants and ASA and other literature generally suggests that MRI is contraindicated.30,31,64–71 However, under specific circumstances and with appropriate patient qualification and monitoring.30,31,64–71 Some descriptive studies and case reports suggest that positioning of the radiofrequency ablation cluster electrode no closer than 5 cm from the pacer leads allowed the procedure to continue uneventfully.40 The majority of Consultants and ASA and HRS members agree that the individual performing the procedure should avoid direct contact between the ablation catheter and the CRMD and leads and should keep the radiofrequency ablation current path as far away from the pulse generator and lead system as possible.

**E. Radiation Therapy.** The literature does not provide sufficient guidance regarding specific management activities related to CRMD patients undergoing radiation therapy. However, none of the Consultants or HRS members and only 10% of the ASA members agree that radiation therapy is contraindicated for all CRMD patients. Fifty-seven percent of the Consultants, 59% of the HRS members, and 37% of the ASA members agree that radiation therapy is contraindicated for some but not all CRMD patients, whereas 43% of the Consultants, 41% of the HRS members, and 53% of the ASA members agree that radiation therapy is not contraindicated for any CRMD patient.

**F. Electroconvulsive Therapy.** No clinical studies were found that report EMI effects or permanent CRMD malfunction associated with ECT. One study reports two cases where patients’ ICDs were turned off before ECT but does not report the effect of the therapy on ICD function.72 However, the author indicates that treatment with ECT might be associated with significant cardiac risks. Transient electrocardiographic changes (e.g., increased P-wave amplitude, altered QRS shape, T-wave and ST-T abnormalities) may result from ECT, and additional cardiac complications (e.g., arrhythmia or ischemia) may occur in patients with preexisting cardiac disease. Finally, physiologic stresses after ECT, such as a period of bradycardia and reduced blood pressure, followed by tachycardia and an increase in blood pressure, may account for cardiac failure in the extended postoperative period (i.e., several hours or days after ECT) among patients with marginal cardiac function.

**Advisory.** The Task Force believes that EMI could be minimized during certain procedures using a variety of intraoperative management techniques.

The Task Force agrees that the risk of intraoperative interference from electrocautery systems may be minimized by (1) positioning the cautery tool and current return pad so that the current pathway does not pass through or near the CRMD system; (2) avoiding proximity of the cautery’s electrical field to the pulse generator and leads, including avoidance of waving the activated electrode over the generator; (3) using short, intermittent, and irregular bursts at the lowest feasible energy levels; and (4) using bipolar electrocautery systems or ultrasonic (harmonic) scalpels if possible. Advising or reminding the individual performing the procedure to implement these management techniques should be considered.

Risk of interference from radiofrequency ablation may be reduced by avoiding direct contact between the ablation catheter and the pulse generator and leads and by keeping the radiofrequency’s current path (electrode tip to current return pad) as far away from the pulse generator and leads as possible. During all radiofrequency ablative procedures, consider discussing with the individual performing the procedure any concerns regarding the proximity of the ablation catheter to the CRMD leads.

During lithotripsy, the lithotripsy beam should not be focused near the pulse generator. If the lithotripsy system triggers on the R wave, atrial pacing might need to be disabled before the procedure.

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1 For some cases, the electrosurgical receiving plate will need to be placed on a site different from the thigh. For example, in head and neck cases, the receiving plate can be placed on the posterior superior aspect of the shoulder contralateral to the generator position.2 An inhibitory effect could occur even when the active electrode of the electrocautery is not touching the patient.
The Task Force believes that MRI is generally contraindicated for CRMD patients. If MRI must be performed, consult with the ordering physician, the patient’s pacemaker specialist or cardiologist, the diagnostic radiologist, and the CRMD manufacturer. The Task Force believes that radiation therapy can be safely performed for CRMD patients. The device must be outside the field of radiation. Therefore, some pulse generators will require surgical relocation before commencing radiation. Most manufacturers recommend verification of pulse generator function during and at the completion of radiation. Problems may include pacemaker failure and runaway pacemaker. †††

Although transient or long-term myocardial and nervous system effects may be associated with ECT, the Task Force believes that such therapies may be administered to CRMD patients without significant damage to a disabled CRMD. If ECT must be performed, consult with the ordering physician and the patient’s cardiologist to plan for the first and subsequent ECTs. All CRMDs should undergo a comprehensive interrogation before the procedure(s). ICD functions should be disabled for shock therapy during ECT; however, be prepared to treat ventricular arrhythmias that occur secondary to the hemodynamic effects of ECT. CRMD-dependent patients may require a temporary pacing system to preserve cardiac rate and rhythm during shock therapy. Also, the CRMD may require programming to asynchronous activity to avoid myopotential inhibition of the device in pacemaker-dependent patients.

3. Emergency Defibrillation or Cardioversion.

During the perioperative period, emergency defibrillation or cardioversion may become necessary for a CRMD patient. In this case, the primary concern is to minimize the current flowing through the pulse generator and lead system. Recent and earlier case reports suggest that optimal positioning of the defibrillation or cardioversion pads or paddles may be an important factor in the prevention of adverse CRMD-related outcomes. 75–77 The majority of Consultants and ASA and HRS members agree that the defibrillation or cardioversion pads should be positioned as far as possible from the pulse generator. The majority of Consultants and ASA and HRS members also agree that the anterior–posterior position should be used and that a clinically appropriate energy output should be used regardless of the type of CRMD.

Advisory. The Task Force believes that before attempting emergency defibrillation or cardioversion of a patient with an ICD and magnet-disabled therapies, all sources of EMI should be terminated, and the magnet should be removed to reenable antitachycardia therapies. The patient should then be observed for appropriate CRMD therapy. For patients with an ICD and antiarrhythmic therapies that have been disabled by programming, consider reenabling therapies through programming. If the above activities do not restore ICD function, proceed with emergency external defibrillation or cardioversion.

Overriding the above discussion is the need to follow existing Advanced Cardiac Life Support and emergency guidelines78 to provide rapid cardioversion or defibrillation, and attention should be turned to providing this therapy as quickly as possible.

If a life-threatening arrhythmia occurs, follow Advanced Cardiac Life Support guidelines for energy level and for paddle placement. If possible, attempt to minimize the current flowing through the pulse generator and lead system by (1) positioning the defibrillation or cardioversion pads or paddles as far as possible from the pulse generator and (2) positioning defibrillation or cardioversion pads or paddles perpendicular to the major axis of the CRMD pulse generator and leads to the extent possible by placing them in an anterior–posterior location. A clinically appropriate energy output should always be used regardless of the presence of a CRMD, and the paddles should be positioned as best as can be done in an emergency.

IV. Postoperative Management

Postoperative treatment of CRMD patients primarily consists of interrogating and restoring CRMD function. Although no recent studies were found examining outcomes associated with interrogating or restoring CRMD function, an earlier case report indicates that postoperative evaluation resulted in the discovery and correction of a pacemaker problem. 79 The majority of Consultants and ASA and HRS members agree that postoperative patient treatment should include interrogating and restoring CRMD function in the postanesthesia care unit or intensive care unit.

Advisory. The Task Force believes that cardiac rate and rhythm should be continuously monitored throughout the immediate postoperative period. Backup pacing capability and cardioversion–defibrillation equipment should be immediately available at all times.

Postoperative interrogation and restoration of CRMD function are basic elements of postoperative management. The CRMD first should be interrogated to assess postoperative device functions. If interrogation determines that CRMD settings are inappropriate, the device should be reprogrammed to appropriate settings. For an ICD, all antitachycardia therapies should be restored. Consultation with a cardiologist or pacemaker–ICD service may be necessary.

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††† Runaway pacemaker is a potentially catastrophic pulse generator malfunction characterized by the sudden onset of rapid, erratic pacing. Runaway pacemaker is the result of multiple internal component failure, and it is relatively uncommon in modern devices. Circuitry in modern pacemakers (and ICDs) limits the runaway pacing rate to less than 210 beats/min.
Appendix 1: Generic Pacemaker and Defibrillator Codes

The generic pacemaker and defibrillator codes were developed as joint projects by the North American Society of Pacing and Electrophysiology (NASPE)‡‡‡ and the British Pacing and Electrophysiology Group (BPEG). The five positions refer to the order of the programmed settings on the CRMD (tables 1 and 2).

### Table 1. Generic Pacemaker Code (NBG*): NASPE/BPEG Revised (2002)

<table>
<thead>
<tr>
<th>Position I, Pacing Chamber(s)</th>
<th>Position II, Sensing Chamber(s)</th>
<th>Position III, Response(s) to Sensing</th>
<th>Position IV, Programmability</th>
<th>Position V, Multisite Pacing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>O</strong> = none</td>
<td><strong>O</strong> = none</td>
<td><strong>O</strong> = none</td>
<td><strong>O</strong> = none</td>
<td><strong>O</strong> = none</td>
</tr>
<tr>
<td><strong>A</strong> = atrium</td>
<td><strong>A</strong> = atrium</td>
<td><strong>I</strong> = inhibited</td>
<td><strong>R</strong> = rate modulation</td>
<td><strong>A</strong> = atrium</td>
</tr>
<tr>
<td><strong>V</strong> = ventricle</td>
<td><strong>V</strong> = ventricle</td>
<td><strong>T</strong> = triggered</td>
<td><strong>V</strong> = ventricle</td>
<td><strong>D</strong> = dual (A + V)</td>
</tr>
<tr>
<td><strong>D</strong> = dual (A + V)</td>
<td><strong>D</strong> = dual (A + V)</td>
<td><strong>D</strong> = dual (T + I)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Examples:

**AAI** = Atrial-only antibradycardia pacing. In the AAI mode, any failure of the atrium to produce an intrinsic event within the appropriate time window (determined by the lower rate limit) results in an atrial pacing pulse emission. There is no ventricular sensing; thus, a premature ventricular event will not likely reset the pacing timer.

**AOO** = Asynchronous atrial-only pacing. In this mode, the pacing device emits a pacing pulse regardless of the underlying cardiac rhythm.

**DDD** = Dual-chamber antibradycardia pacing function in which every atrial event, within programmed limits, is followed by a ventricular event. The DDD mode implies dual-chamber pacing with atrial tracking. In the absence of intrinsic activity in the atrium, it will be paced, and, after any sensed or paced atrial event, an intrinsic ventricular event must occur before the expiration of the atrioventricular timer or the ventricle will be paced.

**DDI** = Dual-chamber behavior in which the atrial activity is tracked into the ventricle only when the atrial event is created by the antibradycardia pacing function of the generator. In the DDI mode, the ventricle is paced only when no intrinsic ventricular activity is present.

**DOO** = Asynchronous atrioventricular sequential pacing without regard to the underlying cardiac rhythm.

**VOO** = Asynchronous ventricular-only pacing without regard to the underlying cardiac rhythm.

**VVI** = Ventricular-only antibradycardia pacing. In the VVI mode, any failure of the ventricle to produce an intrinsic event within the appropriate time window (determined by the lower rate limit) results in a ventricular pacing pulse emission. There is no atrial sensing; thus, there can be no atrioventricular synchrony in a patient with a VVI pacemaker and any intrinsic atrial activity.

* NBG: N refers to NASPE, B refers to BPEG, and G refers to generic.

### Table 2. Generic Defibrillator Code (NBD): NASPE/BPEG

<table>
<thead>
<tr>
<th>Position I, Shock Chamber(s)</th>
<th>Position II, Antitachycardia Pacing Chamber(s)</th>
<th>Position III, Tachycardia Detection</th>
<th>Position IV,* Antibradycardia Pacing Chamber(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>O</strong> = none</td>
<td><strong>O</strong> = none</td>
<td><strong>E</strong> = electrogram</td>
<td><strong>O</strong> = none</td>
</tr>
<tr>
<td><strong>A</strong> = atrium</td>
<td><strong>A</strong> = atrium</td>
<td><strong>H</strong> = hemodynamic</td>
<td><strong>A</strong> = atrium</td>
</tr>
<tr>
<td><strong>V</strong> = ventricle</td>
<td><strong>V</strong> = ventricle</td>
<td></td>
<td><strong>V</strong> = ventricle</td>
</tr>
<tr>
<td><strong>D</strong> = dual (A + V)</td>
<td><strong>D</strong> = dual (A + V)</td>
<td></td>
<td><strong>D</strong> = dual (A + V)</td>
</tr>
</tbody>
</table>

* For robust identification, position IV is expanded into its complete NBG code. For example, a biventricular pacing–defibrillator with ventricular shock and antitachycardia pacing functionality would be identified as VWE-DDDRV, assuming that the pacing section was programmed DDDR, and the current hemodynamic sensors have been approved for tachycardia detection (position III).

‡‡‡ Now called the Heart Rhythm Society (HRS).

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Appendix 2: Summary of Practice Advisory

Preoperative Evaluation
- Establish whether a patient has a CRMD.
  - Conduct a focused history (patient interview, medical records review, review of available chest x-ray films, electrocardiogram, or any available monitor or rhythm strip information).
  - Conduct a focused physical examination (check for scars, palpate for device).
- Define the type of CRMD.
  - Obtain manufacturer’s identification card from patient or other source.
  - Order chest x-ray studies if no other data are available.
  - Refer to supplemental resources (e.g., manufacturer’s databases).
- Determine dependency on pacing function of the CRMD.
  - History of symptomatic bradyarrhythmia resulting in CRMD implantation.
  - History of successful atrioventricular nodal ablation.
  - Inadequate escape rhythm at lowest programmable pacing rate.
- Determine CRMD function.
  - Interrogate device (consultation with a cardiologist or pacemaker–ICD service may be necessary).
  - Determine whether the device will capture when it paces (i.e., produce a mechanical systole with a pacemaker impulse).
  - Consider contacting the manufacturer for perioperative recommendations.

Preoperative Preparation
- Determine whether EMI is likely to occur during the planned procedure.
- Determine whether reprogramming pacing function to asynchronous mode or disabling rate responsive function is advantageous.
- Suspend antiarrhythmic functions if present.
- Advise individual performing the procedure to consider use of a bipolar electrocautery system or ultrasonic (harmonic) scalpel.
- Temporary pacing and defibrillation equipment should be immediately available.
- Evaluate the possible effects of anesthetic techniques and of the procedure on CRMD function and patient CRMD interactions.

Intraoperative Management
- Monitor operation of the CRMD.
  - Conduct electrocardiographic monitoring per ASA standard.
  - Monitor peripheral pulse (e.g., manual pulse palpation, pulse oximeter plethysmogram, arterial line).
- Manage potential CRMD dysfunction due to EMI.
  - Electrocautery.
    - Ensure that the electrocautery is compatible with the CRMD.
    - Determine the type of CRMD.
    - Establish whether a patient has a CRMD.
    - Determine dependency on pacing function of the CRMD.
    - Interrogate and restore CRMD function in the immediate postoperative period.
- Electroconvulsive therapy.
  - Advise individual performing the procedure to use short, intermittent, and irregular bursts at the lowest feasible energy levels.
  - Advise individual performing the procedure to avoid direct contact between the ablation catheter and the pulse generator and leads.
- Radiofrequency ablation.
  - Advise individual performing the procedure to avoid direct contact between the ablation catheter and the pulse generator and leads.
  - Lithotripsy.
    - Advise individual performing the procedure to avoid focusing the lithotripsy beam near the pulse generator.
    - If the lithotripsy system triggers on the R wave, consider preoperative disabling of atrial pacing.
- MRI.
  - MRI is generally contraindicated in patients with CRMDs.
  - If MRI must be performed, consult with the ordering physician, the patient’s cardiologist, the diagnostic radiologist, and the CRMD manufacturer.
- Radiation therapy.
  - Radiation therapy can be safely performed in patients who have CRMDs.
  - Surgically relocate the CRMD if the device will be in the field of radiation.
- Electroconvulsive therapy.
  - Consult with the ordering physician, the patient’s cardiologist, a CRMD service, or the CRMD manufacturer.
- Emergency defibrillation or cardioversion.
  - For a patient with an ICD and magnet-disabled therapies:
    - Advise individual performing the procedure to terminate all sources of EMI while magnet is removed.
    - Remove the magnet to reenable antitachycardia therapies.
    - Observe the patient and the monitors for appropriate CRMD therapy.
    - If the above activities do not restore ICD function, proceed with emergency external defibrillation or cardioversion.
  - For a patient with an ICD and programming-disabled therapies:
    - Advise individual performing the procedure to terminate all sources of EMI while magnet is removed.
    - Reenable therapies through programming if the programmer is immediately available and ready to be used.
    - Observe the patient and the monitors for appropriate CRMD therapy.
    - If the above activities do not restore ICD function, proceed with emergency external defibrillation or cardioversion.
- For external defibrillation:
  - Position defibrillation/cardioversion pads or paddles as far as possible from the pulse generator.
  - Position defibrillation/cardioversion pads or paddles perpendicular to the major axis of the CRMD to the extent possible by placing them in an anterior–posterior location.
  - If it is technically impossible to place the pads or paddles in locations that help to protect the CRMD, defibrillate/cardiovert the patient in the quickest possible way and be prepared to provide pacing through other routes.
  - Use a clinically appropriate energy output.

Postoperative Management
- Continuously monitor cardiac rate and rhythm and have backup pacing and defibrillation equipment immediately available throughout the immediate postoperative period.
- Interrogate and restore CRMD function in the immediate postoperative period.
  - Interrogate CRMD; consultation with a cardiologist or pacemaker–ICD service may be necessary.
  - Restore all antiarrhythmic therapies in ICDs.
  - Ensure that all other settings of the CRMD are appropriate.

Refer to Table 3 for an example of a stepwise approach to the perioperative treatment of the patient with a CRMD.

ASA = American Society of Anesthesiologists; CRMD = cardiac rhythm management device; EMI = electromagnetic interference; ICD = implantable cardioverter–defibrillator; MRI = magnetic resonance imaging.
<table>
<thead>
<tr>
<th>Perioperative Period</th>
<th>Patient/CRMD Condition</th>
<th>Intervention</th>
</tr>
</thead>
</table>
| **Preoperative evaluation** | Patient has CRMD | • Focused history  
                       • Focused physical examination  

Determine CRMD type (pacemaker, ICD, CRT) | | • Manufacturer’s CRMD identification card  
                       • Chest x-ray studies (no data available)  
                       • Supplemental resources*  

Determine whether patient is CRMD-dependent for pacing function | | • Verbal history  
                       • Bradyarrhythmia symptoms  
                       • Atrioventricular node ablation  
                       • No spontaneous ventricular activity†  

Determine CRMD function | | • Comprehensive CRMD evaluation‡  
                       • Determine whether pacing pulses are present and create paced beats  

**Preoperative preparation** | EMI unlikely during procedure | • If EMI unlikely, special precautions are not needed  
                       • Reprogram to asynchronous mode when indicated  
                       • Suspend rate-adaptive functions§  

EMI likely: CRMD is pacemaker | | • Suspend antitachyarrhythmia functions  
                       • If patient is dependent on pacing function, alter pacing functions as above  

EMI likely: CRMD is ICD | | • Use bipolar cauterity; ultrasonic scalpel  
                       • Temporary pacing and external cardioversion–defibrillation available  

EMI likely: all CRMD | | • Plan for possible adverse CRMD–patient interaction  

**Intraoperative management** | Monitoring | • Electrocardiographic monitoring per ASA standard  
                       • Peripheral pulse monitoring  

Electrocautery interference | | • CT/CRP—no current through PG/leads  
                       • Avoid proximity of CT to PG/leads  
                       • Short bursts at lowest possible energy  
                       • Use bipolar cauterity; ultrasonic scalpel  

Radiofrequency catheter ablation | | • Avoid contact of radiofrequency catheter with PG/leads  
                       • Radiofrequency current path far away from PG/leads  
                       • Discuss these concerns with operator  

Lithotripsy | | • Do not focus lithotripsy beam near PG  
                       • R wave triggers lithotripsy? Disable atrial pacing|  

MRI | | • Generally contraindicated  
                       • If required, consult ordering physician, cardiologist, radiologist, and manufacturer  

RT | | • PG/leads must be outside of RT field  
                       • Possible surgical relocation of PG  
                       • Verify PG function during/after RT course  

ECT | | • Consult with ordering physician, patient’s cardiologist, a CRMD service, or CRMD manufacturer  

**Emergency defibrillation–cardioversion** | ICD: magnet disabled | • Terminate all EMI sources  
                       • Remove magnet to reenable therapies  
                       • Observe for appropriate therapies  

ICD: programming disabled | | • Programming to reenable therapies or proceed directly with external cardioversion–defibrillation  

ICD: either of above | | • Minimize current flow through PG/leads  
                       • PP as far as possible from PG  
                       • PP perpendicular to major axis PG/leads  
                       • To extent possible, PP in anterior–posterior location  

Regardless of CRMD type | | • Use clinically appropriate cardioversion/defibrillation energy  

**Postoperative management** | Immediate postoperative period | • Monitor cardiac R&R continuously  
                       • Backup pacing and cardioversion/defibrillation capability  

Postoperative interrogation and restoration of CRMD function | | • Interrogation to assess function  
                       • Settings appropriate?#  
                       • Is CRMD an ICD?**  
                       • Use cardiology/pacemaker–ICD service if needed  

---

* Manufacturer’s databases, pacemaker clinic records, cardiology consultation.  
† With cardiac rhythm management device (CRMD) programmed VVI at lowest programmable rate.  
‡ Ideally CRMD function assessed by interrogation, with function altered by reprogramming if required.  
§ Most times this will be necessary; when in doubt, assume so.  
| Atrial pacing spikes may be interpreted by the lithotriptor as R waves, possibly inciting the lithotriptor to deliver a shock during a vulnerable period in the heart.  
# If necessary, reprogram appropriate settings.  
** Restore all antitachycardia therapies.  
CRP = current return pad; CRT = cardiac resynchronization therapy; CT = cautery tool; ECT = electroconvulsive therapy; EMI = electromagnetic interference; ICD = internal cardioverter–defibrillator; MRI = magnetic resonance imaging; PG = pulse generator; PP = external cardioversion–defibrillation pads or paddles; R&R = rhythm and rate; RT = radiation therapy.  

Anesthesiology, V 103, No 1, Jul 2005
Appendix 3: Literature Review and Consensus-based Evidence

A. State of the Literature

For this Advisory, a literature review was used in combination with opinions obtained from experts and other sources (e.g., professional society members, open forums, Web-based postings) to provide guidance to practitioners regarding the perioperative treatment of patients with CRMDs. Both the literature review and opinion data were based on evidence linkages, consisting of directional statements about relations between specific perioperative management activities and CRMD function or clinical outcomes.

A study or report that appears in the published literature is included in the development of an advisory if the study (1) is related to one of the specified linkage statements, (2) reports a finding or set of findings that can be tallied or measured (e.g., articles that contain only opinion are not included), and (3) is the product of an original investigation or report (i.e., review articles or follow-up studies that summarize previous findings are not included). Because CRMDs represent a rapidly changing technology, earlier literature (i.e., literature published before 1990) was rarely included in the evaluation of evidence for this Practice Advisory.

Although evidence linkages are designed to assess causality, few of the reviewed studies exhibited sufficiently acceptable quantitative methods and analyses to provide a clear indication of causality. Therefore, the published literature could not be used as a source of quantitative support (required for the development of practice guidelines). However, many published studies were evaluated that provided the Task Force with important noncausal evidence. For example, descriptive literature (i.e., reports of frequency or incidence) is often useful in providing an indication of the scope of a problem. Information regarding whether a particular adverse outcome is common or rare may have considerable bearing on the practicality of an advisory. Case reports are typically used as a forum for reporting and recognizing unusual or adverse outcomes and may suggest caution when devising an advisory.

For the literature review, potentially relevant studies were identified via electronic and manual searches of the literature. The electronic search covered a 39-yr period from 1966 through 2004. The manual search covered a 45-yr period from 1961 through 2005. More than 1,500 citations were initially identified, yielding a total of 411 nonoverlapping articles that addressed topics related to the evidence linkages. After review of the articles, 283 studies did not provide direct evidence and were subsequently eliminated. A total of 128 articles (from 39 journals) contained direct linkage-related evidence. No evidence linkage contained enough studies with well-defined experimental designs and statistical information to conduct a quantitative analysis (i.e., meta-analysis).

Interobserver agreement among Task Force members and two methodologists was established by interrater reliability testing. Agreement levels using a \( \kappa \) statistic for two-rater agreement pairs were as follows: (1) type of study design, \( \kappa = 0.72-0.90 \); (2) type of analysis, \( \kappa = 0.80-0.90 \); (3) evidence linkage assignment, \( \kappa = 0.84-1.00 \); and (4) literature inclusion for database, \( \kappa = 0.70-1.00 \). Three-rater chance-corrected agreement values were (1) study design, \( \text{Sav} = 0.81, \text{Var} (\text{Sav}) = 0.010 \); (2) type of analysis, \( \text{Sav} = 0.86, \text{Var} (\text{Sav}) = 0.009 \); (3) linkage assignment, \( \text{Sav} = 0.82, \text{Var} (\text{Sav}) = 0.005 \); and (4) literature database inclusion, \( \text{Sav} = 0.78, \text{Var} (\text{Sav}) = 0.031 \). These values represent moderate to high levels of agreement.

Future studies should focus on prospective methodologies, when possible, that use traditional hypothesis testing techniques. Use of the following methodologic procedures for assessing the impact of perioperative management of CRMDs is recommended: (1) comparison studies (i.e., one technique vs. another) when clinically feasible; (2) randomization; and (3) full reporting of sample size, effect size estimates, test scores, measures of variability, and \( P \) values.

B. Consensus-based Evidence

Consensus was obtained from multiple sources, including (1) survey opinion from Consultants who were selected based on their knowledge or expertise in perioperative management of CRMDs, (2) survey opinions from randomly selected samples of active members of the American Society of Anesthesiologists and active members of the HRS, (3) testimony from attendees of two publicly held open forums at a national anesthesia meeting and at a major cardiology meeting, and (4) Internet commentary, and (5) Task Force opinion and interpretation. The survey rate of return was 56% (\( n = 23 \) of 41) for Consultants, 15% (\( n = 89 \) of 600) for the HRS membership, and 15% (\( n = 44 \) of 300) for the HRS membership. Survey results are presented in the text of the document and in table 4.

The ASA Consultants were also asked to indicate which, if any, of the evidence linkages would change their clinical practices if the Advisory was instituted. The rate of return was 39% (\( n = 16 \) of 41). The percent of responding Consultants expecting no change associated with each linkage were as follows: preoperative evaluation—67%; preoperative patient preparation—67%; intraoperative monitoring of CRMDs—67%; emergency defibrillation or cardioversion—87%; postoperative monitoring of CRMDs—73%; postoperative interrogation and restoration of CRMD function—60%; intraoperative management of EMI during electrocautery—73%, radiofrequency ablation—73%, liothryps—80%, MRI—80%, radiation therapy—80%, and electroconvulsive therapy—73%. Forty percent of the respondents indicated that the Advisory would have no effect on the amount of time spent on a typical case. Nine respondents (60%) indicated that there would be an increase in the amount of time they would spend on a typical case with the implementation of this Advisory. The amount of increased time anticipated by these respondents ranged from 5 to 30 min.
Table 4. Consultant and Membership Survey Responses: Percent Agreement/Disagreement

<table>
<thead>
<tr>
<th>Survey Item</th>
<th>Consultants</th>
<th>ASA Members</th>
<th>HRS Members</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. To perform a preoperative evaluation:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Establish whether a patient has a CRMD.</td>
<td>23 100/0</td>
<td>89 100/0</td>
<td>44 100/0</td>
</tr>
<tr>
<td>Define the type of device.</td>
<td>23 100/0</td>
<td>87 95/0</td>
<td>44 100/0</td>
</tr>
<tr>
<td>Determine whether a patient is CRMD dependent for pacemaking function.</td>
<td>23 96/0</td>
<td>89 96/0</td>
<td>44 96/0</td>
</tr>
<tr>
<td>Determine CRMD function.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. To prepare a CRMD patient for a procedure:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Determine whether EMI is likely to occur.</td>
<td>23 96/4</td>
<td>89 91/2</td>
<td>44 96/2</td>
</tr>
<tr>
<td>Turn pacemaking rate-adaptive therapy off.</td>
<td>23 52/35</td>
<td>89 35/35</td>
<td>44 34/34</td>
</tr>
<tr>
<td>Program pacemaking function to asynchronous mode:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All CRMD patients.</td>
<td>22 0/82</td>
<td>88 21/48</td>
<td>43 9/84</td>
</tr>
<tr>
<td>Pacemaker-dependent patients only.</td>
<td>22 73/23</td>
<td>83 47/27</td>
<td>43 54/28</td>
</tr>
<tr>
<td>Suspend antitachyarrhythmia functions.</td>
<td>21 86/5</td>
<td>87 54/21</td>
<td>43 63/21</td>
</tr>
<tr>
<td>Consider using a bipolar electrocautery system (when applicable).</td>
<td>22 91/0</td>
<td>86 90/2</td>
<td>44 77/14</td>
</tr>
<tr>
<td>Consider using an ultrasonic (harmonic) scalpel (when applicable).</td>
<td>22 68/18</td>
<td>88 63/3</td>
<td>44 34/9</td>
</tr>
<tr>
<td>Assure the availability of temporary pacing and defibrillation equipment.</td>
<td>22 100/0</td>
<td>87 95/1</td>
<td>44 69/7</td>
</tr>
<tr>
<td>Consider the possible effects of anesthetic agents or techniques on CRMD function.</td>
<td>22 64/18</td>
<td>86 77/9</td>
<td>44 66/21</td>
</tr>
<tr>
<td>3. Intraoperative monitoring should include:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continuous electrocardiography.</td>
<td>23 100/0</td>
<td>88 100/0</td>
<td>44 100/0</td>
</tr>
<tr>
<td>Continuous peripheral pulse monitoring.</td>
<td>23 96/0</td>
<td>88 86/11</td>
<td>44 61/18</td>
</tr>
<tr>
<td>4. For procedures using electrocautery:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Position the electrospacial receiving plate so current pathway does not pass through or near the generator or leads.</td>
<td>23 100/0</td>
<td>88 97/0</td>
<td>44 96/0</td>
</tr>
<tr>
<td>Avoid proximity of the cautery’s electrical field to the pulse generator or leads.</td>
<td>23 100/0</td>
<td>87 100/0</td>
<td>44 96/2</td>
</tr>
<tr>
<td>Use short, intermittent, and irregular bursts at the lowest feasible energy levels.</td>
<td>23 96/0</td>
<td>87 83/2</td>
<td>44 91/7</td>
</tr>
<tr>
<td>Use a bipolar electrocautery system (when applicable).</td>
<td>21 91/0</td>
<td>88 94/1</td>
<td>44 84/2</td>
</tr>
<tr>
<td>Use an ultrasonic (harmonic) scalpel (when applicable).</td>
<td>23 57/13</td>
<td>88 65/1</td>
<td>44 41/9</td>
</tr>
<tr>
<td>5. For radiofrequency ablation:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avoid direct contact between the ablation catheter and the CRMD and leads.</td>
<td>23 83/0</td>
<td>87 76/0</td>
<td>44 91/2</td>
</tr>
<tr>
<td>Keep the current path (electrode tip to return plate) as far away from the pulse generator and lead system as possible.</td>
<td>23 87/0</td>
<td>87 78/0</td>
<td>44 89/5</td>
</tr>
<tr>
<td>6. For lithotripsy:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Avoid focusing the lithotripsy beam near the pulse generator.</td>
<td>23 91/0</td>
<td>86 78/1</td>
<td>44 86/0</td>
</tr>
<tr>
<td>If the lithotripsy system triggers on the R wave, disable atrial pacing before procedure.</td>
<td>23 39/26</td>
<td>86 38/13</td>
<td>44 39/9</td>
</tr>
<tr>
<td>7. For MRI:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRI is contraindicated for all CRMD patients.</td>
<td>21 81</td>
<td>79 80</td>
<td>44 55</td>
</tr>
<tr>
<td>MRI is contraindicated for some but not all CRMD patients.</td>
<td>21 19</td>
<td>79 18</td>
<td>44 39</td>
</tr>
<tr>
<td>MRI is not contraindicated for any CRMD patient.</td>
<td>21 0</td>
<td>79 2</td>
<td>44 6</td>
</tr>
<tr>
<td>8. For RT:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RT is contraindicated for all CRMD patients.</td>
<td>21 0</td>
<td>73 10</td>
<td>44 0</td>
</tr>
<tr>
<td>RT is contraindicated for some but not all CRMD patients.</td>
<td>21 57</td>
<td>73 37</td>
<td>44 59</td>
</tr>
<tr>
<td>RT is not contraindicated for any CRMD patient.</td>
<td>21 43</td>
<td>73 53</td>
<td>44 41</td>
</tr>
<tr>
<td>9. For emergency defibrillation or cardioversion:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Position the defibrillation or cardioversion pads as far as possible from the pulse generator.</td>
<td>23 83/0</td>
<td>87 69/13</td>
<td>44 91/7</td>
</tr>
<tr>
<td>Use an anterior–posterior position.</td>
<td>23 74/9</td>
<td>84 61/6</td>
<td>44 68/25</td>
</tr>
<tr>
<td>Use a clinically appropriate energy output regardless of the device.</td>
<td>23 100/0</td>
<td>87 87/0</td>
<td>44 100/0</td>
</tr>
<tr>
<td>10. To treat CRMD patients postoperatively:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Interrogate and restore CRMD function in the PACU or ICU.</td>
<td>23 96/4</td>
<td>88 98/1</td>
<td>44 77/21</td>
</tr>
</tbody>
</table>

* The percentages of respondents who agreed/disagreed with each item are presented. The percentages of respondents who were uncertain are not presented. † Respondents were asked to select one of the three choices. Therefore, the numbers represent percent agreement only.

ASA = American Society of Anesthesiologists; CRMD = cardiac rhythm management device; EMI = electromagnetic interference; HRS = Heart Rhythm Society; ICU = intensive care unit; MRI = magnetic resonance imaging; PACU = postanesthesia care unit; RT = radiation therapy.
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PRACTICE ADVISORY

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Guidelines for pre-operative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery

The Task Force for Preoperative Cardiac Risk Assessment and Perioperative Cardiac Management in Non-cardiac Surgery of the European Society of Cardiology (ESC) and endorsed by the European Society of Anaesthesiology (ESA)

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Keywords
Non-cardiac surgery • Pre-operative cardiac risk assessment • Pre-operative cardiac testing • Pre-operative coronary artery revascularization • Perioperative cardiac management • Renal disease • Pulmonary disease • Neurological disease • Anaesthesiology • Post-operative cardiac surveillance

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List of acronyms and abbreviations

AAA  abdominal aortic aneurysm
ACC  American College of Cardiology
ACE  angiotensin-converting enzyme
ACS  acute coronary syndrome
AHA  American Heart Association
AR  aortic regurgitation
ARB  angiotensin receptor blocker
AS  aortic stenosis
AF  atrial fibrillation
BBSA  β-blocker in spinal anaesthesia
BNP  brain natriuretic peptide
CABG  coronary artery bypass grafting
CARP  coronary artery revascularization prophylaxis
CASS  coronary artery surgery study
CI  confidence interval
COX-2  cyclooxygenase-2
COPD  chronic obstructive pulmonary disease
CPET  cardiopulmonary exercise testing
CPG  Committee for Practice Guidelines
CRP  C-reactive protein
CT  computed tomography
cTnI  cardiac troponin I
cTnT  cardiac troponin T
CVD  cardiovascular disease
DECREASE  Dutch Echocardiographic Cardiac Risk Evaluating
Applying Stress Echo
DES  drug-eluting stent
DIPOM  Diabetes Postoperative Mortality and Morbidity
DSE  dobutamine stress echocardiography
ECG  electrocardiography
ESC  European Society of Cardiology
FEV1  forced expiratory volume in 1 s
FRISC  fast revascularization in instability in coronary disease
HR  hazard ratio
ICU  intensive care unit
IHD  ischaemic heart disease
INR  international normalized ratio
LMWH  low molecular weight heparin
LQTS  long QT syndrome
LR  likelihood ratio
LV  left ventricular
MaVS  metoprolol after surgery
MET  metabolic equivalent
MI  myocardial infarction
MR  mitral regurgitation
MRI  magnetic resonance imaging
MS  mitral stenosis
NICE-SUGAR  normoglycaemia in intensive care evaluation and survival using glucose algorithm regulation
NSTE-MI  non-ST-segment elevation myocardial infarction
NT-proBNP  N-terminal pro-brain natriuretic peptide
NYHA  New York Heart Association
OPUS  orbofibin in patients with unstable coronary syndromes
OR  odds ratio
PaCO2  mixed expired volume of alveolar and dead space gas
PAH pulmonary arterial hypertension  
PETCO₂ end-tidal expiratory CO₂ pressure  
PCI percutaneous coronary intervention  
PDA personal digital assistant  
POISE PeriOperative ISehemic Evaluation trial  
QUO-VADIS QUinapril On Vascular ACE and Determinants of ISchemia  
ROC receiver operating characteristic  
SD standard deviation  
SMVT sustained monomorphic ventricular tachycardia  
SPECT single photon emission computed tomography  
SPVT sustained polymorphic ventricular tachycardia  
STEMI ST-segment elevation myocardial infarction  
SVT supraventricular tachycardia  
SYNTAX synergy between percutaneous coronary intervention with taxus and cardiac surgery  
TACTICS treat angina with agrastat and determine cost of therapy with an invasive or conservative strategy  
TIA transient ischaemic attack  
TIMI thrombolysis in myocardial infarction  
TOE transoesophageal echocardiography  
UFH unfractionated heparin  
VCO₂ carbon dioxide production  
VE minute ventilation  
VHD valvular heart disease  
VKA vitamin K antagonist  
VO₂ oxygen consumption  
VPB ventricular premature beat  
VT ventricular tachycardia

Preamble

Guidelines and Expert Consensus Documents aim to present management and recommendations based on the relevant evidence on a particular subject in order to help physicians to select the best possible management strategies for the individual patient suffering from a specific condition, taking into account not only the impact on outcome, but also the risk–benefit ratio of particular diagnostic or therapeutic means. Guidelines are no substitutes for textbooks. The legal implications of medical guidelines have been discussed previously.¹

A great number of Guidelines and Expert Consensus Documents have been issued in recent years by the European Society of Cardiology (ESC) and also by other organizations or related societies. Because of the impact on clinical practice, quality criteria for development of guidelines have been established in order to make all decisions transparent to the user. The recommendations for formulating and issuing ESC guidelines and Expert Consensus Documents can be found on the ESC website in the guidelines section (www.escardio.org).

In brief, experts in the field are selected and undertake a comprehensive review of the published evidence for management and/or prevention of a given condition. A critical evaluation of diagnostic and therapeutic procedures is performed, including assessment of the risk–benefit ratio. Estimates of expected health outcomes for larger societies are included, where data exist. The level of evidence and the strength of recommendation of particular treatment options are weighted and graded according to predefined scales, as outlined in Tables 1 and 2.

The experts of the writing panels have provided disclosure statements of all relationships they may have which might be perceived as real or potential sources of conflicts of interest. These disclosure forms are kept on file at the European Heart House, headquarters of the ESC. Any changes in conflict of interest that arise during the writing period must be notified to the ESC. The Task Force report is entirely supported financially by the ESC without any involvement of industry.

The ESC Committee for Practice Guidelines (CPG) supervises and coordinates the preparation of new Guidelines and Expert Consensus Documents produced by Task Forces, expert groups, or consensus panels. The Committee is also responsible for the endorsement process of these Guidelines and Expert Consensus Documents or statements. Once the document has been finalized and approved by all the experts involved in the Task Force, it is submitted to outside specialists for review. The document is revised, and finally approved by the CPG and subsequently published.

After publication, dissemination of the message is of paramount importance. Pocketsize versions and personal digital assistant (PDA)-downloadable versions are useful at the point of care. Some surveys have shown that the intended end-users are sometimes not aware of the existence of guidelines, or simply do not translate them into practice, so this is why implementation programmes for new guidelines form an important component of the dissemination of knowledge. Meetings are organized by the ESC, and are directed towards its member National Societies and key opinion leaders in Europe. Implementation meetings can also be undertaken at national levels, once the guidelines have been endorsed by the ESC member societies, and translated into the national language. Implementation programmes are needed because it has been shown that the outcome of disease may be favourably influenced by the thorough application of clinical recommendations.²

Thus, the task of writing Guidelines or Expert Consensus Documents covers not only the integration of the most recent research, but also the creation of educational tools and implementation programmes for the recommendations. The development of clinical guidelines and implementation into clinical practice can then only be completed if surveys and registries are performed to verify its use in real-life daily practices. Such surveys and registries also make it possible to evaluate the impact of implementation of the guidelines on patient outcomes. Guidelines and recommendations should help physicians and other healthcare providers to make decisions in their daily practice. However, the physician in charge of his/her care must make the ultimate judgement regarding the care of an individual patient.

Introduction

Magnitude of the problem

The present guidelines focus on the cardiological management of patients undergoing non-cardiac surgery, i.e. patients where heart
disease is a potential source of complications during surgery. The risk of perioperative complications depends on the condition of the patient prior to surgery, the prevalence of co-morbidities, and the magnitude and duration of the surgical procedure. More specifically, cardiac complications can arise in patients with documented or asymptomatic ischaemic heart disease (IHD), left ventricular (LV) dysfunction, and valvular heart disease (VHD) who undergo procedures that are associated with prolonged haemodynamic and cardiac stress. In the case of perioperative myocardial ischaemia, two mechanisms are important: (i) chronic mismatch in the supply-to-demand ratio of blood flow response to metabolic demand, which clinically resembles stable IHD due to a flow limiting stenosis in coronary conduit arteries; and (ii) coronary plaque rupture due to vascular inflammatory processes presenting as acute coronary syndromes (ACSs). Hence, although LV dysfunction may occur for various reasons in younger age groups, perioperative cardiac mortality and morbidity are predominantly an issue in the adult population undergoing major non-cardiac surgery.

The magnitude of the problem in Europe can best be understood in terms of (i) the size of the adult non-cardiac surgical cohort; and (ii) the average risk of cardiac complications within this cohort. Unfortunately, at a European level, no systematic data are available on the annual number and type of operations, nor on patient outcome. Information is collected at the national level in several countries, but data definitions, amount of data, and data quality vary greatly. In The Netherlands, with a population of 16 million, throughout 1991–2005, 250 000 major surgical procedures were conducted on average annually in patients above the age of 20 years, implying an annual rate of 1.5%. When applied to Europe, with an overall population of 490 million, this figure translates into a crude estimate of 7 million major procedures annually in patients who present with cardiac risk.

Data on cardiac outcome can be derived from the few large-scale clinical trials and registries that have been undertaken in patients undergoing non-cardiac surgery. Lee et al. studied 4315 patients undergoing elective major non-cardiac procedures in a tertiary care teaching hospital throughout 1989–1994. They
observed that 92 (2.1%) patients suffered major cardiac complications, including cardiac death and myocardial infarction (MI). In a cohort of 108,593 consecutive patients who underwent surgery throughout 1991–2000 in a university hospital in The Netherlands, perioperative mortality occurred in 1877 (1.7%) patients, with a cardiovascular cause being identified in 543 cases (0.5%).6 The Dutch Echocardiographic Cardiac Risk Evaluating Applying Stress Echo (DECREASE) -I, -II and -IV trials enrolled 3893 surgical patients throughout 1996–2008, and these comprised intermediate- and high-risk patients of whom 136 (3.5%) suffered perioperative cardiac death or MI.7–9 A final piece of evidence with respect to patient outcome is derived from the Perioperative Ischaemic Evaluation (POISE) trial, which was conducted throughout 2002–2007, and enrolled 8351 patients undergoing non-cardiac surgery.10 Perioperative mortality occurred in 226 patients (2.7%), of whom 133 (1.6%) suffered cardiovascular death, whereas non-fatal MI was observed in another 367 (4.4%) subjects. Differences in incidences between the studies are mainly explained by patient selection and endpoint MI definitions—major non-cardiac surgery is associated with an incidence of cardiac death of between 0.5 and 1.5%, and of major cardiac complications of between 2.0 and 3.5%. When applied to the population in the European Union member states these figures translate into 150,000–250,000 life-threatening cardiac complications due to non-cardiac surgical procedures annually.

Impact of the ageing population

Within the next 20 years, the acceleration in ageing of the population will have a major impact on perioperative patient management. It is estimated that elderly people require surgery four times more often than the rest of the population.11 Although exact data regarding the number of patients undergoing surgery in Europe are lacking, it is estimated that this number will increase by 25% by 2020, and for the same time period the elderly population will increase by >50%. The total number of surgical procedures will increase even faster because of the rising frequency of interventions with age.12 Results of the US National Hospital Discharge Survey show that, in general, the number of surgical procedures will increase in almost all age groups, but that the largest increase will occur in the middle aged and elderly (Table 3).

Demographics of patients undergoing surgery show a trend towards an increasing number of elderly patients and co-morbidities.13 Although mortality from cardiac disease is decreasing in the general population, the prevalence of IHD, heart failure, and cardiovascular risk factors, especially diabetes, is increasing. Among the significant co-morbidities in elderly patients presenting for general surgery, cardiovascular disease (CVD) is the most prevalent. It is estimated from primary care data that in the 75–84 year age group 19% of men and 12% of women have some degree of CVD.14 Age per se, however, seems to be responsible for only a small increase in the risk of complications; greater risks are associated with urgency and significant cardiac, pulmonary, and renal disease. The number of affected individuals is likely to be higher in countries with high CVD mortality, particularly in Central and Eastern Europe. These conditions should, therefore, have a greater impact on the evaluation of patient risk than age alone.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Change in numbers of discharges for surgical procedures by age for the time periods 1994/95 and 2004/05 as reported from the 2005 US National Hospital Discharge Survey (non-federal short-stay hospitals)15</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Number of procedures (in thousands)</td>
</tr>
<tr>
<td>18–44</td>
<td>7311</td>
</tr>
<tr>
<td>45–64</td>
<td>4111</td>
</tr>
<tr>
<td>65–74</td>
<td>3069</td>
</tr>
<tr>
<td>75 and over</td>
<td>3479</td>
</tr>
<tr>
<td>18 and over</td>
<td>17,969</td>
</tr>
</tbody>
</table>

Purpose

Currently there are no official ESC guidelines on pre-operative risk assessment and perioperative cardiac management. The objective is to endorse a standardized and evidence-based approach to perioperative cardiac management. The guidelines recommend a practical, stepwise evaluation of the patient, which integrates clinical risk factors and test results with the estimated stress of the planned surgical procedure. This results in an individualized cardiac risk assessment, with the opportunity to initiate medical therapy, coronary interventions, and specific surgical and anaesthetic techniques in order to optimize the patient’s perioperative condition. Compared with the non-surgical setting, data from randomized clinical trials, which are the ideal evidence base for the guidelines, are sparse. Therefore, when no trials are available on a specific cardiac management regimen in the surgical setting, data from the non-surgical setting are used, and similar recommendations made, but with different levels of evidence. Emphasis is placed on the restricted use of prophylactic coronary revascularization, as this is rarely indicated simply to ensure the patient survives surgery. Pre-operative evaluation requires an integrated multidisciplinary approach from anaesthesiologists, cardiologists, internists, pulmonologists, geriatricians, and surgeons. Anaesthesiologists, who are experts on the specific demands of the proposed surgical procedure, usually coordinate the process.

Guidelines have the potential to improve post-operative outcome. However, as shown in an observational study of 711 vascular surgery patients from The Netherlands, adherence to guidelines is poor.16–18 Although 185 of a total of 711 patients (26%) fulfilled the ACC/AHA guideline criteria for pre-operative non-invasive cardiac testing, clinicians had performed testing in only 38 of those cases (21%).16 The guideline-recommended medical therapy for the perioperative period, namely the combination of aspirin and statins in all patients and β-blockers in patients with ischaemic heart disease, was followed in only 41% of cases.18 Significantly, the use of evidence-based medication during the perioperative period was associated with a reduction in 3-year mortality after adjustment for clinical characteristics [hazard ratio (HR), 0.65; 95% confidence interval (CI), 0.45–0.94]. These data
highlight the existence of a clear opportunity for improving the quality of care in this high-risk group of patients.

In addition to promoting an improvement in immediate perioperative care, guidelines should provide long-term advice, as patients should live long enough to enjoy the benefits of surgery. Following the development and introduction of perioperative cardiac guidelines, their effect on outcome should be monitored. The objective evaluation of changes in outcome will be an essential part of future perioperative guideline developments.

Pre-operative evaluation

Surgical risk for cardiac events

Cardiac complications after non-cardiac surgery depend not only on specific risk factors but also on the type of surgery and the circumstances under which it takes place. Surgical factors that influence cardiac risk are related to the urgency, magnitude, type, and duration of the procedure, as well as the change in body core temperature, blood loss, and fluid shifts.

Every operation elicits a stress response. This response is initiated by tissue injury and mediated by neuroendocrine factors, and may induce tachycardia and hypertension. Fluid shifts in the perioperative period add to the surgical stress. This stress increases myocardial oxygen demand. Surgery also causes alterations in the balance between prothrombotic and fibrinolytic factors, resulting in hypercoagulability and possible coronary thrombosis (elevation of fibrinogen and other coagulation factors, increased platelet activation and aggregation, and reduced fibrinolysis). The extent of such changes is proportionate to the extent and duration of the intervention. All these factors may cause myocardial ischaemia and heart failure. Certainly in patients at elevated risk, attention to these factors should be given and lead, if indicated, to adaptations in the surgical plan.

Although patient-specific factors are more important than surgery-specific factors in predicting the cardiac risk for non-cardiac surgical procedures, the type of surgery cannot be ignored when evaluating a particular patient undergoing an intervention. With regard to cardiac risk, surgical interventions can be divided into low-risk, intermediate-risk, and high-risk groups with estimated 30-day cardiac event rates (cardiac death and MI) of <1%, 1–5%, and >5%, respectively (Table 4). Although only a rough estimation, this risk stratification provides a good indication of the need for cardiac evaluation, drug treatment, and assessment of risk for cardiac events.

The high-risk group consists of major vascular interventions. In the intermediate-risk category the risk also depends on the magnitude, duration, location, blood loss, and fluid shifts related to the specific procedure. In the low-risk category the cardiac risk is negligible unless strong patient-specific risk factors are present.

The need for, and value of, pre-operative cardiac evaluation will also depend on the urgency of surgery. In the case of emergency surgical procedures, such as those for ruptured abdominal aortic aneurysm (AAA), major trauma, or perforated viscus, cardiac evaluation will not change the course and result of the intervention but may influence the management in the immediate postoperative period. In non-emergent but urgent untreated surgical conditions such as bypass for acute limb ischaemia or treatment of bowel obstruction, the morbidity and mortality of the untreated underlying condition will outweigh the potential cardiac risk related to the intervention. In these cases, cardiological evaluation may influence the perioperative measures taken to reduce the cardiac risk, but will not influence the decision to perform the intervention. In some cases, the cardiac risk can also influence the type of operation and guide the choice to less invasive interventions, such as peripheral arterial angioplasty instead of infrainguinal bypass, or extra-anatomic reconstruction instead of aortic procedure, even when these may yield less favourable results.

<table>
<thead>
<tr>
<th>Table 4 Surgical riska estimate (modified from Boersma et al.)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low-risk &lt;1%</strong></td>
</tr>
<tr>
<td>Breast</td>
</tr>
<tr>
<td>Dental</td>
</tr>
<tr>
<td>Endocrine</td>
</tr>
<tr>
<td>Eye</td>
</tr>
<tr>
<td>Gynaecology</td>
</tr>
<tr>
<td>Reconstructive</td>
</tr>
<tr>
<td>Orthopaedic—minor (knee surgery)</td>
</tr>
<tr>
<td>Urologic—minor</td>
</tr>
</tbody>
</table>

aRisk of MI and cardiac death within 30 days after surgery.
results in the long term. Lastly, in some situations, the cardiac evaluation, in as far as it can reliably predict perioperative cardiac complications and estimate late survival, should be taken into consideration even when deciding whether to perform an intervention or not. This is the case in certain prophylactic interventions such as the treatment of small AAAs or asymptomatic carotid stenosis where the life expectancy of the patient and the risk of the operation are important factors in evaluating the potential benefit of the surgical intervention.

Vascular interventions are of specific interest, not only because they carry the highest risk of cardiac complications, explained by the high probability that the atherosclerotic process also affects the coronary arteries, but also because of the many studies that have shown that this risk can be influenced by adequate perioperative measures in these patients. Open aortic and infra-inguinal procedures have both to be considered as high-risk procedures. Although a less extensive intervention, infra-inguinal revascularization entails a cardiac risk similar to or even higher than aortic procedures. This can be explained by the higher incidence of diabetes, renal dysfunction, IHD, and advanced age in this patient group. This also explains why the risk related to peripheral artery angioplasties, which are minimally invasive procedures, is not negligible. Several randomized trials, as well as community-based studies, have shown that the cardiac risk is substantially lower after endovascular aortic aneurysm repair compared with open repair. This can be related to the lesser tissue damage and the avoidance of aortic cross-clamping and post-operative ileus. However, long-term survival does not seem to be influenced by the surgical technique that is used, but is determined by the underlying cardiac disease. Carotid endarterectomy is considered to be an intermediate-risk procedure. Nevertheless, elevated cardiac risk and late survival should be taken into account in the decision-making process and can influence the choice between endarterectomy or stenting.

Laparoscopic procedures have the advantage of causing less tissue trauma and intestinal paralysis compared with open procedures, resulting in less incisional pain and diminished post-operative fluid shifts related to bowel paralysis. On the other hand, the pneumoperitoneum used in these procedures results in elevated intra-abdominal pressure and a reduction in venous return. It will result in a decrease in cardiac output and an increase in systemic vascular resistance. Therefore, cardiac risk in patients with heart failure is not diminished in patients undergoing laparoscopy compared with open surgery, and both should be evaluated in the same way. This is especially true in patients undergoing interventions for morbid obesity.

### Table 5 Lee index and Erasmus model: clinical risk factors used for pre-operative cardiac risk stratification

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Lee index</th>
<th>Erasmus model</th>
</tr>
</thead>
<tbody>
<tr>
<td>IHD (angina pectoris and/or MI)</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Surgical risk</td>
<td>High-risk surgery</td>
<td>High, intermediate-high, intermediate-low, low risk</td>
</tr>
<tr>
<td>Heart failure</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Stroke/transient ischaemic attack</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Diabetes mellitus requiring insulin therapy</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Renal dysfunction/haemodialysis</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Age</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

IHD = ischaemic heart disease; MI = myocardial infarction.

### Recommendation/statement on surgical risk estimate

<table>
<thead>
<tr>
<th>Recommendation/statement</th>
<th>Classa</th>
<th>Levelb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laparoscopic procedures demonstrate a cardiac stress similar to open procedures and it is recommended that patients be screened prior to intervention accordingly</td>
<td>I</td>
<td>A</td>
</tr>
</tbody>
</table>

*aClass of recommendation.  
*bLevel of evidence.

### Functional capacity

Determination of functional capacity is considered to be a pivotal step in pre-operative cardiac risk assessment. Functional capacity is measured in metabolic equivalents (METs). One MET equals the basal metabolic rate. Exercise testing provides an objective assessment of functional capacity. Without testing, functional capacity can be estimated by the ability to perform the activities of daily living. Given that 1 MET represents metabolic demand at rest, climbing two flights of stairs demands 4 METs, and strenuous sports such as swimming >10 METS (Figure 1).

The inability to climb two flights of stairs or run a short distance (<4 METs) indicates poor functional capacity and is associated with an increased incidence of post-operative cardiac events. After thoracic surgery, a poor functional capacity has been associated with an increased mortality (relative risk 18.7, 95% CI 5.9–59). However, in comparison with thoracic surgery, a poor functional status was not associated with an increased mortality after other non-cardiac surgery (relative risk 0.47, 95% CI 0.09–2.5). This may reflect the importance of pulmonary function, strongly related to functional capacity, as a major predictor of survival after thoracic surgery. These findings were confirmed in a study of 5939 patients scheduled for non-cardiac surgery in which the prognostic importance of pre-operative functional capacity was measured in METs. Using receiver operating characteristic (ROC) curve analysis, the association of functional capacity with post-operative cardiac events or death showed an area under...
the ROC curve of just 0.664, compared with 0.814 for age. Considering the relatively weak association between functional capacity and post-operative cardiac outcome, what importance should we attach to functional capacity assessment in the pre-operative evaluation of the risk of non-cardiac surgery? When functional capacity is high, the prognosis is excellent, even in the presence of stable IHD or risk factors.

In this case, perioperative management will rarely be changed as a result of further cardiac testing and the planned surgical procedure can proceed. Using functional capacity evaluation prior to surgery, the ability to climb two flights of stairs or run for a short distance indicated a good functional capacity. On the other hand, when functional capacity is poor or unknown, the presence and number of risk factors in relation to the risk of surgery will determine pre-operative risk stratification and perioperative management.

Risk indices
Effective strategies aimed at reducing the risk of perioperative cardiac complications should involve cardiac evaluation using medical history prior to the surgical procedure, for two main reasons. First, patients with an anticipated low cardiac risk—after thorough evaluation—can be operated on safely without further delay. It is unlikely that risk reduction strategies can reduce the perioperative risk further. Secondly, risk reduction by pharmacological treatment is most cost-effective in patients with a suspected increased cardiac risk. Additional non-invasive cardiac imaging techniques are tools to identify patients at higher risk. However, imaging techniques should be reserved for those patients in whom test results would influence and change management. Obviously, the intensity of the pre-operative cardiac evaluation must be tailored to the patient’s clinical condition and the urgency of the circumstances requiring surgery. When emergency surgery is needed, the evaluation must necessarily be limited. However, most clinical circumstances allow the application of a more extensive, systematic approach, with cardiac risk evaluation that is initially based on clinical characteristics and type of surgery, and then extended—if indicated—to resting electrocardiography (ECG), laboratory measurements, and non-invasive (stress) testing.

During the last 30 years, several risk indices have been developed, based on multivariable analyses of observational data, which represent the relationship between clinical characteristics and perioperative cardiac mortality and morbidity. The indices that were developed by Goldman (1977), Detsky (1986), and Lee (1999) became well known. The Lee index, which is in fact a modification of the original Goldman index, is considered by many clinicians and researchers to be the best currently available cardiac risk prediction index in non-cardiac surgery. It was developed using prospectively collected data on 2893 unselected patients (and validated in another 1422 patients) who underwent a wide spectrum of procedures. They were followed systematically throughout the post-operative phase for a range of clinically relevant cardiac outcomes. The Lee index contains five independent clinical determinants of major perioperative cardiac events: a history of IHD, a history of cerebrovascular disease, heart failure, insulin-dependent diabetes mellitus, and impaired renal function. High-risk type of surgery is the sixth factor that is included in the index. All factors contribute equally to the index (with 1 point each), and the incidence of major cardiac complications is estimated at 0.4, 0.9, 7, and 11% in patients with an index of 0, 1, 2, and ≥3 points, respectively. The area under the ROC curve in the validation data set was 0.81, indicating that the index has a high capability for discriminating between patients with and without a major cardiac event.

However, the patients studied by Lee et al. cannot be considered to be an average, unselected non-cardiac surgical cohort. Patients...
undergoing thoracic (12%), vascular (21%), and orthopaedic surgery (35%) were over-represented. Furthermore, despite its respectable size, the study was too underpowered to reveal a broad range of cardiac outcome determinants, as only 56 cardiac events were observed in the derivation cohort. Several external validation studies have suggested that the Lee index is probably suboptimal for identifying patients with multiple risk factors. In fact, the type of surgery was only classified as two subtypes: first, high-risk, including intraperitoneal, intrathoracic, and suprapoinal vascular procedures; and, secondly, all remaining non-laparoscopic procedures, mainly including orthopaedic, abdominal, and other vascular procedures. Evidence exists that a more subtle classification, such as the Erasmus model, results in better risk discrimination. In this model, an extensive description of the type of surgery and age increased the prognostic value of the model for perioperative cardiac events (area under the ROC curve for the prediction of cardiovascular mortality increased from 0.63 to 0.85).

Recommendations/statements on cardiac risk stratification

<table>
<thead>
<tr>
<th>Recommendations/statements</th>
<th>Classa</th>
<th>Levelb</th>
</tr>
</thead>
<tbody>
<tr>
<td>It is recommended clinical risk indices be used for post-operative risk stratification</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>It is recommended that the Lee index model applying six different variables for perioperative cardiac risk be used</td>
<td>I</td>
<td>A</td>
</tr>
</tbody>
</table>

*aClass of recommendation.
*bLevel of evidence.

Biomarkers

A biological marker—biomarker—is a characteristic that can be objectively measured and evaluated which is an indicator of abnormal biological and pathogenic processes or responses to therapeutic interventions. In the perioperative setting, biomarkers can be divided into markers focusing on myocardial ischaemia and damage, inflammation, and LV function.

Cardiac troponins T and I (cTnT and cTnI) are the preferred markers for the diagnosis of MI because they demonstrate sensitivity and tissue specificity superior to other available biomarkers. The prognostic information is independent of, and complementary to, other important cardiac indicators of risk such as ST deviation and LV function. The prognostic significance of even small elevations in troponins has been independently confirmed in community-based studies and in clinical trials (TACTICS-TIMI 18, FRISC II, OPUS-TIMI), not only in high-risk, but also in intermediate-risk groups. cTnl and cTnT seem to be of similar value for risk assessment in ACS in the presence and absence of renal failure. The prognosis for all-cause death in patients with end-stage renal disease and with even minor elevations in cTnT is 2–5 times worse than for those with undetectable values. Existing evidence suggests that even small increases in cTnT in the perioperative period reflect clinically relevant myocardial injury with worsened cardiac prognosis and outcome. The development of new biomarkers, including high-sensitivity troponins, will further enhance the assessment of myocardial damage. It should be noted that troponin elevation may be observed in many other conditions. The diagnosis of non-ST-segment elevation myocardial infarction (NSTEMI) should never be made solely on the basis of biomarkers.

Inflammatory markers might identify pre-operatively those patients with an increased risk of unstable coronary plaque. C-reactive protein (CRP) is an acute-phase reactant produced in the liver. CRP is also expressed in smooth muscle cells within diseased atherosclerotic arteries and has been implicated in many aspects of atherogenesis and plaque vulnerability, including expression of adhesion molecules, induction of nitric oxide, altered complement function, and inhibition of intrinsic fibrinolysis. However, in the surgical setting, no data are currently available using CRP as a marker for the initiation of risk reduction strategies.

Pre-operative biomarker use from prospective controlled trials are sparse. Based on the present data, routine assessment of serum biomarkers for patients undergoing non-cardiac surgery cannot be proposed for routine use as an index of cell damage.

Recommendations/statements on biomarkers

<table>
<thead>
<tr>
<th>Recommendations/statements</th>
<th>Classa</th>
<th>Levelb</th>
</tr>
</thead>
<tbody>
<tr>
<td>NT-proBNP and BNP measurements should be considered for obtaining independent prognostic information for perioperative and late cardiac events in high-risk patients</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Routine biomarker sampling to prevent cardiac events is not recommended</td>
<td>III</td>
<td>C</td>
</tr>
</tbody>
</table>

*aClass of recommendation.
*bLevel of evidence.

Non-invasive testing

Pre-operative non-invasive testing aims at providing information on three cardiac risk markers: LV dysfunction, myocardial ischaemia, and heart valve abnormalities, all major determinants of adverse post-operative outcome. LV function is assessed at rest, and various imaging modalities are available. For myocardial ischaemia detection, exercise ECG and non-invasive imaging techniques may be used. The overall theme is that the diagnostic algorithm for risk stratification of myocardial ischaemia and LV function should be similar to that proposed for patients in the non-surgical setting with known or suspected IHD. Non-invasive testing should not
only be considered for coronary artery revascularization but also for patient counselling, change of perioperative management in relation to type of surgery, anaesthetic technique, and long-term prognosis. Echocardiography is preferred for evaluation of valve disease (see section on specific diseases, subheading valvular heart disease).

Non-invasive testing of cardiac disease

Electrocardiography

The 12-lead ECG is commonly performed as part of pre-operative cardiovascular risk assessment in patients undergoing non-cardiac surgery. In IHD patients, the pre-operative electrocardiogram contains important prognostic information and is predictive of long-term outcome independent of clinical findings and perioperative ischaemia. However, the electrocardiogram may be normal or non-specific in a patient with either ischaemia or infarction. The routine use of ECG prior to all types of surgery is a subject of increasing debate. A retrospective study investigated 23,036 patients scheduled for 28,457 surgical procedures; patients with abnormal ECG findings had a greater incidence of cardiovascular death than those with normal ECG results (1.8% vs. 0.3%). In patients who underwent low-risk or low- to intermediate-risk surgery, the absolute difference in the incidence of cardiovascular death between those with and without ECG abnormalities was only 0.5%.

<table>
<thead>
<tr>
<th>Recommendations on ECG</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recommendations</strong></td>
</tr>
<tr>
<td>Pre-operative ECG is recommended for patients who have risk factor(s) and are scheduled for intermediate- or high-risk surgery</td>
</tr>
<tr>
<td>Pre-operative ECG should be considered for patients who have risk factor(s) and are scheduled for low-risk surgery</td>
</tr>
<tr>
<td>Pre-operative ECG may be considered for patients who have no risk factor and are scheduled for intermediate-risk surgery</td>
</tr>
<tr>
<td>Pre-operative ECG is not recommended for patients who have no risk factor and are scheduled for low-risk surgery</td>
</tr>
</tbody>
</table>

Class of recommendation.
Level of evidence.
ECG = electrocardiography.

Non-invasive testing of ischaemic heart disease

Physiological exercise using a treadmill or bicycle ergometer is the preferred method for detection of ischaemia. Physiological exercise provides an estimate of functional capacity, provides blood pressure and heart rate response, and detects myocardial ischaemia through ST-segment changes. The accuracy of exercise ECG varies significantly among studies. Meta-analysis of the reported studies using treadmill testing in vascular surgery patients showed a rather low sensitivity (74%, 95% CI 60–88%) and specificity (69%, 95% CI 60–78%), comparable with daily clinical practice. The positive predictive value was as low as 10%, but the negative predictive value was very high (98%). However, risk stratification with exercise is not suitable for patients with limited exercise capacity due to their inability to reach an ischaemic threshold. Furthermore, pre-existing ST-segment abnormalities, especially in the pre-cordial leads V₅ and V₆ at rest, hamper reliable ST-segment analysis. A gradient of severity in the test result relates to the perioperative outcome: the onset of a myocardial ischaemic response at low exercise workloads is associated with a significantly increased risk of perioperative and long-term cardiac events. In contrast, the onset of myocardial ischaemia at high workloads is associated with significantly less risk. Pharmacological stress testing with either nuclear perfusion imaging or echocardiography is more suitable in patients with limited physical capabilities.

The role of myocardial perfusion imaging for pre-operative risk stratification is well established. In patients with limited exercise capacity, pharmacological stress (dipyridamole, adenosine, or dobutamine) is an alternative stressor. Images reflect myocardial blood distribution at the time of injection. Studies are performed both during stress and at rest to determine the presence of reversible defects, reflecting jeopardized ischaemic myocardium, or fixed defects, reflecting scar or non-viable tissue.

The prognostic value of the extent of ischaemic myocardium, using semi-quantitative dipyridamole myocardial perfusion imaging, has been investigated in a meta-analysis of studies in vascular surgery patients. Study endpoints were perioperative
cardiac death and MI. The authors included nine studies, totalling 1179 vascular surgery patients, with a 7% 30-day event rate. In this analysis, reversible ischaemia in <20% of the LV myocardium did not change the likelihood of perioperative cardiac events, compared with those without ischaemia. Patients with more extensive reversible defects were at increased risk: 20–29% reversibility [likelihood ratio (LR) 1.6, 95% CI 1.0–2.6], 30–39% reversibility (LR 2.9, 95% CI 1.6–5.1), 40–49% reversibility (LR 2.9, 95% CI 1.4–6.2), and ≥50% reversibility (LR 11, 95% CI 5.8–20).

A second meta-analysis, that assessed the prognostic value of six diagnostic tests, reported a sensitivity of 83% (95% CI 77–92%) with a much lower specificity of 47% (95% CI, 41–57%) for myocardial perfusion imaging. The positive and negative predictive values were 11 and 97%, respectively.

A third meta-analysis pooled the results of 10 studies evaluating dipyridamole thallium-201 imaging in vascular surgery candidates over a 9-year period (1985–1994). The 30-day cardiac death or non-fatal MI rates were 1% in patients with normal test results, 7% in patients with fixed defects, and 9% in patients with reversible defects on thallium-201 imaging. Moreover, three out of the 10 studies analysed used semi-quantitative scoring, demonstrating a higher incidence of cardiac events in patients with two or more reversible defects.

Overall, the positive predictive value of reversible defects for perioperative death or MI has decreased over recent years. This is probably related to changes in perioperative management and surgical procedures, resulting in a reduced cardiac event rate in patients with myocardial ischaemia as detected by pre-operative cardiac stress tests. However, because of the high sensitivity of nuclear imaging studies for detecting IHD, patients with a normal scan have an excellent prognosis. Myocardial perfusion imaging using dobutamine stress has a good safety profile. Hypotension, a systolic blood pressure decrease of ≥40 mmHg, occurred in 3.4%, and serious cardiac arrhythmias in 3.8% of cases, in a consecutive series of 1076 patients. All arrhythmias terminated either spontaneously or after metoprolol administration.

Stress echocardiography using exercise or pharmacological (dobutamine, dipyridamole) stress has been widely used for pre-operative cardiac risk evaluation. The test combines information on LV function at rest, heart valve abnormalities, and the presence and extent of stress-inducible ischaemia. In one study, 530 patients were enrolled to evaluate the incremental value of dobutamine stress echocardiography (DSE) for the assessment of cardiac risk before non-vascular surgery. Multivariable predictors of post-operative events in patients with ischaemia were found to be a history of heart failure [odds ratio (OR) 4.7, 95% CI 1.6–14.0] and ischaemic threshold <60% of age-predicted maximal heart rate (OR 7.0, 95% CI 2.8–17.6). DSE identified 60% of patients as low risk (no ischaemia), 32% as intermediate risk (ischaemic threshold ≥60%), and 8% as high risk (ischaemic threshold <60%); post-operative event rates were 0, 9, and 43%, respectively. A recent meta-analysis showed that the sensitivity and specificity of DSE for perioperative cardiac death and MI are high (85 and 70%, respectively). DSE can be performed safely with reasonable patient tolerance [incidence of cardiac arrhythmias and hypotension (defined as a systolic blood pressure decrease of ≥40 mmHg)]. DSE has some limitations, e.g. it should not be used in patients with severe arrhythmias, significant hypertension, large thrombus-laden aortic aneurysms, or hypotension.

In general, stress echocardiography has a high negative predictive value (between 90 and 100%): a negative test is associated with a very low incidence of cardiac events and indicates a safe surgical procedure. However, the positive predictive value is relatively low (between 25 and 45%); this means that the post-surgical probability of a cardiac event is low, despite wall motion abnormality detection during stress echocardiography.

In a meta-analysis of 15 studies comparing dipyridamole thallium-201 imaging and DSE for risk stratification before vascular surgery, it was demonstrated that the prognostic value of stress imaging abnormalities for perioperative ischaemic events is comparable when using available techniques, but that the accuracy varies with IHD prevalence. In patients with a low incidence of IHD, the diagnostic accuracy is reduced compared with those with a high incidence of IHD.

MRI can also be used for detection of ischaemia; both perfusion and wall motion can be detected during stress and at rest. Ischaemia, more than IHD, is associated with adverse post-operative cardiac events. Therefore, functional testing is preferred to the detection of anatomical stenosis. The accuracy for assessment of ischaemia is high, with a sensitivity of 83% (95% CI 79–88%) and specificity of 86% (95% CI 81–91%) when wall motion is used (14 studies, 754 patients). When perfusion is added on top of wall motion abnormalities (24 studies, 1516 patients), sensitivity in the assessment of ischaemia increases to 91% (95% CI 88–94%); however, specificity decreases to 81% (95% CI 77–85%). MRI with dobutamine stress was used in 102 patients undergoing major non-cardiac surgery. New wall motion abnormalities were used as a marker of ischaemia. Applying multivariable analysis, myocardial ischaemia was the strongest predictor of perioperative cardiac events (death, MI, and heart failure). MRI enabled non-invasive angiography and meta-analysis of existing data to be undertaken, using IHD detected by coronary angiography as a reference, and demonstrated sensitivity and specificity of 75% (95% CI 68–80%) and 85% (95% CI 78–90%), respectively, on a vessel basis (16 studies, 2041 vessels); on a patient basis (13 studies, 607 subjects), sensitivity and specificity were 88% (95% CI 82–92%) and 56% (95% CI 53–68%) respectively. Currently no data are available in the setting of pre-operative risk stratification.

CT can be used to detect coronary calcium, which reflects coronary atherosclerosis. In addition, both electron beam and multislice CT have been used for non-invasive angiography, and a meta-analysis of existing data, using IHD detected by coronary angiography as a reference, demonstrated a sensitivity and a specificity of 82% (95% CI 80–85%) and 91% (95% CI 90–92%), respectively, on a vessel basis (eight studies, 2726 vessels); on a patient basis (21 studies, 1570 patients), sensitivity and specificity were 96% (95% CI 94–98%) and 74% (95% CI 65–84%), respectively. Data in the setting of pre-operative risk stratification are not yet available. A word of caution should be given with respect to the risk of radiation. In patients undergoing heart valve surgery, CT angiography has been used to exclude
concomitant IHD, thereby avoiding the need for invasive coronary angiography.62 This approach may also be of use for pre-operative risk stratification; however, currently no data are available in the setting of pre-operative risk stratification.

How can these data be put into a practical algorithm? Testing should only be performed if it changes perioperative management. Patients with extensive stress-induced ischaemia represent a high-risk population in whom standard medical therapy appears to be insufficient to prevent perioperative cardiac events.63 Pre-operative testing may be considered in high-risk surgery patients with fewer than three clinical risk factors. However, in these patients, the beneficial effect of cardioprotective therapy appears to be sufficient to preclude pre-operative stress testing. The results of the randomized, multicentre DECREASE-II study showed that the perioperative cardiac event rate of vascular surgery patients on β-blocker therapy was already so reduced that test results and subsequent alteration in perioperative management were redundant.8 No differences in cardiac death and MI at 30 days were observed between 770 patients assigned to no cardiac stress testing vs. testing (1.8 vs. 2.3%; OR 0.78; 95% CI 0.28–2.1). Importantly, pre-operative testing delayed surgery (mean of 3 weeks) in high-risk surgery patients on β-blocker therapy.64 The overall mortality was 5.9%. Patients who had a VO2peak <11 mL/kg/min (n = 55) had a mortality of 18% compared with those who had a VO2peak >11 mL/kg/min (n = 132) whose mortality was 0.8% (risk ratio 24, 95% CI 3.1–183). In patients who exhibited signs of myocardial ischaemia during testing, the mortality was 42% for patients whose VO2peak was <11 mL/kg/min and only 4% for those whose VO2peak was >11 mL/kg/min (P < 0.001). CPET also carries accurate prognostic information in the setting of heart failure patients: an abnormally high relationship between minute ventilation (VE) and carbon dioxide production (VCO2), expressed as the VE/VCO2 slope measured between the onset of loaded exercise and the end of the isocapnic buffering period, identified by the rise in the VE/VCO2 slope and the reduction of end-tidal expiratory CO2 pressure (PETCO2) (or mixed expired value of alveolar and dead space gas, PaCO2), is associated with a poor outcome, as is an oscillatory pattern of ventilation during exercise, defined as cyclic fluctuations in minute ventilation at rest that persist during effort.68 There are potential discrepancies between a CPET and functional assessment using METs that preclude a widespread use of CPET. Non-cardiac and non-respiratory factors such as skeletal muscle function and physical training can underestimate aerobic metabolic activity. A further consideration must be the availability of CPET testing, which at present is not available in all centres. The role of CPET in pre-operative risk assessment has not been established and CPET should not be considered to be a substitute for stress testing in routine practice.

Recommendations on stress testing prior to surgery

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress testing is recommended in high-risk surgery patients with ≥ 3 clinical factors*</td>
<td>I</td>
<td>C</td>
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<tr>
<td>Stress testing may be considered in intermediate-risk surgery patients with ≤ 2 clinical factors</td>
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<td>Stress testing may be considered in intermediate-risk surgery patients</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>Stress testing is not recommended in low-risk surgery</td>
<td>III</td>
<td>C</td>
</tr>
</tbody>
</table>

*Class of recommendation.
| Level of evidence.
| Clinical risk factors are presented in Table 13.

Angiography

Coronary angiography is a well-established invasive diagnostic procedure but is rarely indicated to assess the risk of non-cardiac surgery. There is a lack of information derived from randomized clinical trials on its usefulness in patients scheduled for non-cardiac surgery. Moreover, adopting an invasive coronary angiography assessment may cause an unnecessary and unpredictable delay in an already planned surgical intervention. Nevertheless, IHD may be present in a significant number of patients in whom non-cardiac surgery is indicated. In patients with known IHD, indications for pre-operative coronary angiography and revascularization are similar to angiography indications in the non-surgical setting.47, 69–71 The control of ischaemia before surgery, either medically or with intervention, is recommended whenever non-cardiac surgery procedures can be delayed.
Recommendations on pre-operative coronary angiography

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Classa</th>
<th>Levelb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-operative angiography is recommended in patients with acute STEMI</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Pre-operative angiography is recommended in patients with NSTEMI and unstable angina</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Pre-operative angiography is recommended in patients with angina not controlled with adequate medical therapy</td>
<td>I</td>
<td>A</td>
</tr>
<tr>
<td>Pre-operative angiography may be considered in cardiac-stable patients undergoing high-risk surgery</td>
<td>IIb</td>
<td>B</td>
</tr>
<tr>
<td>Pre-operative angiography may be considered in cardiac-stable patients undergoing intermediate-risk surgery</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>Pre-operative angiography is not recommended in cardiac-stable patients undergoing low-risk surgery</td>
<td>III</td>
<td>C</td>
</tr>
</tbody>
</table>

\*aClass of recommendation.  
\*bLevel of evidence.  
STEMI = ST-segment elevation myocardial infarction; NSTEMI = non-ST-segment elevation myocardial infarction.

### Risk reduction strategies

#### Pharmacological

The occurrence of MI during the intra- or early post-operative period is frequently preceded by prolonged or recurrent myocardial ischaemia. The stress of surgery and anaesthesia may trigger ischaemia through an imbalance between myocardial oxygen demand and supply. Besides specific risk reduction strategies adapted to patient characteristics and the type of surgery, pre-operative evaluation is an opportunity to check and optimize the control of all cardiovascular risk factors.

#### β-Blockers

During the perioperative period, there is a catecholamine surge, resulting in an increased heart rate and myocardial contractility and subsequent increased myocardial oxygen consumption. The main rationale for perioperative β-blocker use is to decrease myocardial oxygen consumption by reducing heart rate, resulting in a lengthening of the diastolic filling period, and decreased myocardial contractility. Additional cardioprotective factors are redistribution of coronary blood flow to the subendocardium, plaque stabilization, and an increase in the threshold for ventricular fibrillation. Randomized studies have shown that β-blockers and other drugs that lower the heart rate can reduce perioperative myocardial ischaemia as assessed by continuous ST-segment monitoring. However, whether this translates into a clinical benefit can be established only through trials analysing the incidence of cardiovascular events. Seven multicentre randomized trials evaluating the effect of perioperative β-blockade on clinical endpoints have been published in peer-reviewed journals (Table 6 and Figure 2).
Three trials targeted patients at high risk for perioperative complications because of the type of surgery, the presence of IHD, or risk factors for perioperative cardiac complications. Three other trials did not require the presence of clinical risk factors, except for diabetes in one case. The POISE trial included patients with a wide spectrum of risk of perioperative cardiac complications.

The first trial randomized 200 patients with at least two risk factors for IHD or with known IHD, who were scheduled for non-cardiac surgery under general anaesthesia, including 40% major vascular surgery procedures. Atenolol was associated with a significant decrease in overall mortality and an increase in event-free survival at 6 months, and this benefit was sustained for up to 2 years. The Dutch Echographic Cardiac Risk Evaluating Applying Stress Echo (DECREASE) trial selected 112 out of 1453 vascular surgery patients who combined at least one clinical risk factor and positive DSE, excluding patients with extensive wall motion abnormalities. Patients were randomized to standard care or bisoprolol, which was started at least 1 week before surgery and titrated according to heart rate. There was an 89% reduction in cardiac mortality and/or MI in the bisoprolol group (3.4% vs. 34%, \( P < 0.001 \)), which was sustained for up to 3 years.

The PeriOperative Beta-BlockadE (POBBLE) trial included 103 low-risk patients undergoing elective infrarenal vascular surgery, randomized to metoprolol tartrate or placebo. The incidence of death, MI, or stroke at 30 days did not differ between the metoprolol and placebo groups (13 and 15%, respectively, \( P = 0.78 \)). Patients were at low cardiac risk and those with a history of MI within the previous 2 years were excluded. In the Metoprolol after Vascular Surgery (MaVS) trial, 497 patients undergoing abdominal or infringuinal vascular surgery were randomized to metoprolol succinate or placebo. The combined endpoint of death, MI, heart failure, arrhythmias, or stroke at 30 days did not differ between the metoprolol and placebo groups (10.2 and 12%, respectively, \( P = 0.57 \)). The Lee index was ≤2 in 90% of patients and ≤1 in 60%.

The Diabetes Postoperative Mortality and Morbidity (DIPOM) trial selected 921 patients with diabetes, age >39 years, and a duration of surgery of >1 h (39% low-risk surgery). Patients were randomized to receive metoprolol succinate or placebo. The combined endpoint of death, MI, unstable angina, or heart failure at 30 days did not differ between the metoprolol and placebo groups (6 and 5%, respectively, \( P = 0.66 \)). However, only 54% of the patients had a history of IHD, or an additional cardiac risk factor, and underwent high- or intermediate-risk surgery.

In the POISE trial, 8351 patients were randomized to metoprolol succinate or placebo. Patients were aged ≥45 years and were included if they had known CVD, at least three out of seven clinical risk factors, or were scheduled for major vascular surgery. Treatment consisted of metoprolol succinate, 100 mg 2–4 h prior to surgery, 100 mg during the first 6 h after surgery, but withheld if systolic blood pressure dipped below 100 mmHg. Maintenance therapy was started 12 h later, bringing the total dose of metoprolol succinate in the first 24 h to 400 mg, at least in a number of patients. There was a 17% decrease in the composite endpoint, defined as death, MI, or non-fatal cardiac arrest at 30 days (5.8% vs. 6.9%, \( P = 0.04 \)). However, the 30% decrease in non-fatal MI (3.6% vs. 5.1%, \( P < 0.001 \)) was partially offset by a 33% increase in total mortality (3.1% vs. 2.3%, \( P = 0.03 \)) and a 2-fold increase in stroke (1.0% vs. 0.5%, \( P = 0.005 \)). Hypotension was more frequent in patients receiving metoprolol (15.0% vs. 9.7%, \( P < 0.0001 \)). Post hoc analysis showed that hypotension had the largest population-attributable risk for death and stroke.

Seven meta-analyses have pooled 5, 11, 6, 15, 8, 22 and 33 randomized published trials on perioperative \( \beta \)-blockers, totalling respectively 586, 866, 632, 1077, 2437, 2057, and 12306 patients. Five meta-analyses gave consistent results showing a significant reduction in perioperative myocardial ischaemia and MI in patients receiving \( \beta \)-blockers. These meta-analyses gave consistent results showing a significant reduction in perioperative myocardial ischaemia, MI, and cardiac mortality in patients.
receiving β-blockers.\textsuperscript{84,85} Risk reduction was more marked in high-risk patients. The most recent meta-analysis concluded that β-blockers result in 16 fewer non-fatal MIs per 1000 patients treated, but at the expense of three non-fatal disabling strokes and (possibly) three fatal cardiac or non-cardiac complications.\textsuperscript{86} However, it should be acknowledged that the recent POISE trial had the greatest weight in all of the above analyses. Indeed, ~80% of the deaths, MIs, and strokes in this meta-analysis are derived from POISE, and this proportion was as high as 84% in the trials labelled low-bias risk. Hence, a more detailed analysis of the results of POISE compared with non-POISE trials is warranted (Table 7). First, in POISE, all-cause mortality was increased by 34% in patients receiving β-blockers; in the non-POISE trials the point estimate of treatment effect was consistent with a reduced, although not statistically significant, all-cause and cardiovascular mortality by β-blockers. The differential treatment effect seems to be caused by the high mortality in POISE patients who are given β-blockers (3.1% vs. 1.9% in non-POISE trials), and not by differences in patients allocated to control therapy (2.3% vs. 2.5%). Therefore, understanding of the cause and timing of deaths in POISE is important. Perioperative death in POISE patients allocated to metoprolol succinate was associated with perioperative hypotension, bradycardia, and stroke. A history of cerebrovascular disease was associated with an increased risk of stroke. Hypotension can be related to the use of a high dose of metoprolol without dose titration. It is considered that 200 mg of metoprolol has approximately the same strength of β-blockade as 100 mg of atenolol and 10 mg of bisoprolol.

Discrepancies in the protective role of β-blockers can be explained by differences in patient characteristics, type of surgery, and the modalities of β-blockade (timing of onset, duration, dose titration, and type of drug). Also, these findings may be hampered by the inclusion of numerous trials which were not designed to assess the effect on perioperative cardiac risk or which used only a single β-blocker dose before anaesthesia without continuation after surgery.\textsuperscript{84} A recent meta-analysis suggested that most differences between trials on the cardioprotective effect of β-blockers could be attributed to the variability in heart rate response.\textsuperscript{86} In particular, the decrease in post-operative MI was highly significant when there was tight heart rate control.

Although observational studies should be interpreted with caution, they provide additional insights into the interactions between risk stratification and perioperative β-blockade. In a prospective cohort comprising 1351 patients undergoing vascular surgery, 360 (27%) were treated using β-blockers.\textsuperscript{63} In a study population of 1351 patients, 83% had <3 clinical risk factors. They experienced a lower risk of death or MI when using β-blockers (0.8%) than without (2.3%). In the 17% of patients who had ≥3 risk factors, the risk of death or MI was reduced using β-blockers from 5.8 to 2.0% when stress-induced ischaemia was absent and from 33 to 2.8% when stress-induced ischaemia was limited (1–4 myocardial segments). Patients with extensive stress-induced ischaemia (≥5/16 myocardial segments) had a particularly high risk of death or MI whatever the treatment used (33% with β-blockers and 36% without). A large retrospective cohort drawn from a quality of care database analysed 663 635 patients undergoing non-cardiac surgery (30% high risk surgery).\textsuperscript{87}
comparison of in-hospital mortality between 119,632 patients receiving β-blockers and 216,220 propensity-matched patients without β-blockers showed no difference overall (2.3% vs. 2.4%, respectively, \( P = 0.68 \)). However, there were marked differences according to patient risk profile. β-Blocker use was associated with a significant decrease in mortality when the Lee index was \( \geq 3 \). No significant difference was observed for a Lee index of 1 or 2. Mortality was increased in the lowest risk group (Lee index of 0).

Randomized trials selecting high-risk patients, cohort studies, and meta-analyses provide consistent evidence supporting a decrease in cardiac mortality and MI by β-blockers in patients with clinical risk factors undergoing high-risk (mainly vascular) surgery. Perioperative β-blockade is also cost-effective in these patients. However, patients with extensive ischaemia as demonstrated by stress testing are at particularly high risk of perioperative cardiac complications, despite perioperative β-blockers.

Conversely, randomized trials including low-risk patients and cohort studies suggest that perioperative β-blockade does not decrease the risk of cardiac complications in patients without clinical risk factors. The possibility of a harmful effect on mortality has been suggested by a retrospective cohort\(^9\) and the POISE trial.\(^10\) Bradycardia and hypotension may be harmful in patients with atherosclerosis, and possibly favour stroke.

This does not justify exposing low-risk patients to potential side effects in the absence of proven benefit. The issue remains debatable in intermediate-risk patients, i.e. those with one or two clinical risk factors. Results of the DECREASE IV trial suggest that β-blockers should also be used in patients undergoing intermediate-risk surgery.\(^98\) Patients randomized to bisoprolol (n = 533) had a lower incidence of the primary efficacy endpoint than those randomized to bisoprolol-control therapy (2.1% vs. 6.0% events, HR 0.34, 95% CI 0.17–0.67). An increased mortality following pre-operative β-blocker withdrawal has been reported in observational studies.\(^89,90\) β-Blockers should be continued when prescribed for IHD or arrhythmias. When β-blockers are prescribed for hypertension, the absence of evidence in favour of a perioperative cardioprotective effect with other antihypertensive drugs does not support a change of therapy. β-Blockers should not be withdrawn in patients treated for stable heart failure due to LV systolic dysfunction. In decompensated heart failure, β-blocker therapy may need to be reduced, or temporarily omitted.\(^91\) If possible, non-cardiac surgery should be deferred so that it can be performed under optimal medical therapy in a stable condition. Contra-indications to β-blockers (asthma, severe conduction disorders, symptomatic bradycardia, and symptomatic hypotension) should be respected. β-Blockers are not contra-indicated in patients with intermittent claudication, as in randomized trials, worsening of symptoms has not been shown to occur more frequently.\(^92\) Furthermore, a recent study showed that cardioselective β-blockers were associated with reduced mortality in patients with chronic obstructive pulmonary disease (COPD) undergoing vascular surgery.\(^93\) In the absence of contra-indications, β-blocker dose should be titrated to achieve a heart rate between 60 and 70 beats/min. β1-Selective blockers without intrinsic sympathomimetic activity are favoured.

### Recommendations on β-blockers\(^a\)

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class(^b)</th>
<th>Level(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-Blockers are recommended in patients who have known IHD or myocardial ischaemia according to pre-operative stress testing(^a)</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>β-Blockers are recommended in patients scheduled for high-risk surgery(^a)</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Continuation of β-blockers is recommended in patients previously treated with β-blockers because of IHD, arrhythmias, or hypertension</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>β-Blockers should be considered for patients scheduled for intermediate-risk surgery(^a)</td>
<td>IIA</td>
<td>B</td>
</tr>
<tr>
<td>Continuation in patients previously treated with β-blockers because of chronic heart failure with systolic dysfunction should be considered</td>
<td>IIA</td>
<td>C</td>
</tr>
<tr>
<td>β-Blockers may be considered in patients scheduled for low-risk surgery with risk factor(s)</td>
<td>IIB</td>
<td>B</td>
</tr>
<tr>
<td>Perioperative high-dose β-blockers without titration are not recommended</td>
<td>III</td>
<td>A</td>
</tr>
<tr>
<td>β-Blockers are not recommended in patients scheduled for low-risk surgery without risk factors</td>
<td>III</td>
<td>B</td>
</tr>
</tbody>
</table>

\(^a\)Treatment should be initiated optimally between 30 days and at least 1 week before surgery. Target: heart rate 60–70 beats/min, systolic blood pressure > 100 mmHg.

\(^b\)Class of recommendation.

\(^c\)Level of evidence.

IHD = ischaemic heart disease.

Treatment onset and the choice of the optimal dose of β-blockers are closely linked. Perioperative myocardial ischaemia and troponin release are reduced, and long-term outcome is improved, in patients who have a lower heart rate.\(^94\) On the other hand, bradycardia and hypotension should be avoided. This highlights the importance of preventing overtreatment with fixed high initial doses. The dose of β-blockers should be titrated, which requires that treatment be initiated optimally between 30 days and at least 1 week before surgery. It is recommended that treatment start with a daily dose of 2.5 mg of bisoprolol or 50 mg of metoprolol succinate which should then be adjusted before surgery to achieve a resting heart rate of between 60 and 70 beats/min with systolic blood pressure > 100 mmHg. The goal for heart rate is the same during the whole perioperative period, using i.v. administration when oral administration is not possible. Post-operative tachycardia should result in the first instance in the treatment of the underlying cause, for example hypovolaemia, pain, blood loss, or infection, rather than the β-blocker dose simply being increased.

The optimal duration of perioperative β-blocker therapy cannot be derived from randomized trials. The occurrence of delayed cardiac events is an incentive to continue β-blocker therapy for at least several months. Long-term β-blocker therapy should be used in patients who had a positive pre-operative stress test. Current concepts of cardioprotection have led to recommendations to use selective β\(_1\)-blockers without intrinsic sympathomimetic activity and with a long half-life, e.g. bisoprolol.
**Statins**

3-Hydroxy-3-methylglutaryl co-enzyme A reductase inhibitors (statins) are widely prescribed in patients with or at risk of IHD because of their lipid-lowering effect. Patients with non-coronary atherosclerosis (carotid, peripheral, aortic, renal) should receive statin therapy for secondary prevention, independently of non-cardiac surgery. Statins also induce coronary plaque stabilization by decreasing lipid oxidation, inflammation, matrix metalloproteinase, and cell death, and by increasing tissue inhibitor of metalloproteinase and collagen. These so-called non-lipid or pleiotropic effects may prevent plaque rupture and subsequent MI in the perioperative period.

Multiple large clinical trials and observational studies have demonstrated a beneficial effect of perioperative statin use. In the first prospective, randomized controlled trial, 100 patients scheduled for vascular surgery were allocated to 20 mg of atorvastatin or placebo once a day for 45 days, irrespective of their serum cholesterol concentration. Vascular surgery was performed on average 31 days after randomization, and patients were followed-up over 6 months. During these 6 months of follow-up, atorvastatin significantly reduced the incidence of cardiac events (8% vs. 26%, P = 0.03). A meta-analysis of 223,010 patients from 12 retrospective and three prospective trials showed that statins reduced mortality significantly by 44% in non-cardiac surgery and by 59% in vascular surgery. The most recent randomized controlled trial was the DECREASE III study. A total of 497 vascular surgery patients were allocated to either fluvastatin (extended release 80 mg once daily) or placebo, starting 37 days prior to surgery. The incidence of myocardial ischaemia in patients allocated to fluvastatin or placebo was 10.8% vs. 19.0%, respectively (OR 0.55, 95% CI 0.34–0.88). Failure to detect statin-induced myopathy and rhabdomyolysis may then lead to the statin being continued and the subsequent effects may prevent plaque rupture and subsequent MI in the perioperative period.

A concern related to the use of perioperative statin therapy has been the risk of statin-induced myopathy and rhabdomyolysis. Perioperatively, factors increasing the risk of statin-induced myopathy are numerous, e.g., the impairment of renal function after major surgery, and multiple drug use during anaesthesia. Furthermore, the use of analgesic drugs and post-operative pain may mask signs of myopathy. Failure to detect statin-induced myopathy may then lead to the statin being continued and the subsequent development of rhabdomyolysis and acute renal failure. However, no studies have been published that support this concern, except for some case reports. In a retrospective study of 981 consecutive patients undergoing vascular surgery, no cases of rhabdomyolysis, significantly higher creatine kinase level, or increased incidence of myopathy were observed in statin users.

Recently it has been suggested that discontinuation of statins may cause a rebound effect and be disadvantageous. A potential limitation of perioperative statin use is the lack of an i.v. formulation.

Therefore, statins with a long half-life or extended release formulations such as rosuvastatin, atorvastatin, and fluvastatin extended release are recommended, to bridge the period immediately after surgery when oral intake is not feasible.

**Nitrates**

Nitroglycerin is well known to reverse myocardial ischaemia. One small but controlled study has demonstrated decreased perioperative myocardial ischaemia in patients with stable angina given i.v. nitroglycerin during non-cardiac surgery. However, no effect was observed on the incidence of MI or cardiac death. These observations were confirmed in a similar study, showing no effect on either myocardial ischaemia, MI, or cardiac death. Furthermore, perioperative use of nitroglycerin may pose a significant haemodynamic risk to the patients. Decreased preload may lead to tachycardia, and hypotension.

**Angiotensin-converting enzyme inhibitors**

Independently of the blood pressure-lowering effect, angiotensin-converting enzyme (ACE) inhibitors preserve organ function. This effect is related to improvement of endothelial function, anti-inflammatory properties, and a direct interference with atherogenesis. The inhibition of ACE may prevent events related to myocardial ischaemia and LV dysfunction. Therefore, it seems reasonable to suggest that perioperative treatment with ACE inhibitors may have beneficial effects on post-operative outcome.

The QUO VADIS study compared the effect of the ACE inhibitor quinapril with that of placebo in patients undergoing cardiac surgery. Quinapril treatment was started 4 weeks before elective surgery and was continued up to 1 year after surgery. This trial demonstrated that post-operative cardiovascular events were significantly reduced (HR 0.23, 95% CI 0.06–0.87) in patients treated with quinapril. The beneficial effect in the QUO VADIS study, however, could be the result of the post-operative treatment. A recent review provided conflicting data concerning ACE inhibitors after cardiac surgery.
Additionally, perioperative use of ACE inhibitors carries a risk of severe hypotension under anaesthesia, in particular following induction and concomitant β-blocker use. Hypotension is less frequent when ACE inhibitors are discontinued the day before surgery. Although this remains debated, ACE inhibitor withdrawal may be considered 24 h before surgery when they are prescribed for hypertension. They should be resumed after surgery as soon as volume is stable. The risk of hypotension is at least as high with angiotensin receptor blockers (ARBs) as with ACE inhibitors, and the response to vasopressors may be impaired. In patients with LV systolic dysfunction who are in a stable clinical condition, it seems reasonable to continue ACE inhibitors during the perioperative period under close monitoring. When LV dysfunction is discovered during pre-operative evaluation in untreated patients in stable condition, surgery should be postponed, if possible, to introduce ACE inhibitors and β-blockers as recommended by the ESC Guidelines on heart failure.91

### Recommendations on ACE inhibitor use

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Classa</th>
<th>Levelb</th>
</tr>
</thead>
<tbody>
<tr>
<td>It is recommended that ACE inhibitors be continued during non-cardiac surgery in stable patients with LV systolic dysfunction.</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>ACE inhibitors are recommended in cardiac-stable patients with LV systolic dysfunction scheduled for high-risk surgery</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>ACE inhibitors should be considered in cardiac-stable patients with LV systolic dysfunction scheduled for low-/intermediate-risk surgery</td>
<td>IIa</td>
<td>C</td>
</tr>
<tr>
<td>Transient discontinuation of ACE inhibitors before non-cardiac surgery in hypertensive patients should be considered.</td>
<td>IIa</td>
<td>C</td>
</tr>
</tbody>
</table>

*aClass of recommendation.

*bLevel of evidence.

ACE = angiotensin-converting enzyme; LV = left ventricular.

### Calcium channel blockers

The effect of calcium channel blockers on the balance between myocardial oxygen supply and demand makes them theoretically suitable for risk reduction strategies. It is necessary to distinguish between dihydropyridines that do not act directly on heart rate and diltiazem or verapamil that lower the heart rate.

The relevance of randomized trials assessing the perioperative effect of calcium channel blockers is limited by their small size, the lack of risk stratification, and the absence of the systematic reporting of cardiac death and MI. A meta-analysis pooled 11 randomized trials totalling 1007 patients. All patients underwent non-cardiac surgery under calcium channel blockers (diltiazem in seven trials, verapamil in two, and nifedipine in one, and one other trial incorporated three arms: control, diltiazem, and nifedipine).109 There was a significant reduction in the number of episodes of myocardial ischaemia and supraventricular tachycardia (SVT) in the pooled analyses on calcium channel blockers. However, the decrease in mortality and MI reached statistical significance only when both endpoints were combined in a composite endpoint of death and/or MI (relative risk 0.35, 95% CI 0.08–0.83, P = 0.02). Subgroup analyses favoured diltiazem. Another study in 1000 patients having acute or elective aortic aneurysm surgery showed that dihydropyridine calcium channel blocker use was independently associated with an increased incidence of perioperative mortality.110 The use of short-acting dihydropyridines, in particular nifedipine capsules, should be avoided.

Thus, although heart rate-reducing calcium channel blockers are not indicated in patients with heart failure and systolic dysfunction, in patients who have contra-indications to β-blockers the continuation or the introduction of heart rate-reducing calcium channel blockers may be considered.

### Recommendations on calcium channel blockers

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Classa</th>
<th>Levelb</th>
</tr>
</thead>
<tbody>
<tr>
<td>It is recommended that calcium channel blockers be continued during non-cardiac surgery in patients with Prinzmetal angina pectoris</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Heart rate-reducing calcium channel blockers, in particular diltiazem, may be considered before non-cardiac surgery in patients who have contra-indications to β-blockers</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>Routine use of calcium channel blockers to reduce the risk of perioperative cardiovascular complications is not recommended</td>
<td>III</td>
<td>C</td>
</tr>
</tbody>
</table>

*aClass of recommendation.

*bLevel of evidence.

### Ivabradine

Ivabradine is a specific inhibitor of the pacemaker in the sino-atrial node and reduces heart rate independently of sympathetic activation. It does not affect blood pressure or myocardial contractility. In a randomized trial of 111 vascular surgery patients, both ivabradine and metoprolol succinate reduced the incidence of ischaemia and MI significantly when compared with placebo. These preliminary findings need to be confirmed by future studies; ivabradine might be considered for patients with strict contra-indications to β-blockers.111

### α2 Receptor agonists

α2 Receptor agonists reduce post-ganglionic noradrenaline output and therefore might reduce the catecholamine surge during surgery. The European Mivazerol trial randomized 1897 patients with IHD who underwent intermediate- or high-risk non-cardiac surgery.112 Mivazerol did not decrease the incidence of death or MI in the whole population. However, there was a reduction of post-operative death or MI observed in a subpopulation of 904 vascular surgery patients. A more recent study including 190 patients with clinical risk factors or IHD showed a decrease in 30-day and 2-year mortality after perioperative use of clonidine.113 However, there was no decrease in MI. A meta-analysis pooled 23 randomized trials, which included cardiac surgery in 10, vascular surgery in eight, and non-vascular surgery in three cases.114
Perioperative use of α2 receptor agonists was associated with a decrease in mortality and MI only in the subgroup having vascular surgery, while there was no benefit in non-vascular surgery.

<table>
<thead>
<tr>
<th>Recommendations on α₂ receptor agonists</th>
<th>Classa</th>
<th>Levelb</th>
</tr>
</thead>
<tbody>
<tr>
<td>α₂ Receptor agonists may be considered to reduce the risk of perioperative cardiovascular complications in vascular surgery patients</td>
<td>IIb</td>
<td>B</td>
</tr>
</tbody>
</table>

**Level of evidence.**

Diuretics

Diuretics are a frequent pharmacological treatment in patients with hypertension or heart failure as underlying diseases. In hypertension, diuretics are usually used at low dose with relatively moderate blood pressure-lowering effect. In general, diuretics for hypertension can be discontinued on the day of surgery, and resumed orally when possible. If blood pressure reduction is required before oral therapy can be continued, other antihypertensive agents given i.v. may be preferred. In heart failure, diuretics are often used at high dose. Dosage increase should be considered if signs of fluid retention are present. Dosage reduction should be considered if there is risk of hypovolaemia, hypotension, and electrolyte disturbances. In general, diuretic treatment, if necessary to control heart failure, should be continued up to the day of surgery, and resumed orally when possible. In the perioperative period, volume status in patients with heart failure should be carefully monitored and loop diuretics may be given i.v. to control volume overload.

In any patient given diuretics, the possibility of electrolyte disturbance should be considered, as diuretics increase renal excretion of K and Mg. Hypokalaemia is reported to occur in up to 34% of patients undergoing surgery (mostly non-cardiac). Hypokalaemia is well known to increase significantly the risk of ventricular tachycardia (VT) and ventricular fibrillation in cardiac disease. In a study of 688 patients with cardiac disease undergoing non-cardiac surgery, hypokalaemia was independently associated with perioperative mortality. On the other hand, in a study of 150 patients undergoing non-cardiac surgery, no increase in intraoperative arrhythmias was observed with hypokalaemia. However, this latter study was relatively small and most patients had no evidence of cardiac disease. Significantly, the use of K- and Mg-sparing diuretics, i.e. aldosterone antagonists (spironolactone and eplerenone), is now well known to reduce mortality in severe heart failure. In general, K and Mg homeostasis should be evaluated pre-operatively. Special attention should be given to patients on diuretics and patients prone to develop arrhythmia. Any electrolyte disturbance—especially hypokalaemia and hypomagnesaemia—should be corrected in due time before surgery. Dietary advice to increase intake of K and Mg should be given; depleting drugs should, if possible, be reduced; sparing diuretics may be added or preferred; and supplementation may be given. Acute pre-operative repletion in asymptomatic patients may be associated with more risks than benefits. Thus, minor, asymptomatic electrolyte disturbances should not delay acute surgery.

<table>
<thead>
<tr>
<th>Recommendations on diuretics</th>
<th>Classa</th>
<th>Levelb</th>
</tr>
</thead>
<tbody>
<tr>
<td>It is recommended that electrolyte disturbances be corrected before surgery</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>It is recommended that hypertensive patients discontinue low-dose diuretics on the day of surgery and resume orally when possible</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>It is recommended that diuretics be continued in heart failure patients up to the day of surgery, resumed intravenously perioperatively, and continued orally when possible</td>
<td>I</td>
<td>C</td>
</tr>
</tbody>
</table>

**Class of recommendation.**

**Level of evidence.**

Aspirin

Though aspirin is widely used in patients with IHD and especially after coronary stent placement, the evidence of aspirin in the perioperative period setting is limited. In a randomized trial of 232 patients undergoing carotid endarterectomy, aspirin was shown to be effective in preventing intraoperative and post-operative stroke, though no effect on death or MI was noted. A meta-analysis in 2001 demonstrated a reduction in serious vascular events and vascular death in vascular surgery patients. This study included 10 trials of antiplatelet treatment in lower limb bypass surgery of which six involved aspirin treatment. However, the benefit of antiplatelet therapy did not reach statistical significance for the combined endpoint of vascular events (OR = 0.8, 95% CI 0.5–1.1) in this vascular surgery population.

Concerns of promoting perioperative haemorrhagic complications often led to the discontinuation of aspirin in the perioperative period. A large meta-analysis, including 41 studies in 49 590 patients, which compared peri-procedural withdrawal vs. bleeding risks of aspirin, concluded that the risk of bleeding complications was increased by 1.5 but that aspirin did not lead to higher severity levels of bleeding complications. A systematic review in subjects at risk of or with IHD demonstrated that aspirin non-adherence/withdrawal was associated with a 3-fold higher risk of major adverse cardiac events (OR = 3.14, 95% CI 1.8–5.6). Aspirin should only be discontinued if the bleeding risk outweighs the potential cardiac benefit. Prior to minor surgical or endoscopic procedures, a careful consideration should be given to the question of withdrawing antithrombotic medications. In principle and based on individualized ‘risk to benefit’ assessments, there is often no need for stopping the antiplatelet treatment prior to the aforementioned procedures in patients who are taking antiplatelet medications. For patients receiving antiplatelet therapy, i.e. aspirin, clopidogrel, or both, with excessive or life-threatening perioperative bleeding, transfusion of platelets or administration of other prohaemostatic agents is recommended.
Anticoagulant therapy

Anticoagulant therapy is associated with increased bleeding during non-cardiac surgery. In some patients, this risk will be outweighed by the benefit of anticoagulant therapy, and drug therapy should be maintained or modified, whereas in other patients with low risk of thrombosis, therapy should be stopped in order to minimize bleeding complications.

Patients treated with oral anticoagulant therapy with vitamin K antagonists (VKAs) have an increased risk of periprocedural and post-procedural bleeding. If the international normalized ratio (INR) is <1.5, surgery can be performed safely (Table 8). However, in patients with a high risk of thromboembolism, discontinuation of VKAs is hazardous and these patients will need bridging therapy with unfractionated heparin (UFH) or therapeutic-dose low molecular weight heparin (LMWH) i.v. or s.c.\textsuperscript{123–125} A high thromboembolic risk is present among other conditions, in patients with atrial fibrillation (AF), mechanical prosthetic heart valves, biological prosthetic heart valves or mitral valvular repair within the last 3 months, or recent venous thromboembolism (<3 months) plus thrombophilia. Bridging therapy is now most often performed with therapeutic-dose s.c. LMWH. VKAs are stopped 5 days (i.e. five doses of VKA) prior to surgery; LMWH or UFH are started 1 day after acenocoumarol interruption, and 2 days after warfarin interruption. In high thromboembolic risk patients, 70 U/kg of antifactor Xa twice daily are recommended and prophylactic once-daily doses in low-risk patients (Table 9).\textsuperscript{126} The last dose of LMWH should be administered at least 12 h before the procedure. In patients with mechanical prosthetic heart valves, the evidence for i.v. UFH is more solid. Thus, in some centres these patients are hospitalized and treated with i.v. UFHs up until 4 h prior to surgery, and treatment with UFH is resumed after surgery until the INR is in the therapeutic range.\textsuperscript{124} On the day of the procedure, the INR is checked.

Table 8  Bridging therapy of VKA with UFH or LMWH in high- and low-risk patients/procedures\textsuperscript{125}

<table>
<thead>
<tr>
<th>INR</th>
<th>LMWH or UFH is continued until the INR has returned to therapeutic levels.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Low thromboembolic risk/low bleeding risk</strong></td>
</tr>
<tr>
<td></td>
<td>• Continue anticoagulant therapy with INR in therapeutic range.</td>
</tr>
<tr>
<td></td>
<td><strong>Low thromboembolic risk/high bleeding risk</strong></td>
</tr>
<tr>
<td></td>
<td>• Discontinue anticoagulant therapy 5 days before the procedure.</td>
</tr>
<tr>
<td></td>
<td>• Start LMWH prophylaxis once daily or UFH i.v. 1 day after acenocoumarol</td>
</tr>
<tr>
<td></td>
<td>interruption, and 2 days after warfarin interruption. Administer the</td>
</tr>
<tr>
<td></td>
<td>last dose of LMWH at least 12 h before the procedure or give UFH i.v.</td>
</tr>
<tr>
<td></td>
<td>up to 4 h prior to surgery.</td>
</tr>
<tr>
<td></td>
<td>• Resume LMWH or UFH at the pre-procedural dose 1–2 days (at least 12 h)</td>
</tr>
<tr>
<td></td>
<td>after the procedure according to haemostatic status. Resume anticoagulant</td>
</tr>
<tr>
<td></td>
<td>therapy 1 to 2 days after surgery at the pre-procedural dose + 50%</td>
</tr>
<tr>
<td></td>
<td>boost dose for two consecutive days according to the haemostatic status.</td>
</tr>
<tr>
<td></td>
<td><strong>High thromboembolic risk</strong></td>
</tr>
<tr>
<td></td>
<td>• Discontinue anticoagulant therapy 5 days before the procedure.</td>
</tr>
<tr>
<td></td>
<td>• Start therapeutic LMWH twice daily or UFH i.v. 1 day after acenocoumarol</td>
</tr>
<tr>
<td></td>
<td>interruption, and 2 days after warfarin interruption. Administer the</td>
</tr>
<tr>
<td></td>
<td>last dose of LMWH at least 12 h before the procedure or give UFH i.v.</td>
</tr>
<tr>
<td></td>
<td>up to 4 h prior to surgery.</td>
</tr>
<tr>
<td></td>
<td>• Resume LMWH or UFH at the pre-procedural dose 1–2 days (at least 12 h)</td>
</tr>
<tr>
<td></td>
<td>after the procedure according to haemostatic status. Resume anticoagulant</td>
</tr>
<tr>
<td></td>
<td>therapy 1–2 days after surgery at the pre-procedural dose + 50% boost</td>
</tr>
<tr>
<td></td>
<td>dose for two consecutive days according to the haemostatic status.</td>
</tr>
<tr>
<td></td>
<td>• LMWH or UFH is continued until the INR has returned to therapeutic levels.</td>
</tr>
</tbody>
</table>

\textsuperscript{125}LMWH = low molecular weight heparin; UFH = unfractionated heparin.
Consideration should be given to postponing the procedure if the INR is >1.5. LMWH or UFH is resumed at the pre-procedural dose 1–2 days after surgery, depending on the haemostatic status, but at least 12 h after the procedure. Oral anticoagulants should be resumed on day 1 or 2 after surgery depending on haemostasis sufficiency (if the patient can take oral therapy) at the pre-operative maintenance dose plus a boost dose of 50% for two consecutive days; the maintenance dose should be administrated thereafter. LMWH or UFH should be continued until the INR returns to therapeutic levels.

Furthermore, the type of surgical procedure should be taken into consideration, as the bleeding risk varies considerably and affects the ability to ensure haemostatic control. Procedures with a high risk of serious bleeding complications are those where compression cannot be performed. In these cases, discontinuation of oral anticoagulants and bridging therapy with LMWH are warranted. In patients undergoing surgery with a low risk of serious bleeding, such as cataract surgery, no changes in oral anticoagulant therapy are needed.

In patients who are receiving VKAs and require reversal of the anticoagulant effect for an urgent surgical procedure, low-dose (2.5–5.0 mg) i.v. or oral vitamin K is recommended. For more immediate reversal of the anticoagulant effect of VKAs, treatment with fresh-frozen plasma or another prothrombin concentrate in addition to low-dose i.v. or oral vitamin K is recommended. In patients receiving UFH and requiring reversal of the anticoagulant effect for an urgent surgical procedure, cessation of therapy is enough. When given as an infusion, the anticoagulant effect of UFH reaches steady state within 4–6 h. So on cessation of an infusion, coagulation should be mostly normal after 4 h. When UFH is given s.c., the anticoagulant effect is more prolonged. For immediate reversal, the antidote is protamine sulfate. However, protamine sulfate can potentially provoke anaphylactic reactions with cardiovascular collapse, especially if infused too quickly. The dose of protamine sulfate for reversal for a heparin infusion then is 1 mg per 100 U of heparin sodium. If the heparin infusion was stopped for >30 min but <2 h, then use half the dose of protamine sulfate; if the heparin infusion was stopped for >2 h but <4 h, then use a quarter of the dose. The maximum dose of protamine sulfate is 50 mg. In patients who are receiving LMWH the anticoagulant effect may be reversed within 8 h of the last dose because of the short half-life. If immediate reversal is required, i.v. protamine sulfate can be used, but anti-Xa activity is never completely neutralized (maximum of 60–75%).

A summary of the recommended way to minimize bleeding and thromboembolic events during surgery is given in Table 8.

### Table 9: Anticoagulation protocols applied according to patient thromboembolic risk

<table>
<thead>
<tr>
<th>Weight, kg</th>
<th>Nadroparin (twice daily, s.c.) (IU)</th>
<th>Enoxaparin (twice daily, s.c.) (IU)</th>
<th>Nadroparin (once daily, s.c.) (IU)</th>
<th>Enoxaparin (once daily, s.c.) (IU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50</td>
<td>2850</td>
<td>2000</td>
<td>2850</td>
<td>4000</td>
</tr>
<tr>
<td>50–69</td>
<td>3800</td>
<td>4000</td>
<td>3800</td>
<td>4000</td>
</tr>
<tr>
<td>70–89</td>
<td>5700</td>
<td>6000</td>
<td>5700</td>
<td>4000</td>
</tr>
<tr>
<td>90–110</td>
<td>7600</td>
<td>8000</td>
<td>5700</td>
<td>4000</td>
</tr>
<tr>
<td>&gt;110</td>
<td>9500</td>
<td>10 000</td>
<td>5700</td>
<td>4000</td>
</tr>
</tbody>
</table>

IU = international units; LMWH = low molecular weight heparin; SC = subcutaneous.

### Revascularization

The main objective of prophylactic myocardial revascularization is the prevention of potentially lethal perioperative MI. While revascularization may be particularly effective in treating high-grade stenoses, it cannot prevent rupture of vulnerable plaques during the stress of surgery. The latter mechanism has been advocated in at least half of fatal cases of perioperative MI and may explain the lack of specificity of stress imaging techniques in predicting infarct-related coronary artery lesions.37,127

Patients who are clinically stable in the years after coronary artery bypass grafting (CABG) have a diminished risk of cardiac complications after subsequent non-cardiac surgery. Data from the CASS registry indicate that this is particularly the case in patients with triple vessel disease and/or depressed LV function but also in the case of high-risk surgery.128 Therefore, patients who had CABG within the previous 5 years can be sent for surgery, if their clinical condition has remained unchanged since their last examination.

Patients with previous percutaneous revascularization may be at higher risk of cardiac events during or after subsequent non-cardiac surgery, particularly in cases of unplanned or urgent surgery after coronary stenting. After the introduction of angioplasty, it seemed that conventional percutaneous coronary intervention (PCI) did not worsen outcomes after surgery, even if
performed as early as 11 days after PCI. The advent of stenting in the mid 1990s dramatically changed the scenario. Indeed, extremely high mortality rates (up to 20%) were reported in relation to acute stent thrombosis at the time of surgery if performed within weeks after coronary stenting with discontinuation of antiplatelet therapy. Therefore, it is preferred that elective surgery be postponed for a minimum period of 6 weeks and optimally up to 3 months after bare metal stent implantation and that dual antiplatelet therapy be continued. When surgery was performed within this period, discontinuation of dual antiplatelet therapy was associated with an increased incidence of stent thrombosis. After 3 months, patients can be sent for non-cardiac surgery, with continuation of at least aspirin therapy.

In 2002, DESs were introduced in Europe and became widely accepted as an efficient tool to reduce in-stent restenosis further. However, their major drawback is the need for prolonged dual antiplatelet therapy by aspirin and clopidogrel for at least 12 months. When surgery was performed within this period, discontinuation of dual antiplatelet therapy was associated with an increased incidence of stent thrombosis. It is now generally accepted that after DES implantation, elective surgery should not take place until after at least 12 months of continuous dual antiplatelet therapy (Figure 3). After 12 months, patients can be sent for non-cardiac surgery, with continuation of at least aspirin therapy. The need for surgery in relation to its timing and the specific pathology (e.g. malignant tumour, vascular aneurysm repair) should be balanced against the excessive risk of stent thrombosis during the first year following DES implantation and a careful ‘case-by-case’ consideration is advisable. Discussion between the surgeon, the anaesthesiologist, and the treating cardiologist about this matter is recommended in order to achieve a reasonable expert consensus.

In patients who require temporary interruption of aspirin- or clopidogrel-containing drugs before surgery or a procedure it is recommended that this treatment be stopped at least 5 days and, preferably as much as 10 days, prior to the procedure. Therapy can be resumed after ~24 h (or the next morning) after surgery when there is adequate haemostasis. In patients in need of an urgent surgical or other invasive procedure, with potential excessive or life-threatening perioperative bleeding, transfusion of platelets or administration of other prohaemostatic agents is recommended.

### Recommendations on timing of non-cardiac surgery in cardiac-stable/asymptomatic patients with prior revascularization

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class</th>
<th>Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>It is recommended that patients with previous CABG in the last 5 years be sent for non-cardiac surgery without further delay</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>It is recommended that non-cardiac surgery be performed in patients with recent bare metal stent implantation after a minimum 6 weeks and optimally 3 months following the intervention</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>It is recommended that non-cardiac surgery be performed in patients with recent drug-eluting stent implantation no sooner than 12 months following the intervention</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Consideration should be given to postponing non-cardiac surgery in patients with recent balloon angioplasty until at least 2 weeks following the intervention</td>
<td>IIa</td>
<td>B</td>
</tr>
</tbody>
</table>

*Class of recommendation. Level of evidence. CABG = coronary artery bypass grafting.

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**Figure 3** Recommendations for timing of non-cardiac surgery after PCI. PCI = percutaneous coronary intervention.
Prophylactic revascularization in patients with stable ischaemic heart disease

Only two randomized studies have addressed the role of prophylactic revascularization prior to non-cardiac surgery in stable patients scheduled for vascular surgery. The Coronary Artery Revascularization Prophylaxis (CARP) trial was the first to compare optimal medical therapy with revascularization (by CABG or PCI) in patients with stable IHD prior to major vascular surgery. Of 5859 patients screened at 18 US Veterans Affairs hospitals, 510 patients were randomized to one or other of the treatment options. Patients were included on the basis of a combination of cardiovascular risk factors and the detection of ischaemia on non-invasive testing as assessed by the consultant cardiologist. There was no difference in the primary endpoint of long-term mortality at 2.7 years after randomization: 22% (revascularization) vs. 23% (no-intervention) (P = 0.92). Furthermore, there was no difference in perioperative MI: 12% vs. 14%, respectively (P = 0.37). The second trial, DECREASE-V, was a pilot study and applied a different, more precise screening methodology and a more contemporary perioperative medical management. A total of 1880 patients scheduled for surgery were screened for the presence of the following risk factors: age >70 years, angina pectoris, prior MI, compensated or a history of congestive heart failure, drug therapy for diabetes mellitus, renal dysfunction, and prior stroke or transient ischaemic attack (TIA). In the presence of ≥3 risk factors, DSE or nuclear stress testing was performed and in the presence of extensive ischaemia (>5/16 segments or >3/6 walls), patients were randomized to either revascularization or no revascularization. Importantly, β-blocker therapy was initiated and aspirin was continued during surgery in all patients. Three-vessel or left main disease was present in 75% of cases. Also 43% of patients had a depressed ejection fraction of ≤35%. PCI was performed in 65% of patients (n = 32, of whom 30 had DECs). There was no difference in the composite primary endpoint (all-cause mortality and non-fatal MI at 30 days): 43% for revascularization vs. 33% for no revascularization (P = 0.30).

CARP was the first trial to indicate that prophylactic revascularization prior to vascular surgery does not improve clinical outcomes in stable patients. Nevertheless, inclusion in the trial was based on subjective indicators and the study population was a relatively low risk group. DECREASE-V included high risk patients with extensive stress-induced ischaemia, as assessed by non-invasive stress testing. Despite the relatively small study cohort, DECREASE-V extends the conclusions of CARP to a higher risk population, with a majority of patients having three-vessel disease and a substantial proportion having asymptomatic LV dysfunction.

Successful achievement of a vascular procedure without prophylactic revascularization in a stable coronary patient does not imply that this patient would not need any revascularization afterwards. The limited data from DECREASE-V indicate a potential late catch-up phenomenon in the medically treated group. Despite the lack of more scientific data, myocardial revascularization may therefore be recommended in patients prior to foreseen non-cardiac surgery without complications and who present with or have persistent signs of extensive ischaemia, according to the ESC Guidelines for non-surgical settings.

Both CARP and DECREASE-V have been conducted in the setting of vascular surgery, a type of surgery presenting particular risk to the patient with coronary heart disease. Despite this limitation, the conclusions of these trials can probably be extrapolated to other types of surgery.

Type of prophylactic revascularization in patients with stable ischaemic heart disease

Occasionally, patients with stable IHD may require elective surgery, meaning that surgery may be postponed for several months or even up to ≥1 year. There are no solid data to guide a revascularization strategy in this case, and recommendations can therefore only be based on experts’ recommendations. Yet, these patients may to some extent be compared with patients who had previous revascularization. It seems therefore reasonable to propose a cardiovascular work-up according to the ESC Guidelines on stable angina pectoris. CABG should be performed to improve prognosis and relieve symptoms in patients with significant left main disease or its equivalent, for significant three-vessel disease, in particular in the case of depressed LV function, as stated in these guidelines. PCI should be performed to improve symptoms in stable symptomatic patients with single or multivessel disease in whom intervention is technically suitable and in whom the procedural risk does not outweigh the potential benefit.

The choice between PCI and CABG, often a matter of debate, will depend on several factors. Recently, the 1 year results of the SYNTAX trial, in which 1800 patients with three-vessel or left main IHD were randomized to undergo CABG or PCI, have been published. They indicate that CABG remains the treatment of choice in these patients but that PCI is a valuable alternative. As mentioned before, current guidelines on the management of stable angina indicate a role for both treatments. Nevertheless, if PCI is performed prior to non-cardiac surgery the use of bare metal stents, in order not to delay surgery unnecessarily, is recommended.
Revascularization in patients with unstable ischaemic heart disease

No trial has investigated the role of prophylactic revascularization in patients with unstable angina pectoris requiring non-cardiac surgery. Unstable angina pectoris, in particular non-ST-segment elevation ACS, is considered to be a high-risk clinical entity and requires prompt diagnosis, risk stratification, and revascularization. Therefore, as long as the clinical condition for non-cardiac surgery is not life threatening, priority should be given to the diagnosis and proper treatment of unstable angina. In this case, the recent ESC Guidelines on the management of non-ST-segment elevation ACS apply. The cornerstone of treatment includes antiplatelet and anticoagulant therapy, β-blocking agents, and prompt revascularization. Careful attention should be paid to avoiding overt anticoagulation and/or antithrombotic management of unstable coronary patients with concomitant surgical conditions, due to the risk of increased bleeding tendency secondary to the background surgical disease (malignancy, etc.). Except for the previously mentioned well-recognized indications for emergency CABG, most patients undergo PCI. In the exceptional situation of unstable angina and the need for subsequent non-cardiac surgery, preference should again be given to bare metal stents, in order not to delay surgery beyond 3 months.

Recommendation on type of prophylactic revascularization in stable patients

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>Class*</th>
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<tbody>
<tr>
<td>It is recommended that PCI or CABG be performed</td>
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<td>A</td>
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</table>

*Class of recommendation.
*Level of evidence.
CABG = coronary artery bypass grafting; PCI = percutaneous coronary intervention.

Revascularization in patients with unstable ischaemic heart disease

Specific diseases

So far, the guidelines have discussed cardiac risk markers and risk reduction strategies. However, patients presenting with specific diseases prior to surgery benefit from an integrated evaluation and management of their disease in the perioperative period. In the following sections the most common cardiovascular diseases are discussed.

Chronic heart failure

The prevalence of chronic heart failure in the adult population in the UK has been estimated to be 1.8%, and this increases with age. In patients >75 years the prevalence is a high as 8.0%.

The predictive value of heart failure for perioperative cardiac events is well recognized and is an important factor of clinical risk indices, such as Goldman’s or Detsky’s risk score. A study evaluating LV function prior to vascular surgery in 1988 found an LV ejection fraction of ≤ 35% to be an optimal predictor of post-operative cardiac events. In 2008, another study confirmed these findings and concluded that elderly patients with chronic heart failure scheduled for vascular surgery have higher risks of operative mortality and hospital readmission than other patients (including those with IHD) admitted for the same procedure. The prognostic pre-operative value of heart failure with preserved LV ejection fraction is ill defined. Long-term outcome is similar to that of patients with reduced LV ejection fraction. These patients could present an increased cardiovascular risk when undergoing surgery. In the absence of evidence-based studies, the committee recommends similar perioperative management in patients with preserved LV ejection fraction as in patients with a reduced ejection fraction.

The ability to assess myocardial viability during stress testing has allowed further risk stratification of cases with LV dysfunction. As shown in a study of 295 patients with a LV ejection fraction < 35% scheduled for vascular surgery, post-operative cardiac events were related to the presence of stress-induced ischaemia and scar tissue. However, there was an inverse relationship to the presence and extent of dysfunctional but viable segments, showing an improved function without signs of ischaemia during inotropic stimulation. Using multivariable analysis, the number of ischaemic segments was associated with perioperative cardiac events (OR per segment 1.6, 95% CI 1.05–1.8), whereas the number of segments with sustained improvement was associated with improved outcome (OR per segment 0.2, 95% CI 0.04–0.7). The stratification using stress testing enables the physician to identify a subgroup of patients with sustained improvement who have a relatively benign post-operative outcome, unlike patients with a predominantly ischaemic response.

Current ESC Guidelines recommend the use of ACE inhibitors (or ARBs in patients intolerant of ACE inhibitors) and β-blockers as primary treatment in chronic heart failure patients, to improve morbidity and mortality. Unless contra-indicated or not tolerated, they should be given in optimal doses in all patients with symptomatic heart failure and an LV ejection fraction ≤ 40%. Either an ARB or an aldosterone antagonist may subsequently be added, depending on clinical condition and patient characteristics. In all patients with an LV ejection fraction ≤ 35% who remain severely symptomatic [New York Heart Association (NYHA) functional class III or IV], the addition of a low dose of aldosterone antagonist should be considered (in the absence of hyperkalaemia and significant renal...
dysfunction). As an alternative option, addition of an ARB is recommended in heart failure patients with an LV ejection fraction ≤40% who remain symptomatic despite optimal treatment with an ACE inhibitor and β-blocker, unless also taking an aldosterone antagonist. Diuretics are recommended in heart failure patients with signs or symptoms of congestion.

It has been concluded that the perioperative use of ACE inhibitors, β-blockers, statins, and aspirin is independently associated with a reduced incidence of in-hospital mortality in patients with LV dysfunction who are undergoing major non-cardiac vascular surgery. Thus, it is recommended that life-saving therapies in stable heart failure patients be continued until the surgery and that they be reinstated post-operatively, as soon as clinical conditions are satisfactory.

The diagnosis of post-operative heart failure is often difficult to make since it often presents atypically and may have a different aetiology compared with the non-surgical setting. The evaluation should include physical examination, ECG, serial biomarker measurements, X-ray, and echocardiography. Special attention should be given to the patient’s volume status since high-volume infusion is often needed in the intra- and immediate post-operative setting. In the period after surgery, fluids given during the operation may be mobilized to cause hypervolaemia and even heart failure, if not adequately handled. Fluid overloading may cause decompensation of chronic heart failure or development of de novo acute heart failure. Heart failure may develop perioperatively either immediately after surgery (due to prolonged procedure, myocardial ischaemia, rapid fluid shift) or some days later (due to third-space fluid re-absorption).

According to the recent ESC Guidelines on heart failure, an attempt should be made to optimize pharmacological therapy before surgery. This may be of particular importance for β-blockers, which are recommended in the perioperative period in all high-risk patients. To avoid uncontrolled hypotension, routine use of i.v. β-blockers is not recommended. Importantly, if a heart failure patient is not receiving a β-blocker, such therapy should be initiated early enough before elective surgery to ensure optimal dose titration.

Once the aetiology of post-operative heart failure is diagnosed, treatment is similar to the non-surgical setting. Patients with heart failure have a significantly higher risk of hospital readmission after surgical procedures. This confirms the need for careful discharge planning and close follow-up, optimally using a multidisciplinary approach.

## Arterial hypertension

In general, the presence of arterial hypertension is not considered to be an independent risk factor for cardiovascular complications in non-cardiac surgery. Pre-operative evaluation allows the identification of patients with hypertension, enables a search for target organ damage and evidence of associated cardiovascular pathology to be undertaken, and allows initiation of appropriate therapy. This is particularly important for those with comorbid factors.

There is no clear evidence favouring one mode of antihypertensive therapy over another in patients undergoing non-cardiac surgery. Patients with arterial hypertension should be managed according to existing ESC Guidelines. However, in hypertensive patients with concomitant IHD who are at high risk of cardiovascular complications, perioperative administration of β-blockers is recommended. In patients with hypertension, antihypertensive therapy should be continued up to the morning of surgery and restarted promptly in the post-operative period. In patients with grade 1 or 2 hypertension, there is no evidence that delay in surgery in order to optimize therapy is beneficial. In these cases, antihypertensive medications should be continued during the perioperative period. In patients with grade 3 hypertension (systolic blood pressure ≥180 mmHg and/or diastolic blood pressure ≥110 mmHg), the potential benefits of delaying surgery to optimize the pharmacological therapy should be weighed against the risk of delaying the surgical procedure.

### Valvular heart disease

Patients with VHD are at higher risk of perioperative cardiovascular complications during non-cardiac surgery. Echocardiography should be performed in patients with known or suspected VHD, to assess its severity and consequences. On the basis of existing data, the following recommendations are particularly applicable in these patients.

#### Recommendation on VHD

<table>
<thead>
<tr>
<th>Recommendation</th>
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<tbody>
<tr>
<td>In the presence of severe VHD it is recommended that a clinical and echocardiographic evaluation be performed and, if needed, treatment before non-cardiac surgery</td>
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</table>

*Class of recommendation.  
Level of evidence.  
VHD = valvular heart disease.

#### Aortic stenosis

Aortic stenosis (AS) is the most common VHD in Europe, particularly among the elderly. Severe AS (defined as aortic valve area <1 cm², <0.6 cm²/m² body surface area) constitutes a well-established risk factor for perioperative mortality and MI. In the case of urgent non-cardiac surgery in patients with severe AS, such procedures should be performed under haemodynamic monitoring. In the case of elective non-cardiac surgery, the presence of symptoms is a key for decision making.

In asymptomatic patients, aortic valve replacement should be considered before elective surgery. In patients who are not candidates for valve replacement either due to high risks associated with serious co-morbidities or those who refuse, non-cardiac surgery should be performed only if is essential. In these patients, balloon aortic valvuloplasty or transcatheter valve implantation may be a reasonable therapeutic option before surgery.

In asymptomatic patients, non-cardiac surgery of low to intermediate risk can be safely performed. If high-risk surgery is planned, further clinical assessment is necessary for aortic valve replacement. In those at high risk for aortic valve replacement, elective surgery under strict haemodynamic monitoring should be performed only if strictly needed. In the remaining patients, aortic valve replacement should be considered as the initial procedure.

#### Mitral stenosis

Non-cardiac surgery can be performed at relatively low risk in patients with non-significant mitral stenosis (MS) (valve area > 1.5 cm²) and in...
Asymptomatic patients with significant MS (valve area <1.5 cm²) and systolic pulmonary artery pressure <50 mmHg. Pre-operative surgical correction of MS in these patients is not indicated. It needs to be remembered that control of heart rate is essential to avoid tachycardia, which may cause pulmonary oedema. Strict control of fluid overload is also important. Also development of AF may cause serious clinical deterioration.\textsuperscript{20,124} With the high risk of embolism, anticoagulation control is important. In asymptomatic patients with significant MS and systolic pulmonary artery pressure >50 mmHg and in symptomatic patients, the risk related to the non-cardiac procedure is significantly higher, and these patients may benefit from percutaneous mitral commissurotomy (or open surgical repair) particularly before high-risk surgery.\textsuperscript{20,124}

**Aortic regurgitation and mitral regurgitation**

Non-significant aortic regurgitation (AR) and mitral regurgitation (MR) do not independently increase the risk of cardiovascular complications during non-cardiac surgery. In asymptomatic patients with severe AR and MR (detailed classification presented in the ESC Guidelines\textsuperscript{124}) and preserved LV function, non-cardiac surgery can be performed without additional risk. Symptomatic patients and those who are asymptomatic with severely impaired LV ejection fraction (<30%) are at high risk of cardiovascular complications, and non-cardiac surgery should be performed only if necessary.\textsuperscript{124} Patients with severe MR and AR may benefit from optimization of pharmacological therapy to produce maximal haemodynamic stabilization before high-risk surgery.

**Patients with prosthetic valve(s)**

Patients who have undergone surgical correction of VHD and have a prosthetic valve can undergo non-cardiac surgery without additional risk, when there is no evidence of valve or ventricular dysfunction. In these patients, endocarditis prophylaxis is recommended and a modification of the anticoagulation regimen needs to be considered in the perioperative period, with oral anticoagulants being temporarily replaced by i.v. UFH, s.c. UFH, or s.c. LMWH at therapeutic doses.

**Prophylaxis of infective endocarditis**

In patients with VHD and those with prosthetic valves who are undergoing non-cardiac surgery at risk of bacteraemia, antibiotic prophylaxis against infective endocarditis should be initiated. This issue is discussed in detail in the ESC and AHA guidelines.\textsuperscript{148,149}

**Arrhythmias**

The occurrence of perioperative arrhythmias has been reported in 70% of patients subjected to general anaesthesia for various surgical procedures.\textsuperscript{150,151} The incidence has been reported to vary from 16 to 62% with intermittent ECG monitoring\textsuperscript{152} and 89% with continuous Holter monitoring\textsuperscript{153}

**Ventricular arrhythmias**

Almost half of all high-risk patients undergoing non-cardiac surgery have frequent ventricular premature beats (VPBs) or non-sustained VT. There is no evidence that VPBs or non-sustained VTs alone are associated with a worse prognosis. ACC/AHA/ESC Guidelines for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death recommend approaches based on large clinical trials.\textsuperscript{154} Regardless of the cause, sustained monomorphic ventricular tachycardia (SMVT) with serious haemodynamic compromise must be treated promptly with electric cardioversion.\textsuperscript{154} I.v. amiodarone can be used for initial treatment of patients with stable SMVT.\textsuperscript{154} It is also reasonable in patients with SMVT that is haemodynamically unstable, refractory to conversion with countershock, or recurrent despite other agents. In sustained polymorphic ventricular tachycardia (SPVT), if haemodynamic compromise is present, immediate electrical cardioversion should be performed. β-Blockers are useful for patients with recurrent SPVT, especially if ischaemia is suspected or cannot be excluded. Amiodarone is reasonable for patients with recurrent SPVT in the absence of long QT syndrome (LQTS).\textsuperscript{154} Torsades de Pointes rarely occurs, and withdrawal of any offending drugs and correction of electrolyte abnormalities are recommended. Management with magnesium sulfate is reasonable for patients with Torsades de Pointes and LQTS. β-Blockade combined with pacing is suggested in patients who have Torsades de Pointes and sinus bradycardia. Isoproterenol is recommended in patients with recurrent pause-dependent Torsades de Pointes who do not have congenital LQTS.\textsuperscript{154} In the event of perioperative pulseless VT or ventricular fibrillation, immediate defibrillation is required.

**Supraventricular arrhythmias**

A greater number of patients undergoing non-cardiac surgery may suffer from SVT and AF compared with ventricular arrhythmias.\textsuperscript{153 – 158} Sympathetic activity is the primary autonomic mechanism responsible for the trigger of AF.\textsuperscript{155} Vagal manoeuvres may terminate SVT in some cases and these arrhythmias respond well to treatment with adenosine. When SVT is refractory to adenosine, effective therapy for termination of the arrhythmia includes a short-acting β-blocking agent or a non-dihydropyridine calcium channel blocker (diltiazem and verapamil) or amiodarone i.v.\textsuperscript{160 – 162} Verapamil should be used with care because of its negative inotropic effect. The use of calcium channel blockers is not recommended in pre-excited SVT/AF. For perioperative AF, the goal of management is ventricular rate control.\textsuperscript{163} β-Blockers and non-dihydropyridine calcium channel blockers (diltiazem and verapamil) are the drugs of choice for the rate control in AF. Digoxin may be used as a first-line drug only in patients with chronic heart failure, since it is not effective in high adrenergic states such as surgery. β-Blockers have been shown to accelerate the conversion of AF to sinus rhythm after non-cardiac surgery.\textsuperscript{164} In several studies, the pre-operative administration of β-blockers was associated with better control of arrhythmias.\textsuperscript{165,166}

**Bradyarrhythmias**

Severe perioperative bradyarrhythmias requiring treatment have been reported in 0.4% of 17,021 patients, 6.4% of whom were American Association of Anaesthesiologists physical status 3 or 4.\textsuperscript{151} These patients were monitored with routine intraoperative and early post-operative ECG monitoring. In general, perioperative bradyarrhythmias respond well to short-term pharmacological therapy, non-invasive transoesophageal atrial pacing in...
anaesthetized individuals, or non-invasive transcutaneous pacing in awake or anaesthetized patients. Temporary cardiac pacing is rarely required, even in the presence of pre-operative asymptomatic bifascicular block or left bundle branch block. The indications for temporary pacemakers during the perioperative period are generally the same as those for permanent pacemakers. Asymptomatic bifascicular block, with or without first degree atrio-ventricular block, is not an indication for temporary endocardial pacing.

**Pacemaker/implantable cardioverter defibrillator**

The use of unipolar electrocautery represents a significant risk to pacemaker-dependent patients. The electrical stimulus from electrocautery may inhibit demand pacemakers or may reprogramme the pacemaker. However, these problems can be avoided by positioning the ground plate for the electrical circuit, such that the electrical current travels away from the generator. Keeping the electrocautery device away from the pacemaker, giving only brief, bursts and using the lowest possible amplitude may decrease the interference. In many studies, the authors recommended setting the pacemaker in an asynchronous or non-sensing mode in patients who are pacemaker dependent and whose underlying rhythm is unreliable, and interrogating the device after surgery to ensure appropriate programming and sensing pacing thresholds. Interference with implantable cardioverter defibrillator function can also occur during non-cardiac surgery as a result of electrical current generated by electrocautery. The implantable cardioverter defibrillator should be turned off during surgery and switched on in the recovery phase before discharge to the ward. In addition, it is recommended that written instructions regarding the responsibility for surveillance and restarting of the implantable cardioverter defibrillator should be available.

### Recommendations on ventricular arrhythmias

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Classa</th>
<th>Levelb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-arrhythmic drugs are recommended for patients with recurrent sustained VT</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Continuation of amiodarone and β-blockers before surgery is recommended</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>It is recommended that wide QRS tachycardia be considered to be VT if the diagnosis is unclear</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Prompt electrical cardioversion in patients with sustained VT with haemodynamic compromise is recommended</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>Anti-arrhythmic drugs for initial treatment of patients with stable sustained monomorphic VT should be considered</td>
<td>IIa</td>
<td>B</td>
</tr>
<tr>
<td>Anti-arrhythmic drugs for patients with non sustained VT are not recommended</td>
<td>III</td>
<td>B</td>
</tr>
<tr>
<td>Anti-arrhythmic drugs for patients with VPBs are not recommended</td>
<td>III</td>
<td>A</td>
</tr>
</tbody>
</table>

*aClass of recommendation.

bLevel of evidence.

VPB = ventricular premature beat; VT = ventricular tachycardia.

### Recommendations on implantable devices

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Classa</th>
<th>Levelb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interrogation of implantable devices pre-operatively and post-operatively is recommended</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>It is recommended that the hospital management state who is responsible for programming the devices before and after surgery</td>
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<td>C</td>
</tr>
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</table>

*aClass of recommendation.

bLevel of evidence.

AF = atrial fibrillation; SVT = supraventricular tachycardia.

### Renal disease

Reduced kidney function is an independent risk factor for adverse post-operative cardiovascular outcomes including MI, stroke, and progression of heart failure. In most risk indices, renal function is taken into account. Traditionally, this function is assessed by serum creatinine concentration. For example, the serum creatinine cut-off value of 2.0 mg/dL (177 μmol/L) is used in the Lee index. However, estimated creatinine clearance (mL/min) incorporating serum creatinine, age, and weight provides a more accurate assessment of renal function than serum creatinine alone. Most commonly used is the Cockcroft–Gault formula, where:

\[
\text{Estimated Creatinine Clearance (mL/min)} = \frac{140 - \text{age in years}}{72 + \text{weight in kg}} \times \text{serum creatinine in mg/dL} \times 0.85 \quad \text{(females)}
\]

For example, if a patient’s serum creatinine is 2.0 mg/dL, the estimated creatinine clearance would be:

\[
\text{Estimated Creatinine Clearance} = \frac{140 - 70}{72 + 70} \times 2.0 \times 0.85 = 5.2 \text{ mL/min}
\]

However, it might be argued that patients with less pronounced renal insufficiency also do worse compared with patients with normal serum creatinine values. A 10 mL/min decrease in creatinine clearance was associated with a 40% increased risk of post-operative mortality (OR 1.4, 95% CI 1.2 – 1.5; ROC area: 0.70, 95% CI 0.63 – 0.76). ROC curve analysis showed that the cut-off value of 64 mL/min for creatinine clearance yielded the highest sensitivity/specificity to predict post-operative mortality.
In addition to the pre-operative renal function, worsening of function after surgery is a prognostic factor for adverse late outcome. In 1324 patients who underwent elective open AAA surgery, creatinine clearance was measured pre-operatively and on days 1, 2, and 3 after surgery. Patients were divided into three groups according to the change in renal function after surgery compared with baseline. Group 1 showed an improved or no change (change in creatinine clearance, ±10% of function compared with baseline); group 2 showed a temporary worsening (worsening >10% at day 1 or 2, then complete recovery within 10% of baseline at day 3); and group 3 experienced a persistent worsening (>10% decrease compared with baseline). Mortality during 30 days after surgery was 1.3, 5.0, and 12.6% in groups 1, 2, and 3, respectively. Adjusted for baseline characteristics and post-operative complications, 30-day mortality was highest in patients with persistent worsening of renal function (HR 7.3, 95% CI 2.7–19.8), followed by those with temporary worsening (HR 3.7, 95% CI 1.4–9.9). During 60 ± 3.4 years of follow-up, 348 patients (36.5%) died. The risk of late mortality was 1.7 (95% CI 1.3–2.3) in the persistent worsening group followed by those with temporary worsening (HR 1.5, 95% CI 1.2–1.4). This study showed that, although renal function may recover completely after aortic surgery, temporary worsening of renal function was associated with an increased long-term mortality.

Identification of patients who might experience perioperative worsening of renal function is important in order to initiate supportive measures such as maintenance of adequate intravascular volume for renal perfusion and vasopressor use. In a large retrospective study, risk factors for post-operative acute renal failure within the first 7 days after major non-cardiac surgery among patients with previously normal renal function were evaluated. Thirty-day, 60-day, and 1-year all-cause mortality was also assessed. A total of 65 043 cases throughout 2003 and 2006 were reviewed. Of these, 15 102 patients met the inclusion criteria; 121 patients developed acute renal failure (0.8%), and 14 required renal replacement therapy (0.1%). Seven independent pre-operative predictors were identified (P <0.05): age, emergency surgery, liver disease, high body mass index, high-risk surgery, peripheral arterial occlusive disease, and COPD necessitating chronic bronchodilator therapy.

Contrast-induced nephropathy, caused by renal hypoperfusion and direct tubular toxicity, occurs in up to 15% of patients with chronic renal dysfunction undergoing radiographic procedures. Between 0.5 and 12% of these patients require hemodialysis and prolonged hospitalization. A considerable number of patients experience worsening of renal function, possibly progressing to end-stage renal failure. The cornerstone of prevention consists of periprocedural hydration and antioxidant drugs. Recently, three randomized studies have compared the effects of sodium bicarbonate vs. isotonic saline in humans, resulting in an impressive reduction in contrast nephropathy in the sodium bicarbonate group, with an incidence <2%. These results were recently evaluated in an adequately powered randomized trial comparing the efficacy of hydration with sodium bicarbonate vs. isotonic saline in addition to oral N-acetylcysteine for prophylaxis of contrast-induced nephropathy in a population of patients with chronic kidney dysfunction undergoing planned coronary angiography or intervention. A total of 502 patients with an estimated creatinine clearance <60 mL/min were randomized to receive infusion of either saline (0.9% NaCl) or sodium bicarbonate before and after administration of contrast medium on top of N-acetylcysteine orally (600 mg b.i.d.). Treatment with isotonic saline consisted of 1 mL/kg/h 0.9% sodium chloride for 12 h before and after the procedure, and treatment with sodium bicarbonate (154 mEq/L in dextrose and water) consisted of 3 mL/kg for 1 h before the contrast medium, followed by an infusion of 1 mL/kg/h for 6 h after the procedure. Contrast-induced nephropathy was defined as an absolute increase in serum creatinine ≥0.5 mg/dL measured within 5 days after contrast exposure. No difference was observed between the two study groups; contrast-induced nephropathy occurred in 54 patients (10.8%); 25 (10%) were treated with sodium bicarbonate and 29 (11.5%) with saline (P = 0.60). Thus, hydration with sodium bicarbonate plus oral N-acetylcysteine before contrast medium exposure was no more effective than hydration with isotonic sodium chloride plus oral N-acetylcysteine for prophylaxis of contrast-induced nephropathy in patients with moderate renal dysfunction. The discrepancies among randomized studies might be explained by differences in the concomitant use of N-acetylcysteine, use of contrast medium, or baseline renal dysfunction among randomized patients. Sodium bicarbonate requires only 1 h of pre-treatment and may represent an option in patients scheduled for urgent agent injection or for outpatient procedures.

Cerebrovascular disease

Cerebrovascular disease is the third leading cause of death in Western countries, with ~500 TIA's and 2400 new strokes per million inhabitants. One-third of new stroke patients die within 1 year, and <50% make a full recovery and regain independence. An increasing number of elderly patients are referred for non-cardiac surgery, including those with concomitant vascular diseases affecting the cerebral circulation. Risk factors for perioperative symptomatic or asymptomatic transient or permanent cerebrovascular events (TIA/stroke) are embolism or haemodynamic compromise in large (aorta, carotid, vertebral, and main cerebral arteries intracranially) or small vessels (perforating
and penetrating arterioles and capillaries). Although fatal and non-fatal stroke can be reduced significantly in symptomatic patients with moderate/severe carotid stenosis associated with ipsilateral symptoms, in particular if treated early (2–4 weeks, but at least within 3–6 months after the onset of symptoms), the benefit of this interventional/surgical treatment is smaller in neurologically asymptomatic subjects. Thus medical measures to prevent stroke are of utmost general importance and include a multifaceted strategy aimed at control of hypertension, hyperlipidaemia, diabetes, etc. The usefulness of specific antiplatelet agents or anticoagulants has been demonstrated in many randomized controlled trials for primary and secondary prevention, and may even be increased in elderly subjects undergoing non-cardiac surgery and anaesthesia.\(^{184}\)

Apart from stroke and TIA, transient or permanent changes in mental status characterized by disturbances of attention, orientation, memory dysfunction, illusions, hallucinations, aphasia, etc. (the key diagnostic features of delirium) may occur, including anxiety and depression, which are often under-recognized or misdiagnosed. They may be due to perioperative medication, surgery itself, intraoperative hypo- or hypertension, and cerebral microembolism causing multiple small vessel occlusion and ischaemia, evidenced by transcranial Doppler and MRI diffusion-weighted imaging. In cardiac surgery, mental changes are common and may be associated with transient and occasionally even permanent cognitive dysfunction (25–30%). It is very likely that they also occur in the elderly high-risk patient undergoing non-cardiac surgery.

Current concepts of perioperative stroke are summarized in three major reviews\(^{185–187}\) which compare the incidence of stroke for various surgical procedures (0.08–0.07% in general surgery, 1–5% in peripheral and carotid surgery, and 2–10% in cardiac surgery). Contrary to common belief, most strokes are not related to hypoperfusion, but occur mainly in the presence of an intact cerebral autoregulation.\(^{187}\) Ischaemic and embolic mechanisms are far more common than haemodynamic compromise. Delayed stroke is mainly attributed to various sources of cardiac embolism, followed by hypercoagulability and increased risk of thrombogenic events. Many strokes remain undiagnosed because of a lack of major sensory–motor symptoms or the presence of only subtle neuropsychological deficits, which are more difficult to identify. Several patient- and procedure-related factors are associated with an increased risk of perioperative stroke—they should be investigated carefully to evaluate the individual risk/benefit ratio and optimize care, including appropriate risk modification and timing of surgery. A history of recent cardiac events (8%/year), but not for stroke (1–2%/year).\(^{96}\) However, the overall perioperative stroke risk tends to be overstated. There is no evidence-based recommendation to treat carotid stenosis prior to non-cardiac surgery, but there are exceptional cases prior to cardiac surgery.

Discontinuation of warfarin or antiplatelet agents in anticipation of surgery exposes patients to an increased risk of perioperative stroke. A review of perioperative outcome in patients requiring warfarin showed 0.6% thromboembolic events in those who continued therapy vs. 7.0% in patients who received i.v. heparin as bridging therapy.\(^ {188}\) Whether this is due to insufficient control or dosage of heparin administration is uncertain. In knee or hip replacement, continued use of moderate dose warfarin therapy during the perioperative period was safe and effective and was similar to patients undergoing dental procedures, cataract surgery, and diagnostic endoscopy without interrupting their antiplatelet agents or oral anticoagulants regimen. Lengthy operations are associated with higher risks for perioperative stroke; the choice of surgical technique is also important and the types of anaesthesia and anaesthetic agents require additional consideration. Optimal selection of individually guided best levels of blood pressure during surgery and thereafter, as well as management of the patient’s body temperature and control of blood glucose, are suggested to reduce rates of incidental stroke and death. Pre-, intra-, and post-operative use of antiplatelet agents is useful. Whether or not so-called neuroprotective agents are needed is a matter of controversy.

### Pulmonary disease

The co-existence of pulmonary disease in patients having non-cardiac surgery may increase the risk of operation. Such diseases include acute respiratory infections, COPD, asthma, cystic fibrosis, interstitial lung disease, and other conditions causing impairment of respiratory function. Pre-existing pulmonary disease has a significant impact on perioperative risk, but the most common effect is to increase the risk of post-operative pulmonary complications. These complications are mainly a consequence of the development of atelectasis during general anaesthesia. Post-operative shallow breathing, reduced lung expansion, and other factors may cause the lung collapse to persist and promote respiratory infection. These complications occur especially after abdominal or thoracic surgery, and the risk seems to be increased in smokers. Specific perioperative management is required to reduce the risks of pulmonary complications. There are some
respiratory conditions which are associated with cardiovascular abnormalities and which may require special cardiac risk assessment and management in addition to dealing with pulmonary complications per se. Two such conditions are COPD and pulmonary arterial hypertension (PAH).

COPD, defined as airways obstruction which is not completely reversible, is well recognized as a major cause of morbidity and mortality. The prevalence of COPD in adults in Europe has been found to vary between ~5 and 10%, with rates tending to be higher in males than females. Thus, up to one in 10 patients having non-cardiac surgery may have COPD.

Cor pulmonale with right heart failure is a direct complication of severe COPD. However, COPD is also associated with an increased risk of coronary heart disease. In a systematic review of 12 population cohort studies, those with a reduced forced expiratory volume in 1 s (FEV\textsubscript{1}) had a 75% increased risk of cardiovascular mortality compared with those with a normal FEV\textsubscript{1}.\textsuperscript{189} Reduced expiratory flow has also been associated with a higher incidence of non-fatal coronary heart disease and stroke, carotid stenosis, low ankle-brachial index, and cerebral white matter lesions. These associations occur in both men and women and, despite a strong relationship of smoking with both COPD and CVD, are independent of traditional cardiovascular risk factors. For every 10% decrease in FEV\textsubscript{1}, cardiovascular mortality increases by ~30% and non-fatal coronary events by ~20%.

In patients undergoing aortic aneurysm repair, conflicting results have been found with short-term mortality (often due to cardiac complications). For example, COPD has been associated with operative death, but not 30-day mortality. In vascular surgery patients as a whole, COPD has not been associated with increased 30-day mortality. Thus, despite an association with CVD, there is no convincing evidence that COPD is related to a higher risk of perioperative cardiac complications.

PAH may be idiopathic, due to congenital heart disease, familial, or associated with specific conditions such as collagen vascular disease. It must be distinguished from other causes of PAH due to COPD, thromboembolism, and congenital disease. The diagnosis is based on a mean arterial pulmonary pressure of >25 mmHg at rest and a pulmonary wedge pressure of ≤15 mmHg. In surveys in Europe, the prevalence has varied between about 15 and 50 cases per million adults. Half the cases were idiopathic. The prevalence is thus low and consequently the condition is uncommon in surgical practice.

PAH increases surgical complications, especially right ventricular failure, myocardial ischaemia, and post-operative hypoxia. In patients having cardiopulmonary bypass surgery, a mean pre-operative arterial pressure >30 mmHg is an independent predictor of mortality. In a study of patients with pulmonary hypertension undergoing non-cardiac surgery, of whom over half had PAH, outcome predictors included NYHA functional class ≥II, intermediate- to high-risk surgery, right ventricular function, and duration of anaesthesia.\textsuperscript{190} There is a need for further research on factors predicting poor outcomes. However, the study above did confirm that such patients are at high risk, the perioperative cardiopulmonary complication rate being 38% and mortality 7%.

Pre-existing COPD is often considered in terms of the risk of post-operative pulmonary complications. For perioperative cardiac risk, the lack of convincing evidence that COPD increases risk may have arisen because in COPD patients extra care was taken with cardiac management, thus negating any association. Nevertheless, COPD has not been included in pre-operative cardiac risk indices, such as Goldman, Detsky, and Lee and, indeed, no improvement was found in the prognostic value of the Lee index in vascular surgery patients when COPD was included.\textsuperscript{191} For PAH, on the other hand, the condition is so uncommon that its inclusion in an integrated risk model has not been considered.

In patients with pulmonary disease having non-cardiac surgery, the treatment goals pre-operatively are to optimize pulmonary function and minimize respiratory complications. For COPD, treatment goals would include eliminating active infection with antibiotics; minimizing wheeze associated with any reversible disease using inhaled bronchodilators or steroids; reducing right and LV failure with diuretics; ensuring adequate oxygenation; and, finally, encouraging smoking cessation prior to surgery. In relation to perioperative cardiac management, patients with COPD should be managed in the same way as those without COPD and, in particular, there are no special contra-indications to the use of cardioselective β-blockers or statins in COPD patients.\textsuperscript{93,192} PAH is incurable and the treatment goal is to reduce symptoms, and improve exercise capacity and right ventricular function. Anaesthesia and surgery may be complicated by acute right heart failure due to increase of pulmonary vascular resistance related to the impairment of lung ventilation, typical of the operative and post-operative state of thoracic and abdominal surgery. Specific drug therapy for PAH includes calcium channel blockers (only for the few patients who are responders to the acute vasoreactivity test), prostanooids, endothelin receptor antagonists, and phosphodiesterase type-5 inhibitors.\textsuperscript{143,193} Ideally, patients with PAH should have an optimized treatment regimen before any surgical intervention. It is recommended also that PAH-specific drug therapy is not withheld for >12 h due to the perioperative fasting state. In case of progression of right heart failure in the post-operative period, it is recommended that the diuretic dose be optimized and, if necessary, that inotropic support with dobutamine be initiated. The role of starting new specific PAH drug therapy in the perioperative period has not been established. In the case of severe right heart failure, not responsive to supportive therapy, the administration of temporary inhaled nitric oxide or i.v. epoprostenol with the guidance of a physician experienced in the treatment of PAH may be indicated. In this case, a period of progressive weaning from these medications may be required.

Patients with COPD and PAH have a relatively high frequency of heart failure and coronary heart disease. There is no consistent evidence indicating that COPD patients are at higher risk of perioperative cardiac complications and death, so that they can be managed in the same way as patients without COPD. On the other hand, PAH increases perioperative risk, and requires pre-operative assessment and, if severe, perioperative treatment.
Perioperative monitoring

Electrocardiography

Although even a single post-operative ECG demonstrating ischaemia in the recovery room is predictive of a major cardiac complication later during the hospital stay, ECG monitoring alone is not adequate to detect ischaemia in real time in the intensive care unit (ICU) and intraoperative settings. Specifically, conventional visual ECG monitoring for the detection of transient ST-segment changes is inaccurate. Although lead V5 has been known as the best choice for the detection of intraoperative ischaemia for many years, one study found that lead V4 was more sensitive and appropriate than lead V5 for detecting prolonged post-operative ischaemia and infarction. Leads are not specific for ischaemic events, and, furthermore, ischaemic events are dynamic and may not always appear in the same lead. If a single lead is used for monitoring, there is an increased risk of missing ischaemic events. With the use of selected lead combinations, more ischaemic events can be precisely diagnosed in the intraoperative setting. In one study, although the best sensitivity was obtained with lead V5 (75%), followed by lead V4 (61%), combining leads V4 and V5 increased the sensitivity to 90%. In the same study, when three leads (II, V4, and V5) were used simultaneously, the sensitivity increased to 96%. Similarly, in another study in which two or more pre-cordial leads were used, the sensitivity of ECG monitoring was >95% for detection of perioperative ischaemia and infarction. It was also shown that ECG monitoring with fewer leads (as few as three leads) had lower sensitivity than monitoring with 12 leads, and there was a statistically significant association, independent of perioperative troponin values, between perioperative ischaemia on a 12-lead ECG and long-term mortality. Thus, 12-lead ECG monitoring is recommended especially with high-risk patients.

ST-segment monitoring has been shown to be limited in patients who have intraventricular conduction defects (e.g. left bundle branch block) and ventricular paced rhythms. The secondary ST–T changes, which were present in these patients, were due to abnormal depolarization, which also distorted the repolarization process. The distorted ST-segments can limit the sensitivity of the ST-segment monitoring system. Because detection of ST-segment changes of the electrocardiogram by visual inspection is poor, computerized analysis has become standard in modern monitors. Continuous automated ST trending monitors are included in most new operating room ECG monitors to facilitate ischaemia detection. Such devices increase the sensitivity of ECG ischaemia detection. In one study, Holter recordings were used as the reference standard for detection of intraoperative ischaemia, and the ST trending monitors were found to have overall sensitivity and specificity of 74 and 73%, respectively. Several conditions contributed to the inaccuracy of ST trend monitoring, and additional modification of their performance was necessary to achieve better agreement with the Holter analysis.

In a series of studies during the past decade, the presence of ECG changes during monitoring in high-risk cohorts has been linked to a higher incidence of perioperative MI and cardiac events. In addition, the duration of ST-segment changes positively correlates with the incidence of perioperative MI. Therefore, when ST-segment changes occur, the clinician should assume that myocardial ischaemia is present. However, it is not clear if ECG monitoring is sufficiently sensitive to identify patients at low risk. In addition, the usefulness of this test in the general population is limited because many studies have excluded patients with ECG findings that preclude accurate evaluation of ischaemia.

Transoesophageal echocardiography

Transoesophageal echocardiography (TOE) has frequently been used as a monitoring tool during cardiac surgery since the mid 1980s. However, few evidence-based data support TOE use in non-cardiac surgery. TOE has several advantages over alternative monitoring methods, such as the use of a pulmonary artery catheter. It is rapidly available, relatively non-invasive, and provides more versatile and comprehensive information. However, although TOE is in general a safe procedure, serious adverse events can
occur. The complication rates relate to the experience of the operator and the presence of severe oesophageal or gastric diseases. Specific training of users is mandatory to avoid inaccurate interpretation.

Myocardial ischaemia can be identified by abnormalities in regional wall motion and thickening. The concordance between intraoperative TOE and ECG is rather weak. Both ST-segment changes and regional wall motion abnormalities can be present in the absence of acute ischaemia. Wall motion abnormalities may be difficult to interpret in the presence of left bundle branch block, ventricular pacing, AF, or right ventricular overload. The resolution of ischaemia is not necessarily detectable if ischaemia is followed by myocardial stunning. Episodes of new or worsened wall motion abnormalities have been shown to be relatively infrequent (20%) in high-risk patients undergoing non-cardiac surgery. They were more common in patients submitted to aortic vascular surgery. Episodes were poorly correlated with post-operative cardiac complications.

When compared with pre-operative clinical data and intraoperative monitoring using 2-lead ECG, routine monitoring for myocardial ischaemia during surgery has little incremental clinical value in identifying patients at high risk of perioperative ischaemic outcomes.

The main advantage of TOE over pulmonary artery catheterization is the more comprehensive evaluation of cardiac structure and function. Information is quickly available on regional or global, right and/or LV dysfunction, the presence of tamponade or cardiac thrombi, and preload estimation through the measurement of end-diastolic volume. Numerous indices of ventricular and atrial function have been proposed. However, most parameters are load dependent.

The role of TOE for haemodynamic monitoring in patients at risk is more controversial. Automated analysis systems exist but are not yet sufficiently validated. There is no evidence that haemodynamic monitoring by TOE accurately stratifies risk or predicts outcome.

TOE can be useful in the operating room in patients with severe valvular lesions. The loading conditions during general anaesthesia differ from those present in the pre-operative evaluation. Functional and ischaemic mitral regurgitation are usually reduced during general anaesthesia. Organic mitral regurgitation can, conversely, increase. In the setting of severe mitral regurgitation, the LV ejection fraction overestimates LV function, and other parameters may be more accurate, such as myocardial velocities or deformation obtained by tissue Doppler imaging or 2D speckle tracking, an angle-independent method. These are promising techniques, but more validation is needed before they can be used routinely in this setting. In patients with severe aortic stenosis, appropriate preload is important during surgery. Monitoring of LV end-diastolic volume may be more accurate than that of pulmonary capillary pressure. An appropriate heart rate is crucial in patients with mitral stenosis and aortic regurgitation: a long diastolic period in the former and shorter duration of diastole in the latter. When inappropriate control of heart rate occurs, the consequences should be assessed: changes in transmural mean gradient and pulmonary arterial pressures in mitral stenosis and changes in LV volumes and indices of LV function in aortic regurgitation.

### Recommendations on intraoperative and/or perioperative transoesophageal echocardiography for detection of myocardial ischaemia

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class(^a)</th>
<th>Level(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>The use of TOE should be considered in patients who develop ST-segment changes on intraoperative or perioperative ECG monitoring</td>
<td>Ila</td>
<td>C</td>
</tr>
<tr>
<td>The use of TOE may be considered in patients at high risk of developing myocardial ischaemia who undergo major non-cardiac surgery</td>
<td>Ilb</td>
<td>C</td>
</tr>
</tbody>
</table>

\(^a\) Class of recommendation.  
\(^b\) Level of evidence.  
ECG = electrocardiography; TOE = transoesophageal echocardiography.

TOE is recommended if acute and severe haemodynamic instability or life-threatening abnormalities develop during or after surgery. The main advantage of TOE over pulmonary artery catheterization is the more comprehensive evaluation of cardiac structure and function. Information is quickly available on regional or global, right and/or LV dysfunction, the presence of tamponade or cardiac thrombi, and preload estimation through the measurement of end-diastolic volume. Numerous indices of ventricular and atrial function have been proposed. However, most parameters are load dependent.

The role of TOE for haemodynamic monitoring in patients at risk is more controversial. Automated analysis systems exist but are not yet sufficiently validated. There is no evidence that haemodynamic monitoring by TOE accurately stratifies risk or predicts outcome.

TOE can be useful in the operating room in patients with severe valvular lesions. The loading conditions during general anaesthesia differ from those present in the pre-operative evaluation. Functional and ischaemic mitral regurgitation are usually reduced during general anaesthesia. Organic mitral regurgitation can, conversely, increase. In the setting of severe mitral regurgitation, the LV ejection fraction overestimates LV function, and other parameters may be more accurate, such as myocardial velocities or deformation obtained by tissue Doppler imaging or 2D speckle tracking, an angle-independent method. These are promising techniques, but more validation is needed before they can be used routinely in this setting. In patients with severe aortic stenosis, appropriate preload is important during surgery. Monitoring of LV end-diastolic volume may be more accurate than that of pulmonary capillary pressure. An appropriate heart rate is crucial in patients with mitral stenosis and aortic regurgitation: a long diastolic period in the former and shorter duration of diastole in the latter. When inappropriate control of heart rate occurs, the consequences should be assessed: changes in transmural mean gradient and pulmonary arterial pressures in mitral stenosis and changes in LV volumes and indices of LV function in aortic regurgitation.

### Recommendations on intraoperative and/or perioperative transoesophageal echocardiography in patients with or at risk of haemodynamic instability

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class(^a)</th>
<th>Level(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOE is recommended when acute sustained severe haemodynamic disturbances develop during surgery or in the perioperative period</td>
<td>I</td>
<td>C</td>
</tr>
<tr>
<td>TOE monitoring may be considered in patients at increased risk of significant haemodynamic disturbances during and after major non-cardiac surgery</td>
<td>Ilb</td>
<td>C</td>
</tr>
<tr>
<td>TOE monitoring may be considered in patients who present severe valvular lesions during major non-cardiac surgical procedures accompanied by significant haemodynamic stresses</td>
<td>Ilb</td>
<td>C</td>
</tr>
</tbody>
</table>

\(^a\) Class of recommendation.  
\(^b\) Level of evidence.  
TOE = transoesophageal echocardiography.

### Right heart catheterization

Most post-operative ischaemic episodes are silent and not accompanied by changes in pulmonary capillary wedge pressure. Right heart catheterization is not recommended for monitoring patients with intraoperative ischaemia. Indeed, both a large observational study and a randomized multicentre clinical trial did not show a benefit associated with the use of right heart catheterization after major non-cardiac surgery. A case–control analysis was carried out on a subset of patients from the observational study who underwent pulmonary artery catheter placement and who were matched with a similar number of patients who did not undergo right heart catheterization. Patients, who were adjusted for surgical procedure and propensity of catheterization,
Disturbed glucose metabolism

Diabetes mellitus is an important risk factor for perioperative cardiac complications and death. This condition promotes atherosclerosis, endothelial dysfunction, and activation of proinflammatory cytokines. Surgical stress is associated with haemodynamic stress and vasospasm and further enhances the prothrombotic state, while inhibiting fibrinolysis. This may lead to instability of pre-existing coronary plaques, thrombus formation, vessel occlusion, and MI. Also, hyperglycaemia in the absence of established diabetes plays an important role, emphasizing the need for pre-operative management of hyperglycaemia where possible. This is illustrated by studies on patients with pre-diabetes glucose levels who undergo non-cardiac vascular or non-vascular surgery, showing 2- to 4-fold increases in risk of myocardial ischaemia, troponin release, 30-day and long-term cardiac events, and risk of death or cardiovascular mortality in particular. Importantly, impaired glucose tolerance is often identified only after glucose loading. Critical illness is another condition characterized by disturbed glucose homeostasis (‘stress diabetes’ or ‘diabetes of injury’), which develops independently of previously diagnosed diabetes and has repeatedly been identified as an important risk factor for morbidity and/or mortality.

Data from the International Diabetes Foundation reveal a high and increasing prevalence of diabetes in Europe, rising from 7.8% in 2003 to 8.4% in 2007, with an estimated prevalence of at least 9.1% by 2025. More than 30% of the cases were previously undiagnosed, pointing to underestimation of the problem. With ~48 million people affected, diabetes has become one of the main causes of morbidity and mortality in Europe. According to the World Health Organization, ~50% of these patients die of CVDs. It has been well established that surgery in patients with diabetes is associated with longer hospital stay, higher healthcare resource utilization, and greater perioperative mortality. More recently, the emphasis has shifted from diabetes to hyperglycaemia on its own. New-onset hyperglycaemia, as compared with hyperglycaemia in known diabetics, may hold a much higher risk of adverse outcome.

Evidence for strict blood glucose control for patients without known diabetes undergoing non-cardiac surgery is largely derived from studies in critically ill patients. In 2001 the landmark Leuven prospective randomized controlled study demonstrated major clinical benefits for surgical ICU patients whose blood glucose levels were maintained normal (5.0–5.6 mmol/L; 90–100 mg/dL) with intensive insulin therapy, compared with patients who received conventional glucose management and developed hyperglycaemia (8.3–8.9 mmol/L; 150–160 mg/dL). These benefits included lower ICU and in-hospital mortality and prevention of several critical illness-associated complications (critical illness polyneuropathy, severe infections, acute renal failure, and prolonged dependency on mechanical ventilation and intensive care). Also, long-term outcome improved, as shown for the cardiac surgery subgroup. Five years later the Leuven group reported findings from the medical ICU, showing prevention of morbidity, but no mortality benefit from intensive glucose control, except in a subgroup requiring critical care for ≥3 days. Based on these two trials recommendations were made aiming at tight glucose control. Several observational implementation studies on tight glucose management or small, randomized studies in selected ICU patient groups supported the clinical benefits of the Leuven studies. Pooled analysis of the Leuven studies revealed reduced mortality and morbidity for all major clinical diagnostic subgroups, including cardiovascular, respiratory, gastrointestinal/hepatic disease or surgery, active malignancy, and sepsis upon ICU admission. Patients with known diabetes tended to experience less morbidity but a survival benefit appeared absent. All studies described above started glucose control after ICU admission. Timing of initiating insulin therapy is controversial, but a recent medical ICU study showed better outcome when initiated within the first 48 h than after 48 h. Tight intraoperative glucose control may provide additional benefit but appears a challenge and, so far, studies have mainly been set up for cardiac surgery. Moderate intraoperative glycaemic control during CABG (not continued in the ICU) resulted in decreased need for pacing, lower incidence of Af and infections, shortening of the ICU and hospital stay, and decreased recurrent ischaemic events in the long-run. In contrast, implementation of glycaemic control during cardiac surgery, superimposed upon post-operative ICU glycaemic control, did not further reduce perioperative mortality or morbidity. In an observational study, stricter glucose control during liver transplantation was associated with a lower infection rate and 1-year mortality than poor glycaemic control. Studies in the field of critical care have demonstrated the detrimental effect of hyperglycaemia, due to an adverse effect on renal and hepatic function, endothelial function, and immune response, particularly in patients without underlying diabetes. In the Leuven studies, risk of death and degree of hyperglycaemia were positively correlated. Unequivocal demonstration that glycaemic control rather than direct insulin effects mediated the survival and most morbidity benefits of insulin therapy was provided in a rabbit model of critical illness. Several risk factors for cardiac events after non-cardiac surgery are attenuated with strict blood glucose control in the ICU, including endothelial injury/dysfunction, CRP, and asymmetric dimethylarginine, apart from effects on mitochondrial damage, serum lipid profile, and the cortisol response. No effects, or only marginal ones, were seen on cytokines, coagulation, and fibrinolysis.

Recently, the favourable outcomes of the Leuven findings using tight glucose control were questioned. The NICE-SUGAR study investigators randomized ~6000 patients (63% medical ICU and 37% surgical ICU) to either tight glucose control (target glucose level, 4.5–6.0 mmol/L: 81–108 mg/dL) or conventional glucose control (target glucose level, 8.0–10.0 mmol/L: 144–180 mg/dL). Patients were randomized to treatment within 24 h after admission using i.v. insulin infusions for glucose control. The primary endpoint, death by 90 days after randomization, was increased with intensive glucose control (27.5%) as compared with 24.9% with conventional control. There was no morbidity difference between the two study groups, and hence the excess...
mortality remains unexplained. As could be expected, hypoglycaemia (<40 mg/dL) occurred in more patients in the intensive-control group than in the conventional-control group (6.8% vs. 0.5%, P < 0.001). The strength of the NICE-SUGAR trial was its large and multicentre design using a computer-guided insulin infusion protocol. However, this protocol used an if–then algorithm based upon inaccurate and non-standardized stand-alone glucometers for blood glucose measurements. In addition, NICE-SUGAR had an open-label design, a small imbalance between the groups with respect to corticosteroid therapy, and 10% of patients randomized to intensive glucose control discontinued the study prematurely. The differences in outcome between the two studies should be explained.

(i) The Leuven trials were performed in a single centre with standardized care which included early parenteral nutrition supplementing enteral feeding, whereas in the NICE-SUGAR trial enteral nutrition predominated, resulting in hypocaloric feeding in particular during the first week after admission to ICU.

(ii) The target for initiating insulin in the standard treatment group was different, with insulin being advocated in the Leuven study only when blood glucose exceeded the renal threshold of >215 mg/dL, an approach that considers hyperglycaemia as a possible beneficial adaptation, whereas in NICE-SUGAR a target of 144–180 mg/dL was used in the standard group, which resulted in 70% of the patients receiving insulin and reaching an average blood glucose level of 8.0 mmol/L (144 mg/dL).

(iii) Also in the intervention group of NICE-SUGAR, the compliance to therapy was much lower than in the Leuven studies, which resulted in an average glucose level of 6.6 mmol/L (118 mg/dL) and a very large overlap with the glucose levels in the control group.

(iv) The use of inaccurate glucometers in NICE-SUGAR may have misguided the insulin therapy and may have overlooked hypokalaemia, a possible cause of excess cardiovascular mortality, which is prevented with the use of blood gas analysers for glucose measurement.

(v) The nurse experience with the intervention in NICE-SUGAR was much less than in the Leuven studies, in view of the limited number of patients recruited per centre (<15% of all patients screened in the participating ICUs) as compared with 70–95% in the Leuven studies.

The results of the NICE-SUGAR trial may suggest that intensive glucose control could harm patients admitted to the ICU, in terms of death, when glucose levels are below the range of 7.8–10.0 mmol/L (140–180 mg/dL). In contrast, evidence derived from previous studies suggests the clinical benefit of maintenance of normoglycaemia (4.4–6.1 mmol/L; 80–110 mg/dL) as compared with tolerating hyperglycaemia up to 11.9 mmol/L (215 mg/dL) for adult critically ill patients (Table 10).

Until further data become available clarifying the reasons for the different outcomes between the studies, it is recommended that the management of blood glucose in the ICU be optimized, avoiding the extremes of hyperglycaemia and also hypoglycaemia. The available data indicate that this therapy should be started immediately after ICU admission. It may be advisable to target a level of ~8.0 mmol/L (144 mg/dL) for settings and patient populations that are comparable with those studied in NICE-SUGAR.

### Table 10 Clinical benefits of intensive insulin therapy in critically ill patients with a non-cardiac diagnosis upon ICU admission

<table>
<thead>
<tr>
<th></th>
<th>ICU stay ≥3 days</th>
<th>P-value</th>
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<tbody>
<tr>
<td></td>
<td>CIT</td>
<td>IIT</td>
</tr>
<tr>
<td>ICU mortality</td>
<td>27.4%</td>
<td>22.7%</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>38.7%</td>
<td>32.1%</td>
</tr>
<tr>
<td>Renal replacement therapy</td>
<td>11.2%</td>
<td>7.3%</td>
</tr>
<tr>
<td>Critical illness polyneuropathy&lt;sup&gt;a&lt;/sup&gt;</td>
<td>51.3%</td>
<td>34.4%</td>
</tr>
<tr>
<td>Bacteremia</td>
<td>13.5%</td>
<td>10.6%</td>
</tr>
<tr>
<td>Mechanical ventilation (days)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>8 (4–17)</td>
<td>7 (3–13)</td>
</tr>
<tr>
<td>ICU stay (days)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>9 (4–18)</td>
<td>8 (4–15)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Percentage of those screened of screened.
<sup>b</sup>Median (interquartile range). CIT = conventional insulin therapy; IIT = intensive insulin therapy.

### Recommendations on blood glucose control

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Class&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Level&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-operative prevention of hyperglycaemia [targeting levels at least below 10.0 mmol/L (180 mg/dL)] with intensive insulin therapy is recommended in adults after high-risk or complicated major surgery requiring admission to ICU</td>
<td>I</td>
<td>B</td>
</tr>
<tr>
<td>Intraoperative prevention of hyperglycaemia with insulin may be considered</td>
<td>IIb</td>
<td>C</td>
</tr>
<tr>
<td>Post-operative prevention of hyperglycaemia with insulin after uncomplicated elective surgery may be considered</td>
<td>IIb</td>
<td>C</td>
</tr>
</tbody>
</table>

<sup>a</sup>Class of recommendation.
<sup>b</sup>Level of evidence.

ICU = intensive care unit.

### Anaesthesia

An optimal perioperative course stems from a close cooperation between cardiologists, surgeons, pulmonologists, and anaesthesiologists. Pre-operative risk assessment and pre-operative optimization of cardiac disease should be performed jointly.

There is a paucity of strong evidence-based data supporting the choice of a particular perioperative approach and thus several options are available. Sufficiently powered randomized trials addressing the potential relationship between patient outcome and perioperative management are still lacking for cardiac patients undergoing non-cardiac surgery.
Intraoperative anaesthetic management

The choice of the anaesthetic agent has been considered to be of little importance with regard to patients’ outcome provided the vital functions are adequately supported. There is conflicting evidence from cardiac surgery over whether a specific method is advantageous in cardiac disease, but there is no evidence of superiority of any specific anaesthetic agent in non-cardiac surgery.224,225

Most anaesthetic techniques reduce sympathetic tone, leading to vasodilatation and reduction in systemic blood pressure. Thus, anaesthesiological management must ensure the proper maintenance of organ perfusion pressure.

Neuraxial techniques

Spinal and epidural anaesthesia also induce sympathetic blockade. Depending on the height of the block, it induces peripheral vasodilation with fall in blood pressure. When reaching the thoracic dermatome level 4, a reduction in cardiac sympathetic drive with subsequent reduction in myocardial contractility, heart rate, and change in cardiac loading conditions will appear. The speed and strength of sympathetic blockade will depend on dosage and drugs as well as the patient’s condition. There is conflicting evidence on the effect of neuraxial blocks on patient outcome after non-cardiac surgery. One meta-analysis reported significantly improved survival and reduced incidence of post-operative thromboembolic, cardiac and pulmonary complications with neuraxial blockade compared with general anaesthesia.226 A major criticism of this study has been the inclusion of older studies, which may have made the results invalid for current practice. A recent analysis of a large cohort of patients (10 564 patients without and 2253 patients with epidural) undergoing colon resection confirmed the improved survival with epidural analgesia at 7 and 30 days after surgery, but it was not possible to identify the cause of death.227 Also cardiac morbidity was not different between the two groups.

Randomized studies and a meta-analysis of several randomized clinical trials in non-cardiac surgery patients, comparing outcome with regional and general anaesthetic techniques have shown little consistent evidence of improved outcome and reduced post-operative morbidity and mortality.228–230 It has been estimated that the number of patients needed for a randomized clinical trial to determine whether epidural anaesthesia and analgesia would affect mortality in patients undergoing high-risk vascular surgery would be ~24 000, while enrolment of 1.2 million would be needed in a low-risk procedure.227 Thus, present studies are underpowered for a valid analysis of risk of death for procedures with low surgical risk. No study has clearly demonstrated a difference in outcome with different monitoring techniques, fluid management, or transfusion strategies. Most studies have used different pre-determined therapeutic goals, often requiring inotropic support, a factor that may have been of importance for the results.231 The importance of skilled anaesthesiological management in keeping adequate circulation is often underlined.231

Post-operative pain management

Post-operative pain is a major concern, reported in 5–10% of the patients. It may increase sympathetic drive and delay recovery.232,233 The evidence that pain causes organ complications after surgery is less clear. Neuroaxial analgesia with local anaesthetics/opioids and/or α2-agonists, i.e., opioids alone or in combination with non-steroidal anti-inflammatory drugs seems to be the most effective. The benefit of invasive analgesic techniques should be weighed against potential dangers. This is of special importance when considering the use of neuraxial blockade in patients under chronic antithrombotic therapy due to increased potential of a neuraxial haematoma. It is beyond the scope of these guidelines to give recommendations for the use of neuraxial blocks in patients with coagulation disturbances.

Patient-controlled analgesia is an alternative for post-operative pain relief. Recent meta-analyses of controlled randomized trials show that patient-controlled analgesia has some advantage with regard to patient satisfaction over nurse-controlled or on-demand analgesia.234 No difference with regard to morbidity or final outcome was demonstrated. Patient-controlled analgesia is an adequate alternative in patients and situations not suited for regional anaesthesia. Routines for follow-up and documentation of effects should be in place.232,235–237 Non-steroid anti-inflammatory drugs and the cyclooxygenase-2 (COX-2) inhibitors have the potential for promoting heart and renal failure as well as thromboembolic events and should be avoided in patients with myocardial ischaemia. The COX-2 inhibitors cause less gastrointestinal ulceration and bronchospasm. The final role for these drugs in the treatment of post-operative pain in cardiac patients undergoing non-cardiac surgery has not been defined. The drugs should be avoided in patients with renal and heart failure, elderly patients, patients on diuretics, as well as patients with unstable haemodynamics.238

Recommendations on anaesthesia

<table>
<thead>
<tr>
<th>Recommendations</th>
<th>Classa</th>
<th>Levelb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consideration should be given to performing thoracic epidural anaesthesia in high-risk surgery for patients with cardiac disease</td>
<td>IIa</td>
<td>A</td>
</tr>
<tr>
<td>Use of non-steroidal anti-inflammatory drugs and COX-2 inhibitors for post-operative pain control is not recommended in patients with renal and heart failure, myocardial ischaemia, elderly patients, as well as in patients taking diuretics or having unstable haemodynamics</td>
<td>III</td>
<td>B</td>
</tr>
</tbody>
</table>

aClass of recommendation.  
bLevel of evidence.  
COX-2 = cyclooxygenase-2.

Putting the puzzle together

Figure 4 presents in algorithmic form an evidence-based stepwise approach for determining which patient benefits from cardiac testing, coronary artery revascularization, and cardiovascular therapy prior to surgery. For each step the committee has included the level of the recommendations and the strength of evidence in the accompanying Table 11.

Step 1. The urgency of the surgical procedure should be assessed. In urgent cases, patient- or surgical-specific factors dictate the
Figure 4 Summary of pre-operative cardiac risk evaluation and perioperative management.
strategy, and do not allow further cardiac testing or treatment. In these cases, the consultant provides recommendations on perioperative medical management, surveillance for cardiac events, and continuation of chronic cardiovascular medical therapy.

Step 2. If the patients is unstable, as presented in Table 12, this condition should be clarified and treated appropriately prior to surgery. Examples are unstable coronary syndromes, decompenstated heart failure, severe arrhythmias, or symptomatic valvular disease. This usually leads to cancellation or delay of the surgical procedure. For instance, patients with unstable angina pectoris should be referred for coronary angiography to assess the therapeutic options. Treatment options should be discussed in a multidisciplinary team, involving all perioperative care physicians, because interventions might have implications for anaesthesiological and surgical care. For example, the initiation of dual antiplatelet therapy after coronary artery stent placement might complicate loco-regional anaesthesia or

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### Table 11  
Summary of pre-operative cardiac risk evaluation and perioperative management

<table>
<thead>
<tr>
<th>Step</th>
<th>Urgency</th>
<th>Cardiac condition</th>
<th>Type of surgery</th>
<th>Functional capacity</th>
<th>Number of clinical risk factors</th>
<th>LV echo</th>
<th>ECG</th>
<th>Stress Testing</th>
<th>β-Blockers</th>
<th>ACE-inhibitors</th>
<th>Aspirin</th>
<th>Status</th>
<th>Coronary Revascularisation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Urgent</td>
<td>surgery</td>
<td></td>
<td></td>
<td>III C</td>
<td>Ia C</td>
<td>C</td>
<td>C</td>
<td>I C</td>
<td>I C</td>
<td>I C</td>
<td>I C</td>
<td>III C</td>
</tr>
<tr>
<td>2</td>
<td>Elective surgery</td>
<td>Unstable</td>
<td></td>
<td></td>
<td>I C</td>
<td>I C</td>
<td>C</td>
<td>III C</td>
<td>III C</td>
<td>III C</td>
<td>I C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Elective surgery</td>
<td>Stable</td>
<td>Low risk (&lt;1%)</td>
<td></td>
<td>None</td>
<td>III B</td>
<td>III B</td>
<td>III B</td>
<td>III B</td>
<td>III B</td>
<td>III B</td>
<td>III B</td>
<td>III C</td>
</tr>
<tr>
<td>4</td>
<td>Elective surgery</td>
<td>Intermediate risk (1-5%)</td>
<td>Moderate or poor</td>
<td></td>
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<td>III B</td>
<td>III B</td>
<td>III B</td>
<td>III B</td>
<td>III B</td>
<td>III B</td>
<td>III C</td>
</tr>
<tr>
<td>5</td>
<td>Elective surgery</td>
<td>High risk (&gt;5%)</td>
<td>Moderate or poor</td>
<td></td>
<td>≤ 2</td>
<td>IIa C</td>
<td>I B</td>
<td>IIa C</td>
<td>III A (no titration)</td>
<td>IIa C</td>
<td>I B</td>
<td>IIa C</td>
<td>II B</td>
</tr>
<tr>
<td>6</td>
<td>Elective surgery</td>
<td>High risk (&gt;5%)</td>
<td>Moderate or poor</td>
<td></td>
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<td>IIa C</td>
<td>I C</td>
<td>I B</td>
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<td>IIa C</td>
<td>I B</td>
<td>IIa C</td>
<td>II B</td>
</tr>
</tbody>
</table>

### Table 12  
Unstable cardiac conditions

- Unstable angina pectoris
- Acute heart failure
- Significant cardiac arrhythmias
- Symptomatic valvular heart disease
- Recent MI* and residual myocardial ischemia

*An MI within 30 days, according to the universal definition of MI.
specific surgical procedures. Depending on the outcome of this discussion, patients can proceed for coronary artery intervention, namely CABG, balloon angioplasty, or stent placement with the initiation of dual antiplatelet therapy if the index surgical procedure can be delayed, or directly for operation if delay is incompatible with optimal medical therapy.

Step 3. Determine the risk of the surgical procedure (Table 4). If the estimated 30-day cardiac risk of the procedure in cardiac-stable patients is low, <1%, it is unlikely that test results will change management and it would be appropriate to proceed with the planned surgical procedure. The consultant can identify risk factors and provide recommendations on lifestyle and medical therapy according to the ESC Guidelines for post-operative care to improve long-term outcome.

Step 4. Consider the functional capacity of the patient. If an asymptomatic or cardiac-stable patient has moderate or good functional capacity, >4 METs, perioperative management is unlikely to be changed on the basis of test results irrespective of the planned surgical procedure. Even in the presence of clinical risk factors, it is appropriate to refer the patient for surgery. In patients with IHD or risk factor(s), statin therapy and a titrated low-dose β-blocker regimen can be initiated prior to surgery, as outlined in Table 11.

Step 5. It is recommended that chronic aspirin therapy be continued. Discontinuation of aspirin therapy should be considered only in those patients in which haemostasis is difficult to control during surgery.

Step 6. In patients with a moderate or poor functional capacity, consider the risk of the surgical procedure, as outlined in Table 4. Patients scheduled for intermediate-risk surgery can proceed for surgery; statin therapy and a titrated low-dose β-blocker regimen appears appropriate prior to surgery. In patients with systolic LV dysfunction, evidenced by LV ejection fraction <40%, ACE inhibitors (or ARBs in patients intolerant of ACE inhibitors) are recommended before surgery. In patients with one or more clinical risk factors, a pre-operative baseline ECG is recommended to monitor changes during the perioperative period. In patients scheduled for high-risk surgery, as described in Table 4, clinical risk factors (Table 13) are noted. In patients with up to two clinical risk factors, statin therapy and a titrated low-dose β-blocker regimen are recommended prior to surgery. In patients with systolic LV dysfunction, evidenced by LV ejection fraction <40%, ACE inhibitors (or ARBs in patients intolerant of ACE inhibitors) are recommended before surgery.

Consider non-invasive testing in patients with ≥3 clinical risk factors (Table 13). Non-invasive testing can also be considered prior to any surgical procedure for patient counselling, or change of perioperative management in relation to type of surgery and anaesthesia technique.

Step 7. Interpretation of non-invasive stress test results. Patients without stress-induced ischaemia, or mild to moderate ischaemia suggestive of one- or two-vessel disease, can proceed with the planned surgical procedure. It is recommended that statin therapy and a titrated low-dose β-blocker regimen be initiated. In patients with extensive stress-induced ischaemia, as assessed by non-invasive testing, individualized perioperative management is recommended, taking into consideration the potential benefit of the proposed surgical procedure compared with the predicted adverse outcome. Also, the effect of medical therapy and/or coronary revascularization must be assessed, not only for immediate post-operative outcome, but also for long-term follow-up. In patients referred for percutaneous coronary artery intervention, the initiation and duration of antiplatelet therapy will interfere with the planned surgical procedure. In patients referred for angioplasty, non-cardiac surgery can be performed within 2 weeks after intervention with continuation of aspirin treatment. In patients with bare metal stent placement, non-cardiac surgery can be performed after 6 weeks to 3 months following intervention. Dual antiplatelet therapy should be continued for at least 6 weeks, preferably for up to 3 months. After this period, at least aspirin therapy should be continued. In patients with recent DES placement, non-cardiac surgery can be performed after 12 months following intervention, before which time dual antiplatelet therapy is recommended. After this period, at least aspirin therapy should be continued.

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**Table 13 Clinical risk factors**

- Angina pectoris
- Prior Mi
- Heart failure
- Stroke/transient ischaemic attack
- Renal dysfunction (serum creatinine >170 μmol/L or 2 mg/dL or a creatinine clearance of <60 mL/min)
- Diabetes mellitus requiring insulin therapy

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*According to the universal definition of Mi."
References


OVER THE LAST 2 DECADES, utilization of percutaneous coronary interventions (PCIs) for the treatment of coronary artery disease has increased by more than 320%. In contemporary practice, most nonsurgical interventions for coronary artery disease involve placement of stents in the diseased coronary circulation because coronary artery stent placement improves the short- and long-term patency rate of coronary vessels compared with simple balloon angioplasty. In 2003 alone, 84% of the 660,000 coronary procedures performed in the United States involved placement of at least 1 coronary stent. The initial trials of coronary artery stents were complicated by unacceptably high rates of stent thrombosis (up to 8.6% incidence if PCI was performed during myocardial infarction). Stent thrombosis is a potentially lethal event characterized by the formation of platelet-rich thrombus on the metal stent struts before the development of a protective endothelial barrier. Mortality rates between 30% and 50% have been reported when stent thrombosis occurs and myocardial infarction always follows. This rate of thrombosis has subsequently decreased to less than 1% due, in large part, to a better understanding of the pathophysiology of thrombosis, implementation of effective antiplatelet agents, and advances in stent deployment and design.

Given the increasing role of PCI in the management of coronary artery disease and the aging of the population, there will be many more patients presenting in the perioperative period with a history of coronary stent placement, either recent or remote. Perioperative physicians need to be aware of the issues surrounding antiplatelet therapy, stent thrombosis, and bleeding risks as they pertain to this patient population. The problem is further confounded by the fact that this is one of the fastest changing areas of medicine, making it difficult to stay current and deliver optimum patient care. In addition, the popularity of drug-eluting stents (DESs) combined with the lack of large, prospective studies of these patients in the perioperative period add to the complexity of clinical management.

PATHOPHYSIOLOGY OF STENT OCCLUSION

Two possible mechanisms exist to explain the closure of a previously patent coronary artery stent: in-stent restenosis (ISR) or stent thrombosis. It is important that the reader understand the difference between these 2 clinical entities because the pathophysiology and clinical implications differ markedly. Some of these differences are shown in Figure 1.

Coronary artery ISR has been and continues to be a key limiting factor in the long-term success of PCI procedures. Before 2002, only bare metal stents (BMSs) were placed. The use of BMSs, however, may be complicated by the development of neointimal hyperplasia resulting in narrowing or occlusion of the coronary vessel. This complication occurs in more than 30% of high-risk subgroups, including those patients with diabetes mellitus, small coronary vessels, or long lesions. Angioplasty and the placement of coronary artery stents result in coronary artery de-endothelialization and deposition of a layer of platelets and fibrin in the injured artery. Smooth muscle cells release cytokines that attract leukocytes. Growth factors released by these leukocytes and platelets lead to the migration of smooth muscle cells to the neointima. Over time, this matrix becomes less cellular as the production of extracellular elements increases, leading to partial or complete occlusion of the stent. Essentially, the problem of native artery atherosclerotic disease is replaced by the problem of scar tissue growth inside the stent. Until recently, there have been no effective interventions to prevent this complication, and percutaneous treatment options have been of little help in the treatment of ISR.

In 2002, the Food and Drug Administration approved the use of DESs. These stents currently account for approximately 85% of stents placed in the United States. Both Taxus (Boston Scientific, Natick, MA) (paclitaxel-eluting) and Cypher ( Cordis, Johnson and Johnson, Miami Lakes, FL) (sirolimus-eluting) stents make use of slowly released molecules that contain anti-inflammatory and antiproliferative properties. This change in technology has proven useful in the prevention of ISR. In the TAXUS-IV trial, paclitaxel-eluting stents were shown to significantly reduce the rates of target vessel
failure and major adverse cardiac events versus BMSs at the 1-year follow-up.\textsuperscript{15} In the SIRIUS trial of 1,058 patients, Moses et al\textsuperscript{11} showed a statistically significant reduction in the rate of target vessel failure at 9 months in patients treated with sirolimus-eluting stents versus patients treated with BMSs. Despite the usefulness of DESs in preventing ISR, as of yet, they have not been shown to influence the rates of myocardial infarction or death.\textsuperscript{16}

In contrast to ISR, which develops over a period of months and can be asymptomatic in 50\% of cases, stent thrombosis is a sudden, potentially catastrophic complication of PCI. Stent thrombosis is defined as partial or total stent occlusion and historically was thought most likely to occur within 30 days of PCI.\textsuperscript{17} It manifests as an acute myocardial infarction with sudden onset of chest pain; is generally associated with ST-segment elevation on the electrocardiogram; and can lead to ventricular arrhythmias, cardiogenic shock, or sudden death. This “early stent thrombosis” (<30 days after placement) is typically because of mechanical causes such as coronary artery dissection or incomplete deployment of the stent\textsuperscript{13} and has a frequency of approximately 0.5 to 2\%. Although late stent thrombosis is known to occur with BMSs,\textsuperscript{18} the incidence is thought to be very low. With the recent use of predominantly DESs, an ever-increasing number of cases of late stent thrombosis months to years after placement are being reported with many of these events occurring in the perioperative period.\textsuperscript{18-25}

The cause of late stent thrombosis, especially with the DES, remains incompletely understood. Potential causes include delayed arterial healing,\textsuperscript{26} delayed endothelialization of the DES,\textsuperscript{27,28} stent malapposition, and possible resistance to the antiplatelet effects of aspirin or thienopyridines.\textsuperscript{13} The acute and often complete nature of stent thrombosis has severe consequences because most cases result in a transmural myocardial infarction (MI) or death.\textsuperscript{6,20,29,30}

Regardless of timing, platelets play a central role in the development of stent thrombosis, and their activation is an important early step in the pathophysiology of thrombosis. Platelet activation involves 3 essential steps: (1) a conformational change increases the effective surface area of the platelet membrane; (2) the secretion of prothrombotic, inflammatory, and chemoattractant mediators that propagate the thrombotic process; and (3) the activation of the glycoprotein IIb/IIIa receptor from its inactive form that allows binding of fibrinogen and cross-linking with other platelets.\textsuperscript{31} Multiple agonists including thromboxane and adenosine diphosphate contribute to the activation of platelets. Aspirin antagonizes the production of thromboxane by inhibiting the enzyme cyclooxygenase 1. The thienopyridines (ticlopidine and clopidogrel) irreversibly inhibit binding of adenosine diphosphate to its receptor. The ultimate effect of combining these 2 agents is a synergistic reduction in platelet aggregation\textsuperscript{32-34} and represents the current recommended antplatelet therapy after PCI.\textsuperscript{35}

The early trials of thienopyridines combined with aspirin essentially all used ticlopidine. Clopidogrel (Bristol-Myers Squibb Company, New York, NY), an acetate derivative of ticlopidine, has subsequently emerged as the thienopyridine of choice in the United States and in many other countries. The full antiplatelet effects of ticlopidine are delayed for several days after initiation of therapy, whereas the near-maximal effects of clopidogrel are seen only 2 hours after a 300-mg oral loading dose.\textsuperscript{31} Clopidogrel also has been shown to exert more
powerful platelet antiaggregant effects.36 Lastly, ticlopidine use may be complicated by severe neutropenia in about 1% of patients37 and thrombotic thrombocytopenic purpura in 1:1,000 patients.38 These pharmacologic differences, combined with the fact that numerous trials have now shown the efficacy of clopidogrel and ticlopidine to be at least equal,39-41 have led to the use of clopidogrel and aspirin combination therapy as the standard of care for the prevention of coronary stent thrombosis. Despite clopidogrel being the current thienopyridine of choice, it should be noted that recent evidence suggests that 4% to 30% of patients will not show an adequate platelet response to conventional doses.32 These “nonresponders” may represent a group of patients at high risk for stent thrombosis.

Without adequate antiplatelet therapy, patients remain at high risk of stent thrombosis until complete endothelialization of the stent has occurred, at which time the risk of thrombosis decreases significantly.43 Endothelialization of bare metal stents typically occurs 2 to 6 weeks after placement; however, this process is delayed for an undetermined amount of time when DESs are placed (see later). The American College of Cardiology, American Heart Association, and Society for Cardiovascular Angiography and Interventions (ACC/AHA/SCAI) recently released updated guidelines for oral antiplatelet therapy after PCI. In summary, patients already taking aspirin should continue this therapy before PCI, and patients not previously on aspirin should be given 300 to 325 mg at least 2 hours before PCI. Postprocedurally, patients should continue to take 325 mg of aspirin daily for 1 month after a BMS, for 3 months after placement of sirolimus-eluting stents, and for 6 months after placement of paclitaxel-eluting stents; following these intervals, aspirin therapy should be continued indefinitely at 75 to 162 mg/d. In addition, patients should receive 300 mg of clopidogrel 6 hours before PCI and continue with 75 mg/d for 1 month after BMS, for at least 3 (sirolimus stents) to 6 (paclitaxel stents) months after DESs, and ideally up to 12 months if not at high risk of bleeding complications.35

Although DESs have proven useful in decreasing the rate of neointimal hyperplasia that leads to restenosis, they also likely inhibit the normal endothelialization process.28 Endothelialization is important in providing a protective covering of the thrombogenic stent and thus preventing thrombosis. As a consequence, patients with DES actually require longer courses of antiplatelet therapy and are potentially at higher risk of thrombosis should these agents be discontinued prematurely.

Stabile et al recently described 2 interesting cases of late stent thrombosis. Both patients had multivessel coronary disease treated with combinations of BMSs and DESs. One patient discontinued clopidogrel 3 months after stenting and stopped aspirin 12 months after stenting. The second patient stopped both aspirin and clopidogrel 11 months after stent placement in preparation for colonoscopy and polyectomy. Both patients subsequently developed symptoms of an acute coronary syndrome. Angiographic studies of both patients revealed thrombosis of the DES while the BMS remained patent.22 This report highlights the potential for late stent thrombosis after discontinuation of antiplatelet therapy in patients who have received DESs and may indicate clinically important differences in the rate of endothelialization between BMSs and DESs.

SURGERY AFTER CORONARY STENTING

Several case series have attempted to evaluate the risk of noncardiac surgery (NCS) after recent PCI with stent placement. In 2000, Kaluza et al published a series of 40 patients who underwent BMS placement 1 to 39 days (average of 13 days) before NCS. They found an alarmingly high rate of adverse outcomes with 8 deaths, 7 MIs, and 11 major bleeding episodes. The authors attributed 6 of the 8 deaths to MI, whereas 2 resulted from bleeding complications. Four of the patients who died had both MI and bleeding complications. Angiography confirmed stent thrombosis in 2 of the patients suffering MIs. All deaths and the majority of the bleeding complications occurred in patients who underwent NCS less than 14 days after stent placement. The mortality rate for the 25 patients undergoing surgery less than 14 days after stent placement was 32%. Most of the patients in the group suffering complications had their aspirin and ticlopidine withheld only 1 to 2 days before operation.44

Subsequently, Wilson et al described their experience in a series of patients from the Mayo Clinic Percutaneous Coronary Intervention and Surgical Databases. They identified 207 patients who underwent NCS within 2 months of BMS placement. Eight of these 207 patients (4%) suffered a major adverse cardiac event, and 6 of these patients died. All of the patients suffering major adverse events underwent surgery within 6 weeks of stent placement; there were no complications in the 39 patients undergoing NCS 7 to 9 weeks after stent placement. Compared with the report of Kaluza et al, Wilson and colleagues found a significantly lower occurrence of both thrombotic complications and excessive perioperative bleeding. Twenty-six percent of patients received aspirin and a thienopyridine up to the time of surgery. Another 14% of study patients continued aspirin and had received the last dose of thienopyridine within 10 days of surgery. Only 2 of these patients were described as having “excessive bleeding.” Continuing antiplatelet therapy up to the day of surgery did not appear to influence transfusion requirements compared with stopping therapy >10 days before surgery (p = 0.54).45 These authors hypothesized that the decrease in adverse perioperative events when patients underwent NCS >6 weeks after stent placement corresponded to the time course of re-endothelialization and that, when possible, elective surgery should be delayed for at least 6 weeks to allow completion of an antiplatelet therapy with aspirin and a thienopyridine.43

Two additional studies provide support for this recommendation.46,47 These 2 retrospective reports also showed that the risk of adverse events was related to the timing of surgery after PCI with BMS, with the optimal waiting period appearing to be approximately 6 weeks. These 2 studies failed to show an increased risk of bleeding complications when antiplatelet agents were continued up to the day of surgery, and, in fact, 1 study showed lower mortality with this approach.47

Recently, the first review of a prospectively maintained database of patients undergoing NCS after PCI has been published.48 This series included 103 patients undergoing NCS within 1 year of stent placement. The authors attempted to identify the type of stent placed but were largely unsuccessful because of poor documentation. However, this cohort included
at least 5 patients who had previously undergone DES placement. In this study, antiplatelet therapy was either continued throughout the perioperative period or it was discontinued <3 days before surgery, and patients were maintained on either low–molecular-weight heparin (LMWH) (1 mg/kg/d) or unfractionated heparin infusions (>1.5-fold activated partial thromboplastin time). Five patients died (4.9%) because of cardiac events. Four patients had “excessive” bleeding with no patient receiving more than 6 units of packed red blood cells. The proximity of PCI to surgery was again found to be an important factor in outcome; patients undergoing NCS <35 days after PCI had a 2-fold increased risk of adverse events versus patients undergoing NCS >90 days after PCI.

The vast majority of the patients enrolled in the previously described studies received a BMS, making these data of decreasing relevance in the modern era of predominant DES placement. However, a recent series begins to shed light on the subject of DES in the perioperative period. Schouten et al described the outcome of 192 patients undergoing NCS within 2 years of stent placement. Importantly, 99 of these patients had received DESs. There was a wide range of surgery, and the decision of whether or not to continue antiplatelet therapy into the perioperative period was left to the discretion of the primary physician. Ultimately, 101 patients (53%) were maintained on their antiplatelet therapy throughout the perioperative period, and 91 patients had clopidogrel and aspirin withheld 1 week prior to surgery. Five patients died of cardiac complications with 4 of the deaths caused by stent thrombosis (2 BMSs and 2 DESs). The patients who died had all had their antiplatelet agents withheld. Indeed, cessation of clopidogrel before the period suggested by the ACC/AHA/SCAI guidelines conferred a 30.7% risk of death versus no deaths for a similar group of patients who were continued on antiplatelet therapy. There was 1 patient with a DES that had stent thrombosis 253 days after placement when antiplatelet agents were withheld.

PERIOPERATIVE DECISION-MAKING IN PATIENTS WITH CARDIAC STENTS

The previously described studies permit some conclusions to be reached while leaving other questions unresolved. Timing of surgery after PCI is consistently a factor in the complication rate. For BMSs, the minimum safe waiting period appears to be 6 weeks. This information is not yet available for patients with a DES, but current ACC/AHA/SCAI guidelines suggest that patients with DESs should complete a minimum of 3 (sirolimus) to 6 (paxilaxel) months of antiplatelet therapy before elective surgery. The numerous reports describing late and unpredictable thrombotic complications suggest that there may be no completely “safe” time to stop antiplatelet therapy. An important finding in these reports is that many cases of thrombosis occurred more than 1 year after stent placement. There is literature to suggest that prolonged antiplatelet therapy (up to 12 months) after PCI decreases the incidence of cardiovascular ischemic events, and a recent trial showed that beneficial reductions in death and MI may be seen if clopidogrel is continued for 24 months after DES placement.

Furthermore, the ACC/AHA/SCAI guidelines suggest that clopidogrel therapy be continued ideally up to 12 months in patients who are not at risk for bleeding complications. The prolonged course of antiplatelet therapy may be required to protect the DES until endothelialization has occurred. The risk of late stent thrombosis with DESs is currently undergoing extensive scrutiny by the Food and Drug Administration with recognition that there is a small but definite increased risk with DESs compared with BMSs; whether prolongation of dual antiplatelet therapy will reduce this excess risk is uncertain.

One further conclusion that can be reached from the reported studies is that the risk of thrombotic complications appears to significantly outweigh the risk of bleeding problems. This is particularly exemplified in the study of Vicenzi et al. Of the 46 (out of a total of 103) patients suffering a perioperative complication, only 4 patients had bleeding complications; all other adverse events were cardiac in nature. Importantly, the 5 deaths in this study were from cardiac causes. In 3 of the reported studies, continuing antiplatelet therapy into the perioperative period did not increase the risk of bleeding complications. These studies and previous experience from the cardiac surgery literature suggest that, at a minimum, aspirin may be safely continued perioperatively for the majority of scheduled procedures.

The optimal timing of clopidogrel cessation before surgery that would prevent hemorrhagic complications has yet to be determined. The effects of both clopidogrel and aspirin are irreversible for the lifespan of each individual platelet they bind. Thus, recovery of platelet function is dependent on the generation of new platelets. At least 3 to 5 days are likely needed to accumulate a significant number of new, unaffected platelets. The bleeding consequences of clopidogrel exposure before surgery have been described in the cardiac surgery literature. Data from the CURE trial indicate that, at least in cardiac surgery, withholding clopidogrel 5 days before operation decreases the risk of hemorrhagic complications. The decision of when or if to stop clopidogrel may also be influenced by the choice of anesthesia. The American Society of Regional Anesthesia advises discontinuation of ticlopidine 10 days and clopidogrel 7 days before the performance of neuraxial anesthesia techniques to avoid spinal or epidural hematoma. Lastly, the type of surgical procedure will be an important factor in determining optimal management of antiplatelet therapy. Patients undergoing open procedures in which bleeding sites may be readily identified are potentially at less risk of catastrophic bleeding complications when compared with those undergoing intracranial, urologic, neuraxial, or laparoscopic procedures.

In the previously described studies, clopidogrel was stopped from 0 to 10 days preoperatively. This decision as to whether or not to continue antiplatelet therapy into the perioperative period must be weighed against the risk of thrombotic complications and its devastating effects. A consistent finding in the trials evaluating stent thrombosis in nonsurgical patients is the premature cessation of antiplatelet therapy. The hypercoagulable state seen in the perioperative period likely adds another risk factor for thrombosis.

Although the use of heparin and LMWH to prevent stent thrombosis when antiplatelet agents are withheld has been described, caution should be used in applying this practice. Stent thrombosis is a platelet-mediated event as described...
earlier and neither heparin nor LMWH is likely to offer significant protection. The 2 studies describing anticoagulation to prevent stent thrombosis were nonrandomized and likely much too small to show success in preventing a relatively rare, albeit devastating, event.\textsuperscript{55,56} Lastly, data from the interventional cardiology literature suggest that LMWH is of little benefit in preventing stent thrombosis.\textsuperscript{50,60} If an agent with a shorter half-life is desired for transition off of clopidogrel, a small molecule glycoprotein IIb/IIIa inhibitor, such as tirofiban or eptifibatide, both of which have relatively short half-lives, may be an effective choice. These agents are profound inhibitors for platelet function, and their use in the perioperative period for prevention of stent thrombosis has been described in at least 1 case report.\textsuperscript{60} Prospective trials will be required to study the use of these agents in this setting before any strong recommendations can be made.

All of the previously described factors will be important variables in considering how best to proceed with this complex patient population. Patients having undergone PCI within the last year presenting for elective but necessary surgery (eg, excision of colon cancer) should be discussed and managed with the input of a knowledgeable cardiologist, anesthesiologist, and surgeon. Truly elective surgeries should be avoided in the first 3 months after a sirolimus stent and the first 6 months after a paclitaxel stent. Given the recent ACC/AHA/SCAI recommendation that clopidogrel ideally be continued for up to 12 months in patients receiving DES and the recent evidence indicating the beneficial effects of prolonged antiplatelet therapy,\textsuperscript{51} it may be reasonable to postpone truly elective surgery (eg, knee arthroscopy, hip arthroplasty, and so on) until that interval has elapsed.

Patients found to have significant coronary disease during a preoperative cardiac evaluation deserve a similar discussion and may have more options. If coronary revascularization is desired preoperatively and the procedure can be safely delayed for 6 weeks, a BMS may be used. In the contemporary practice of using β-adrenergic blockade at-risk patients,\textsuperscript{62} and in view of the lack of evidence supporting revascularization before NCS,\textsuperscript{63,64} it may be reasonable to proceed with the surgical procedure using judicious β-blockade with postoperative cardiac risk stratification and treatment. Lastly, simple balloon angioplasty followed by surgery also would be a reasonable option.\textsuperscript{65}

The patients most at risk are likely those presenting for urgent or emergent surgery with the history of recent PCI. In patients at high risk of thrombotic complications consideration may be given to performing the procedure at an institution where prompt access to the cardiac catheterization laboratory is available should stent thrombosis occur. Again, the relative risk of stent thrombosis must be weighed against the risks of bleeding in making the decision to continue or withhold antiplatelet therapy in these urgent or emergent situations.

In considering all of the available data, the authors believe that strong consideration should be given to continuing clopidogrel and aspirin up to the time of surgery and reinstuting therapy as soon as possible after surgery in any patient having undergone placement of a sirolimus DES less than 3 months before NCS or a paclitaxel DES <6 months before NCS.\textsuperscript{55} It should be further noted that even if patients are outside of this time course, they may still be at significant risk for stent thrombosis and should be monitored for such. If the risks of perioperative bleeding complications are considered low, continuing antiplatelet therapy should be considered in any patient undergoing surgery less than 1 year after DES placement. When the risk of bleeding complications is believed to be unacceptably high, the antiplatelet agents should be withheld for the shortest period possible and reinstated as soon as possible postoperatively.

**CONCLUSION**

Patients with coronary artery disease treated with PCI present a unique and potentially underappreciated challenge to the perioperative physician. Many physicians may believe that the presence of a coronary stent guarantees flow in a treated coronary vessel without fully appreciating the tenuous balance of factors maintaining stent patency and coronary blood flow, the real risk of stent thrombosis, and the potentially severe consequences associated with this complication. Although the optimum time frame for NCS after PCI is still undetermined, current data suggest postponing elective procedures for at least 6 weeks in patients with BMSs and possibly up to 12 months in patients with DESs to minimize the risk of stent thrombosis. A growing body of literature, however, suggests that there may be no truly “safe” time to stop antiplatelet therapy, and these patients should be managed as though they are at continued risk of stent thrombosis. Although the risks of stent thrombosis versus bleeding should be carefully weighed for each individual patient, the literature strongly suggests that the balance should be weighted toward avoiding thrombotic complications.

**Note Added in Proof**

Shortly after the acceptance of this article for publication, the American Heart Association, American College of Cardiology, Society for Cardiovascular Angiography and Interventions, American College of Surgeons, and American Dental Association released an advisory statement regarding the risks and prevention of premature discontinuation of dual antiplatelet therapy in patients with coronary artery stents.\textsuperscript{66} While this statement and its recommendations are consistent with those made in this article, readers are encouraged to familiarize themselves with this important advisory statement.

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The pulmonary circulation is normally a low pressure, low resistance circulation. In patients with pulmonary arterial hypertension, altered vascular endothelial and smooth muscle function lead to a combination of vasoconstriction, localized thrombosis, and vascular growth and remodeling. These processes increase pulmonary vascular resistance, resulting in right ventricular failure, inadequate oxygenation, and ultimately death. Pulmonary hypertension markedly increases morbidity and mortality among patients undergoing surgery.1-6 Understanding the pathophysiology and etiology of pulmonary hypertension in the individual patient allows accurate risk assessment, optimization prior to surgery, and rational intraoperative and postoperative treatment.7-12

An approach to understanding the pathophysiology of an individual patient with pulmonary hypertension is derived from the equation for pulmonary vascular resistance: \( \text{PVR} = (\text{PAP} - \text{LAP}) \times \frac{80}{\text{CO}} \), where PVR represents pulmonary vascular resistance (in dynes.s.cm\(^{-5}\)), PAP represents mean pulmonary artery pressure (in mmHg), LAP represents left atrial pressure (in mmHg), and CO represents cardiac output (in L.min\(^{-1}\)). Rearranging this equation for PAP demonstrates that \( \text{PAP} = \text{LAP} + (\text{CO} \times \text{PVR})/80 \).

Thus, the three factors that account for increased PAP are increased left atrial pressure, increased cardiac output, and increased pulmonary vascular resistance. Therapy of the perioperative patient with pulmonary hypertension should involve an assessment of the quantitative contribution of each of these three components. For example, patients with mitral stenosis who have increased PAP due solely to increased left atrial pressure have uncomplicated perioperative courses, but patients with mitral stenosis who have increased PAP due to increased PVR from pulmonary vascular modeling commonly have severe right ventricular failure after mitral valve replacement and may not succeed in weaning from cardiopulmonary bypass. Pulmonary vasodilator therapy would be inappropriate in one patient but life-saving in the other.
Similarly, patients with chronic left ventricular failure who undergo heart transplantation tend to do well perioperatively if the pulmonary hypertension is due solely to elevated left atrial pressure but may have severe right ventricular failure after transplantation if there is also a significant component of increased PVR. In patients with pulmonary arterial hypertension, analyzing whether cardiac output is maintained or is markedly decreased has significant prognostic value in assessing perioperative risk (see section on risk assessment).

The current World Health Organization classification of pulmonary hypertension involves five major categories (pulmonary arterial hypertension, pulmonary venous hypertension, pulmonary hypertension associated with disorders of the respiratory system and/or hypoxemia, chronic thrombotic and/or embolic disease, and pulmonary hypertension due to disorders directly affecting the pulmonary vasculature). For the physician who is treating a perioperative patient with pulmonary hypertension, the equation for pulmonary artery pressure can be used to review the common etiologies. Increased left atrial pressure includes left ventricular failure and valvular heart disease (particularly mitral stenosis and/or regurgitation). Increased cardiac output includes patients with congenital heart disease with cardiac shunts such as ventricular septal defects. The major categories of chronically increased PVR are pulmonary disease (parenchymal or airway), hypoxia without pulmonary disease (hypoventilation syndromes, high altitude), pulmonary arterial obstruction (thromboembolism, schistosomiasis), and idiopathic pulmonary arterial hypertension. Because of pulmonary vascular remodeling, all these etiologies of pulmonary hypertension can result in increased PVR.

In addition to these etiologies of chronic pulmonary hypertension, acute increases in PVR may result from hypoxia, hypercarbia, acidosis, increased sympathetic tone, and endogenous or exogenous pulmonary vasoconstrictors such as catecholamines, serotonin, thromboxane, and endothelin. Most perioperative patients with decompensated pulmonary hypertension have a combination of chronic pulmonary hypertension with an acute increase in PVR and therapy should be directed at reversing this acute PVR increase.

**Perioperative Risk Assessment**

In the face of increased impedance to right ventricular ejection, the compensatory reserves of the right ventricle are limited. Reduction in right ventricular stroke volume and cardiac output as well as ventricular interdependence, with decreased left ventricular filling and output, occur. In the patient with pulmonary hypertension, anesthesia and surgery may produce progressive hemodynamic deterioration and death due to additional increases in PVR combined with decreases in right ventricular function. For example, patients with pulmonary hypertension undergoing cardiac surgery may fail to wean off cardiopulmonary bypass due to inadequate myocardial right ventricular protection during the ischemic period of aortic cross-clamping, increased endogenous pulmonary vasoconstrictors, and decreased endogenous pulmonary vasodilators from pulmonary endothelial injury during cardiopulmonary bypass. Thus patients with pulmonary hypertension have markedly increased perioperative morbidity and mortality. For patients with Eisenmenger syndrome undergoing cesarean section, mortality is as high as 70%. Patients undergoing liver transplantation with pulmonary arterial hypertension have increased mortality related to the severity of the pulmonary hypertension, with
mortality rates as high as 80% when mean PAP >45 mmHg. Reports of successful outcomes of surgery in patients with severe pulmonary hypertension include curative procedures such as lung or heart-lung transplantation, cesarean section, and relatively brief procedures with minor blood loss such as lung biopsy, cholecystectomy, femoral artery repair, and laparoscopic tubal ligation. 15-20

Survival in pulmonary arterial hypertension correlates with the ability of the right ventricle to compensate for the increased PVR as assessed by cardiac output, right atrial pressure, and functional status. These factors also appear to be major predictors of perioperative risk in the surgical patient. However, perioperative risk is also highly correlated to the surgical procedure. 3 Major procedures that result in the systemic inflammatory response syndrome may exacerbate pulmonary hypertension and increase the perioperative risk. Procedures with rapid blood loss may result in fatal hypotension in the patient requiring adequate venous return as compensation for increased right ventricular afterload. Finally, some procedures may pose special risks for the patient with pulmonary hypertension. For example, hip replacement surgery commonly involves pulmonary embolization of air, bone marrow, and cement during placement of the femoral component. Overall, the risk assessment requires balancing the functional reserve of the patient against the anticipated increased demands of the surgical procedure.

Progressive or acute increases in pulmonary artery pressure leading to acute right heart failure are the major complications of anesthesia and surgery. A pulmonary vasodilator trial may provide additional prognostic information and guide therapy if perioperative right ventricular failure occurs. This approach is used in the evaluation for heart transplantation and has been advocated in occasional patients with pulmonary hypertension undergoing noncardiac surgery. Because of pulmonary selectivity inhaled nitric oxide is an ideal agent for screening for pulmonary vascular reactivity. In patients at an unacceptably high risk following optimization of therapy, consideration should be given to lung or heart-lung transplantation or chronic prostacyclin treatment to decrease the pulmonary hypertension to acceptable levels. 1,21

Preparation of the Patient for Anesthesia and Surgery

Whichever anesthetic technique is chosen, surgery and anesthesia in patients with pulmonary hypertension are associated with significant morbidity and mortality. Prior to anesthesia and surgery such patients should be evaluated with electrocardiography, chest x-ray, arterial blood gas (ABG) measurement, and echocardiography. Evidence of significant right ventricular dysfunction should prompt reevaluation of the need for surgery. All attempts to reduce PAP prior to surgery should be performed, such as the administration of oxygen, bronchodilators, antibiotics, and steroids in the patient with lung disease, and vasodilators and inotropes in the patient with cardiac disease. Reduction of PAP is more likely to succeed prior to surgery than after the induction of anesthesia. Digoxin may have beneficial short-term effect on cardiac function and sympathetic activation in pulmonary arterial hypertension. 22 Patients receiving chronic therapy for pulmonary arterial hypertension should continue such therapy throughout the perioperative period. Discontinuation of continuous epoprostenol infusion (Flolan) can precipitate an acute pulmonary hypertensive crisis. Although prostacyclin inhibits platelet aggregation, excess surgical bleeding is not usually a problem. It is
important to coordinate continuation of the prostacyclin infusion with the nursing staff that will care for the patient after surgery. Patients receiving chronic prostacyclin infusion should have the infusion continued throughout the perioperative period, and management of hypotension should be with additional therapy rather than with discontinuation of the prostacyclin infusion.

**Anesthetic Management**
The anesthetic management of patients with pulmonary hypertension undergoing noncardiac surgery has received relatively little attention in the literature. Most discussion has been limited to obstetrical anesthesia case reports in adults and case series of repair of congenital heart defects in pediatrics. Most authors agree that the management of a specific anesthetic technique is as important as the choice of the technique. In the absence of evidence-based recommendations anesthesiologists need to focus on basic hemodynamic principles.

**Physiologic Considerations and Goals**
The anesthetic plan for the patient with pulmonary hypertension is designed to account for the underlying pathophysiology. The major abnormality is the elevated PVR, which increases right ventricular afterload, thereby increasing right ventricular work and decreasing right ventricular, and thus left ventricular, output. Based on the underlying pathophysiology, the major anesthetic considerations include:

1) Preload: Maintenance of preload (intravascular volume) at normal or increased levels is essential to maintain cardiac output in the face of increased ventricular afterload.

2) Systemic vascular resistance: In normal hemodynamic states, this is a major determinant of left ventricular afterload (and, therefore, cardiac output). In pulmonary hypertension, cardiac output is limited by right ventricular function and is, therefore, independent of systemic vascular resistance. Since systemic blood pressure is related to the product of cardiac output and systemic vascular resistance, it is important to maintain systemic vascular resistance in the normal-to-high range, because cardiac output is unable to increase when systemic vascular resistance decreases.

3) Contractility: Maintenance of normal-to-high contractility is essential to maintain cardiac output in the face of increased right ventricular afterload.

4) Heart rate and rhythm: Sinus rhythm is important for adequate filling of a hypertrophied right ventricle. Stroke volume is limited by right ventricular afterload, so bradycardia should be avoided.

5) Avoidance of myocardial ischemia: Right ventricular subendocardial ischemia due to myocardial oxygen supply-demand imbalance is common in pulmonary hypertension. Systemic hypotension and excessive increases in preload, contractility, and heart rate must be avoided.

The above five physiologic considerations for pulmonary hypertension are similar to the considerations in the patient with aortic stenosis (since both situations involve excessive ventricular afterload, specifically right ventricular afterload in pulmonary
hypertension and left ventricular afterload in aortic stenosis). Although many physicians are skilled at the management of aortic stenosis, a final consideration applies only in the case of pulmonary hypertension:

6) Pulmonary vascular resistance: In pulmonary hypertension, this is the major factor governing right ventricular afterload and cardiac output. Therefore, increases in pulmonary vascular resistance must be avoided and therapy to decrease pulmonary vascular resistance may be required.

**Perioperative Monitoring**

Monitoring during anesthesia must be adequate to detect the causes and complications of increased pulmonary vascular resistance. Arterial oxygen saturation should be continuously monitored by pulse oximetry. Arterial catheterization is required both for beat-to-beat blood pressure monitoring and for frequent arterial blood gas measurements. Monitoring of preload requires consideration of the altered physiology in pulmonary hypertension. In the absence of pulmonary hypertension, cardiac output is determined by left ventricular function, and the relevant preload is left ventricular filling, which is usually monitored by pulmonary artery occlusion pressure (PAOP). However, with severe pulmonary hypertension, cardiac output is limited by right ventricular function, and the relevant preload is right ventricular filling, which may correspond to right atrial or central venous pressures. Therefore in severe pulmonary hypertension, volume administration should be governed by central venous pressure rather than PAOP. However, with moderate pulmonary hypertension, cardiac output varies with both left and right ventricular performance. In these cases, the normal relationships between central venous pressure and PAOP may be altered, so that central venous pressure is no longer an indicator of left ventricular preload. Monitoring both central venous pressure and PAOP and observing the response to volume administration is the best method for accurately assessing preload in patients with pulmonary hypertension. Intraoperative volume assessment can be performed with transesophageal echocardiography, which demonstrates the filling of both ventricles.

Pulmonary artery catheterization may be valuable for perioperative management of the pulmonary hypertension patient. First, it allows measurement of both central venous pressure and PAOP and determination of preload. Second, it allows measurement of cardiac output and calculation of pulmonary and systemic vascular resistance. Third, it allows measurement of pulmonary artery pressure, which is necessary for proper management of systemic hypotension or the use of pulmonary vasodilator therapy. The measurement of mixed venous oxygen saturation allows continuous assessment of arterial oxygenation and cardiac output in patients with pulmonary hypertension. The risk of pulmonary artery catheterization in patients with pulmonary hypertension is increased because of the high mortality of associated arrhythmias, pulmonary artery rupture, and venous air embolism or thromboembolism. In addition, thermodilution cardiac output determinations may be misleading when pulmonary hypertension is associated with anatomic shunting or significant tricuspid regurgitation. If there is a left-to-right shunt, thermodilution will measure pulmonary, rather than systemic, blood flow since the cold indicator will be diluted by shunted blood. If there is a right-to-left shunt, thermodilution will measure systemic rather than pulmonary blood flow, since some of the cold indicator will pass through the shunt. Pulmonary artery catheterization is usually not
indicated in patients with intracardiac shunting because of the high risk of catheter misdirection and the limited additional information over measurement of central venous pressure alone.

**Choice of Anesthetic Technique**

All types of anesthetic techniques have been successfully used in individual pulmonary hypertension patients. The choice of anesthetic technique is usually based on pathophysiologial considerations. Since general anesthesia in pulmonary hypertension patients has significant risks, limited regional anesthesia (eg, axillary block for upper extremity surgery, ankle block for foot surgery) should be considered when appropriate. The use of neuraxial regional techniques (spinal or epidural block) with sympatholytic effects may decrease systemic vascular resistance and produce systemic hypotension when cardiac output is fixed due to pulmonary hypertension. Thus, spinal anesthesia may be contraindicated in most patients. Epidural anesthesia has been successful in selected patients, particularly when the magnitude of the block is limited, eg, in management of labor. Epidural anesthesia allows a slow onset of block and titration of the extent of block so that adverse hemodynamic effects may be recognized early and corrected. However, extreme caution is mandatory to avoid excessive sympatholytic effects. Thoracic epidural blockade has only minor hemodynamic effects but may be titrated slowly to avoid bradycardia. Excess sedation, which may decrease systemic vascular resistance and produce respiratory depression, should be avoided when regional anesthesia is used. Intrathecal and epidural narcotics may provide excellent pain relief postoperatively or during labor without sympathetic blockade or respiratory depression.

General anesthesia remains the method of choice for major surgery in patients with pulmonary hypertension. Several techniques of general anesthesia are possible. Potent inhalational agents may decrease systemic vascular resistance, contractility, and heart rate, thereby producing hypotension and low cardiac output. The marked reduction in contractility and the increased incidence of dysrhythmias that occur with halothane are poorly tolerated. Isoflurane, sevoflurane, and desflurane have less effect on contractility and may result in beneficial pulmonary vasodilation; however, the marked reductions in systemic vascular resistance may result in systemic hypotension. In patients with adequate functional reserve sevoflurane can be used as it is shorter-acting and more readily titratable than isoflurane and unlike desflurane does not produced tachycardia during rapid increases in concentration. Narcotic-nitrous oxide techniques maintain systemic vascular resistance, but may produce hypoxia and decreased contractility; in addition, nitrous oxide increases pulmonary resistance in patients with pulmonary hypertension.

“Balanced” anesthetic techniques may have all the above disadvantages but are frequently chosen as a means of limiting the adverse effects of a single technique. One anesthetic technique that maintains preload, systemic afterload, and contractility without increasing pulmonary vascular resistance is the high-dose narcotic-oxygen technique used in cardiac anesthesia. This appears to be the technique of choice in the patient with severe pulmonary hypertension undergoing major surgery. In addition to producing hemodynamic stability, the use of 100% oxygen may produce pulmonary vasodilation in some patients. In patients undergoing short procedures with intense stimulation such as bronchoscopy a
remifentanil infusion can provide short-acting analgesia. The choice of induction agents for general anesthesia is based on similar considerations. Anesthetic induction of the patient with pulmonary hypertension is an unstable period during which patients are prone to develop systemic hypotension and cardiovascular collapse. In addition, patients with right-to-left anatomic shunting have markedly increased responses to intravenous agents and delayed response to inhalation agents. For rapid-sequence induction etomidate maintains systemic hemodynamics without affecting pulmonary resistance. In contrast, pentothal and propofol may adversely affect systemic resistance, venous return, and contractility. Although ketamine maintains systemic hemodynamics, questions have been raised about possible increases in pulmonary vascular resistance with this agent. Studies suggest that there is little or no increase in pulmonary vascular resistance when ventilation is controlled, and that any increase that may occur with ketamine will be less than the increase in systemic vascular resistance. Ketamine is therefore unlikely to produce systemic hypotension or reverse a left-to-right anatomic shunt.

Ventilatory management may markedly affect pulmonary vascular resistance. Alveolar hypoxia is a potent pulmonary vasoconstrictor and use of high inspired oxygen concentrations may result in additional pulmonary vasodilation in some patients. Hypercarbia is a potent pulmonary vasoconstrictor, and hypocarbia is a pulmonary vasodilator. Hyperventilation may decrease the pulmonary hypertensive responses to various stimuli. Pulmonary vascular resistance is dependent on functional residual capacity (FRC), such that it is increased whenever FRC is increased from its normal value. Pulmonary vascular resistance increases when lung volumes above normal FRC result in compression of small intra-alveolar vessels. Pulmonary vascular resistance also increases when lung volumes below normal FRC produce increased large-vessel resistance due to hypoxic pulmonary vasoconstriction. Ventilatory parameters may affect both FRC and peak lung volume. FRC is usually decreased during general anesthesia. This reduction in FRC can be reversed with positive end-expiratory pressure (PEEP), resulting in a decrease in pulmonary vascular resistance. However, excessive PEEP will increase FRC above optimal values, and result in an increase in pulmonary vascular resistance. The effect of tidal volume on pulmonary vascular resistance may similarly be bimodal. At low tidal volumes increased resistance occurs due to alveolar hypoxia and hypercarbia. At high tidal volumes lung volume intermittently exceeds normal FRC, resulting in compression of intra-alveolar vessels and increased pulmonary vascular resistance. Therefore, ventilation of the patient with pulmonary hypertension should use high concentrations of oxygen, moderate tidal volumes, rates sufficient to achieve hypocarbia, and low levels of PEEP (5-10 cm H2O). High-frequency ventilation has been advocated as a means of achieving adequate gas exchange, while maintaining lung volume continuously at normal FRC.

Management of emergence from anesthesia requires maintaining hemodynamic stability and adequate alveolar ventilation. The major factor responsible for hemodynamic stability is the ratio of pulmonary to systemic vascular tone. Extubation in a deep plane of anesthesia to avoid pulmonary vasoconstriction may be complicated by decreased systemic vascular resistance, decreased contractility, and inadequate ventilation (producing hypoxemia or hypercarbia and exacerbating pulmonary hypertension). In addition, reductions in FRC can increase pulmonary
vascular resistance. Extubation in a light plane of anesthesia can result in marked sympathetic tone and severe pulmonary vasoconstriction. The addition of narcotics to a primarily inhalational technique may allow extubation in a light plane of anesthesia without increasing sympathetic tone. A narcotic-oxygen anesthetic technique followed by postoperative mechanical ventilation appears to be the safest technique for major surgery. Pulmonary hypertension patients have limited ability to tolerate any further increase in pulmonary vascular resistance and it is important to avoid introduction of air or particulate matter (eg, precipitated drugs) into the venous system. In patients with anatomic shunting, such venous embolization may result in systemic embolization, as well as provoking hemodynamic decompensation.

**Treatment of Perioperative Hypotension**

Pulmonary hypertension patients should have hemodynamic therapy aimed at maintaining blood pressure, cardiac output, and low pulmonary vascular resistance. When inotropic therapy is required agents such as dobutamine and milrinone, which increase cardiac output, maintain systemic blood pressure, and decrease pulmonary vascular resistance, are indicated. The management of systemic hypotension in the patient with pulmonary hypertension is based on principles of hemodynamic management. As shown in Table 1, systemic hypotension may result from four etiologies, each of which has a specific hemodynamic pattern.

<table>
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<tr>
<th>Etiology</th>
<th>CVP</th>
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<td>Decreased SVR</td>
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<td>Increased PVR</td>
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CO = cardiac output; CVP = central venous pressure; PAOP = pulmonary artery occlusion pressure; PAP = pulmonary artery pressure; PVR = pulmonary vascular resistance; SVR = systemic vascular resistance.

Pulmonary artery catheterization allows differentiation among these etiologies. Decreased preload is the only etiology that decreases central venous pressure; volume therapy is the appropriate treatment. But volume loading of a failing right ventricle can result in further distention and progressive dysfunction and therefore must be monitored closely. Decreased contractility is the only condition that results in an increase in central venous pressure with a decrease in pulmonary artery pressure; inotropic therapy is indicated. Decreased systemic vascular resistance is the only condition in which cardiac output is maintained. Appropriate therapy may be a combination of systemic vasoconstrictors, inotropic agents, and pulmonary vasodilators. The use of vasopressin as a systemic vasoconstrictor has been recommended in some reports. A combined inotropic-vasopressor agent such as epinephrine or norepinephrine may be useful. Finally, if pulmonary artery pressure has increased or remained the same during systemic hypotension, then the elevated pulmonary vascular resistance is preventing generation of adequate cardiac output. The initial approach should be to detect any correctable causes of increased pulmonary vascular resistance such as hypoxia, hypercarbia, acidosis, increased sympathetic tone, and endogenous or exogenous vasoconstrictors. Patients without correctable factors should be considered candidates for acute pulmonary vasodilator.
therapy. Therefore, arterial blood gases should be measured and acid-base status corrected to baseline. When systemic hypotension occurs without a decrease in pulmonary artery pressure, cardiac output measurement will differentiate between a primary fall in systemic resistance (cardiac output increased or unchanged with no change in pulmonary vascular resistance) and worsened pulmonary hypertension (cardiac output decreased with increased pulmonary vascular resistance). A primary fall in systemic vascular resistance may be treated by either increasing cardiac output with inotropic agents or by achieving selective systemic vasoconstriction with phenylephrine, norepinephrine, or vasopressin.

When an increase in pulmonary vascular resistance produces decreased cardiac output and systemic hypotension, pulmonary vasodilator therapy is required to interrupt the cycle of pulmonary hypertension. This cycle is characterized by low cardiac output, systemic hypotension, and decreased right ventricular coronary perfusion with a further decrease in cardiac output; similarly, low cardiac output produces desaturation of mixed venous blood and acidosis, which result in increased pulmonary vasoconstriction. The goals of pulmonary vasodilator therapy are twofold: first, to reduce pulmonary vascular resistance and thereby decrease pulmonary artery pressure and/or increase cardiac output, and, second, to reduce the PVR/SVR ratio so that the increase in cardiac output will prevent hypotension by compensating for any reduction in systemic vascular resistance. Essentially all agents with systemic vasodilator activity (alpha-blockers, beta-agonists, acetylcholine, direct smooth muscle vasodilators, calcium channel blockers, prostacyclin, prostaglandin E1) are capable of producing pulmonary vasodilation. However, use of these agents as pulmonary vasodilators has frequently resulted in systemic hypotension. In pulmonary hypertension, cardiac output varies with right heart function. Both the pulmonary and systemic vasodilator effects of drugs are dose-dependent. For the majority of drugs, systemic vasodilator effects occur at doses that do not produce pulmonary vasodilation. Thus, with a decrease in systemic and no change in pulmonary vascular resistance, cardiac output cannot rise and systemic blood pressure must fall (BP = CO x SVR).

Pulmonary vasodilators include direct-acting nitro vasodilators such as hydralazine, nitroglycerin, and nitroprusside; alpha-adrenergic blockers such as tolazoline and phentolamine; beta-adrenergic agents such as isoproterenol; calcium blockers such as nifedipine and diltiazem; prostaglandins such as prostaglandin E1 and prostacyclin; adenosine; and indirect-acting vasodilators such as acetylcholine which cause nitric oxide release. The ideal pulmonary vasodilator for the perioperative setting should produce preferential pulmonary vasodilation without other direct hemodynamic effects; in addition, the drug should be short-acting when used for acute treatment. A major principle of acute vasodilator drug therapy is that short-acting titratable agents should be used and the effects should be assessed at each dose before increasing to a higher dose.

For severe perioperative pulmonary hypertension resulting in right ventricular failure inhaled vasodilator therapy is the treatment of choice. This approach was first developed with inhaled nitric oxide,23,25-27 which diffuses from the alveoli to the adjacent pulmonary vascular smooth muscle cells to produce pulmonary vasodilation. Inhaled nitric oxiddoes not produce systemic vasodilation because any nitric oxide that is absorbed into the pulmonary circulation is inactivated by
binding to hemoglobin. In addition, inhaled nitric oxide may improve ventilation-perfusion matching in lung disease. Unlike intravenous vasodilators, which may increase blood flow to poorly ventilated alveoli, inhaled vasodilators are preferentially distributed to ventilated alveoli. By increasing blood flow to ventilated alveoli, there is an improvement in ventilation-perfusion matching and gas exchange. Inhaled nitric oxide effectively decreases perioperative pulmonary hypertension in multiple settings, particularly following cardiopulmonary bypass when pulmonary vascular resistance may be elevated due to pulmonary endothelial dysfunction. Inhaled nitric oxide may be useful in patients with allograft dysfunction following lung transplantation since nitric oxide may decrease pulmonary hypertension, improve ventilation-perfusion mismatch, and decrease ischemia-reperfusion lung injury. Inhaled nitric oxide improves outcome in neonatal pulmonary hypertension with hypoxic respiratory failure as judged by a decreased frequency of death or extracorporeal membrane oxygenation use. Although inhaled nitric oxide improves oxygenation and decreases pulmonary hypertension in the acute respiratory distress syndrome, randomized studies have not demonstrated sustained improvement or improved outcome. Patients with hypoxemia may not improve oxygenation with inhaled nitric oxide if the vascular tone in well-ventilated segments is not increased above basal levels. In such cases, combination of inhaled nitric oxide with almitrine bis mesylate or possibly phenylephrine may improve hypoxemia without producing excessive pulmonary hypertension.

In general, the inhaled nitric oxide dose-response curve in patients with pulmonary hypertension demonstrates maximal responses at doses of 10 ppm or less and, in the perioperative setting, a trial of 20 ppm inhaled nitric oxide is usually sufficient to determine if the patient will have a beneficial response. Discontinuation of inhaled nitric oxide may produce rebound pulmonary hypertension, which limits its utility in the perioperative setting. Rebound pulmonary hypertension may be due to progression of underlying pulmonary hypertension, decreased endogenous nitric oxide synthesis, downregulation of guanylyl cyclase, or activation of endogenous vasoconstrictor pathways such as endothelin. Approximately one third of pulmonary hypertension patients have little or no response to inhaled nitric oxide. Possible explanations include an unreactive pulmonary circulation, rapid inactivation of nitric oxide, abnormalities in the guanylyl cyclase system, or rapid metabolism of cGMP. Inhibition of cGMP phosphodiesterase with sildenafil can increase the frequency, the magnitude, and the duration of response to inhaled nitric oxide.

Other inhaled vasodilators may also produce selective pulmonary vasodilation. These include nitrovasodilators (nitroglycerin, nitroprusside) and prostaglandin derivatives such as prostacyclin, prostaglandin E1, and iloprost. The use of a combination of agents that affect different mechanisms of vasodilation (eg, nitric oxide, which increases cGMP and prostacyclin, which increases cAMP) may produce additive pulmonary vasodilation. Patients undergoing cardiac surgery who develop intractable right ventricular failure due to pulmonary hypertension may be candidates for a right ventricular assist device, either on a temporary basis until right ventricular function recovers or as a bridge to transplantation.

Postoperative Management
Although the focus in the literature has been on intraoperative management of pulmonary hypertension, most patients who die in the perioperative period do so
several days after surgery. Causes of death include progressive increases in pulmonary vascular resistance, progressive decreases in myocardial function, and sudden death. Patients should therefore be monitored in an appropriate setting. Deepening of the level of sedation/anesthesia may be effective in selected patients. The use of epidural narcotics, limited thoracic epidural local anesthetics, continuous regional anesthesia, and non-narcotic analgesic adjuvant should be considered for pain management when appropriate.

In summary, pulmonary hypertension patients have markedly increased morbidity and mortality during anesthesia and surgery. However, management based on physiologic principles can allow the majority of patients to safely undergo required surgical procedures.

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Pulmonary arterial hypertension (PAH) is a disease of the pulmonary vasculature that is characterized by a progressive increase in pulmonary vascular resistance (PVR) and pulmonary artery pressure (PAP) resulting in the development of right ventricular (RV) failure, inadequate oxygenation, and ultimately death. Anesthesia and surgery, both cardiac and noncardiac, are associated with significantly increased morbidity and mortality in patients with PAH due mainly to RV failure, arrhythmias, postoperative hypoxemia, and myocardial ischemia. Preoperative risk assessment and successful management of patients with PAH undergoing general surgery involves an understanding of the pathophysiology of the disease, analysis of preoperative and operative risk factors, intraoperative management, and early recognition and treatment of postoperative complications.

Classification
For the physician who is treating a perioperative patient with pulmonary hypertension, it is important to know the underlying etiology of the pulmonary hypertension. Five major categories of pulmonary hypertension are currently classified by the World Health Organization (Group 1: PAH; Group 2: pulmonary venous hypertension related to left heart disease; Group 3: pulmonary hypertension associated with hypoxic respiratory disorders; Group 4: pulmonary hypertension due to chronic thromboembolic disease; and Group 5: miscellaneous causes). PAH is diagnosed hemodynamically as a mean PAP (mPAP) greater than 25 mmHg at rest or greater than 30 mmHg with exercise, PVR greater than 3 Wood units, and pulmonary artery occlusive pressure (PAOP) of 15 mmHg or less (ie, evidence of “precapillary” pulmonary hypertension in patients who fit WHO Group I clinical characteristics).

Pulmonary hypertension regardless of etiology is associated with increased surgical risk compared to patients without pulmonary hypertension. However, the perioperative risk and management among these patients may differ, particularly for patients with pulmonary venous hypertension (ie, “postcapillary” pulmonary hypertension; mPAP greater than 25 mmHg, PVR less than 3 Wood units, PAOP greater than 15 mmHg) or “mixed” pulmonary hypertension (mPAP greater than 25 mmHg, PVR greater than 3 Wood units, PAOP greater than 15 mmHg). This document will address patients with PAH, though most of the principles discussed may apply to patients with other categories of pulmonary hypertension regardless of etiology.

Pathophysiology
The pulmonary vasculature is normally a low resistance, high capacitance circuit compared to the systemic circulation, which is a high resistance circulation. The precapillary pulmonary arterioles have thinner media and fewer smooth muscle cells, resulting in greater compliance. In addition, the cross-sectional area of the pulmonary vascular bed is large, with a great capacity for the recruitment of vessels to accommodate increases in flow (cardiac output) up to three- or fourfold without an increase in PAP. PAH is associated with a combination of pulmonary arteriolar vasoconstriction from vascular smooth muscle cell contraction, vascular remodeling, and in-situ thrombosis. Increases in PVR and PAP increase RV afterload, leading progressively to hypertrophy, chamber dilation, and systolic dysfunction.

Symptoms of the disease are first noted when the right ventricle is unable to increase contractility sufficiently to augment left ventricular (LV) preload and cardiac output during exercise. As the disease progresses, LV filling and cardiac output may be
Pounded by tachycardia. Consumption due to increased wall stress that can be com-
temic hypotension in a ventricle with high myocardial oxygen of reduced coronary perfusion pressure in the setting of sys-
and superimposed myocardial ischemia may occur as a result
hemodynamic deterioration and collapse as a result of acute
increases in PVR and RV workload, systemic hypotension, myocardial ischemia, and progressive RV failure.

Preoperative Risk Assessment: Predictors of Good and Poor Outcome
There is limited evidence-based literature describing the peri-
operative risk of morbidity and mortality in patients with PAH undergoing noncardiac surgery, with most of the reports being focused on patients with pulmonary hypertension undergoing cardiopulmonary surgeries, usually with cardiopulmonary bypass. Cardiac surgery and cardiopulmonary bypass are asso-
ciated with an increased risk of morbidity and mortality com-
pared with noncardiac operations, independent of the presence of pulmonary hypertension. However, compared with other “high-risk” patient populations undergoing noncardiac surgery, the perioperative risk in patients with PAH appears to be greater. Moreover, the risks associated with PAH seem to be more frequent than with other etiologies of pulmonary hyper-
tension. Perioperative risk assessment in such patients should involve an individualized approach taking into account the type of surgery, the patient’s functional capacity, hemodynamic severity of the PAH and RV function, and any comorbid condi-
tions. Patients with low-risk clinical characteristics and/or those who are to undergo low-risk operations will generally have a good outcome, whereas those who have high-risk features and/or those undergoing intermediate- to high-risk surgeries with general anesthesia have much poorer outcomes.

Potential Adverse Hemodynamic Effects of Anesthesia
Since, for the most part, the pulmonary vasculopathy in pa-
ients with PAH is associated with a sustained elevation in PVR and PAP with relatively little vascular reactivity, anesthetic administration for surgery may cause significant systemic hypotension due to greater systemic than pulmonary vasodila-
tion and a limited ability of the right ventricle to compensate with an increase in cardiac output. In addition, the negative inotropic effects of some anesthetic agents may exacerbate hypotension and precipitate RV failure. RV failure may be man-
ifest by an increase in RV diastolic and right atrial pressures, and superimposed myocardial ischemia may occur as a result of reduced coronary perfusion pressure in the setting of sys-
temic hypotension in a ventricle with high myocardial oxygen consumption due to increased wall stress that can be com-
pounded by tachycardia.

In contrast to the systemic arteries, pulmonary vessels con-
strict with hypoxia and relax in the presence of hyperoxia. Pulmonary vasoconstriction and acute increases in PVR also occur in the presence of hypercarbia, acidosis, hypothermia, increased sympathetic tone (eg, pain or agitation), and increased endogenous or exogenous mediators such as cate-
cholamines. Therefore, anesthesia and surgery can lead to hemodynamic deterioration and collapse as a result of acute

decreased even at rest as a result of reduced RV stroke volume
and impaired LV diastolic filling related to the leftward shift
of the interventricular septum. Thus, PAH patients presenting
for surgery may have varying degrees of RV dysfunction and
remodeling.

Table 1. Risk Stratification of Noncardiac Surgical Procedures

<table>
<thead>
<tr>
<th>Low-Risk Operations</th>
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<tbody>
<tr>
<td>Dermatologic surgeries</td>
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<tr>
<td>Endoscopic procedures</td>
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<tr>
<td>Cataract surgery</td>
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<tr>
<td>Breast surgery</td>
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<table>
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<tr>
<th>Intermediate-Risk Operations</th>
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<tbody>
<tr>
<td>Carotid endarterectomy</td>
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<tr>
<td>Head and neck surgery</td>
</tr>
<tr>
<td>Gynecologic surgery</td>
</tr>
<tr>
<td>Gastrointestinal/ intraabdominal surgery</td>
</tr>
<tr>
<td>Orthopedic surgery</td>
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<tr>
<td>Prostate surgery</td>
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<tr>
<td>Thoracic surgery</td>
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<table>
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<tr>
<th>High-Risk Operations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emergent major surgery</td>
</tr>
<tr>
<td>Aortic or other major vascular surgery</td>
</tr>
<tr>
<td>Liver transplantation</td>
</tr>
<tr>
<td>Other major operations with anticipated large fluid shifts and/or blood loss</td>
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Type of Surgery Predicts Perioperative Risk
The type of noncardiac surgery being performed significantly influences the perioperative risk (Table 1). Ramakrishna et al. published the only study to date of perioperative outcomes in patients with pulmonary hypertension undergoing noncardiac surgery. They retrospectively analyzed the outcomes of a hetero-
egeneous group of 145 patients with pulmonary hypertension diagnosed by echocardiography undergoing noncardiac surgery (note that the types of surgeries categorized as low versus inter-
mediate to high risk in this study differ from Table 1), and they found that short-term perioperative mortality was 7%. Thoracic followed by orthopedic surgeries were associated with the high-
est perioperative morbidity.3,5

Thoracic surgery may be associated with changes in intrathoracic pressure, lung volumes, and oxygenation that can acutely increase PVR and reduce RV preload and cardiac out-
put with a substantial risk of hemodynamic collapse. Orthopedic surgeries, such as hip or knee replacement, can lead to embolization of air, bone marrow, or cement to the pul-
monary circulation that can cause hypoxia, substantial increas-
es in PVR, and acute RV failure. Pneumoperitoneum associ-
ed with laparoscopic surgeries may compromise cardiovascular hemodynamic status by reducing ventricular preload and increasing afterload. Procedures that cause rapid blood loss may lead to hypotension and hemodynamic deterioration in the setting of PAH and RV systolic and diastolic dysfunction where RV stroke volume and cardiac output are dependent on ade-
quate preload. Gynecologic surgery in nonpregnant women with PAH may be associated with low to high risk, depending on the clinical setting and surgery type. Cesarean section has been performed successfully in pregnant women with PAH in isolat-
ed small reports. However, it must be emphasized that pregnancy is poorly tolerated in patients with PAH and is contraindicated because of the very high associated maternal and fetal mortality rates. Marked increases in hemodynamic stress and fluid shifts associated with labor and both vaginal and cesarean deliveries are associated with a high puerperal mortality rate, which was 24% in one study of patients with Eisenmenger syndrome.6 Since most of these deaths occur well after surgery, they are probably not related to anesthesia per se but rather to fluid shifts and neurohormonal changes. Although elective surgery is generally not recommended in patients with PAH because of increased risk, laparoscopic tubal ligation may be performed with relatively low risk in patients with PAH and is a consideration for women of childbearing age who are not candidates for double barrier methods of contraception.7,8 Alternatively, the Essure micro-insert device is an attractive method of permanent contraception that is implanted noninvasively and appears to be very effective. Other reports of successful outcomes of surgery include patients with PAH undergoing cholecystectomy, hysterectomy, and femoral artery and abdominal aortic aneurysm repairs.9-11

**Low- Versus High-Risk Clinical Characteristics**

**Predict Surgical Outcome**

Ramakrishna et al found that in 145 adult patients with pulmonary hypertension undergoing noncardiac surgery under general anesthesia, New York Heart Association (NYHA) functional class II or higher, right-axis deviation on electrocardiography, RV hypertrophy by 2D-echocardiography, Doppler RV index of myocardiographic performance 0.75 or higher, RV systolic pressure/systolic blood pressure ratio 0.66 or higher, and a history of pulmonary embolism were associated with increased morbidity and mortality.3 Pulmonary artery catheterization was not routinely performed in this patient population.

In the absence of more evidence-based literature, other clinical factors that are predictors of perioperative risk are generally felt to be similar to those known to correlate with survival in PAH,12 and they include patient's functional status and indices of the severity of PAH and RV function, as well as patient comorbidities. Although the PAP itself has not been clearly demonstrated to be an independent predictor of survival in PAH, in children with PAH undergoing noncardiac surgery or catheterization, suprasystemic PAP is a significant risk factor for major perioperative complications, including cardiac arrest and pulmonary hypertensive crisis.13 In addition, Krowka et al found that the perioperative mortality rate was 100% in patients with postpulmonary hypertension and mPAP of 50 mmHg or greater undergoing liver transplantation, whereas survival was much better in patients with an mPAP under 35 mmHg.14

A complete perioperative assessment in patients with PAH should involve transthoracic echocardiography, electrocardiography, assessment of NYHA/WHO functional classification, some laboratory studies, and in most cases, preoperative right heart catheterization with or without acute vasodilator testing. Pulmonary artery catheterization with continuous hemodynamic monitoring is recommended in patients undergoing intermediate- to high-risk procedures and in patients with symptomatic PAH or a history of RV failure.

**Table 2. Low- Versus High-Risk Clinical Predictors**

<table>
<thead>
<tr>
<th>Low-Risk Predictors</th>
<th>NYHA/WHO functional class I</th>
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<tbody>
<tr>
<td>Hemodynamics</td>
<td></td>
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<tr>
<td>Normal right atrial pressure (≥ 7 mmHg; off diuretics)</td>
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<tr>
<td>PVR:SVR ratio &lt; 0.5</td>
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<tr>
<td>Mean PAP &lt; 35 mmHg</td>
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<tr>
<td>Normal left ventricular filling pressure (PAOP 8 to 12 mmHg)</td>
<td></td>
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<tr>
<td>Normal cardiac output (cardiac index ≥ 2.8 L/min/m²)</td>
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<tr>
<td>Echocardiography</td>
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<tr>
<td>Normal right atrial size</td>
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<tr>
<td>Absence of interventricular septal flattening</td>
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<tr>
<td>Absence of right ventricular hypertrophy</td>
<td></td>
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<tr>
<td>Right ventricular myocardial performance index &lt; 0.75</td>
<td></td>
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<tr>
<td>TAPSE score ≥ 0.8 cm</td>
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<tr>
<td>Electrocardiography</td>
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<tr>
<td>Absence of right axis deviation</td>
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<tr>
<td>Laboratory</td>
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<tr>
<td>Normal serum BNP level</td>
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<tr>
<th>High-Risk Predictors</th>
<th>NYHA/WHO functional class III or IV</th>
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<tbody>
<tr>
<td>Hemodynamics</td>
<td></td>
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<tr>
<td>Right atrial pressure ≥ 12 mmHg</td>
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<tr>
<td>Severely elevated PAP (mean PAP ≥ 55 mmHg, PVR:SVR ratio ≥ 0.75)</td>
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<tr>
<td>Reduced cardiac output (cardiac index &lt; 2.2 L/min/m²)</td>
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<tr>
<td>Abnormal right ventricular stroke*work index</td>
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<tr>
<td>Echocardiography</td>
<td></td>
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<tr>
<td>Severe right atrial enlargement</td>
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<tr>
<td>Interventricular septal diastolic flattening</td>
<td></td>
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<tr>
<td>Pericardial effusion</td>
<td></td>
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<tr>
<td>Right ventricular myocardial performance index ≥ 0.75</td>
<td></td>
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<tr>
<td>Right ventricular hypertrophy</td>
<td></td>
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<tr>
<td>RVSP:SBP ratio ≥ 0.66</td>
<td></td>
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<tr>
<td>TAPSE score &lt; 0.8 cm</td>
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<tr>
<td>Electrocardiography</td>
<td></td>
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<tr>
<td>Right axis deviation</td>
<td></td>
</tr>
<tr>
<td>Laboratory</td>
<td></td>
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<tr>
<td>BNP level &gt; 330 pg/mL</td>
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<tr>
<td>Reduced creatinine clearance &lt; 60 mL/min</td>
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BNP = B-type natriuretic protein; NYHA = New York Heart Association; PAOP = pulmonary artery occlusive pressure; PAP = pulmonary artery pressure; PVR = pulmonary vascular resistance; RVSP = right ventricular systolic pressure; SBP = systolic blood pressure; SVR = systemic vascular resistance; TAPSE = tricuspid annular systolic excursion; WHO = World Health Organization.

Table 2 lists low versus high perioperative clinical risk factors.3,12,14-21 Although other parameters of functional capacity, such as 6-minute walk distance (6MWD) and exercise peak VO2, are predictors of survival in patients with PAH, Ramakrishna et al found that the 6MWD did not predict early mortality associated with general surgery, possibly indicating that it may be more predictive of long-term outcome.3,22

A pulmonary vasodilator trial may provide additional information that can guide perioperative therapy and it has been advocated in patients with PAH undergoing general surgery.11 There are no generally accepted criteria for a beneficial
response. However, a drop in mPAP or PVR by at least 20% associated with an increase in cardiac output is perhaps significant (although not sufficient for identifying patients who are candidates for chronic calcium channel blocker therapy). The pulmonary vasodilators inhaled nitric oxide with FiO2 1.0, intravenous epoprostenol, and adenosine are typically used for acute vasodilator testing. Of these, the selective pulmonary vasodilator inhaled nitric oxide is the most common agent used, and its pulmonary vasodilatory effects are typically at least as great as those of the intravenous vasodilators.23,24

Although acute preoperative testing with intravenous nitroglycerine and oxygen was reported to cause a greater reduction in PAP and increase in cardiac output compared with inhaled nitric oxide or nifedipine in one patient,11 caution should be exercised when administering nonselective vasodilators in patients with PAH because of the potential development of severe systemic hypotension. It must be recognized that patients with pulmonary venous hypertension whose baseline LV filling pressures are elevated (PAOP greater than 15 mmHg) are at risk for the development of pulmonary edema if given relatively selective pulmonary vasodilators such as inhaled nitric oxide or epoprostenol, and in such cases intravenous nitroprusside, nesiritide, or nitroglycerin are more appropriate agents to reduce the LV filling pressure and PAP.

Major comorbid conditions as previously described by Eagle et al25 can also substantially increase the risk of any surgery. A history of pulmonary embolism in particular has been associated with increased perioperative risk in patients with pulmonary hypertension undergoing noncardiac surgery.3

If there is baseline evidence of significant RV failure, such as markedly increased right atrial pressure and reduced cardiac output, or suprasystemic PAPs, serious consideration should be given to delaying surgery if possible until the hemodynamics can be optimized to a more acceptable level. Patients who have indicators of poor prognosis should be considered for chronic therapy with epoprostenol. Other pulmonary vasodilator therapies, such as oral endothelin receptor antagonists, phosphodiesterase type 5 inhibitors, or other prostenoids may be used as alternatives according to evidence-based guidelines26 alone or in combination with epoprostenol.

Recommendations to Anesthesiologists
In cases of elective surgery, a preoperative evaluation should be performed by an anesthesiologist and it is advisable that only anesthesiologists with experience in the care of patients with PAH should be utilized for these patients. Hemodynamic monitoring with a pulmonary artery catheter is recommended in patients undergoing intermediate- to high-risk procedures, patients with symptomatic PAH, or a history of RV failure, for both preoperative risk assessment and to guide therapy perioperatively. Although the risk of pulmonary artery catheterization in patients with pulmonary hypertension is increased because of a higher mortality associated with arrhythmias, pulmonary artery rupture, and venous air or thromboemboli, the overall risk of serious adverse events is only 1.1% with a procedure-related mortality of 0.055% in experienced hands.27
thetic agents and techniques have been used successfully in patients with PAH may be prone to develop systemic hypotension and cardiovascular collapse. Many different types of anesthetic agents make them either preferable or undesirable for use in these patients. Alveolar and pulmonary arterial hypoxia and hypercarbia cause hypoxic pulmonary vasoconstriction, which can be improved with low levels of positive end-expiratory pressure (PEEP), resulting in a decrease in PVR.

On the other hand, high levels of PEEP (greater than 15 cm H2O) and hyperinflation of the lungs lead to compression of the infra-alveolar vessels with marked increases in PVR. The resultant increase in RV afterload may cause or worsen RV failure and in patients with interatrial communications such as a patent foramen ovale, right-to-left shunting may occur as the right atrial pressure exceeds left atrial pressure leading to arterial oxygen desaturation. Ventilator management of the patient with PAH should therefore entail the use of high oxygen concentrations, hyperventilation to achieve a PCO2 of 30 to 35 mmHg or less, low levels of PEEP between 5 and 10 cm H2O, and maintenance of lung volumes at normal functional residual capacity.

Treatment of Acute Perioperative Right Ventricular Failure

Despite all precautions, acute decompensated RV failure (ADRVF) and hypotension can develop perioperatively in patients with PAH undergoing surgery. Treatment of these patients involves the reduction of RV afterload and an increase in systemic pressure. The development of RV failure is indicated by a rising RV diastolic and right atrial pressure and decreasing cardiac output. In addition to ventilatory maneuvers to reduce PVR as discussed above, pulmonary vasodilators should be administered, if needed.

The most suitable vasodilators for use in the perioperative setting to decrease PVR are the inhaled agents, which are selective to the pulmonary vascular bed and have the added poten-

| Table 3. Perioperative Hemodynamic Goals |

| Mean arterial pressure ≥ 55 to 60 mmHg | Systolic blood pressure ≥ 80 mmHg | Systemic blood pressure ≥ 100% |
| Right atrial pressure < 10 mmHg | Mean pulmonary artery pressure < 35 mmHg | PVR:SVR ratio < 0.5 (if possible) |
| Pulmonary artery occlusion pressure 8 to 12 mmHg | Cardiac index ≥ 2.2 L/min/m² |

PVR = pulmonary vascular resistance; SVR = systemic vascular resistance.

As a guide for perioperative management, Table 3 outlines the hemodynamic goals, which should be achieved: The cardiac output should be typically determined using the Fick equation and mixed venous oxygenation saturation measurement, because in many patients with PAH and significant tricuspid regurgitation, the cardiac output may be underestimated by the thermodilution technique.

Anesthetic induction is an unstable period, during which patients with PAH may be prone to develop systemic hypotension and cardiovascular collapse. Many different types of anesthetic agents and techniques have been used successfully in patients with PAH. However, the anesthetic technique should be chosen carefully. The potential hemodynamic effects of anesthetic agents have been previously described in this manuscript. Although anesthetic agents do not change the PVR related to fixed pulmonary vascular disease, they can produce changes in PVR related to vascular reactivity, alterations of cardiac output and pulmonary blood flow, RV afterload, and potentially, intracardiac shunting.

Limited regional anesthesia (ie, local nerve block), which has very little hemodynamic effect, should be considered in appropriate patients, such as those undergoing minor surgery. Neuraxial regional anesthesia (eg, spinal or epidural block) can be associated with profound systemic hypotension due to the sympatholytic effects and resultant decreases in SVR in these patients with limited ability to augment RV stroke volume and cardiac output. Thus, spinal anesthesia is clearly contraindicated in most patients. On the other hand, epidural anesthesia has less systemic effects when administered carefully, and it has been used successfully in patients undergoing femoral artery repair, cholecystectomy, cesarean section, and therapeutic abortion.

General anesthesia is usually needed for higher risk operations, and there is some evidence to suggest that most perioperative deaths in patients receiving general anesthesia are due to the surgical procedure and disease and not the anesthesia. That being said, the hemodynamic effects of some general anesthetic agents make them either preferable or undesirable in patients with PAH. For instance, inhalational anesthetics such as nitrous oxide increase PVR and decrease contractility and halothane may cause a marked reduction in contractility and increased incidence of dysrhythmias. Isoflurane, sevoflurane and desflurane may result in pulmonary vasodilation with less effect on contractility and therefore may be preferable agents in patients with PAH. Intravenous anesthetics such as propofol and pentothal may also adversely affect contractility and systemic vascular resistance, causing hypotension. Ketamine appears to have little effect on systemic hemodynamics. However, there is conflicting evidence with respect to increases in PVR. Rapid-sequence etomidate induction is reported to maintain systemic hemodynamics without affecting PVR. Combination or “balanced” anesthetic techniques (eg, inhalational and intravenous or intravenous and epidural) are used frequently as a means of limiting the adverse effects of a single technique. The high-dose narcotic-oxygen technique, which can produce hemodynamic stability and pulmonary vasodilation with 100% oxygen, has been touted as the technique of choice for patients with PAH undergoing major surgery.
milrinone). Intravenous epoprostenol, which has positive postinil and iloprost), and phosphodiesterase-3 inhibitor (eg, erin), prostaglandins (eg, epoprostenol, prostaglandin E1, tre-

failure include nitric oxide donors (eg, nitroprusside, nitroglyc-

discontinuation. Alternatively, one could use inhaled iloprost

and the potential for rebound pulmonary hypertension with its

(ie, methemoglobin, peroxynitrite, nitrogen dioxide), and the potential for rebound pulmonary hypertension with its
discontinuation. Alternatively, one could use inhaled iloprost

alone or in combination with inhaled nitric oxide.

Other intravenous agents available for the treatment of RV
failure include nitric oxide donors (eg, nitroprusside, nitroglycer-
erin), prostaglandins (eg, epoprostenol, prostaglandin E1, tre-
postinil and iloprost), and phosphodiesterase-3 inhibitor (eg, milrinone). Intravenous epoprostenol, which has positive

inotropic properties by increasing cardiomyocyte intracellular
CAMP levels in addition to its effect on vascular smooth muscle,
has also been used in the perioperative setting, although mostly in patients who have been receiving it as chronic thera-
py. Treprostinil is also typically used in patients receiving it as chronic therapy. In patients with systemic hypotension related
to low cardiac output state from severe RV failure, intravenous
epoprostenol and other prostaglandins may lead to an increase
in blood pressure by reducing RV afterload and improving stroke volume, LV preload and cardiac output. However, there is the
potential for causing worsened hypotension and/or ventilation-
perfusion mismatching with arterial desaturation with all these
drugs.

Inotropes, such as the beta-adrenergic agents dobutamine

or dopamine, may be required to restore adequate tissue perfu-
sion. Dobutamine is typically preferred over dopamine.

However, in the setting of systemic hypotension/hypoperfusion,
dopamine or norepinephrine should be considered to support
RV function, improve systemic pressure, and preserve coronary
perfusion. The inodilator milrinone is a phosphodiesterase-3
inhibitor that vasodilates the systemic and pulmonary vascula-
ture and increases cardiac output. Its potent systemic vasodila-
tory properties can, however, overwhelm its inotropic effect and
cause severe, sustained hypotension in patients with PAH, who
often have mostly fixed pulmonary vascular disease. Its use
should therefore be avoided in such patients. For the same rea-
son, intravenous nitric oxide donors such as nitroprusside or
nitroglycerin should not be used in acute compensated right
heart failure due to PAH as they can exacerbate systemic
hypotension. The recombinant B-type natriuretic peptide nesiri-
tide, an effective treatment of pulmonary hypertension associ-
ated with left heart failure, does not appear to decrease PVR in
patients with PAH when given acutely, and because of concerns of systemic hypotension its use in PAH patients is not rec-

ommended. Perioperative Management

In general, perioperative management of the patient with PAH
undergoing general surgery includes serial assessment and opti-
mization of baseline hemodynamics, the administration of chronic and acute pulmonary vasodilators in most cases, and the early identification and treatment of ADRVF and its precipitating factors. Once the baseline hemodynamics are obtained, preferably with retention of the pulmonary artery catheter in preparation for anesthesia and surgery, therapies aimed at optimizing the hemodynamics (Table 3) should be instituted, such as diuretics to reduce the right atrial pressure or the addition or up-titration of pulmonary vasodilators or inotropes if needed and surgery cannot be delayed.

Chronic pulmonary hypertension-specific therapies should be continued throughout the perioperative period. Arrangements should be made with the anesthesiologists and nursing staff to continue catheter-based therapies such as epoprostenol or treprostinil throughout the perioperative period. Although epoprostenol causes platelet inhibition, it typically does not cause significant bleeding with surgery. Short-term administration of digoxin may improve cardiac output and reduce sympathetic activation in patients with PAH and RV failure. Patients should receive prophylaxis perioperatively to prevent deep vein thrombosis and pulmonary thromboembolism.

In patients with PAH undergoing general surgery, death when it occurs, can be sudden and often occurs in the postoperative period within the first several days. This is perhaps due to fluid shifts, increased sympathetic tone, increased pulmonary vasoconstriction, and pulmonary thromboembolism that leads to worsened RV failure, sometimes with arrhythmias. In order to minimize sympathetic activation, adequate pain control should be emphasized at all times and sufficient sedation should be given in order to prevent agitation, especially while the patient is being ventilated. Sedatives with fewer negative inotropic and vasodilatory properties are preferred. Narcotic analgesics have less hemodynamic effect and may provide sufficient sedation alone. Weaning from the ventilator has been associated with paroxysms of severe pulmonary hypertension and pulseless electrical activity. Exitation in a light plane of anesthesia with an inhalational anesthetic and the addition of narcotics has been advocated. Selective pulmonary vasodilators, such as inhaled nitric oxide and high-flow oxygen should be used liberally if needed to manage the patient through this period.

Frequent serial examinations should be performed in order to promptly identify and treat patients who develop ADRVF. Common precipitating factors of ADRVF include dysrhythmias, infection, anemia, acidosis, hypoxia, hypothermia, and pulmonary embolism. Atrial tachyarrhythmias should be slowed with digoxin, amiodarone, or diltiazem, and amiodarone may also facilitate chemical cardioversion. If the patient is hypotensive, electrical cardioversion is indicated. The use of beta-blockers or the calcium channel blocker verapamil should be avoided because of their negative inotropic and vasodilatory that may cause hypotension. Infection is poorly tolerated in patients with PAH in whom RV contractile reserve is limited. Anemia also increases RV work and should be corrected if significant, although no evidence-based guidelines for transfusion therapy currently exist. Oxygen is a pulmonary vasodilator and maintenance of adequate oxygenation is of paramount importance in patients with PAH and RV failure. Acidemia increases PVR and therefore acidosis should be aggressively treated. In fact, small degrees of alkalemia appear to be beneficial.

Respiratory acidosis should be avoided (goal: Paco₂ 30 to 35 mmHg or less) and the prompt correction of metabolic acidosis is also indicated (goal: pH higher than 7.4). Avoidance of hypothermia and shivering is accomplished by maintenance of a body temperature around 37°C.

**Summary**

General surgery in patients with PAH is associated with increased perioperative morbidity and mortality. Perioperative risk assessment involves an individualized approach taking into account the type of surgery as well as the hemodynamic severity of the patient’s PAH, functional status, and other comorbid conditions, if any. General anesthesia is associated with higher perioperative mortality. However, this is likely related to the type of surgical procedure and severity of disease and is less often due to the anesthesia itself. A comprehensive preoperative evaluation should typically include right heart catheterization in most cases. Perioperative management must include serial assessment and optimization of hemodynamics, avoidance of factors known to cause pulmonary vasoconstriction, careful ventilatory management, administration of acute and chronic pulmonary vasodilators in most cases, and early postoperative identification and treatment of ADRVF and its precipitating factors.

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**References**


Dr Channick: Good morning, gentlemen. The challenges of general surgery in pulmonary hypertension patients are something all of us face, and we are doing so more and more often. As more patients are surviving longer with medical therapies, many practical issues arise. Let’s start with Stuart Rich. As a physician taking care of patients with pulmonary hypertension, very briefly tell us what you feel are the greatest challenges you face with patients being considered for a surgical procedure.

Dr Rich: We’re talking noncardiac surgery?

Dr Channick: Yes.

Dr Rich: What we’ve encountered is undue anxiety over the underlying presence of pulmonary hypertension, especially in stable patients being sent for a surgical procedure, and the problem of what I call “fiddling.” Fiddling is having anesthesiologists place a Swan-Ganz catheter into the patients for monitoring during surgery, to monitor the pulmonary artery pressure, which we strongly discourage because the level of the pulmonary artery pressure for all practical purposes is irrelevant. These patients have pulmonary hypertension, and if they are clinically stable, the focus should be on the general clinical parameters, which include blood pressure, heart rate, oxygen saturation, etc. The problem with putting the Swan in is that there is this inclination to try to lower the pulmonary pressure, either because the patients become unstable or because they think they can lower it a bit, and that’s where the problems begin. So that’s one fundamental problem. One should assume that the pulmonary artery pressure is as good as it’s going to get. That’s why the patients were referred on therapy for this other procedure. The other category of things to focus on is the nuances that are typical of pulmonary hypertension patients. They tend to get hypoxic easily when their cardiac output falls. A lot of them have underlying lung disease that is not obvious. They tend to get vagal very easily, so with the occurrence of unexplained hypotension or bradycardia, we advise just giving the atropine first and thinking afterward. And lastly, and this should be obvious, if they have a Hickman catheter for intravenous therapy, it is a dedicated line and should never be interrupted or tampered with for another infusion.

Dr Channick: Do you like to talk to the anesthesiologist yourself prior to any surgical procedure?

Dr Rich: Absolutely. It’s really not the surgeon or the procedure that’s the problem; it’s usually the anesthesiologist who’s overseeing the “hemodynamic environment” of the patient where the problems are encountered.

Dr Channick: Excellent. Dr Pearl, as an anesthesiologist, what are some of the mistakes or issues that you see with your anesthesiologist colleagues or that you think about with these patients?

Dr Pearl: A few things. A major problem involves patients who are receiving a continuous intravenous infusion such as epoprostenol (Flolan) for treatment of pulmonary hypertension. When the patients become hypotensive, the anesthesiologists want to decrease the rate of the infusion, and the subsequent increased pulmonary hypertension is frequently disastrous. As a general rule, we never titrate the infusion rate in the perioperative setting, neither increasing nor decreasing the rate. In places that are not used to taking care of patients receiving continuous infusions for pulmonary hypertension, there can be confusion as...
to what to do with the infusion in the operating room and how to switch it over to something we may be more used to being able to manage in terms of different pumps and infusion systems. The switch from the patient’s chronic pump to the hospital system can cause problems for the team that is not used to doing so. There is a tendency, as was noted, to try to manipulate pulmonary artery pressures in order to make the pulmonary hypertension better than it was before. Anesthesiologists frequently overtreat the patient with stable pulmonary hypertension. On the other hand, these patients do need to be treated much more gently than other patients. They can decompensate very easily, particularly during extubation in terms of worsening pulmonary hypertension as they emerge from anesthesia.

Dr Channick: This is backing up a little bit. We always debate over which type of anesthesia is best or worst in these patients—general versus spinal, certain agents versus others. What is your feeling on that?

Dr Pearl: Over time we have learned that many of these patients will tolerate regional anesthesia techniques. Certainly for peripheral surgery anesthesiologists who are reasonably skilled at nerve blocks can often very effectively provide anesthesia without having to deal with the impact of general anesthesia or the marked hemodynamic changes of spinal-epidural anesthesia. Even patients undergoing a lower abdominal procedure, or patients with pulmonary hypertension who are pregnant, will commonly tolerate epidural or continuous spinal anesthesia. One needs to titrate slowly and allow the physiology to adjust to the changes that occur rather than have rapid changes such as may occur in a typical spinal, which is likely to decompensate the patient. So regional anesthesia works well for many of the patients and avoids some of the problems of general anesthesia but, as in many things with anesthesia, one can be successful with almost any approach. It’s much more the way the approach is done than the choice itself.

Dr Rich: That’s right on the money. I’ve always felt uncomfortable recommending to anesthesiologists how to anesthetize a patient for a surgical procedure. That’s their specialty and really not ours. I think the general principle that allows the patient to have the least stress is probably the one that is in his or her best interest, combined with the surgical technique and the type of anesthesia delivered. I prefer to leave it to their judgment, and I think the points Ron made are right on in terms of having an appreciation for the nuances. And then there’s the old rule—that it’s always easier to stay out of trouble than to get out of trouble. They can’t have too normal a heart rate, too normal a blood pressure. If you pay attention to these signals early on, you can probably avoid getting into a problem, rather than ignoring them and allowing the patient to decompress.

Dr Channick: Dr McCurry, I assume that as a surgeon you have operated on a number of patients who had pulmonary hypertension. Are there any issues that have come up for you?

Dr McCurry: I’m a cardiac thoracic surgeon and direct our heart-lung transplant programs here, so the majority of the patients I have operated on have been in the setting of replacement and correction of their disease, if you will, with transplantation. I would echo some of the comments Stuart and Ron made because we have had the opportunity to offer nontransplant surgery, either thoracic surgery or abdominal surgery, to some of the patients with either primary or secondary pulmonary hypertension on our lung transplant waiting list. Obviously those are patients whose condition in general was more advanced, who were not responding to medical therapy or had a transient response and then declined and ultimately had been referred to our program for consideration for transplantation. The two main procedures we have offered prior to getting into a transplant are bariatric surgery—we’ve had a handful of patients with pulmonary hypertension doing bariatric surgery, to try to get them to lose weight prior to transplantation—and the second is in the setting of secondary pulmonary hypertension associated with mixed connective tissue disease, primarily scleroderma. We’ve done a few esophagectomies preoperatively prior to transplantation in patients with very severe esophageal dysmotility. A lot of the points Stuart and Ron have made are right on with regard to management of those patients intraoperatively and in the postoperative period.

Dr Channick: One of the issues I have dealt with is that it’s not easy if patients are getting continuous infusion of prostacyclin, but now a number of our patients are getting intermittent oral therapy or even inhaled therapy. How have you dealt with that intraoperatively? For instance, have you used continuous prostacyclin therapy intraoperatively or nitric oxide during the surgical procedure or in the immediate postoperative period in these patients who may not be able to take oral or inhaled therapies? How have you dealt with those issues?

Dr Pearl: Patients receiving oral therapy tend to be relatively simple to manage because you can have them take it in the morning. The duration of the surgery is almost always much shorter than the duration of the oral therapy. For patients who are not eating after surgery, you can usually put it down the nasogastric tube. Most of these patients are not undergoing surgery where they can’t take medications directly afterward. So that has not been a problem. In general, they also do not have rapid rebound from discontinuing oral agents. We have not had much experience with inhaled iloprost. We’re trying to decide what to do. Certainly we have them take it immediately before surgery and we might try to
use nebulized in place of inhaled therapy during or after surgery. I don’t know that inhaled nitric oxide would provide necessarily the same benefit as inhaled iloprost. It’s something that we would consider if we saw the patients getting into trouble. But ideally we would try to replace it with inhaled therapy at the same time.

Dr Channick: Are you prepared to use intravenous prostacyclin intraoperatively even if patients have not been receiving it, if they get into trouble?

Dr Pearl: Yes, but when you’re talking about intravenous prostanoids, one is probably at that point using them for their acute pulmonary vasodilatory effects, which inhaled nitric oxide may adequately replace instead.

Dr Rich: I agree. In patients who become hemodynamically unstable, initiating a prostacyclin at that point is probably not the wisest thing. You just go back to the fundamentals. If they’re hypotensive you give them a pressor to raise the blood pressure or cardiac output, etc. On another theme here, and Ron, I don’t know if you agree, but the referral centers need to have one or more anesthesiologists designated as the only ones who will do the cases with pulmonary hypertension. That’s what we’ve done at the University of Chicago. We just have a handful of anesthesiologists who are comfortable with pulmonary hypertension because the general anesthesiologists we have encountered are very frightened. I think having the presence of pulmonary hypertension qualifies as a Class IV risk. We’re sending a lot of patients to bariatric surgery also. Unless the anesthesiologist is experienced, he or she will be very reluctant to do these cases because, at least on paper, they carry an inordinate risk.

Dr Pearl: I completely agree.

Dr Rich: I would follow with another suggestion. Even community hospital types of procedures belong in a referral center for patients with pulmonary hypertension. I don’t care if it’s a laparoscopic cholecystectomy or a small surgical procedure, because familiarity is really essential. I can also tell you some horror stories of things that Ron also referred to. They’ve never seen a CADD pump before, so they switch them to a regular IMED pump. They don’t know how to mix the Flolan correctly, so someone in pharmacy is trying to mix it without experience. They see a Hickman catheter in a patient with lousy venous access and they try to drip something else in that. And we’ve had very tragic deaths occur in patients undergoing minor surgical procedures at community hospitals because of our healthcare system, which puts barriers to having these patients sent to specialty centers.

Dr McCurry: That has not been my experience in the setting of transplantation. Certainly you can see some preexisting thrombocytopenia but, in general, bleeding has not been a major problem in these patients.

Dr Pearl: It has not been a problem for us either.

Dr McCurry: Ron, may I ask you about the value of echocardiography, intraoperative transesophageal echocardiography? Do you see a value of that in this patient population, depending on the severity of illness? What do you see as the role there?

Dr Pearl: We commonly do it unless it’s a relatively straightforward surgical procedure. However, I don’t think we’ve seen it to be extremely useful in general during surgery. There is obviously always right ventricular dilatation and decreased function. We normally have interventricular dependence, so the left ventricle is small. You can diagnose left ventricular underfilling. But what to do about that is often very difficult, especially when it is due to worsening pulmonary hypertension. The major set of cases where intraoperative transesophageal echocardiography might be useful is those where there is going to be very large blood loss and where it is often difficult to figure out whether the problems you are getting into are related to lack of intravascular volume versus the pulmonary hypertension versus some cardiac depression. – Dr Pearl

Dr Channick: We’ve had similar horror stories even in our own institution, and if we hadn’t intervened, there would have been a bad outcome. In terms of the types of surgery our patients face, you name it, from gall bladder removal to total colectomy, I don’t think there is necessarily any particular operation that these patients cannot undergo. One potential issue is bleeding. We generally consider intravenous epoprostenol to have antiplatelet effects. Have you observed that these patients seem to bleed more intra- or postoperatively?

Dr Rich: May I comment on that? We have been involved in the management of this patient group at the University of Chicago, and I think I can confirm that they appear to bleed a little bit more than the average patient. That is a potential issue to consider. Dr Pearl: I guess that gets back a little bit to Stuart’s point about the dangers of putting in a PA catheter, because you actually may respond to the information in an inappropriate way. One issue that comes up with our patients is
obviously the volume status, and the one thing I talk to anesthesiologists about is paying attention to the volume status so they don’t get more concerned about overloading the patients than losing too much. It’s a problem on both ends. Theoretically, that would be one potential advantage of having some sort of central monitoring, to make sure they are not getting overloaded.

Dr Rich: I hate to be so basic, but lots of times those neck veins are so distended going into the OR that unless they’re invisible in the patient, the volume status is more than adequate. The problem that you are alluding to, Rich, the knee-jerk reaction of the inexperienced physician, is that if the blood pressure falls, give fluids. We have people going into the OR with ascites, and the last thing they need is more fluids.

Dr Pearl: The overwhelming majority of the surgical procedures these patients undergo are not large blood-loss procedures, and having to give volume should usually not be an issue. Sometimes they’re undergoing major procedures, and there are those where you may have a couple of liters of blood loss. There, the issue of giving volume does come up. That is uncommon.

Dr Rich: Then I would move to my adage that it is easier to stay out of trouble than to get out of trouble. We will tolerate mild anemia going into the OR for a major procedure in normal patients, but in these patients I want the hemoglobin to be above 12 g/dL if there is any concern about blood loss, because they have no reserve. They may tolerate going from 12 to 9 g/dL but they can easily become very ischemic and I want to be very protective and get all those numbers as ideal as I can before the surgical procedure starts.

Dr Channick: Although it is fairly basic, are there any specific pressors you like or do not like to achieve better responses in these patients?

Dr Rich: Our bias has always been toward phenylephrine. I know that is not widely popular. Typically the problem is one of hypotension, which leads to right ventricular ischemia and failure acutely, so simply raising systemic blood pressure with phenylephrine is all that we generally need to do if hypotension is a problem. If it’s hypotension with low cardiac output, then we prefer dopamine.

Dr Pearl: I would say that phenylephrine has for two decades been recognized as extremely valuable. Often it tends to be underutilized in this setting because the concept in the physician’s mind is that the problem is low cardiac output and we have to do something to raise cardiac output. The right ventricle becomes ischemic very easily. Right ventricular perfusion is highly dependent in pulmonary hypertension on maintenance of systemic blood pressure, so I completely agree with the idea of using phenylephrine to maintain blood pressure. Some institutions might use norepinephrine instead of phenylephrine to try to maintain blood pressure. There are some settings where one needs to do something for more inotropic support. That’s more common, for example, when we talk about pulmonary hypertension in the setting of cardiac surgery. Dobutamine is a very good choice in that setting. Outside of cardiac surgery the emphasis probably should be much more on maintaining blood pressure with vasoconstrictors.

Dr Channick: I think we’re all in agreement there. I’ve seen inotropes make people more tachycardic, which isn’t a good thing either for these patients. Is there something else that we should be discussing about surgery in these patients that we haven’t thought of?

Dr Pearl: Let me say that I do like to use pulmonary artery catheters in the bigger surgical procedures. It’s not specifically done to try to reduce pulmonary artery pressures. The value of pulmonary artery pressure monitoring is often seen during the emergence of anesthesia, when patients can develop marked increases in their pulmonary artery pressure, often with increases in systemic blood pressure. That we will sometimes treat. It’s not to improve the pulmonary artery pressure from where it began but to prevent decompensation from exacerbation of the chronic pulmonary hypertension. If the patient seems to be decompensating and the systemic blood pressure is good, we will treat that at that point in time. One can make the same decision without a pulmonary artery catheter as well, but it helps us to determine if there is a need to do something. I agree with the earlier comments that, in general, one should avoid intervening if possible. But we have seen patients who develop marked increases in pulmonary pressure during the emergence from anesthesia and who, if allowed to continue on that path, do get into trouble.

Dr McCurry: One other thought on the intraoperative management of these patients might be in that subpopulation of patients who might have a patent foramen ovale coexisting and, at least intraoperatively, the risk of a paradoxical air embolus. Those of us who work in the operating room know that it is not uncommon with intravenous lines and everything else in the operating room to get some air on the right side of the heart, particularly in the setting where there might be some intermittent right to left shunt or a positive pressure ventilation, a greater preponderance of left to right shunting.

(continued on page 96)
don’t know what you think, Ron, but we try to be very fastidious about avoiding air entry via intravenous catheters.

Dr Pearl: I agree. We treat patients as though they had congenital heart disease with shunting lesions and make sure when we give medications that we do not allow air bubbles. Does anyone have experience with patients receiving inhaled iloprost coming for surgery?

Dr McCurry: We use very little of it here.

Dr Channick: We do have some experience with that group of patients. It has been a challenge. We’ve taken the approach that they do a treatment before and then after. We have once or twice delivered iloprost through the ventilator circuit although, to be honest, we really don’t know exactly the dose or method by which to deliver this therapy in a mechanically ventilated patient, given the relative inefficiency of delivering it and the loss of the drug with a standard nebulizer system. We actually have had patients to whom we gave a low dose of IV epoprostenol intraoperatively at 2 to 3 ng/kg/min and then we resumed the inhaled therapy after the patient was able to use the ultrasonic nebulizer. But I know of cardiac anesthesiologists who are very fond of it intraoperatively. As far as I know there is no accepted method of dosing, of how to give it. That is a big issue. I think I can summarize by saying that it is fairly clear that patients with pulmonary hypertension can undergo virtually any kind of surgery as long as the proper attention is paid to these patients. That is the important message I am getting from this conversation. Yes, our patients can undergo surgery, but it needs to be done at the right center with trained anesthesiologists and clinicians who are used to managing these patients.

Dr Pearl: In the past the sense has been that surgery cannot be tolerated by these patients. The majority of patients can undergo surgery safely, but there does need to be an appropriate risk/benefit analysis. These patients are at increased risk. It depends in many ways on their functional status. The patient who is decompensated from pulmonary hypertension and has a short life expectancy should not undergo major surgery that puts him or her at high risk for morbidity and mortality. I agree with the important message that patients with pulmonary hypertension can undergo surgery, but they need to be in relatively good compensation in order to do so.
The patient with a cardiac pacemaker or implanted defibrillator and management during anaesthesia

Marc A. Rozner

Purpose of review
Worldwide, nearly 3 million patients have cardiac pacemakers and more than 300 000 have implantable cardioverter-defibrillators. Many factors cause confusion regarding perioperative care of these patients, since conventional wisdom, case reports, textbooks, and literature reviews have either not kept pace with technologic developments or contain incorrect statements. Additionally, recalls or alert notices have prompted programming changes that might not be understood or recognized.

Recent findings
The complexity of the devices, as well as features designed to improve both the quality of life and the survival of the patient, can masquerade as pacing malfunction. Additionally, algorithms designed to detect heart rate, ST segment behavior, and arrhythmias in electrocardiographic monitors may lead to inappropriate behavior on the part of the perioperative team.

Summary
Appropriate education of perioperative practitioners, as well as preoperative interrogation of a pacemaker or implantable cardioverter-defibrillator, may prevent perioperative delays, cancellations, and deaths. Additionally, evidence suggests that postoperative re-interrogation of any cardiac generator is warranted if an operative event includes the use of monopolar electrosurgery (‘Bovie’) or significant fluid or blood component administration.

Keywords
cardiac pacemaker, implantable cardioverter-defibrillator, review

Introduction
Battery-operated pacemakers were developed to treat bradycardia in 1958, and implantable cardioverter-defibrillators (ICDs) to treat tachyarrhythmias followed in 1980. ICD advancements have three important results. First, all ICDs have brady-pacing capability, and the presence of pacing artifacts on an ECG might lead a practitioner to mistake an ICD for a (non-ICD) pacemaker. If ECGs are routinely collected from patients with ‘pacemakers’ using a magnet, then some ICDs from Guidant/CPI might be permanently deactivated with magnet placement [1]. Second, ICD brady-pacing is never converted to asynchronous mode with magnet placement. Third, ICDs respond to, and process, electromagnetic interference (EMI) differently than a pacemaker.

The complexity of cardiac generators limits generalizations that can be made about the perioperative care of these patients. Population aging, continued enhancements, and new indications for implantation of cardiac devices will lead to increased implantations. Whether pacemaker or ICD patients have increased perioperative morbidity/mortality remains an area ripe for investigation. Levine et al. reported increases in pacing thresholds in some thoracic operations [2]. In 1995, Badrinath et al. retrospectively reviewed ophthalmic surgery cases in one hospital in Madras, India from 1979 through 1988 (14 787 cases) and reported that the presence of a pacemaker significantly increased the probability of a mortal event within 6 weeks postoperatively, regardless of the anesthetic technique [3]. In abstract form, Samain et al. reported that three of 73 pacemaker patients (4.1%) undergoing significant surgery (not including open-heart surgery) died postoperatively of cardiac cause, although a time-frame was not specified [4]. Also in abstract form, Rozner et al. reported preop to postop pacing threshold increases in nonthoracic surgery [5]. These issues led the American Society of Anesthesiologists to publish a Practice Advisory for these patients [6]. Other guidelines have been published as well [7–10], although not all authors recommend ICD disablement in the perioperative period [11]. ICDs also perform permanent cardiac pacing, so ICD issues related primarily to antibrady pacing should be reviewed in the Pacing section. Table 1 shows perioperative guidelines adapted from a number of sources.

Also, some generator manufacturers have issued a variety of notices regarding potential failures in both pacemakers.
Table 1 Perioperative guidelines for the patient with a cardiac generator

<table>
<thead>
<tr>
<th>Preoperative key points</th>
<th>Intraoperative key points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have the pacemaker or defibrillator interrogated by a competent authority shortly before the anesthetic</td>
<td>Monitor cardiac rhythm/peripheral pulse with pulse oximeter or arterial waveform</td>
</tr>
<tr>
<td>Obtain a copy of this interrogation. Ensure that the device will pace the heart with appropriate safety margins</td>
<td>Disable the ‘artifact filter’ on the EKG monitor</td>
</tr>
<tr>
<td>Consider replacing any device near its elective replacement period in a patient scheduled to undergo either a major surgery or surgery within 25 cm of the generator</td>
<td>Avoid use of monopolar electrosurgery</td>
</tr>
<tr>
<td>Determine the patient’s underlying rhythm/rate to determine the need for backup pacing support</td>
<td>Use bipolar ESU if possible; if not possible, then pure cut (monopolar ESU) is better than ‘blend’ or ‘coag’</td>
</tr>
<tr>
<td>Identify the magnet rate and rhythm, if a magnet mode is present and magnet use is planned</td>
<td>Place the ESU current return pad in such a way to prevent electricity from crossing the generator-heart circuit, even if the pad must be placed on the distal forearm and the wire covered with sterile drape</td>
</tr>
<tr>
<td>Program minute ventilation rate responsiveness off, if present</td>
<td>If the ESU causes ventricular oversensing, pacer quiescence, or tachycardia, limit the period(s) of asystole or reprogram the device</td>
</tr>
<tr>
<td>Program all rate enhancements off</td>
<td>Postoperative key points</td>
</tr>
<tr>
<td>Consider increasing the pacing rate to optimize oxygen delivery to tissues for major cases</td>
<td>Have the device interrogated by a competent authority postop. Some rate enhancements can be re-initiated and optimum heart rate and pacing parameters should be determined. The ICD patient must be monitored until the antitachycardia therapy is restored</td>
</tr>
<tr>
<td>Disable antitachycardia therapy if a defibrillator</td>
<td>ESU, electrosurgery; ICD, implantable cardioverter-defibrillator.</td>
</tr>
</tbody>
</table>

[12–14] and ICDs [15–17]. For some ICDs, Guidant has found that 45 000 devices are at risk for improperly entering the ‘magnet mode’, which prevents any detection (and, therefore, treatment) of tachyarrhythmias. As a ‘work-around’, Guidant has recommended the permanent disabling of the magnet mode through programming [18]. Although pacemakers and ICDs are more reliable than almost any other technology, some devices fail prematurely. Using data from the FDA, Maisel et al. reported that for every 1000 implants, 1.4 pacemaker and 36.4 ICD patients underwent device explanation for unexpected device failure during 2001–2002 [19**].

These systems consist of an impulse generator and lead(s). Leads can have one (unipolar), two (bipolar), or multiple (multipolar) electrodes with connections in multiple chambers. In unipolar pacing, as well as defibrillation, the generator case serves as an electrode, and tissue contact in a pacemaker has been disrupted by pocket gas [20]. Pacing in a unipolar mode (unusual in an ICD system) produces larger ‘spikes’ on an analogue-recorded ECG, and unipolar sensing is more sensitive to EMI. Most pacemaking systems use bipolar pacing/sensing configuration, since bipolar pacing usually requires less energy and bipolar sensing is more resistant to interference from muscle artifacts or stray electromagnetic fields. Often, bipolar electrodes can be identified on the chest film since they will have a ring electrode 1–3 cm proximal to the lead tip. ICDs can be distinguished from conventional pacemakers by the presence of a shock coil on the right ventricular lead (Fig. 1).

Finally, devices resembling cardiac pulse generators are being implanted at increasing rates for pain control, thalamic stimulation to control Parkinson’s disease, phrenic nerve stimulation to stimulate the diaphragm in paralyzed patients, and vagus nerve stimulation to control epilepsy and possibly obesity [21]. These devices can be confused for a cardiac generator as well.

For ease of reading, this review is divided into a section on conventional pacemakers and a section on ICDs.

Pacemaker overview

The Pacemaking Code of the North American Society of Pacing and Electrophysiology (NASPE) and the British Pacing and Electrophysiology Group (BPEG) describes basic pacing behavior Table 2 [22]. Single chamber pacemakers can pace the atrium (AAI) or the ventricle (VVI) Dual chamber programming (DDD) is used to provide atrio-ventricular synchrony; VDD pacing (single wire device providing atrio-ventricular synchrony) can be found in patients with atrio-ventricular nodal disease but normal sinus node function. Some patients with atrial dysrhythmias have DDI programming (atrio-ventricular synchrony is provided only when the pacemaker provides atrial pacing). Biventricular pacing is being investigated as a means to prevent atrial fibrillation [23], and biventricular pacing [also called Cardiac Resynchronization Therapy (CRT)] is used to treat dilated cardiomyopathy [24–26].

Permanent pacing indications (Table 3) are reviewed in detail elsewhere [27]. In order to be effective, pacing for CRT, hypertrophic cardiomyopathy, and dilated cardiomyopathy must provide the stimulus for ventricular activation, and atrio-ventricular synchrony must be preserved [28]. Pacemaker inhibition, loss of pacing (i.e. from native conduction, junctional rhythm, EMI), or atrio-ventricular dys-synchrony can lead to deteriorating hemodynamics in these patients. Biventricular pacing can lengthen the Q-T interval in some patients, producing torsade-de-points [29]. Thus access to rapid defibrillation is required for the patient with biventricular pacing.
This chest film was taken from a 78-year-old man with right upper lobe lung cancer, coronary artery disease, and ischemic cardiomyopathy with ejection fraction of 22%. The implantable cardioverter-defibrillator (ICD) generator is in the left pectoral position with three leads: a conventional, bipolar lead to the right atrium, a tripolar lead to the right ventricle (RV), and a unipolar lead to the coronary sinus (CS). This system is designed to provide ‘resynchronization (bradycardia) therapy’ in the setting of a dilated cardiomyopathy with a prolonged QRS (and frequently with a prolonged P-R interval as well). The bipolar lead in the right atrium will perform both sensing and pacing function. In the RV, the tip electrode functions as the cathode for pacing and sensing functions. The presence of a ‘shock’ conductor (termed ‘shock coil’) on the RV lead in the right ventricle distinguishes a defibrillation system from a conventional pacemaking system. In this particular patient, the RV shock coil also functions as the pacing and sensing anode (this is called an integrated bipolar defibrillator case (called the ‘can’). When the defibrillation circuit includes the ICD case, it is called ‘active can configuration’.

**Table 2 NASPE/BPEG generic pacemaker code (NBG) [Revised 2002]**

<table>
<thead>
<tr>
<th>Position I</th>
<th>Position II</th>
<th>Position III</th>
<th>Position IV</th>
<th>Position V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chambers paced</td>
<td>Chambers sensed</td>
<td>Response to sensing</td>
<td>Programmability</td>
<td>Multi-site pacing</td>
</tr>
<tr>
<td>O = None</td>
<td>O = None</td>
<td>O = None</td>
<td>R = Rate Modulation</td>
<td>A = Atrium</td>
</tr>
<tr>
<td>A = Atrium</td>
<td>A = Atrium</td>
<td>I = Inhibited</td>
<td>O = None</td>
<td>O = None</td>
</tr>
<tr>
<td>V = Ventricle</td>
<td>V = Ventricle</td>
<td>T = Triggered</td>
<td>R = Rate Modulation</td>
<td>V = Ventricle</td>
</tr>
<tr>
<td>D = Dual (A + V)</td>
<td>D = Dual (A + V)</td>
<td>D = Dual (T + I)</td>
<td>D = Dual (T + I)</td>
<td>D = Dual (A + V)</td>
</tr>
</tbody>
</table>

has the potential to create a malignant rhythm in the patient with structurally compromised myocardium [35]. Reprogramming a device will not protect it from internal damage or reset caused by EMI. In general, rate responsiveness and ‘enhancements’ (dynamic atrial overdrive, hysteresis, sleep rate, A-V search, etc.) should be disabled by programming, since many of these features can mimic pacing dysfunction [7,36,37]. It should be noted that for many Guidant and/or CPI devices, Guidant Medical recommends increasing the pacing voltage to ‘5 volts or higher’ when monopolar electrosurgery will be used. Few cardiologists follow this recommendation, but there are reports of threshold changes during both intrathoracic [2] and nonchest surgery [38]. Recently, pacing threshold was shown to be increased by device states [39]. Special attention must be given to any device with a minute ventilation (bioimpedance) sensor (Table 6) since inappropriate tachycardia has been observed secondary to mechanical ventilation [40,41], monopolar (‘Bovie’) electrosurgery [40,42,43], and connection to an ECG monitor with respiratory rate monitoring [39,44–48]. Sometimes, inappropriate therapy producing life-threatening results has been delivered in these settings [41,49**].

Intraoperative (or procedure) management of pacemakers

No special technique or monitoring is needed for the pacemaker patient, but attention must be given to a number of concerns (Table 7). Monopolar ‘Bovie’ electrosurgery use remains the principal intraoperative issue for the patient with a pacemaker. Between 1984 and 1997, the US FDA was notified of 456 adverse events with pulse generators, 255 from electrosurgery, and a ‘significant number’ of device failures [50]. Coagulation electrosurgery is more likely to cause problems than cutting electrosurgery [51]. Magnet placement during electrosurgery might prevent aberrant pacemaker (but not ICD) behavior, and spurious reprogramming with magnet...

**Table 3 Permanent pacemaker indications**

<table>
<thead>
<tr>
<th>Sinus node disease</th>
<th>Atrioventricular node disease</th>
<th>Long Q-T syndrome</th>
<th>Hypertrophic obstructive cardiomyopathy</th>
<th>Dilated cardiomyopathy</th>
</tr>
</thead>
</table>

**Table 4 Usual (or default) effects for most devices of appropriate magnet placement**

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Pacemaker</th>
<th>Implantable cardioverter-defibrillator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biotronik</td>
<td>PROGRAMMABLE</td>
<td>NONPROGRAMMABLE</td>
</tr>
<tr>
<td>ELA Medical (Sorin)</td>
<td>NONPROGRAMMABLE</td>
<td>Disables tachy therapies</td>
</tr>
<tr>
<td>Guidant (also CPI) now Boston Scientific</td>
<td>PROGRAMMABLE OFF MODE</td>
<td>PROGRAMMABLE OFF MODE</td>
</tr>
<tr>
<td>Medtronic Corporation</td>
<td>NONPROGRAMMABLE</td>
<td>NONPROGRAMMABLE</td>
</tr>
<tr>
<td>Pacesetter</td>
<td>PROGRAMMABLE OFF (and VARIO* MODE)</td>
<td>PROGRAMMABLE OFF MODE</td>
</tr>
<tr>
<td>St Jude Medical</td>
<td>Battery OK: AS pacing below 87 bpm</td>
<td>NO confirmation</td>
</tr>
</tbody>
</table>

This table is not meant to be complete. It lists the default (or out-of-box) settings for appropriate magnet placement. Only an interrogation of the generator will reveal the true settings for any programmable device. The term ‘PROGRAMMABLE OFF MODE’ indicates that the magnet response can be eliminated in the generator by programming, AS, asynchronous; ERI, elective replacement indicated; the device is reporting the need for generator replacement due to battery depletion; LRL, lower rate limit; the minimum programmed rate for the device.

*VARIO mode: 32 AS events; the first 16 between 100 bpm and 85 bpm (ERI) to indicate battery performance; the next 15 at 119 bpm with gradually declining ventricular pacing output to demonstrate capture threshold. The final pace is no output to clearly demonstrate no capture. This sequence repeats as long as the magnet is in place.

**For CPI/Guidant ICDs, if magnet mode is programmed to ‘ON’, appropriate magnet placement immediately disables tachy detection and therapy, and tachy therapies remain disabled as long as the magnet remains appropriately applied. If each heartbeat produces a ‘beep’, then the device will be enabled for tachy therapy upon magnet removal. If the device emits a constant tone, then tachy therapy is disabled whether or not a magnet is present. If the ‘Change Tachy Mode with Magnet’ feature also is programmed ‘ON’, after 30 s of continuous magnet application, the tachy mode changes, i.e., it will switch from enabled (in absence of magnet, beeping) to permanently disabled (constant tone) or vice versa. Any CPI/Guidant ICD that does not emit sound when a magnet is applied should undergo an immediate device interrogation.**
placement is unlikely. If monopolar electrosurgery is to be used, then the electrosurgery current-return pad must be placed to ensure that electrosurgery current path does not cross the chest or the pacemaking system. Some authors recommend placement of this pad on the shoulder for head and neck procedures or the distal arm (with sterile draping of the wire) for breast and axillary procedures when the generator is ipsilateral to the surgical site [51,53].

Choice of anesthetic agents should be dictated primarily by the patient’s underlying physiology as well as the procedure. The use of drugs that suppress the atrioventricular or SA node (such as potent opiates or dexmedetomidine), however, can abolish any underlying rhythm that might be present and render the patient truly pacing-dependent. Also, some potent inhalational agents (isoflurane, sevoflurane, and desflurane) may exacerbate the long Q-T syndrome [54–57].

Finally, attention must be given to the electrocardiographic monitor. Most monitors have high-frequency filtering that removes the pacemaker artifact, and many of the monitors can be fooled by the electrosurgery or the nerve stimulator [58]. The monitors frequently report inappropriate heart rates on the electrocardiographic channel. As a result, the pulse must be measured mechanically. Methods for such measurement include pulse oximeter or noninvasive pressure plethysmography, invasive pressure monitor, or Doppler waveforms.

### Pacemaker failure

Pacemaker failure has three etiologies: first, failure to capture; second, lead failure; or third, generator failure. Failure to capture can result from myocardial ischemia/infarction, acid-base disturbance, electrolyte abnormalities, or abnormal antiarrhythmic drug level(s). External pacing can further inhibit permanent pacemaker output due to oversensing of the temporary pacing pulse by the permanent pacemaker, even at temporary pacing energies that do not produce myocardial capture [59,60]. Sympathomimetic drugs generally lower pacing threshold. Outright generator and/or lead failure is rare in an appropriately tested system.

### Postoperative pacemaker evaluation

Any pacemaker that was reprogrammed for the operating room should be reset appropriately. For nonreprogrammed devices, most manufacturers recommend interrogation to ensure proper functioning and remaining battery life if any electrosurgery was used. Attention should be paid to possible perioperative changes in pacing or sensing thresholds, and an appropriate lower pacing rate should be chosen to ensure appropriate delivery of oxygen to the tissues.

### Implantable cardioverter-defibrillator overview

For the patient with ventricular tachycardia or fibrillation, ICDs clearly reduce deaths, and they remain superior to antiarrhythmic drug therapy [61]. Further, studies such as the Multicenter Automatic Defibrillator Implantation Trial II (ischemic cardiomyopathy, ejection fraction less than 0.30 [62]) and the Sudden Cardiac Death – Heart Failure Trial (any cardiomyopathy, ejection fraction less than 0.35 [63]) have demonstrated that placement of ICDs in patients (without evidence of tachyarrhythmias) reduces overall cardiac mortality, thus increasing the number of patients for whom ICD therapy is indicated. Table 8 shows current ICD indications.

Like pacemakers, ICDs have a four-place code (Table 9) [64]. The Pacemaker Code can be used instead of

---

### Table 5 Pacing function reprogramming possibly needed

| Any rate-responsive device problems are well known and have been misinterpreted with potential for patient injury. The US FDA has issued an alert regarding devices with minute ventilation sensors [52]. |
| Special pacing indication (HOCM, DCM, pediatrics) |
| Pacemaker-dependent patient |
| Major procedure in the chest or abdomen |
| Rate enhancements are present that should be disabled |
| Special procedures |
| Lithotripsy |
| Transurethral or hysteroscopic resection |
| Electroconvulsive therapy |
| Succinylcholine use |
| MRI (usually contraindicated by device manufacturers, although now possible in some patients) |

HOCM, hypertrophic obstructive cardiomyopathy; DCM, dilated cardiomyopathy.

---

### Table 6 Pacemakers with minute ventilation sensors

| ELA Medical (Sorin) | Symphony, Brio (212, 220, 222) |
| Guidant Medical and/or (CPI) | Opus RM (4534) |
| Chorus RM (7034, 7134) |
| Talent (130, 213, 223) |
| Pulsar (1172, 1272) |
| Pulsar Max (1170, 1171, 1270) |
| Pulsar Max II (1180, 1181, 1280) |
| Insignia Plus (1194, 1297, 1298) |
| Medtronic | Kappa 400 series (401, 403) |
| Telelectronics/St Jude | Meta (1202, 1204, 1206, 1230, 1250, 1254, 1256) |
| Tempo (1102, 1902, 2102, 2902) |

### Table 7 Essentials of pacemaker monitoring

| EKG monitoring of the patient must include the ability to detect pacemaker discharges (‘artifact filter’ disabled) |
| Perfused (peripheral) pulse must be monitored with a waveform display |
| The pacemaker rate might need to be increased due to an increased oxygen demand |
| BIV and HOCM patients might need beat-to-beat cardiac output monitoring |
| Appropriate equipment must be on hand to provide backup pacing and/or defibrillation |

BIV, biventricular; HOCM, hypertrophic obstructive cardiomyopathy.
chamber (VVI) pacing might decrease survival when compared with single-chamber pacing in an ICD patient approved for patients who need permanent pacing modes (including rate responsiveness) are approved for patients who need permanent pacing (about 20% of ICD patients). It should be noted that the use of dual chamber (DDD) pacing in an ICD patient might decrease survival when compared with single chamber (VVI) pacing.

Also, an inappropriate shock (i.e., no arrhythmia present) can be delivered without prior ECG changes if a lead is damaged or defective, resulting from electrical ‘chatter’ [70]. Currently, several ventricle leads are on ‘alert status’ for such false signal generation.

Implantable cardioverter-defibrillator magnets

Like pacemakers, magnet behavior in many ICDs can be altered by programming, although most ICDs suspend tachydysrhythmia detection (and therefore therapy) when a magnet is appropriately placed (usually over the middle of the ICD generator). Some ICDs from Angiomed, CPI, Pacemaker (St Jude Medical) or Ventritex can be programmed to ignore magnet placement. Depending upon programming, antitachycardia therapy in some Guidant or CPI devices can be permanently disabled by magnet placement for 30 s, and some patients have been discovered with their ICD antitachycardia therapy unintentionally disabled [1]. In general, magnets will not affect the brady pacing mode or rate (except ELA rate change) and Teletronics Guardian 4202/4203 (disabled). Intermedics devices change pacing rate (VVI mode) to reflect battery voltage. Interrogating the device and calling the manufacturer remain the most reliable method for determining magnet response. Table 4 shows the usual (default) behavior for appropriate magnet placement in many ICDs.

Preanesthetic evaluation and implantable cardioverter-defibrillator reprogramming

In addition to evaluating and optimizing comorbid disease(s), every ICD patient should undergo preoperative ICD interrogation. Magnet nonresponsiveness should be identified in this visit. Important features of the preanesthetic device evaluation are shown in Table 1.

All ICD patients should have antitachycardia therapy disabled if monopolar Bovie use is planned, or if there is evidence of lead problems [6,7]. In situations where lead performance is adequate and no monopolar Bovie will be used, magnet placement on a magnet-responsive device (or tachy therapy disablement by programming) might be indicated in any case wherein patient movement could produce disastrous results (such as intra-ocular surgery). The comments in the pacing section apply here for antibradycardia pacing.

### Table 8 Implantable cardioverter-defibrillator indications

<table>
<thead>
<tr>
<th>Ventricular tachycardia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventricular fibrillation</td>
</tr>
<tr>
<td>Post-MI patients with EF ≤ 30% (MADIT II)</td>
</tr>
<tr>
<td>Cardiomyopathy from any cause with EF ≤ 35% (SCD-HeFT)</td>
</tr>
<tr>
<td>Hypertrophic cardiomyopathy</td>
</tr>
<tr>
<td>Awaiting heart transplant</td>
</tr>
<tr>
<td>Long Q-T syndrome</td>
</tr>
<tr>
<td>Arrhythmogenic right ventricular dysplasia</td>
</tr>
<tr>
<td>Brugada syndrome (right bundle branch block, S-T segment elevation in leads V1-V3)</td>
</tr>
</tbody>
</table>

ML, myocardial infarction; EF, ejection fraction; MADIT II, Multicenter Automatic Defibrillator Implantation Trial II; SCD-HeFT, Sudden Cardiac Death – Heart Failure Trial.

Position IV. Current follow-up guidelines suggest a comprehensive device interrogation with a programmer every 3–4 months.

ICDs measure each cardiac R-R interval and categorize the rate as normal, too fast (short R-R interval), or too slow (long R-R interval). When enough short R-R intervals are detected, an antitachycardia event is begun. The internal computer chooses antitachycardia pacing (ATP, less energy use, better tolerated by patient) or shock, depending upon the presentation and device programming. Most ICDs are programmed to ‘reconfirm’ ventricular tachycardia or ventricular fibrillation after charging to prevent inappropriate therapy. Typically, ICDs deliver 6–18 shocks per event. Once a shock is delivered, no further ATP can take place. Despite improvements in detection of ventricular dysrhythmias [65], more than 10% of shocks are for rhythm other than ventricular tachycardia or ventricular fibrillation [66]. Whether inappropriate shocks injure patients remains a subject of considerable debate, but many patients who receive an inappropriate shock will demonstrate elevated troponin levels in the absence of an ischemic event [67].

Supraventricular tachycardia remains the most common etiology of inappropriate shock therapy, and causes of inappropriate shock have been reviewed elsewhere [68]. Most ICDs will begin pacing when the R-R interval is too long. ICDs with sophisticated, dual and three-chamber pacing modes (including rate responsiveness) are approved for patients who need permanent pacing (about 20% of ICD patients). It should be noted that the use of dual chamber (DDD) pacing in an ICD patient might decrease survival when compared with single chamber (VVI) pacing [69].

### Table 9 NASPE/BPEG generic defibrillator code (NBD)

<table>
<thead>
<tr>
<th>Position I</th>
<th>Position II</th>
<th>Position III</th>
<th>Position IV (or use Pacemaker Code)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shock chambers</td>
<td>Antitachycardia pacing chambers</td>
<td>Tachycardia detection</td>
<td>Antibradycardia pacing chambers</td>
</tr>
<tr>
<td>O = None</td>
<td>O = None</td>
<td>E = Electrogram</td>
<td>O = None</td>
</tr>
<tr>
<td>A = Atrium</td>
<td>V = Ventricle</td>
<td>H = Hemodynamic</td>
<td>A = Atrium</td>
</tr>
<tr>
<td>V = Ventricle</td>
<td>D = Dual (A+V)</td>
<td>V = Ventricle</td>
<td>D = Dual (A+V)</td>
</tr>
</tbody>
</table>

Intraoperative (or procedure) implantable cardioverter-defibrillator management

No special monitoring or anesthetic technique (due to the ICD) is required for the ICD patient. ECG monitoring and the ability to deliver external cardioversion or defibrillation must be present during the time of ICD disablement. If emergency cardioversion or defibrillation is needed, the defibrillator pads should be placed to avoid the pulse generator to the extent possible. Nevertheless, one should remember that the patient, not the ICD, is being treated. The recommendations in the section ‘Intraoperative (or procedure) management of pacemakers’ also apply here. ICDs should be disabled prior to insertion of a central line to prevent inappropriate shock and possible ICD failure [71].

Postoperative implantable cardioverter-defibrillator evaluation

The ICD must be reinterrogated and re-enabled, and pacing parameters should be checked and reset as necessary, as discussed in the pacing section. Any recorded tachycardia events should be reviewed and counters should be cleared.

Conclusion

Electronic miniaturization of pacemakers and ICDs has permitted the design and use of sophisticated electronics in patients who have need for artificial pacing and/or automated cardioversion/defibrillation of their heart. These devices are no longer confined to keeping the heart beating between a minimum rate (pacing function) and a maximum rate (ICD functions), as they are being used as therapy to improve the failing heart. The aging of the population and our ability to care for a patient with increasingly complex disease suggest that we will be caring for many more patients with these devices, and we must be prepared for this situation. Safe and efficient clinical management of these patients depends upon our understanding of implantable systems, indications for their use, and the perioperative needs that they create.

References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

• of special interest

•• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 289).


20. Most practitioners do not understand that problems can develop in implanted devices. In this paper, Maisel et al. searched the FDA database to learn that per 1000 implants, 1.4 pacemakers and 36.4 ICDs had been explanted during 2001–2 for failures other than battery depletion.


Anesthesia and medical device


34 Hayes JJ, Juknavorian R, Maloney JD. The role(s) of the industry employed allied professional. Pacing Clin Electrophysiol 2001; 24:398–399.


This article should serve as yet another alarm that medical providers are vastly undertrained in the care of pacemaker (and probably ICD) patients. Lau et al. received [on transfer] a hypotensive, unconscious, intubated patient who had sustained a pacemaker-mediated tachycardia due to connection to an electrocardiographic monitor after he had been treated (unsuccessfully) with amiodarone, sotalol, magnesium sulfate, and 11 electrical shocks for a paced, wide complex rhythm at 135 bpm.


Current Perioperative Management of the Patient With a Cardiac Rhythm Management Device
Marc E. Stone and Andrey Apinis

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Current Perioperative Management of the Patient With a Cardiac Rhythm Management Device

Marc E. Stone, MD, and Andrey Apinis, MD

The safe and effective perioperative management of the patient with a cardiac rhythm management device (ie, pacemaker and/or implantable cardioverter defibrillator) is based entirely on the avoidance of adverse outcomes, including damage to the device, the leads, or the site of lead implantation that might prevent the device from functioning as intended. An important management principle is the potential reprogramming of such a device in the perioperative period to avoid transient interruption of device function or the delivery of inappropriate electrophysiological therapy (eg, unnecessary defibrillation or pacing). Given the large numbers of patients worldwide currently implanted with these devices, the anesthesia practitioner should become electively familiar with the current technology. This article describes the current status of cardiac rhythm management devices and discusses recommended perioperative management.

Keywords: cardiac rhythm management device; pacemaker; implantable cardioverter defibrillator; ICD; heart failure; perioperative management; anesthesia; sudden cardiac death; ventricular fibrillation

It was recently reported that nearly 3 million patients worldwide have a pacemaker, and somewhere between 300,000 and 500,000 patients have an implantable cardioverter defibrillator (ICD) (also T. McNulty, public relations manager, Medtronic, Inc, Minneapolis, MN, personal communication, May 2007). According to the American Heart Association, in the United States alone, 180,000 pacemakers and 91,000 ICDs were implanted in 2005, and it is likely the numbers are increasing. Current industry-wide estimates indicate that approximately one third of the pacemakers annually implanted worldwide are in the United States (T. McNulty, personal communication, May 2007), and it is further estimated that there are currently 1.5 million Americans living with a pacemaker and 500,000 with an ICD (T. McNulty, personal communication, May 2007). Unfortunately, statistics regarding the number of device implants are not tracked systematically, so such numbers tend to be very approximate and no one really knows for certain how many are out there. What is clear is that the anesthesia practitioner can expect to encounter patients with a cardiac rhythm management device (CRMD) fairly frequently, and it is imperative to understand the perioperative management of these patients if eminently preventable complications are to be avoided.

An American Society of Anesthesiologists (ASA) Task Force Practice Advisory outlining the recommended perioperative management of the patient with a CRMD was published in the July 2005 issue of Anesthesiology. As stated in the document, the purpose of the advisory is to facilitate the safe and effective perioperative management of patients with CRMDs and to reduce the incidence of adverse outcomes. Furthermore, the advisory also outlined that although the use of practice guidelines cannot guarantee a specific outcome, following the recommendations therein should prevent the vast majority of untoward events that might arise. Although
individual practitioners may therefore choose to deviate from the recommendations based on their own experience, their medical judgment, and as their own clinical situation warrants, it is important to appreciate that the intention of the task force recommendations was the highest possible level of safety for patients, and not necessarily the highest level of convenience for practitioners.

The following paragraphs illustrate how CRMD technology has evolved over the past decade; practical perioperative management is also discussed. The article concludes with a brief discussion of CRMD management for specific clinical scenarios, including lithotripsy, radiation therapy, electroconvulsive therapy (ECT), and magnetic resonance imaging (MRI).

Pacemakers

Basics of Modern Pacemakers

Pacemakers can be temporary or permanent, and indications for pacing continue to expand as the technology advances. Although a complete list and description of all current indications for pacing is beyond the scope of this article, the most common indications include symptomatic bradycardia of any etiology, high-grade atrioventricular (AV) conduction block of any etiology, documented periods of asystole greater than or equal to 3 seconds, and following catheter ablation of the AV junction.

Pacing can take place in a single chamber (eg, atrium or ventricle only), dual chambers (eg, atrium and ventricle), or multiple chambers (eg, in biventricular pacing) and can employ either unipolar or bipolar leads, although the trend over the past 15 years has been to implant pacemakers with bipolar leads. Figure 1 shows examples of both single-chamber and dual-chamber pacemakers and illustrates the concept of unipolar and bipolar leads. As seen in Figure 1, the distance between the anode and cathode is much smaller with a bipolar lead than with a unipolar lead (where the pulse generator functions as the anode), reducing susceptibility to electromagnetic interference (EMI).

Typically, pacemaker leads are placed in the right atrium, the right ventricle, or both. Depending on how the device is programmed, in a single-chamber mode, the device can sense the intrinsic electrical activity in the chamber where the lead is placed to either inhibit or trigger pacing of that chamber. Depending on the desired heart rate, specific escape intervals (time limits) are programmed. If no spontaneous depolarization of the chamber is sensed within the preset time limit, the device will “trigger” depolarization of the chamber. If a spontaneous depolarization is sensed, the device will inhibit itself and “sense” for a subsequent depolarization during the next preset time interval. Although atrial pacing alone may allow for normal AV synchrony in a patient with a competent AV node, isolated ventricular pacing has some disadvantages, as discussed below.

A dual-chamber mode allows for both sensing and subsequent triggering or inhibition of pacing in one or both chambers where leads are placed and has the distinct physiological advantage of maintaining AV synchrony. In AV sequential pacing (“physiologic pacing”), ventricular systole is immediately preceded by an atrial systole, and the ventricular rate is the same as the atrial rate. As synchronicity of the atrial and ventricular systoles is achieved, cardiac output is optimized, and congestive symptoms are minimized.
because left ventricular (LV) filling is optimized without the need for excessively high left atrial pressures. This synchronicity also promotes normal AV valve function and minimizes the AV valvular insufficiency that occurs with retrograde atrial activation during isolated ventricular pacing. Studies have demonstrated more than doubling of cardiac output with atrial pacing for treatment of AV junctional rhythm in patients with ischemic cardiomyopathy.

**Modern Alphabet Soup**

Table 1 shows the current NASPE/BPEG generic code for antibradycardia, adaptive rate, and multisite pacing. In plain English, this code describes pacemaker programming. Different versions of this code have existed over the years, and this modified version was adopted in October 2001 as an attempt to decrease confusion and enhance communication between multidisciplinary practitioners caring for patients with pacemakers.

The basic 3-letter programming codes did not change in the current version. The first letter specifies the chamber(s) paced, the second letter specifies the chamber(s) where sensing takes place, and the third letter describes the response to what is sensed, resulting in programming designations such as AOO, VVI, or DDD. It is important to understand what these letters imply so that one knows what pacing behavior to expect from a given patient’s device. The brief clinical examples that follow illustrate the basic principles of how the code is used. Note that programming modes other than those specified may be clinically employed in specific patients and those presented here are only examples.

A patient with symptomatic sinus bradycardia but normal AV conduction needs a pacemaker to ensure an adequate heart rate. Such patients may potentially have their pacemakers programmed to AAI. In AAI mode, the atrium is paced at the set demand rate only if no spontaneous atrial depolarization is sensed during the programmed atrial escape interval. If the atrium spontaneously depolarizes within the preset time limit, the device inhibits itself, thus the letter “I” in the third position of the pacer code.

A patient with atrial fibrillation or flutter and a slow ventricular response needs a pacemaker to ensure adequate ventricular rate. Such a patient may have his or her pacemaker programmed to VVI. In VVI mode, the ventricle is paced at a preset rate if no spontaneous ventricular depolarization is sensed within the predetermined time interval.

Patients with complete AV block but normal sinus node function need a pacemaker to ensure that a ventricular depolarization follows each spontaneous atrial depolarization. Such patients might have their device programmed to VAT mode. In VAT mode, the atrial beat triggers ventricular pacing. As explained above, VAT mode will allow physiologic pacing, because the paced ventricular rate will “track” the spontaneous atrial rate. This will allow for overall increased heart rate in response to increased metabolic demand. Clearly, however, this mode is not appropriate for patients predisposed to atrial tachydysrhythmias.

DDD, the most sophisticated and commonly programmed mode today, is capable of both sensing and subsequent triggering or inhibition of pacing of the atrium and/or ventricle. DDD is therefore a “smart” mode, encompassing many of the other
modes, and is capable of providing whatever the patient requires. Most patients presenting with a permanently implanted pacemaker will have their pacemaker programmed to DDD mode.

Pacing modes that preserve AV synchrony therefore include those that simply pace the atria in patients with AV node competency (eg, AOO, AAI, DOO, DVI, DDI, and DDD) and those that sense atrial activity to trigger ventricular pacing (eg, VAT, VDD, and DDD) in patients with slow ventricular rates or AV nodal block.

Asynchronous modes (eg, AOO, VOO, and DOO) are most often used for temporary pacing applications (eg, emergency situations, bradycardia following an acute myocardial infarction or cardiotomy, as a bridge to implantation of a more sophisticated permanent pacemaker, etc). In these modes, the specified chamber(s) is (are) paced at a set rate regardless of intrinsic electrical activity in that chamber. Although asynchronous atrial pacing is effective to increase the heart rate in a patient with symptomatic bradycardia, a competent conduction system is necessary. Asynchronous ventricular pacing can be used in an emergency situation (eg, acute high degree AV conduction block, or asystole) but, as discussed above, isolated ventricular pacing is not particularly physiologic and often leads to decreased stroke volume, AV valve insufficiency, and overall decreased cardiac output.

**New Simplicity at the Fourth and Fifth Positions of the NBG Code**

The main modifications in this current version of the code are at the fourth and fifth positions. In contrast to the codes in those positions previously (which imparted way too much information for routine clinical use and were therefore rarely used by nonelectrophysiologists), position IV now specifies only the presence or absence of rate modulation (discussed in detail below), and position V now specifies only the location or absence of multisite pacing (also discussed below). Although the full 5-digit programming code is not always used, it does provide important information that may potentially change patient management in the perioperative period.

It should be appreciated that sinus node dysfunction is very common in the population of patients who need a pacemaker, and it is clear that the ability to increase the heart rate when needed is crucial to optimal systemic perfusion. Rate modulation (also called rate adaptation) is a functionality incorporated into most modern pacemakers that allows the device to automatically increase the heart rate when needed to meet metabolic demands. With modern rate-adaptive pacing, the paced heart rate automatically changes to more closely approximate what the normal sinus node would do and is adjusted according to a computerized algorithm in proportion to the change in certain monitored physiologic variables. Thus, many patients with permanently implanted pacemakers are programmed to DDDR (though DDD is often all that is communicated). The required sensors can be classified according to the physiological “level” they detect. Table 2 describes some of the different physiological sensors that are currently in use or may one day be possible.

Currently, the sensing of bodily acceleration due to motion is the most commonly used sensor in the industry, with rate-adaptive devices from all 3 major manufacturers employing accelerometers. Determination of minute ventilation through changes in thoracic impedance is also in use, particularly in Boston Scientific (formerly Guidant, Natick, MA) devices. About 50% of the Boston Scientific devices have what is called a “blended sensor” that assess both acceleration and minute ventilation and may deliver a better rate response to exercise than only 1 sensor. Sensing of Q-T interval may be available in some devices, as is sensing of internal cardiac impedance, but these have not yet been made widely available. It is important to be aware of how rate modulation is accomplished because it may be prudent to preoperatively disable the rate-adaptive pacing functionality for some patients, particularly those with devices where assessment of minute ventilation is in use. This sensor is particularly likely to be interfered with by hyperventilation and by other impedance-based monitors, such as telemetry, resulting in unnecessarily rapid rates of pacing.

Position V in the code designates the presence or absence of multisite pacing. Multisite pacing refers to either the presence of more than 1 lead in a single cardiac chamber or to biventricular pacing. The use of more than 1 pacing lead in the right atrium is currently the subject of clinical trials intending to suppress atrial fibrillation and is not particularly clinically relevant at the time of this writing. Biventricular pacing, on the other hand, is extremely clinically relevant. Biventricular pacing is
also commonly known as cardiac resynchronization therapy (CRT).

The progression of disease resulting in advanced cardiac failure is typically accompanied by conduction defects and dysrhythmias. In addition to the well-known defects in sinus or AV node function that develop, intraventricular conduction defects delay the onset and completeness of right or left ventricular systole in at least 30% of patients with advanced heart failure.\(^6\) This discoordination between and within the left and right ventricular contractions further impairs cardiac output and has been reported to increase the risk of death in this population.\(^7\)-\(^10\)

CRT entails biventricular pacing to optimize the timing and completeness of right and left ventricular contractions. Normally, we pace the right side of the heart, and we strive to create sequential AV contractions to optimize cardiac output. In CRT, in addition to AV sequential pacing of the right side of the heart, we also pace the LV, and its paced contraction is carefully timed to improve the synchrony between right ventricular (RV) and LV ejection. Furthermore, the overall pattern of systolic contraction of the LV is improved. Studies have shown that atrial-synchronized biventricular pacing can improve cardiac output and overall hemodynamics. This enhances patients’ ability to exercise, which improves their New York Health Association functional class, and decreases the length and frequency of their hospitalizations, which improves their quality of life.\(^11\) Whether or not CRT can significantly prolong survival remains the subject of national and international multicenter trials.

CRT is currently indicated for the reduction in symptoms of moderate to severe heart failure (NYHA functional class III or IV) in those patients who remain symptomatic despite stable, optimal medical therapy and have a left ventricular ejection fraction of \(\leq 35\%\), a QRS duration of \(\geq 120\) ms, and an ICD indication.

### Implantable Cardioverter Defibrillators

Approximately 300,000 to 350,000 deaths in the United States each year are sudden cardiac deaths (SCDs),\(^12\) with approximately two thirds of these deaths due to ventricular tachycardia (VT) that progressed to ventricular fibrillation (VF).\(^13\) Patients with ischemic heart disease, dilated cardiomyopathy, and advanced stages of congestive heart failure are particularly prone to malignant ventricular arrhythmias. Even in the absence of worsening congestive symptoms, SCD accounts for approximately 40% of all deaths in patients with heart failure\(^14\) and occurs with a frequency 6 to 9 times that in the general population.\(^15\) In these situations, a promptly delivered defibrillatory shock offers the best chance for survival.

Devices capable of detecting a ventricular dysrhythmia and delivering a defibrillatory shock are generically referred to as implantable cardioverter defibrillators. The first automatic ICD (AICD) was developed by NASA in conjunction with Cardiac Pacemakers, Inc (St Paul, MN; a subsidiary of Eli Lilly and Company). The first human implant took place in February 1980. At that time, the large devices employed epicardial leads and were implanted in the abdomen through a thoracotomy. Publications in the peer-reviewed, indexed literature about the clinical use of ICDs first appeared in the mid-1980s. Since that time, ICDs have been miniaturized and can be implanted in a small subcutaneous pectoral
pocket with the leads transvenously inserted into the heart chambers. Modern ICDs have been demonstrated to successfully terminate VF in >98% of episodes,\(^3\) and all such devices now incorporate sophisticated pacemaker technology. Apart from the convenience of having both antibradycardia and antitachycardia functionality in a single device for pacemaker-dependent patients at risk of ventricular dysrhythmias, the purpose of the pacemaker for nondependent patients with an ICD is to act as a backup in case defibrillation results in bradycardia or asystole.

In patients with ischemic cardiomyopathy and decreased LV function, large clinical trials have demonstrated that an ICD increases survival and decreases the risk of SCD.\(^{16-18}\) Although there is some controversy over whether an ICD offers survival benefit compared with anti-dysrhythmic agents alone,\(^{19}\) it is clear that such pharmacologic interventions are not always successful in all patients, and the general consensus is that an ICD does offer survival benefit to these patients.

In patients with nonischemic dilated cardiomyopathy and moderate-to-severe LV dysfunction, the prophylactic implantation of an ICD has been demonstrated to provide a mortality benefit, ostensibly through prevention of more sudden deaths from dysrhythmia than standard pharmacotherapy.\(^{20,21}\)

Thus, ICDs are currently a definitive therapy for patients at high risk for malignant ventricular tachydysrhythmias (primary prophylaxis) and are also being implanted in patients who have survived a malignant tachydysrhythmia (secondary prophylaxis). Table 3 lists the major indications for ICD implantation and provides perspective regarding why so many are being implanted. It is important to realize that ICDs do not reduce the incidence of dysrhythmias per se; they simply prevent the consequences of malignant tachycardias.

### How Does an ICD Work?

ICDs employ a lead in the RV to sense the electrical activity in the chamber and to deliver a defibrillatory shock when indicated. Some systems may also employ a lead in the right atrium, though these are not commonly in clinical use at the time of this writing (unless the patient already requires a pacemaker lead in the right atrium). Programming of predefined heart rate “zones” allows the ICD to distinguish different types of malignant tachydysrhythmias (eg, VT or VF) and provide different therapies to interrupt

---

**Table 3. Common Indications for ICD Implantation**

<table>
<thead>
<tr>
<th>Class 1 Indications(^b)</th>
<th>Class 2 Indications(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>History of prior MI(^c)</strong></td>
<td>LVEF less than 35% and NYHA class II or III, or LVEF less than 30% and NYHA class I</td>
</tr>
<tr>
<td>Hemodynamically unstable, sustained VT and LV dysfunction</td>
<td>Recurrent VT and normal LVEF</td>
</tr>
<tr>
<td>History of nonsustained VT, LVEF less than 40% and inducible VT or VF at electrophysiological study</td>
<td></td>
</tr>
<tr>
<td>History of spontaneous sustained VT/VF associated with primary pathology</td>
<td></td>
</tr>
<tr>
<td><strong>Chronic myocarditis, pericardial disease, hypertrophic or infiltrative cardiomyopathy</strong></td>
<td>History of sustained VT/VF and significant LV dysfunction</td>
</tr>
<tr>
<td><strong>Nonischemic dilated cardiomyopathy</strong></td>
<td>LVEF less than 35% and NYHA class II or III</td>
</tr>
<tr>
<td><strong>Hypertrophic cardiomyopathy, ARVD</strong></td>
<td>History of documented VT or VF</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NOTES:** ICD = implantable cardioverter defibrillator; MI = myocardial infarction; LVEF = left ventricular ejection fraction = NYHA = New York Heart Association; VT = ventricular tachycardia; ARVD = arrhythmogenic right ventricular dysplasia.

\(^a\)Adapted from the ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities.

\(^b\)In all cases chronic medical therapy should be optimized and patients should have reasonable expectations of survival in a good functional status for more than 1 year.

\(^c\)ICD placement generally is not recommended earlier than 40 days after acute MI and earlier than 90 days after myocardial revascularization procedure.
them. These zones are individually determined ranges of heart rates based on specific pathology and risks in a given patient. When a fast ventricular rhythm is sensed, the software compares the rate with the predetermined zones. Treatment for VT usually begins with attempted overdrive pacing followed by lower energy electrical shock if pacing is ineffective. An additional sensing electrode in the right atrium may help distinguish true VT from conducted supraventricular tachycardia and thus avoid unnecessary, uncomfortable, and potentially deleterious ICD discharges. If the sensed rate falls into the higher zone, then the rhythm is most likely interpreted as VF and a high-energy shock is delivered. ICDs store a log of dysrhythmias previously detected and treatments provided.

Perioperative Management of Patients With CRMDs

One needs to understand what will cause problems with a CRMD if one is to avoid them.

As mentioned above, the ASA Task Force Practice Advisory of 2005 outlines the recommended perioperative management of the patient with a CRMD to facilitate the safe and effective perioperative management of patients with CRMDs and to reduce the incidence of adverse outcomes.

As specifically related to a CRMD, adverse outcomes to be avoided are defined as follows:

- Damage to the device, the leads, or site of lead implantation
- Failure to deliver pacing and/or defibrillation
- Changes in pacing behavior
- Inappropriate delivery of a defibrillatory shock (if an ICD is present)
- Inadvertent electrical reset to backup pacing modes

Although some of these may result in significant morbidity or even mortality, any of these may potentially result in hypotension, dysrhythmias, myocardial tissue damage, and ischemia of the heart or other vital organs. Furthermore, these may result in a delay or cancellation of surgery, extended hospital stays, readmission to manage device malfunctions, additional hospital resource use, and increased medical costs.

The most common problem the anesthesia practitioner will encounter in the perioperative period is interference with device function from EMI. If an ICD is present, EMI can result in an inappropriate delivery of a defibrillatory shock. In the case of a pacemaker, EMI can result in

- Inappropriate inhibition or triggering of a paced output,
- Asynchronous pacing (which may compete with a spontaneous rhythm, possibly resulting in an arrhythmia), and
- Reprogramming (usually into a backup mode, often this is VVI or VOO).

Depending on the device present, prolonged EMI may cause the pacemaker to go into what is called a noise reversion mode, or noise suppression protocol in which asynchronous pacing will occur until the noise stops. Again, the problem with this is loss of potential AV synchrony that normally optimizes hemodynamics. In some cases, current can be induced down the leads, resulting in inappropriate electrical discharge to the myocardium causing dysrhythmias or even a burn. Furthermore, there can be actual damage to device circuitry, especially from external defibrillation. In general, however, inhibition of pacing and asynchronous pacing are the most common outcomes of EMI, and unrecognized EMI should be considered if pacing modes appear to change suddenly or intermittently on electrocardiogram (ECG) monitors.

Anything that emits radiofrequency waves between 0 and 10⁹ Hz can generate EMI and cause interference of proper device function. Table 4 provides a list of things commonly encountered in the perioperative setting associated with EMI. Higher frequency waves such as X-rays, γ rays, and infrared and ultraviolet light do not acutely cause interference with CRMD function, though repeated exposure to certain types of radiation may cause deterioration of insulation within the device, resulting in short circuiting or other electrical problems. Precautions for patients undergoing radiation therapy are discussed further below.

The vulnerability of modern devices to EMI compared with those of prior years has decreased tremendously, and probably the biggest factor is the nearly routine use of bipolar leads. Figure 1 demonstrates the difference between unipolar and bipolar leads. The vast majority of devices one will encounter nowadays employ bipolar leads, though unipolar leads are still used sometimes for pediatric applications, for epicardially placed leads, and for any adult...
patient who requires them for optimal device function. The reason bipolar leads result in less susceptibility to EMI is because both the anode and the cathode of the lead are located in close proximity to each other on the lead itself, minimizing the physical distance over which the entire circuit is completed. With unipolar leads, the cathode is still at the tip of the lead, but it is the pulse generator itself that serves to complete the circuit. Thus, like a large antenna, there is a greater potential for interference from electromagnetic waves. In addition to the protective effect of bipolar leads, modern devices are also generally protected by components such as filters and circuit shields, which insulate the internal electronics from the metal device casing, and noise protection algorithms, which filter out signals outside the range of normal cardiac noise.

### Table 4. A List of Factors Associated With the Generation of EMI That Are Commonly Encountered in the Perioperative Setting

- Electrocautery
- Nerve stimulators
- Evoked potential monitors
- Fasciculations
- Shivering
- Large tidal volumes
- External defibrillation
- Magnetic resonance imaging
- Radiofrequency ablation or lesioning
- Extracorporeal shock wave lithotripsy
- Electroconvulsive therapy

Although there are no actual clinical trials that have assessed the need to perform a comprehensive preoperative evaluation of a patient’s CRMD, there are published case reports in which an incomplete evaluation resulted in intraoperative problems.

Once it is established that there is a device present, one needs to define the type of device and how it is programmed. Certainly, depending on where the patient is being evaluated, one can ask to see the device identification card that all patients with implanted CRMDs carry in their wallet, but this is only feasible in a pretesting clinic because very few patients have their wallet on them in the preoperative holding area. Additionally, very few patients (or their families) have an adequate level of sophistication to verbally provide the needed information. If the card is available, the type of device and how it is programmed will be apparent. The requisite information may also be obtained from notes in the chart, or a phone call to the patient’s cardiologist or pacemaker clinic. If the device manufacturer can be determined (try asking the patient which name they recognize—Medtronic, Boston Scientific [formerly Guidant], St Jude, etc), one can call the manufacturer.

The recommendation of the ASA task force is that a comprehensive evaluation of the device be performed by a knowledgeable consultant using the appropriate manufacturer’s programming device. Depending on the practice setting, this may be dedicated EPS staff, a cardiologist, or perhaps a representative from industry.

But the task force also acknowledges that such an evaluation may not always be possible, and in these cases they recommend that at minimum it is necessary to confirm whether pacing impulses are present and create a paced beat. To do so, they further recommend that consultation with a cardiologist or CRMD service may be necessary. However, it is clear that knowledgeable consultants may not always be immediately available without advance planning, especially after hours, or for emergent cases. So what else can one do to get the requisite information?

The chest X-ray can provide valuable information about whether the device is a single-chamber or a dual-chamber pacemaker, a biventricular pacemaker,
and whether or not there is an ICD present. Most practitioners will be able to recognize if the device has 1 lead or 2 leads and where those leads are going (right atrium, right ventricle, or both). The lead of an ICD generally has 2 fat radioopaque sections and goes to the RV. A biventricular system will have 3 leads (1 lead in the right atrium, 1 lead that enters the coronary sinus and travels toward the left side of the heart, and 1 lead in the RV that usually has the fat segments indicating the presence of an ICD).

Knowledge of the supposed programming and of the location of leads does not, however, provide any assurance that the device is functioning properly, nor does it necessarily reveal if the patient is pacemaker dependent. In this regard, the ECG may provide information about both sinus node and pacemaker function. One should examine the ECG for presence or absence of native p-waves and pacing spikes and see what is apparently being captured—atrium, ventricle, perhaps both, perhaps neither. If every cardiac cycle on the baseline ECG is a paced beat and this is also the case on the monitor preoperatively, there may be a good chance that the patient is pacemaker dependent, but the task force recommends 3 specific ways of determining pacemaker dependency.

- A verbal history or chart notes indicating symptomatic bradyarrhythmia or syncope for which the device was implanted.
- A history of successful AV nodal ablation.
- Or, if a consultant is involved with a programming device, no evidence of spontaneous ventricular activity with the device programmed to VVI mode at the lowest possible programmable rate.

Sometimes the history and the ECG on the chart may not provide sufficient information and one might consider performing provocative maneuvers to ensure proper sensing, pacing, and mechanical capture. Obviously, such maneuvers are not always necessary, and extreme caution is advised. Clearly, the assurance of a backup pacing plan (eg, external pacing pads already applied) is prudent. Such maneuvers might include asking the patient to perform a Valsalva maneuver or the administration of a small dose of ephedrine, esmolol, or adenosine. All of these should elicit bradycardia (brief asystole in the case of adenosine) that hopefully would reveal pacemaker function. Again, such maneuvers are not recommended or routinely necessary, but will help in assuring proper pacemaker function.

**Figuring Out What to Do With It**

A decision needs to be made regarding what, if anything actually, needs to be done to prepare the patient for the operating room (OR). First and foremost, one needs to determine if EMI is likely to occur during the care of the patient. EMI is likely to be present during any procedure employing electrocautery, so all of the following recommendations are applicable to surgical procedures in the OR:

1. Determine if reprogramming of the device is necessary. Reprogramming of a pacemaker to an asynchronous mode is generally only done for pacemaker-dependent patients. Where feasible, it is preferable to have all pacemaker reprogramming done by a knowledgeable consultant using the manufacturer’s programming device. Though it is not specifically recommended by the task force, application of a pacemaker magnet is commonly used to create an asynchronous mode with modern devices (ie, implanted since 2000) because it is reliable and much more convenient in the OR setting. It must be appreciated that the magnet must remain in place to maintain the asynchronous mode of pacing. Patients who are not pacemaker dependent generally do not require any reprogramming, especially if there are bipolar leads. Biventricular pacemakers can be programmed to an asynchronous mode when necessary (the carefully timed delays that allow resynchronization are maintained with most manufacturers’ devices) with a programming device or a magnet.

2. Most knowledgeable consultants do recommend that rate-adaptive functionality be suspended in the perioperative period.

3. The antitachyarrhythmia functions of an ICD should be disabled, preferably by the manufacturer programming device, though it is becoming more and more common to employ a magnet for this purpose. Although there are some caveats to this (discussed in detail below), the proper use of a magnet is a reliable and safe way to disable a modern ICD. Very recently manufactured devices may employ enhanced noise protection algorithms that may render the device less susceptible to EMI, especially if the site of surgery is distal from the heart, but the official recommendation is still to disable the tachy therapies of an ICD if EMI is anticipated.

Equally important as having an ICD deactivated is assuring that the patient always remains appropriately monitored in a setting where temporary pacing
or external defibrillation can be immediately performed if necessary. Usually, it is most convenient to place external defibrillation/pacing pads on the patient and keep them connected to a portable monitor/defibrillator. The convention for a patient with a CRMD is to place the external pads in an anterior–posterior configuration (perpendicular to the axis of the leads) instead of the usual apex and base locations because one wants to minimize induction of current down the leads should the pads need to be used.

It is critical to remember that patients with an ICD are ostensibly at high risk for ventricular tachydysrhythmias. Thus, once an ICD has been disabled, the practitioner caring for the patient must remain vigilant and be ready to defibrillate the patient rapidly as required. Again, it is most convenient to apply external defibrillation pads to the patient and keep them connected to a bedside portable defibrillator with the monitor on at all times.

The Use of Magnets

Pacemakers. As mentioned above, an asynchronous mode may be electively employed to protect a patient from the effects of EMI, and application of a magnet to a modern pacemaker will produce an asynchronous mode of pacing. The asynchronous rate obtained usually depends on the charge remaining on the battery, potentially on specific programming of a given patient’s device, and the defaults that vary by manufacturer. Furthermore, the specific mode of asynchronous pacing (eg, AOO, VOO, DOO) depends entirely on the configuration of the patient’s device. The asynchronous mode will persist as long as the magnet remains in place over the pulse generator. Removal of the magnet will result in reversion to baseline device programming.

A notable exception to the rule that a magnet will produce an asynchronous mode of pacing occurs when the CRMD is a combined device (pacemaker and ICD). Application of a magnet to a combined CRMD will deactivate the ICD, but neither primary pacemaker function nor backup “postshock therapy” will be affected by magnet application. This important point is reemphasized again below.

ICDs. Although it is not specifically recommended by the ASA task force, in the event that a patient’s ICD has not been deactivated preoperatively, a magnet can be placed over the pulse generator to deactivate the arrhythmia detection function and prevent accidental discharge.

Medtronic, St Jude, and Biotronik devices always require that the magnet remain on the device to keep it deactivated. Subsequent removal of the magnet will promptly reactivate the ICD.

Deactivation of a Boston Scientific (formerly Guidant) ICD with a magnet is different, because magnet application will elicit audible R-wave synchronous tones (assuming the device is preprogrammed to respond to the magnet application). These tones indicate what the device is sensing from the ECG but can be difficult to hear if the environment is noisy. The next action depends on what occurs after the magnet has been held over the device for 20 to 30 seconds.

- If the R-wave synchronous tones persist (majority of modern device programming at the time of this writing), tachy therapies will be suspended for as long as the magnet remains on the device. Removal of the magnet will reactivate the potential to deliver a defibrillatory shock.
- If the R-wave synchronous tones convert to a solid tone (mostly now with older devices), the device is permanently deactivated and the magnet can be safely removed. This device is now permanently deactivated. To reactivate the Boston Scientific ICD, replace the magnet for 30 seconds, until R-wave synchronous tones are again heard. This indicates that the ECG sensing function of the device has been successfully reactivated.

If no audible signals are heard with magnet application, the device is either programmed to ignore magnet application or is possibly not manufactured by Boston Scientific. In either case, a knowledgeable consultant should formally deactivate the device with a programmer.

One should bear in mind that all ICDs have backup pacing function in the event that defibrillation results in bradycardia or asystole. Even when the ICD is successfully deactivated by a magnet, backup pacemaker function of an ICD will not be affected.

Combined devices. In a patient with a combined primary pacemaker and ICD, the industry standard nominal magnet response will be to deactivate the ICD, and the pacing behavior will not change to an asynchronous mode. Thus, in a patient with a combined device, if it is determined that an asynchronous
mode is required to protect a pacemaker-dependent patient from the effects of intraoperative EMI, this reprogramming will need to be performed by a knowledgeable consultant with a device programmer. If an asynchronous mode of pacing is manifest following application of a magnet, then it is highly unlikely that an ICD is present.

Intraoperative Management

Intraoperatively, it is imperative that the cardiac rate and rhythm be continuously monitored as the patient with a CRMD is ostensibly at high risk of rhythm problems. It is also the recommendation of the ASA task force that the peripheral pulse be continuously monitored. Although clinical data or other evidence to support this is not provided in the task force document, it is reasonable to do so, because pulseless electrical activity does exist, and can happen in this high-risk population. The pulse rate can be monitored easily by the pulse oximeter already in use. Alternatively, one can employ direct palpation, auscultation of heart tones, or observation of the waveform from an indwelling arterial line. Although not every patient will need one for all procedures, it may be reasonable to place an arterial line in high-risk patients for major surgical procedures.

Vigilance of appropriate pacing behavior is necessary throughout the procedure regardless of any reprogramming that may have been done or the perceived decreased vulnerability to EMI with modern devices. Any hemodynamic instability that appears to be related to EMI should prompt one to ask the surgeon to temporarily stop using the cautery until hemodynamics are stabilized. If adverse pacing behavior (or inhibition of pacing) is manifest, application of a magnet to the pulse generator should produce an asynchronous mode. Precautionary measures that may also be employed include placing the cautery dispersal plate as distal as possible with respect to the site of device implantation; suggesting the limitation of cautery use to short, irregular bursts; and using more “cutting” than “coagulating” current. One can also ask the surgeon to use a bipolar cautery unit, but few surgeons outside of the neurosurgical or ophthalmological operating theater will comply. Management of EMI from the electrocautery should not be an issue for a deactivated ICD, but the presence of the leads in contact with the heart still poses a risk if current gets conducted down them.

If the patient does develop a malignant tachyarrhythmia, one should immediately defibrillate the patient while attempting to minimize the current that might flow through the pulse generator and leads. As mentioned above, this is theoretically accomplished by positioning the external pads or handheld paddles as far as possible from the pulse generator. Again, an anterior–posterior position is preferred. Clinically appropriate energy levels and other standard ACLS Advanced Cardiac Life Support recommendations should be employed as needed. In the event that an ICD has been deactivated with a magnet that is still in place, the task force does discuss the possibility of simply removing the magnet and allowing the ICD to defibrillate the patient. Any delay in device function, however, should prompt immediate external defibrillation.

Anesthetic Drugs and Technique

Commonly used agents have not been demonstrated to affect pacing thresholds, though the physiologic consequences of anesthetic management may. Perhaps the biggest consideration is to avoid hyperventilation, which will abruptly lower serum potassium levels. Fasciculations, shivering, and large tidal volumes are all classic factors that result in myopotentials and are a possible source of EMI. Finally, myocardial ischemia and high blood levels of local anesthetics may increase electrophysiologic thresholds but one hardly needs to be cautioned in these areas.

Postoperative Management

Postoperatively, where an ICD has been deactivated, the patient needs to remain appropriately monitored with the immediate availability of an external source of defibrillation (and pacing) until the ICD is reactivated by knowledgeable personnel. This includes the time during transport from the OR to that setting! One of the controversial parts of the ASA task force practice advisory is the recommendation that all devices should ideally be interrogated for the appropriateness of all settings before discharge from the postanesthesia care unit (or intensive care unit) to a nonmonitored setting. Not all consultants, societies, and manufacturers believe this to be necessary, but as mentioned above, the recommendations are intended to result in the highest level of safety for the patient, and not necessarily the highest level of convenience.
for the practitioners, the nurses, the consultants, or, sometimes, the patients themselves. In the full text of the ASA task force document, one can see that although 96% of consultants and 98% of ASA members on the task force voted for this recommendation, only 77% of Heart Rhythm Society members on the task force agreed. Based on the track record of modern devices, representatives from industry and many cardiologists do not believe that all devices need to be routinely evaluated immediately postoperatively because there have not been any reported instances of EMI-induced permanent reprogramming. Additionally, it may not be feasible in all practice settings to get such an evaluation performed. However, interrogation should clearly be performed if defibrillation was required, and if any uncertainty about the function of a device exists, it is prudent to maintain appropriate monitoring and have an interrogation performed as soon as possible.

Recommendations for Specific Procedures

Radiofrequency ablation is associated with the generation of EMI, so an ICD should be disabled and pacemaker-dependent patients should be reprogrammed to an asynchronous mode. Furthermore, the ablation currents should be kept as far away as possible from the pulse generator and leads because the current could potentially be conducted down the leads to their point of attachment to the myocardium, resulting in dysrhythmia or burn.

Radiotherapy is not associated with EMI; however, ionizing radiation may cause cumulative damage to the insulation of the leads and the semiconductor circuitry in the pulse generator. Assuming appropriate shielding is used, radiation therapy is not contraindicated in patients with CRMDs. A recommendation is made, however, to potentially consider relocating the generator if it cannot be adequately shielded.

MRI is generally considered to be contraindicated for patients with CRMDs due to the generation of heat and unacceptably high rates of pacing that might occur if the magnetic fields induce current down the leads. There are some centers, however, that are starting to perform limited MRI scanning of the extremities in patients with CRMDs.

For lithotripsy, ICD should be disabled, and it is also recommended to disable atrial sensing/pacing if the lithotripter triggers on the R-wave because there will be inhibition of pacing, inappropriate tracking, and likely reversion to noise mode anyway. Additionally, the shock wave should be kept as far away from the pulse generator and leads as possible because lithotripter shocks can loosen semiconductor components and lead connections.

For ECT, it is recommended not only to have the ICD deactivated but also to have the CRMD interrogated following the therapy to assure the appropriateness of all settings. Additionally, the hemodynamic effects of ECT bear due consideration and appropriate planning in this high-risk population.

References

8. Unverferth DV, Magorien RD, Moeschberger ML, Baker PB, Fetters JK, Leier CV. Factors influencing the


Validation of the Berlin Questionnaire and American Society of Anesthesiologists Checklist as Screening Tools for Obstructive Sleep Apnea in Surgical Patients


Background: Because of the high prevalence of obstructive sleep apnea (OSA) and its adverse impact on perioperative outcome, a practical screening tool for surgical patients is required. This study was conducted to validate the Berlin questionnaire and the American Society of Anesthesiologists (ASA) checklist in surgical patients and to compare them with the STOP questionnaire.

Methods: After hospital ethics approval, preoperative patients aged 18 yr or older and without previously diagnosed OSA were recruited. The scores from the Berlin questionnaire, ASA checklist, and STOP questionnaire were evaluated versus the apnea–hypopnea index from in-laboratory polysomnography. The perioperative data were collected through chart review.

Results: Of 2,467 screened patients, 33, 27, and 28% were respectively classified as being at high risk of OSA by the Berlin questionnaire, ASA checklist, and STOP questionnaire. The performance of the screening tools was evaluated in 177 patients who underwent polysomnography. The sensitivities of the Berlin questionnaire, ASA checklist, and STOP questionnaire were 68.9—87.2, 72.1—87.2, and 65.6—79.5%, respectively, for being at high risk of OSA by the STOP questionnaire or ASA checklist had a significantly increased incidence of postoperative complications.

Conclusions: Similar to the STOP questionnaire, the Berlin questionnaire and ASA checklist demonstrated a moderately high level of sensitivity for OSA screening. The STOP questionnaire and the ASA checklist were able to identify the patients who were likely to develop postoperative complications.

The prevalence of obstructive sleep apnea (OSA) in surgical patients is higher than in the general population. Studies have shown that undiagnosed OSA is associated with increased perioperative morbidity and mortality. However, none of the screening tools for OSA have been validated in surgical patients.

The Berlin questionnaire (appendix 1) is the most widely used questionnaire for OSA. It includes 11 questions organized into three categories. The predictive performance of the Berlin questionnaire for OSA varies in different patient populations. The sensitivity ranges from 54% to 86% and the specificity ranges from 43% to 87% among primary care patients. It has not been validated for use in surgical patients.

The American Society of Anesthesiologists (ASA) Task Force on Perioperative Management of Patients with Obstructive Sleep Apnea has recommended a checklist (ASA checklist, appendix 2) as a routine screening tool for OSA in surgical patients. It consists of 12 items for adults and 14 items for children. The checklist is a consensus of the Task Force and has not been validated in any patient population.

The STOP questionnaire was developed and validated in surgical patients as a screening tool for OSA. It is a self-administered screening tool and includes four yes/no questions with a mnemonic (S—snoring, T—tiredness, O—observed you stop breathing, P—blood pressure).

The objective of this study was to validate the Berlin questionnaire and the ASA checklist as screening tools for OSA in surgical patients and to compare them with the STOP questionnaire. We also studied the association between the scores of screening tools and the occurrence of postoperative complications.

Materials and Methods

The study was conducted in the same patient population as described in the accompanying article. Details of the inclusion and exclusion criteria, patient screening, sleep study and polysomnography scoring, and diagnosis and severity definition of OSA are described in that article. Approval from the Research Ethics Board of University Health Network and Mount Sinai Hospital (Toronto, Ontario, Canada) was obtained.

All patients who met the inclusion criteria and gave consent were screened by the three screening tools: the Berlin questionnaire, the ASA checklist, and the STOP questionnaire. Following a randomized order list, the STOP and Berlin questionnaires were clipped together and simultaneously administered to patients. Upon completion of the questionnaires and before scoring of the questionnaires, the patient was screened by one of the three research staff (two research anesthesiologists and a research assistant) with the ASA checklist. All patients who completed the questionnaires and the ASA checklist were invited to undergo an overnight in-laboratory poly-
somnographic study before surgery, regardless of their score on the questionnaires. The Berlin questionnaire and the ASA checklist were scored according to standard scoring criteria (appendixes 1 and 2).

The reliability of the screening tools was checked before they were used to screen patients. The agreement and Cohen $\kappa$ coefficient of test-retest were 96.3% ($n = 54$) and 0.9168 (confidence interval, 0.804–1.000), respectively, for the Berlin questionnaire and 96.3% ($n = 55$) and 0.923 (confidence interval, 0.818–1.000) for the STOP questionnaire. The Fleiss $\kappa$ coefficient of the three research staff scoring the ASA checklist was 0.7460 ($n = 29, P < 0.001$).

If the apnea–hypopnea index (AHI) of a patient was greater than 30/h, the anesthesiologist and surgeon who were taking care of the patient were informed. The data regarding the perioperative complications of patients were obtained through chart review by a research anesthesiologist who was blinded to the results of the three questionnaires and polysomnography. The definition of postoperative complications was listed in appendix 3.

The details of the sample size estimation and data analysis are described in the accompanying article. The test-retest agreement for the Berlin and the STOP questionnaire was analyzed with the Cohen $\kappa$ coefficient. Interrater agreement among the three research staff for the ASA checklist was analyzed with the Fleiss $\kappa$ coefficient. The Breslow-Day test was used to check whether there was a significant difference between the screening tools.

Results

The analysis of the validation of the Berlin questionnaire and the ASA checklist, and the comparison of the three screening tools—the Berlin questionnaire, the ASA checklist, and the STOP questionnaire—were based on the 177 patients who underwent polysomnography and completed the three questionnaires. All 416 patients who gave consent were included in the postoperative complication analysis, with focus on the 211 patients who underwent polysomnography. The process of patient screening and the demographic data for the different groups of patients are described in the accompanying article.

In 2,467 screened patients who completed the three screening tools, 35% were classified as being at high risk of having OSA by the Berlin questionnaire, 27% by the ASA checklist, and 28% by the STOP questionnaire.

Demographic Characteristics of the Patients for Validation

Table 1 shows the demographic data of the patients regarding whether they were at high or low risk on the Berlin questionnaire, the ASA checklist, and the STOP questionnaire. Although the STOP questionnaire did not include any question regarding body mass index (BMI) and neck circumference, it was able to distinguish the patients with a significantly higher BMI and a larger neck circumference from patients with a lower BMI and a smaller neck circumference, similar to the Berlin questionnaire and the ASA checklist. Second, all three screening tools recognized the patients with significantly higher AHI.

In addition, the Berlin and STOP questionnaires were able to identify patients with significantly lower minimum arterial oxygen saturation during overnight polysomnography. Third, besides hypertension, which is part of the STOP and Berlin questionnaires, there was a significantly higher prevalence of gastroesophageal reflux disease in patients classified as having a high risk of OSA by the STOP and Berlin questionnaires.

Table 1. Demographic Data

<table>
<thead>
<tr>
<th>Total</th>
<th>STOP Questionnaire</th>
<th>Berlin Questionnaire</th>
<th>ASA Checklist</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Low Risk</td>
<td>High Risk</td>
<td>Low Risk</td>
</tr>
<tr>
<td>(n = 177)</td>
<td>(n = 75)</td>
<td>(n = 102)</td>
<td>(n = 69)</td>
</tr>
<tr>
<td>Gender, M/F, n</td>
<td>88/89</td>
<td>38/37</td>
<td>50/52</td>
</tr>
<tr>
<td>Age, mean ± SD, yr</td>
<td>55 ± 13</td>
<td>54 ± 15</td>
<td>56 ± 12</td>
</tr>
<tr>
<td>BMI, mean ± SD, kg/m²</td>
<td>30 ± 6</td>
<td>28 ± 6</td>
<td>31 ± 6*</td>
</tr>
<tr>
<td>BMI &gt;35 kg/m², n</td>
<td>34</td>
<td>10</td>
<td>24</td>
</tr>
<tr>
<td>Neck circumference, cm</td>
<td>39 ± 6</td>
<td>38 ± 5</td>
<td>40 ± 7*</td>
</tr>
<tr>
<td>AHI/h</td>
<td>20 ± 6</td>
<td>12 ± 14</td>
<td>25 ± 27*</td>
</tr>
<tr>
<td>Minimum SaO₂%, %</td>
<td>82 ± 11</td>
<td>84 ± 9</td>
<td>80 ± 10*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Existing conditions, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>GERD</td>
</tr>
<tr>
<td>Diabetes</td>
</tr>
<tr>
<td>Asthma</td>
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<tr>
<td>Depression</td>
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</tbody>
</table>

* P < 0.05 vs. low risk.

AHI = apnea–hypopnea index; ASA = American Society of Anesthesiologists; BMI = body mass index; GERD = gastroesophageal reflux disease; SaO₂ = arterial oxygen saturation.
Evaluation of the Screening Tools
The scores of the three screening tools were evaluated versus the AHI from overnight in-laboratory polysomnography. The predictive parameters of each screening tool for patients with mild, moderate, or severe OSA are shown in table 2. All three screening tools demonstrated a moderately high level of sensitivity for OSA screening. In terms of the specificity, in almost all situations that were checked, the 95% confidence intervals include 50%, which means that they were not significantly different from chance. When we conducted an overall comparison of the three screening tools, no significant difference was found in terms of the ability of the three screening tools to recognize patients with OSA, because the $P$ values were 0.378, 0.530, and 0.753 with AHI greater than 5, greater than 15, and greater than 30 as cutoffs in the Breslow-Day test for homogeneity of odds ratios.

Table 2. Predictive Parameters for the STOP, Berlin, and ASA Questionnaires

<table>
<thead>
<tr>
<th></th>
<th>STOP Questionnaire (n = 177)</th>
<th>Berlin Questionnaire (n = 177)</th>
<th>ASA Checklist (n = 177)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHI &gt;5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity, %</td>
<td>65.6 (56.4–73.9)</td>
<td>68.9 (59.8–76.9)</td>
<td>72.1 (63.3–79.9)</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>60.0 (45.9–73.0)</td>
<td>56.4 (42.3–69.7)</td>
<td>38.2 (25.4–52.3)</td>
</tr>
<tr>
<td>PPV, %</td>
<td>78.4 (69.2–86.0)</td>
<td>77.9 (68.8–85.2)</td>
<td>72.1 (63.3–79.9)</td>
</tr>
<tr>
<td>NPV, %</td>
<td>44.0 (32.6–56.0)</td>
<td>44.9 (32.9–57.4)</td>
<td>38.2 (25.4–52.3)</td>
</tr>
<tr>
<td>Likelihood ratio</td>
<td>1.639 (1.172–2.385)</td>
<td>1.578 (1.176–2.362)</td>
<td>1.167 (0.940–1.511)</td>
</tr>
<tr>
<td>Odds ratio</td>
<td>2.857 (1.482–5.507)</td>
<td>2.855 (1.481–5.504)</td>
<td>1.599 (0.816–3.133)</td>
</tr>
<tr>
<td>Area under ROC curve</td>
<td>0.703</td>
<td>0.690</td>
<td>0.783</td>
</tr>
<tr>
<td>AHI &gt;15</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity, %</td>
<td>74.3 (62.4–84.0)</td>
<td>78.6 (67.1–87.5)</td>
<td>78.6 (67.1–87.5)</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>53.3 (43.4–63.0)</td>
<td>50.5 (40.6–62.3)</td>
<td>37.4 (28.2–47.3)</td>
</tr>
<tr>
<td>PPV, %</td>
<td>51.0 (41.3–60.7)</td>
<td>50.9 (41.5–60.7)</td>
<td>45.1 (36.1–54.4)</td>
</tr>
<tr>
<td>NPV, %</td>
<td>76.0 (64.8–85.1)</td>
<td>78.3 (66.7–87.3)</td>
<td>72.7 (59.0–83.9)</td>
</tr>
<tr>
<td>Likelihood ratio</td>
<td>1.590 (1.280–2.057)</td>
<td>1.586 (1.276–2.061)</td>
<td>1.255 (1.048–1.524)</td>
</tr>
<tr>
<td>Odds ratio</td>
<td>3.293 (1.707–6.352)</td>
<td>3.736 (1.883–7.413)</td>
<td>2.189 (1.095–4.375)</td>
</tr>
<tr>
<td>Area under ROC curve</td>
<td>0.722</td>
<td>0.672</td>
<td>0.730</td>
</tr>
<tr>
<td>AHI &gt;30</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sensitivity, %</td>
<td>79.5 (63.5–90.7)</td>
<td>87.2 (72.6–95.7)</td>
<td>87.2 (72.6–95.7)</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>48.6 (40.0–63.0)</td>
<td>46.4 (37.9–55.1)</td>
<td>36.2 (28.2–44.8)</td>
</tr>
<tr>
<td>PPV, %</td>
<td>30.4 (21.7–40.3)</td>
<td>31.5 (22.9–41.2)</td>
<td>27.9 (20.1–36.7)</td>
</tr>
<tr>
<td>NPV, %</td>
<td>89.3 (80.4–95.3)</td>
<td>92.8 (83.9–97.6)</td>
<td>90.9 (80.1–97.0)</td>
</tr>
<tr>
<td>Likelihood ratio</td>
<td>1.545 (1.261–2.010)</td>
<td>1.626 (1.349–2.025)</td>
<td>1.367 (1.096–1.648)</td>
</tr>
<tr>
<td>Area under ROC curve</td>
<td>0.769</td>
<td>0.668</td>
<td>0.617</td>
</tr>
</tbody>
</table>

Data are presented as mean (95% confidence interval).

AHI = apnea-hypopnea index; ASA = American Society of Anesthesiologists; NPV = negative predictive value; PPV = positive predictive value; ROC = receiver operating characteristic.

Structural Characteristics of the Three Screening Tools
The structural characteristics of the screening tools are summarized in table 3. Several features make the STOP questionnaire easiest to remember and to use among the three screening tools. These include a smaller number of items, a yes/no format of the question design, the simple mnemonic, and a straightforward scoring procedure.

Postoperative Complications
Table 4 briefly summarizes the demographic data and the postoperative complications of the 416 patients who consented to the study. There were no deaths or life-threatening complications in either group of patients. Compared with the patients who did not show up for polysomnography, the patients who underwent polysomnography had a significantly higher incidence of

Table 3. Structural Characteristics of the Screening Tools

<table>
<thead>
<tr>
<th></th>
<th>Berlin Questionnaire</th>
<th>ASA Checklist</th>
<th>STOP Questionnaire</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of items</td>
<td>11</td>
<td>12 or 14*</td>
<td>4</td>
</tr>
<tr>
<td>Number of category</td>
<td>3</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Format of questions</td>
<td>Multiple choice</td>
<td>Checklist</td>
<td>Yes/no</td>
</tr>
<tr>
<td>Scoring</td>
<td>Categories → final</td>
<td>Categories → final</td>
<td>Final</td>
</tr>
<tr>
<td>Healthcare staff involved</td>
<td>Scoring</td>
<td>Evaluation + scoring</td>
<td>Scoring</td>
</tr>
</tbody>
</table>

* 12 items for adults and 14 items for children.

ASA = American Society of Anesthesiologists.
postoperative complications (22.8% vs. 14.6%; \( P = 0.034 \)), mainly because of the increased incidence of severe desaturation (10.9% vs. 5.4%; \( P = 0.039 \)). The patients who did not show up for polysomnography also had a significantly high rate of smokers (26.8% vs. 14.7%; \( P = 0.002 \)).

Table 5 summarizes the demographic data and postoperative complications in 211 patients who underwent polysomnography. The demographic data showed the same trend as in 177 patients.\(^1\)\(^1\) Compared with patients with an AHI of 5 or less, the patients with an AHI greater than 5 were older and had a higher percentage of male patients. They also had a higher BMI, a larger neck circumference, and a higher prevalence of hypertension. Patients with an AHI greater than 5 had a significantly higher incidence of postoperative complications (table 5), as seen in the incidence of total complications (27.4% vs. 12.3%; \( P = 0.016 \)), respiratory complications (22.6% vs. 9.2%; \( P = 0.021 \)), and desaturation (20.6% vs. 9.2%; \( P = 0.044 \)). As a result, more patients needed prolonged oxygen therapy (14.3% vs. 4.7%; \( P = 0.043 \)). In terms of the incidence of postoperative complications at the different AHI cutoff values, there was no significant difference between patients with an AHI of 15 or less versus patients with an AHI greater than 15, and patients with an AHI of 30 or less versus patients with an AHI greater than 30.

When examining the frequency of postoperative complications from the perspective of the score of the screening tools (table 6), the patients ranked as high risk by the STOP questionnaire had a significantly higher incidence of respiratory complications (23.8% vs. 10.6%; \( P < 0.005 \)), desaturation (22.2% vs. 9.4%; \( P < 0.05 \)), and severe desaturation (15.1% vs. 4.7%; \( P < 0.05 \)). The higher incidences of postoperative respiratory complications (25.7% vs. 9.9%; \( P < 0.05 \)) and desaturation (21.4% vs. 8.5%; \( P < 0.05 \)) were also found in the patients identified as having a high risk of OSA by the ASA checklist.

Table 7 shows the odds ratios for the factors that are possibly related with the incidence of postoperative complications. In this patient population, gender, age older than 50 yr, BMI >35 kg/m\(^2\), neck circumferences greater than 40 cm, hypertension, and gastroesophageal reflux disease were not significantly related to the incidence of postoperative complications. In terms of the screening tools, identification of high risk of having OSA by the STOP-Bang (an alternative scoring model of STOP questionnaire\(^1\)\(^1\)) was significantly associated with the occurrence of postoperative complications. AHI greater than 5 was another significant factor for the occurrence of postoperative complications. When reviewing the subgroups with the dif-
ferent ranges of AHI, an AHI of 15–30 was the most significant risk factor for the postoperative complications.

### Discussion

This study has validated the use of the Berlin questionnaire and the ASA checklist as screening tools for OSA in surgical patients. Similar to the STOP questionnaire, both the Berlin questionnaire and the ASA checklist demonstrated a moderately high level of sensitivity, ranging from 65.6% to 87.2% for the different AHI cutoffs. The patients with OSA had an increased rate of postoperative complications, which was mainly due to the increased frequency of postoperative desaturation. Either having an AHI greater than 5 or being iden-

### Table 5. Demographic Data and Postoperative Complications: AHI >5 versus AHI ≤5

<table>
<thead>
<tr>
<th></th>
<th>Total (n = 211)</th>
<th>AHI ≤5 (n = 64)</th>
<th>AHI &gt;5 (n = 147)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, M/F, n</td>
<td>106/105</td>
<td>23/41</td>
<td>83/64</td>
<td>0.01</td>
</tr>
<tr>
<td>Age, mean ± SD, yr</td>
<td>56 ± 13</td>
<td>50 ± 14</td>
<td>59 ± 12</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>BMI, mean ± SD, kg/m²</td>
<td>30.3 ± 7</td>
<td>27.9 ± 6</td>
<td>30.4 ± 6</td>
<td>0.01</td>
</tr>
<tr>
<td>BMI &gt;35 kg/m², n (%)</td>
<td>42 (19.9)</td>
<td>9 (14.1)</td>
<td>33 (22.5)</td>
<td>0.16</td>
</tr>
<tr>
<td>Neck circumference, cm</td>
<td>39.1 ± 6</td>
<td>36.3 ± 4</td>
<td>40.2 ± 6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>AHI/h</td>
<td>18.9 ± 22</td>
<td>2.5 ± 2</td>
<td>25.9 ± 22</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Preexisting conditions, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>92 (43.6)</td>
<td>20 (31.3)</td>
<td>72 (49.0)</td>
<td>0.02</td>
</tr>
<tr>
<td>GERD</td>
<td>65 (30.8)</td>
<td>17 (26.6)</td>
<td>48 (32.7)</td>
<td>0.38</td>
</tr>
<tr>
<td>Diabetes</td>
<td>38 (18.0)</td>
<td>7 (10.9)</td>
<td>31 (21.1)</td>
<td>0.08</td>
</tr>
<tr>
<td>Total complications, n (%)</td>
<td>48 (22.8)</td>
<td>8 (12.3)</td>
<td>40 (27.4)</td>
<td>0.02</td>
</tr>
<tr>
<td>Respiratory complication, n (%)</td>
<td>39 (18.5)</td>
<td>6 (9.2)</td>
<td>33 (22.6)</td>
<td>0.02</td>
</tr>
<tr>
<td>Total desaturation</td>
<td>36 (17.1)</td>
<td>6 (9.2)</td>
<td>30 (20.6)</td>
<td>0.04</td>
</tr>
<tr>
<td>Mild desaturation, SaO2 90–95%</td>
<td>13 (6.2)</td>
<td>2 (3.1)</td>
<td>11 (7.5)</td>
<td>0.35</td>
</tr>
<tr>
<td>Severe desaturation, SaO2 ≤90%</td>
<td>23 (10.9)</td>
<td>4 (6.2)</td>
<td>19 (13.0)</td>
<td>0.16</td>
</tr>
<tr>
<td>Cardiac complication, n (%)</td>
<td>12 (5.7)</td>
<td>2 (3.1)</td>
<td>10 (6.9)</td>
<td>0.35</td>
</tr>
<tr>
<td>Neurologic complication,† n (%)</td>
<td>2 (0.95)</td>
<td>0</td>
<td>2 (1.4)</td>
<td>1.00</td>
</tr>
<tr>
<td>Prolong oxygen therapy</td>
<td>24 (11.4)</td>
<td>3 (4.7)</td>
<td>21 (14.3)</td>
<td>0.04</td>
</tr>
<tr>
<td>Additional monitoring</td>
<td>9 (4.3)</td>
<td>1 (91.5)</td>
<td>8 (5.5)</td>
<td>0.28</td>
</tr>
<tr>
<td>Total admission to ICU, n</td>
<td>13</td>
<td>1</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Planned ICU admission</td>
<td>3</td>
<td>0</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Unplanned ICU admission</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>ICU admission related OSA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>9</td>
<td>0</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Hospital stay after surgery, median (range), h</td>
<td>44.8 (0.2–352.8)</td>
<td>25.0 (0.75–215.6)</td>
<td>51.6 (0.2–352.8)</td>
<td>0.25</td>
</tr>
<tr>
<td>Readmission within 30 days, n (%)</td>
<td>4 (1.9)</td>
<td>0</td>
<td>4 (2.7)</td>
<td>0.18</td>
</tr>
<tr>
<td>ED visit within 30 days, n (%)</td>
<td>1 (0.5)</td>
<td>1 (1.5)</td>
<td>0</td>
<td>0.31</td>
</tr>
</tbody>
</table>

* Cardiac complications: bradycardia, tachycardia, dysrhythmia, and ischemia. † Neurologic complications: confusion, agitation, and excessive drowsiness.

### Table 6. Distribution of Complications

<table>
<thead>
<tr>
<th></th>
<th>STOP Questionnaire</th>
<th>Berlin Questionnaire</th>
<th>ASA Checklist</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low Risk</td>
<td>High Risk</td>
<td>Low Risk</td>
</tr>
<tr>
<td>n</td>
<td>211</td>
<td>85 (40.3)</td>
<td>126 (59.7)</td>
</tr>
<tr>
<td>Total complications</td>
<td>48 (22.8)</td>
<td>14 (16.5)</td>
<td>34 (27.0)</td>
</tr>
<tr>
<td>Respiratory complications</td>
<td>39 (18.5)</td>
<td>9 (10.6)</td>
<td>30 (23.8)*</td>
</tr>
<tr>
<td>Total desaturation</td>
<td>36 (17.1)</td>
<td>8 (9.4)</td>
<td>28 (22.2)*</td>
</tr>
<tr>
<td>Mild desaturation, SaO2 90–95%</td>
<td>13 (6.2)</td>
<td>4 (4.7)</td>
<td>9 (7.1)</td>
</tr>
<tr>
<td>Severe desaturation, SaO2 ≤90%</td>
<td>23 (10.9)</td>
<td>4 (4.7)</td>
<td>19 (16.1)*</td>
</tr>
<tr>
<td>Cardiac complication†</td>
<td>12 (5.7)</td>
<td>5 (5.9)</td>
<td>7 (5.6)</td>
</tr>
<tr>
<td>Neurologic complication‡</td>
<td>2 (1.0)</td>
<td>1 (1.2)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Prolong oxygen therapy</td>
<td>25 (11.9)</td>
<td>6 (7.1)</td>
<td>19 (15.1)</td>
</tr>
<tr>
<td>Additional monitoring</td>
<td>9 (4.3)</td>
<td>2 (2.4)</td>
<td>7 (5.6)</td>
</tr>
<tr>
<td>Total admission to ICU, n</td>
<td>13 (6.1)</td>
<td>6 (7.1)</td>
<td>7 (5.6)</td>
</tr>
</tbody>
</table>

Data are presented as n (%).  
* P < 0.05 vs. low risk. † Cardiac complications: bradycardia, tachycardia, dysrhythmia, and ischemia. ‡ Neurologic complications: confusion, agitation, and excessive drowsiness.

ASA = American Society of Anesthesiologists; ICU = intensive care unit; SaO2 = arterial oxygen saturation.
to identify patients at high risk of having OSA in the different patient populations. The Berlin questionnaire is a widely used screening tool for OSA. It was an outcome of the Conference on Sleep in Primary Care in April 1996 in Berlin, Germany. It includes 11 questions organized into the three categories: 5 questions related to snoring and the cessation of breathing in category 1, 4 questions related to daytime sleepiness in category 2, 1 question about high blood pressure, and 1 question regarding BMI in category 3. When two of three categories are classified as positive, it includes 11 questions organized into the three categories: 5 questions related to snoring and the cessation of breathing in category 1, 4 questions related to daytime sleepiness in category 2, 1 question about high blood pressure, and 1 question regarding BMI in category 3. When two of three categories are classified as positive, the patient is rated as being at high risk of having OSA (appendix 1).

The predictive performance of the Berlin questionnaire for OSA varies greatly among different patient populations. In primary care patients, the sensitivity and specificity were found to be 86% and 77%, respectively, at a cutoff of AHI greater than 5, and 54% and 97% at a cutoff of AHI greater than 15.7 In a group of patients preselected by excluding all patients with any typical symptoms of OSA or any comorbidity that could significantly increase the risk of having OSA, a modified version of the Berlin questionnaire showed a sensitivity of 86% and a specificity of 96% at a cutoff of AHI greater than 15.22 However, the sensitivity and specificity of the Berlin questionnaire were 62.5% and 53.8% with a cutoff of AHI of 10 or greater in 153 patients undergoing pulmonary rehabilitation. In patients referred to a sleep laboratory, the Berlin questionnaire again showed a very low predictive value. The sensitivity and specificity of the Berlin questionnaire were 68% and 49% at respiratory disturbance index greater than 5, 62% and 43% at respiratory disturbance index greater than 10, and 57% and 43% at respiratory disturbance index greater than 15.9

Compared with the aforementioned studies, our results showed that the Berlin questionnaire had a moderately high level of sensitivity in surgical patients (68.9%) and a higher sensitivity for surgical patients with moderate and severe OSA (78.6–87.2%). However, the specificity is low and is not significant. This finding suggests that in surgical patients, the Berlin questionnaire is helpful in detecting the high risk of having OSA, especially if the OSA is moderate or severe.

The ASA Task Force on the Perioperative Management of Patients with Obstructive Sleep Apnea published a practice guideline in 2006.10 These guidelines recommend the routine screening of surgical patients with a three-category checklist with 12 items for adults and 14 items for children (appendix 2). The ASA checklist has never been validated in any group of patients. Our study is the first study that has evaluated the predictive values of the ASA checklist for OSA. Compared with the Berlin and STOP questionnaires, the ASA checklist demonstrated a similar level of sensitivity and specificity.

The STOP questionnaire was developed and validated in surgical patients.11 There are four yes/no questions in the STOP questionnaire and eight yes/no items in the alternative scoring model STOP-Bang. The scoring is easy and straightforward. The STOP questionnaire performs with similar sensitivity and specificity compared with the Berlin questionnaire and the ASA checklist. The alternative scoring model STOP-Bang demonstrated a high level of sensitivity (84–100%) and negative predictive value (61–100%), especially for moderate and severe OSA. If a patient is ranked as being at low risk of having

### Table 7. Odds Ratios for Effectors on the Incidence of Postoperative Complications

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Value</th>
<th>Point Estimate</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Male vs. female</td>
<td>1.29</td>
<td>0.67–2.46</td>
</tr>
<tr>
<td>Age &gt;50 yr</td>
<td>Yes vs. no</td>
<td>1.14</td>
<td>0.54–2.38</td>
</tr>
<tr>
<td>BMI &gt;35 kg/m²</td>
<td>Yes vs. no</td>
<td>1.94</td>
<td>0.92–4.09</td>
</tr>
<tr>
<td>Neck circumference &gt;40 cm</td>
<td>Yes vs. no</td>
<td>1.21</td>
<td>0.61–2.38</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Yes vs. no</td>
<td>1.18</td>
<td>0.62–2.26</td>
</tr>
<tr>
<td>GERD</td>
<td>Yes vs. no</td>
<td>1.83</td>
<td>0.93–3.59</td>
</tr>
<tr>
<td>Berlin questionnaire</td>
<td>High risk vs. low risk</td>
<td>0.85</td>
<td>0.44–3.63</td>
</tr>
<tr>
<td>ASA checklist</td>
<td>High risk vs. low risk</td>
<td>1.75</td>
<td>0.85–3.63</td>
</tr>
<tr>
<td>STOP questionnaire</td>
<td>High risk vs. low risk</td>
<td>1.94</td>
<td>0.97–3.89</td>
</tr>
<tr>
<td>STOP-Bang</td>
<td>High risk vs. low risk</td>
<td>3.00</td>
<td>1.20–7.53</td>
</tr>
<tr>
<td>AHI &gt;5 vs. ≤5</td>
<td>2.77</td>
<td>1.21–6.32</td>
<td></td>
</tr>
<tr>
<td>AHI &gt;5–15 vs. ≤5</td>
<td>2.23</td>
<td>0.87–5.70</td>
<td></td>
</tr>
<tr>
<td>AHI &gt;15–30 vs. ≤5</td>
<td>4.16</td>
<td>1.54–11.20</td>
<td></td>
</tr>
<tr>
<td>AHI &gt;30 vs. ≤5</td>
<td>2.53</td>
<td>0.92–6.94</td>
<td></td>
</tr>
</tbody>
</table>

AHI = apnea–hypopnea index; ASA = American Society of Anesthesiologists; BMI = body mass index; GERD = gastroesophageal reflux disease.
OSA by the STOP-Bang, the patient will have a very low possibility of having moderate or severe OSA.

Most studies published on postoperative complications among OSA patients are focused on patients who underwent upper airway surgery. Only a few studies have been published on postoperative complications in patients who underwent surgeries other than upper airway surgery. The overall postoperative complication rate in OSA patients undergoing surgery other than upper airway surgery is increased, 39% versus 18% in the control group ($P = 0.01$). The rate of serious complications is 24%, and the rate of respiratory complications is 32%. Compared with the aforementioned studies, the overall rate of postoperative complications in our patients was lower (27.4% vs. 12.3%; $P = 0.02$). The most common complication was desaturation (20.6% vs. 9.2%; $P = 0.04$). There were no deaths or serious complications in our patients.

When individually checking the possible risk factors for postoperative complications, either being identified as being at high risk of having OSA by the STOP-Bang or having an AHI greater than 5 was associated with an increased occurrence of postoperative complications. When the subgroups with different AHI were further examined, patients with moderate OSA (AHI = 15–30) had a significantly increased risk for postoperative complications. However, the patients with severe OSA (AHI >30) did not show a similar increased risk for postoperative complications. Our ethics board required us to inform anesthesiologists if the patient’s AHI was 30 or greater. In one of our study hospitals, we were required to admit all patients with an AHI of 30 or greater to the intensive care unit for postoperative observation for the first night after surgery. This requirement to monitor these patients in the intensive care unit may explain why AHI greater than 30 was not found to be a risk factor for postoperative complications in our study population.

Our data suggest that the patients identified as being at high risk of having OSA by the STOP questionnaire or by the ASA checklist had an increased postoperative complication rate. The finding may provide practical guidelines to anesthesiologists, but it must be confirmed with further study.

There are potential limitations with the study. Self-selection of patients may have been involved during the process of patient screening. The patients who had sleep symptoms might have selectively consented to overnight polysomnography. The patients who underwent polysomnography had a higher frequency of postoperative complications than the patients who did not show up for polysomnography, further supporting that there may have been self-selection from the perspective of patients. Additional potential limitations are discussed in the accompanying article.

In conclusion, the Berlin questionnaire and the ASA checklist have been validated in surgical patients as screening tools for OSA. Both demonstrated a moderately high level of sensitivity and a negative predictive value, as the STOP questionnaire did. The STOP questionnaire and the ASA checklist were also able to identify the patients susceptible to postoperative complications. Because of its easy-to-use format, the STOP questionnaire might be easier for patients to complete and more suitable in the busy preoperative clinics.

The authors thank all of the anesthesiologists at Toronto Western Hospital, Toronto General Hospital, and Mount Sinai Hospital (Toronto, Ontario, Canada).

Appendix 1: Berlin Questionnaire

Height ____ m Weight ____ kg Age ____ Male/Female
Please choose the correct response to each question.

**Category 1**

1. Do you snore?
   a. Yes
   b. No
   c. Don’t know

2. Your snoring is:
   a. Slightly louder than breathing
   b. As loud as talking
   c. Louder than talking
   d. Very loud—can be heard in adjacent rooms

3. How often do you snore?
   a. Nearly every day
   b. 3–4 times a week
   c. 1–2 times a week
   d. 1–2 times a month
   e. Never or nearly never

4. Has your snoring ever bothered other people?
   a. Yes
   b. No
   c. Don’t know

5. Has anyone noticed that you quit breathing during your sleep?
   a. Nearly every day
   b. 3–4 times a week
   c. 1–2 times a week
   d. 1–2 times a month
   e. Never or nearly never

**Category 2**

6. How often do you feel tired or fatigued after your sleep?
   a. Nearly every day
   b. 3–4 times a week
   c. 1–2 times a week
   d. 1–2 times a month
   e. Never or nearly never

7. During your waking time, do you feel tired, fatigued, or not up to par?
   a. Nearly every day
   b. 3–4 times a week
   c. 1–2 times a week
   d. 1–2 times a month
   e. Never or nearly never

8. Have you ever nodded off or fallen asleep while driving a vehicle?
   a. Yes
   b. No
If yes:

9. How often does this occur?
   a. Nearly every day
   b. 3–4 times a week
   c. 1–2 times a week
   d. 1–2 times a month
   e. Never or nearly never

Category 3
10. Do you have high blood pressure?
   a. Yes
   b. No
   c. Don’t know

Scoring Berlin Questionnaire
Adapted from table 2 in Netzer et al.7
The questionnaire consists of three categories related to the risk of having OSA.

Categories and scoring:
Category 1: items 1, 2, 3, 4, and 5
   Item 1: If yes is the response, assign 1 point.
   Item 2: If c or d is the response, assign 1 point.
   Item 3: If a or b is the response, assign 1 point.
   Item 4: If a is the response, assign 1 point.
   Item 5: If a or b is the response, assign 2 points.
   Category 1 is positive if the total score is 2 or more points.
Category 2: items 6, 7, and 8 (item 9 should be noted separately)
   Item 6: If a or b is the response, assign 1 point.
   Item 7: If a or b is the response, assign 1 point.
   Item 8: If a is the response, assign 1 point.
   Category 2 is positive if the total score is 2 or more points.
Category 3 is positive if the answer to item 10 is yes or if the BMI of the patient is greater than 30 kg/m².
High risk of OSA: two or more categories scored as positive
Low risk of OSA: only one or no category scored as positive

Appendix 2: ASA Checklist
Adapted from table 1 in Gross et al.10

Category 1: Predisposing Physical Characteristics
   a. BMI ≥35 kg/m²
   b. Neck circumference >43 cm/17 inches (men) or 40 cm/16 inches (women)
   c. Craniofacial abnormalities affecting the airway
   d. Anatomical nasal obstruction
   e. Tonsils nearly touching or touching the midline

Category 2: History of Apparent Airway Obstruction during Sleep
Two or more of the following are present (if patient lives alone or sleep is not observed by another person, then only one of the following need be present):
   a. Snoring (loud enough to be heard through closed door)
   b. Frequent snoring
   c. Observed pauses in breathing during sleep
   d. Awakens from sleep with choking sensation
   e. Frequent arousals from sleep

Category 3: Somnolence
One or more of the following are present:
   a. Frequent somnolence or fatigue despite adequate “sleep”
   b. Falls asleep easily in a nonstimulating environment (e.g., watching TV, reading, in or driving a car) despite adequate “sleep”
   c. [Parent or teacher comments that child appears sleepy during the day, is easily distracted, is overly aggressive, or has difficulty concentrating]∗
   d. [Child often difficult to arouse at usual awakening time]∗

Scoring:
If two or more items in category 1 are positive, category 1 is positive.
If two or more items in category 2 are positive, category 2 is positive.
If one or more items in category 3 are positive, category 3 is positive.
High risk of OSA: two or more categories scored as positive
Low risk of OSA: only one or no category scored as positive
∗ Items in brackets refer to pediatric patients.

Appendix 3. Definition of Adverse Events

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory complication</td>
<td>Includes desaturation, pulmonary edema, bronchospasm, and arrival in PACU intubated</td>
</tr>
<tr>
<td>Desaturation</td>
<td>( \text{SaO}_2 &lt; 95% ) at any time and/or cyanosis</td>
</tr>
<tr>
<td>Severe desaturation</td>
<td>( \text{SaO}_2 &lt; 90% ) at any time and/or cyanosis</td>
</tr>
<tr>
<td>Prolong oxygen therapy</td>
<td>Requirement of oxygen therapy after discharge from PACU</td>
</tr>
<tr>
<td>Additional monitoring</td>
<td>Electrocardiography or oxygen saturation monitoring</td>
</tr>
<tr>
<td>Cardiac complication</td>
<td>Includes tachycardia, bradycardia, dysrhythmia, and myocardial ischemia</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>Heart rate &gt;120 beats/min for more than 10 min</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>Heart rate &lt;40 beats/min for more than 10 min</td>
</tr>
<tr>
<td>Dysrhythmia</td>
<td>New atrial fibrillation, supraventricular tachycardia, heart block, or premature ventricular beats &gt;5/min</td>
</tr>
<tr>
<td>Myocardial ischemia</td>
<td>&gt;1 mm ST depression, inversion of T wave for more than 1 min</td>
</tr>
<tr>
<td>Neurologic complication</td>
<td>Includes confusion, agitation, and excessive drowsiness</td>
</tr>
<tr>
<td>Readmission within 7 or 30 days</td>
<td>Patients have to be readmitted to hospital within 7 or 30 days after discharge</td>
</tr>
</tbody>
</table>

PACU = postanesthesia care unit; \( \text{SaO}_2 \) = arterial oxygen saturation.
References