by David J. Cullen, MD, and Robert R. Kirby, MD

Case Presentation

A 47-year-old, healthy female underwent general anesthesia for shoulder arthroscopy. Preoperative blood pressure (BP) was 125/83 mmHg. After premedication with 50 mg of meperidine, 40 mg hydroxyzine, and 0.2 mg glycopyrrolate intramuscularly, anesthesia was induced with 200 mg propofol, 100 mg succinylcholine, and 30 mg lidocaine. Because she was hypertensive, just prior to induction, 50 mg of labetalol was given intravenously. Anesthesia was maintained with 2% isoflurane, 60% nitrous oxide, and oxygen. The patient was placed in the “barber-shop” position for the surgery. Twenty minutes into the case, blood pressure decreased to 100/60 mmHg and then remained in the 80-90 mmHg systolic range for the remainder of the case. Oxygen saturation was 100% and end tidal CO2 values were in the 30s throughout the case. Upon arrival in the post-anesthesia care unit (PACU), her blood pressure was 113/60 mmHg but she did not awaken. Naloxone 0.1 mg was given intravenously, but she remained unresponsive and did not move her extremities. Another 0.1 mg of naloxone was given 35 min after arrival in the PACU followed by 3 more doses of naloxone and 2 doses of physostigmine. During this time, her trachea remained intubated and she was well oxygenated. Neurologic evaluation suggested a diencephalic syndrome, possibly brain infarction. She was unresponsive to voice commands or painful stimuli, and reflexes were decreased bilaterally. A computer axial tomography (CAT) scan of the head was normal initially, but 5 days later suggested brain swelling and obliteration of the cistern. Magnetic resonance imaging (MRI) 1 week later showed changes in both cerebral hemispheres suggesting cortical infarcts, involvement of the anterior and medial temporal lobe bilaterally, no significant edema, and no significant herniation. At no time was there any evidence of an intracranial bleed. After 2 weeks, her Glasgow coma scale was 3; her fundi were clear and crisp. She had corneal reflexes, a positive gag, and negative doll’s eyes; she was hyperreflexive with increased tone and was unresponsive to noxious stimuli in all 4 extremities. She is expected to remain in a persistent vegetative state.

Considerations When Using the Beach Chair Position

The beach chair (barbershop) position was developed in the 1980s for orthopedic shoulder arthroscopy procedures. Patients are sat up at angles varying from 30-90° above the horizontal plane with appropriate padding and with the head secured in a headrest. Injuries to the brachial plexus are reduced compared to the lateral decubitus position, and the surgeon has excellent access to the shoulder. The position helps the surgeon because the weight of the arm distracts the shoulder joint while avoiding distortion of the intrarticular anatomy.

However, significant changes can develop when patients are moved to the upright position. Mean arterial pressure (MAP), central venous pressure (CVP), pulmonary artery occlusion pressure (PAOP), stroke volume, cardiac output, and PaO2 all decrease while the alveolar-arterial oxygen gradient (PAO2-PaO2), pulmonary vascular resistance, and total peripheral resistance increase. Under nonanesthetized conditions, these effects are compensated for by an increase in systemic vascular resistance by up to 50-80%. However, this autonomic response is blocked by vasodilating anesthetics, which further exacerbate and compromise cardiac output. Blood pressure remains unchanged or increases slightly in nonanesthetized patients in the sitting position but decreases in the anesthetized state. Cerebral perfusion pressure (CPP) decreases by approximately 15% in the sitting position in non-anesthetized patients and could further decrease under anesthesia because of vasodilatation and impaired venous return. Venous return from the cerebral circulation is usually increased by inspiratory subatmospheric pressure during spontaneous ventilation, but this mechanism is nullified by positive pressure ventilation. Obstruction of the internal jugular veins in the sitting position may also impede cerebral venous drainage, especially with unfavorable positions of the head and neck, such as flexion of the head. Pohl and Cullen reported a series of cases in 2005 that documented blood pressure decreases ranging from 28-42%; consequently, hypotension was thought to be a likely cause of ischemic brain injury. Given the potential for peripheral vasodilatation and myocardial depression that can occur in patients who are anesthetized with potent intravenous and inhalational drugs, the effects of the upright position and anesthesia synergize.

Cerebral autoregulation has been thought to maintain cerebral blood flow (CBF) constant between MAP of 50-150 mmHg. However, it must be remembered that in poorly controlled hypertensive patients, autoregulation of CBF is shifted to the right, requiring higher CPP/MAP to ensure adequate cerebral perfusion. In recent years, Drummond and others have emphasized that the quoted value of 50 mmHg for the lower limit of autoregulation (LLA) should be modified upward to reflect a range of values from 70-93 mmHg with a mean value of 80 ± 8 mmHg rather than the specific number of 50 mmHg. Some orthopedic surgeons request deliberate hypotension for shoulder surgery. With the acquisition of the anesthesiologist or the nurse anesthetist, deliberate hypotension to mean arterial pressures of 50-60 mmHg eliminates any margin for error in case blood pressure falls further. In addition, neither the surgeon nor the anesthesiologist nor the CRNA typically seems to consider the added effect of the beach chair position on cerebral perfusion.
Physicians Lee and Lofsky Named Consultants to Executive Committee

Dr. Lorri Lee and Dr. Ann Lofsky have recently been appointed consultants to the APSF Executive Committee. Their experience and expertise will certainly make them important additions to our organization.

Lorri A. Lee, MD, received her training in anesthesiology at the University of Washington where she is currently an associate professor in the Departments of Anesthesiology and Neurological Surgery (adjunct). As an investigator for the ASA Closed Claims Project, her research is focused on evaluating trends and associated factors in anesthesia-related patient injuries and medical liability. Dr. Lee is director of the ASA Postoperative Visual Loss Registry and served on the ASA Perioperative Blindness Advisory Task Force.

Ann Lofsky, MD, completed both internal medicine and anesthesiology residencies at UCLA before entering private practice in anesthesiology. She is currently a partner in the anesthesia group at Saint John’s Hospital in Santa Monica. For 13 years, Dr. Lofsky served on the board of directors of The Doctors Company, a physician-owned medical malpractice insurer. In that capacity, she has written and lectured extensively on risk management and patient safety concerns for anesthesia providers. She is now a governor emeritus and anesthesia consultant for The Doctors Company.
Consider Correction for Cuff Location

“Perfusion,” From Page 25

In the upright position, MAP at the brain is very different when compared to the site at which the BP is actually measured, usually the arm. Unfortunately this difference may be overlooked. In the supine position, BP measured in the arm and BP perfusing the brain are essentially the same. However, if the patient is upright in the beach chair position, BP will be less in the brain than at the heart or arm. The BP difference will be equal to the hydrostatic pressure gradient between the heart/brain and the arm. For example, suppose the BP at the heart/arm is 120/80 mmHg, (MAP 95 mmHg). If the height of the external auditory meatus (representing the base of the brain) is 20 cm above the heart, the difference in BP at the heart compared to the brain will be 15 mmHg. Thus, the BP at the base of the brain will be 105/65 mmHg (MAP 78 mmHg). Most patients undergoing relatively straightforward procedures such as shoulder arthroscopy or even open shoulder surgery do not have intra-arterial BP monitoring available. Therefore, they do not have a transducer placed at the level of the external auditory meatus to monitor BP at the base of the brain. Instead, it is up to the anesthesiologist and/or nurse anesthetist to correct the BP readings at the arm to account for the height of the brain above the arm. Even accounting for the hydrostatic gradient between the external auditory meatus (base of brain) and the arm does not take into account the added distance from the base of the brain, at the circle of Willis, to the most cephalic portion of the cerebral cortex, an additional distance of 10-12 cm (depending on the patient’s height), which represents a further gradient of about 9 mmHg.

The case presented at the beginning of this article suggests that the gradient between the arm and brain was not appreciated. Blood pressure was measured at the arm with a non-invasive cuff, but was not adjusted upward to maintain an adequate MAP at the level of the brain during the procedure. Systolic BPs of 80-100 mmHg probably corresponded to MAPs of 50-80 mmHg, but in the beach chair or upright position, MAP at the base of the brain was probably 15-20 mmHg lower, and at the top of the cerebral cortex, another 9 mmHg lower. It is reasonable to estimate a MAP of 30-40 mmHg at the cerebral cortex and a little higher at the brainstem. CAT scan on the fifth postoperative day showed brain swelling and obliteration of the cisterns. MRI 1 week later showed cortical infarcts in both cerebral hemispheres and no intracranial bleed. The injury was consistent with the hypoperfusion that occurred intraoperatively.

Estimates of the MAP at the head can be made once the patient is in the beach chair position. The critical variable is the vertical distance between the external auditory meatus and the BP cuff. Once that distance is known, it should be converted to a hydrostatic pressure gradient that then must be incorporated into BP management during the procedure.

To quantitate the hydrostatic gradient, there is a 0.77 mmHg decrease for every centimeter gradient (1 mmHg for each 1.25 cm). In general, the approximate distance between the brain and the site of the BP cuff on the arm in the seated position will be 10-30 cm depending on the angle of the sitting position and the height of the patient; hence the brain MAP will be 8-24 mmHg lower than the measured mean brachial artery pressure. If the beach chair position is combined with the use of deliberate hypotension, cerebral perfusion will be severely compromised. An even more exaggerated occurrence may develop when the BP cuff must be placed on the leg because the contralateral arm is not available for BP measurement, e.g., in a patient with prior lymph node dissection for breast cancer. In the beach chair position, the legs are considerably lower than the trunk, therefore the BP difference between the BP cuff measured on the leg and the BP in the brain will be even greater than the gradient between the arm and the brain.

The following case illustrates this point. A 54-year-old woman underwent left shoulder replacement surgery in the beach chair position. The patient had no history of hypertension or myocardial infarction. Preoperative electrocardiogram, echocardiogram, thallium scan, and exercise tolerance test were normal. The patient received an interscalene block with 40 ml of 0.5% bupivacaine with epinephrine (1:200,000). Because of a previous mastectomy, a 20-gauge intravenous catheter was placed in the right foot and a noninvasive BP cuff was placed on the calf.

There was no documentation that the calf BP was validated to the left arm BP before the patient was anesthetized and the left arm became unavailable. No arterial catheter was placed although deliberate hypotension was used. Anesthesia was induced with 100 mg propofol, 250 mg sodium pentothal, 50 mg rocuronium, and 250 mcg fentanyl. Anesthesia was maintained with 3.5% sevoflurane and 67% nitrous oxide in oxygen. Nitroglycerin, 50 mcg times 3 doses, and labetalol, 5 mg times 4 doses, were used to produce deliberate hypotension. One hour after induction, her systolic BP was between 85-100 mmHg. Two hours later, her BP was 70/40 mmHg and then remained around 90/60 mmHg for the next 40 min, when it decreased to 50/25 and was treated with phenylephrine. Electrocardiography showed sinus rhythm throughout, oxygen saturations were always high, and end-tidal CO2 was in the high 20s for most of the case. In the PACU, emergence was delayed, and she did not breathe spontaneously. A radially arterial catheter was finally placed while she was in the PACU, and BPs were normal. Apnea persisted and her pupils were fixed and dilated. Blood gas analysis on controlled ventilation showed a PaO2 of 236 mmHg, PaCO2 of 35 mmHg, and pH of 7.4, with glucose of 92 mg/dl. Neurologic evaluation revealed brain death with no CBF, flat electroencephalogram, no reflexes, no response to pain, and no lesions on the CAT scan. At autopsy the upper spinal cord and medulla were infarcted. The anesthesia equipment tested normal. In this case, not only was deliberate hypotension used to very low values, but BP was measured in the leg while the patient was in the sitting position. One can only imagine how low the BP was in the brain when BP in the leg was 70/40 or 60/60.

In addition to avoiding deliberate hypotension, one must be extremely vigilant and treat aggressively the unexpected hypotension that often occurs during anesthesia in the beach chair position for the reasons enumerated above. These treatments are well known to all anesthesia providers and include careful control of the inhalation anesthetic concentration, adequate and timely fluid administration, and vasopressor infusion, as needed during the time of the procedure when the patient is upright and at risk.

Head position is also important because some degree of head manipulation is required when positioning the patient in the seated position. Most surgeons use a headrest to immobilize the head. Several studies suggest that CBF can be compromised by mechanical obstruction and injury to major veins or arteries. Blood flow reduction in the vertebral artery caused by extension and rotation or tilt of the head may result in posterior brain circulation infarcts.

Finally, hypotension and generalized circulatory instability can result from gas embolism. This rare complication has been reported with both air and carbon dioxide distension of the joint capsule followed by pressurized injection of irrigation fluid. Thus, anesthesiologists and CRNAs should keep the possibility of venous gas embolism in mind during shoulder arthroscopy in the sitting position if sudden cardiovascular collapse occurs.

Summary

Despite its low incidence, intraoperative stroke associated with shoulder surgery, particularly in healthy patients at no risk for stroke, is a totally unexpected and devastating complication. Patients in the beach chair position are at risk for an intraoperative stroke if borderline low BPs, as measured in the arm, are used without appreciating the effect on CBF. Because of the specific physiologic changes associated with the sitting position, great care should be applied when using and interpreting BP cuff measurements in the nonoperative arm or even more so, if leg measurements of BP must be used. Blood pressure values <80% of preoperative resting values should be treated aggressively to enhance the margin of safety. Deliberate hypotension must be avoided. A thorough understanding of the physiologic changes associated with the upright position, and the physical effects of gravity on BP in the brain is crucial to prevent catastrophic neurologic outcome during shoulder surgery in the sitting position.

Dr. Cullen is formerly Chair of the Department of Anesthesia and Pain Medicine, Caritas St. Elizabeth’s Medical Center and former Professor of Anesthesiology at Tufts University School of Medicine in Boston, MA. Dr. Kirby is an Emeritus Professor of Anesthesiology at the University of Florida College of Medicine in Gainesville.

General References
Doctors Company Reviews Maternal Arrests Cases
(Reprinted with permission from The Doctors Company)

by Ann S. Lofsky, MD

Anesthesia-related maternal arrest is a feared complication that places the lives of both mother and baby at risk. Literature reviews on the subject have been traditionally hampered by a lack of specifics regarding the care provided and the aging of data by the time it could be collected and analyzed. Valid concerns about the privacy of stricken families, the confidentiality of the healthcare providers involved, and liability risks have likely acted together to prevent the wider dissemination of case specifics in an open forum.

Despite recent advances and changing practice patterns in obstetrical anesthesia, malpractice claim reviews indicate that maternal arrest on labor and delivery continues to result in major morbidity and mortality. The Doctors Company recently reviewed 22 anesthesiology claims that were filed after maternal arrests on labor and delivery wards between 1998 and 2006. Anesthesia care was analyzed at the time of initial medical record review from both Standard of Care and patient safety viewpoints. Characteristics of these claims and expert reviewer comments regarding suggested practice changes that might possibly have avoided the arrests or improved the outcomes are presented here with an aim toward improving maternal safety.

Overall Outcome

The mothers, aged 17 to 41, suffered the most severe complications post-arrest. Ten out of the 22 died, including 3 who were declared brain dead and removed from ventilators. Eleven suffered degrees of complications post-arrest. Ten out of the 22 had no apparent residuals post-arrest and was suing primarily for emotional distress.

Surprisingly, the infant outcome in these cases appeared quite different. In all cases where information was available, infants (or children) had been evaluated as developmentally normal at the time of final medical records review. This was true even for the babies born with low Apgar scores, and included not only the 10 babies delivered prior to the maternal arrest, but also the 12 born after their mothers had sustained significant periods of circulatory and/or respiratory arrest.

This disparity suggests that the fetus may well be more resistant to periods of hypoxia and hypotension than is the parturient, and it reaffirms the importance of the anesthesiologist’s primary focus being the welfare of the mother. This raises the question as to whether maternal resuscitation should ever be intentionally delayed in order to expedite delivery of the fetus.

Respiratory Arrests after Regional Anesthetics

The most common scenario in this series (13 patients) was a respiratory arrest following epidural or spinal block. Included in this group were 11 patients who developed unintentionally high neuraxial blockade with resultant apnea and 2 patients who arrested after intravenous sedation was administered post-caesarean section delivery under spinal anesthesia. None of these patients were attached to a maternal monitor with audible alarms at the time of the arrest, making delay in response and resuscitation a frequent reviewer concern.

Labor Epidurals

There were 8 patients in this series who arrested in labor rooms following attempted insertion and dosing of epidural catheters to relieve labor pains. Of these, 7 had subsequent evidence of unintentional subarachnoid blocks, either by positive aspiration of the catheter for cerebrospinal fluid (CSF) (3 patients) or air in the veinsicles on CT scanning (4 patients), presumably introduced into the CSF during injection through the needle or catheter.

All 8 of these arrests occurred within the first 30 minutes of initial catheter placement. In half of the cases, anesthesia providers were not in the room at the time, and the arrest was noted first by other healthcare workers. Reasons given by anesthesia providers for leaving the room after catheter placement included wanting to chart at the nursing desk, being called away to place another labor epidural or to attend to another labor patient’s needs, or needing to locate drugs or airway equipment.

In the 1 case in which the mother recovered without obvious neurologic impairment, she was placed supine immediately by the anesthesiologist on initial complaint of difficulty breathing and ventilated with oxygen by Ambu-bag as soon as respirations appeared inadequate. The obstetrician accomplished a crash cesarean section within minutes while still in the labor room, with only a benzodiazepine provided before incision. Blood pressure was supported with IV fluid infusion.

The other 7 cases involved the transfer of a mother in respiratory and/or circulatory arrest from the labor room to the operating room for STAT cesarean section due to fetal distress. In 4 of these cases, there were documented delays in the ventilation of the mother for reasons including initial failure to notice maternal arrest, desire to wait for more optimal intubating conditions in the OR, difficulty locating an Ambu-bag or airway device, or an anesthesia provider not being in attendance. The improved outcome in the 1 case involving immediate resuscitation suggests that the rapid establishment of adequate ventilation and blood pressure support might be crucial factors after unintentionally high spinal blockade.

Cesarean Sections

There were 5 cases of maternal respiratory arrest following regional anesthesia administered for elective cesarean-section delivery. These all involved spinal anesthetics, possibly because this is a preferred anesthesia choice for purely elective cases. In 2 instances, the mothers received an intravenous benzodiazepine or opioid after delivery; both had also received spinal opioids. Maternal respiratory arrests occurred after delivery in these cases, although there were possible delays in recognition of the arrests.

In the other 3 cases, the mothers received no intravenous anesthetics. One mother arrested immediately after the spinal was placed, with suspected preeclampsia and volume depletion as contributing factors. The other 2 cases involved apparent high spinals, with delay in recognition and/or resuscitation also potential problems.

Contributing Factors

Morbidity obesity, which is known to complicate regional anesthesia, was documented in 3 out of the 8 labor epidural cases and 1 out of the 5 cesarean sections. These proportions would appear to be higher than those present in most labor and delivery populations and suggest that morbid obesity may be a significant relative risk factor for maternal arrest following regional blocks.

Three mothers in this series carried the diagnosis of preeclampsia. Two arrested at the time of induction of anesthesia for cesarean section (1 spinal, 1 general anesthetic). Reviewers raised the possibility of relative hypovolemia in these cases and questioned whether invasive monitoring might have provided useful additional information.

Arrests after Maternal Hemorrhage

There were 7 cases involving arrests in mothers after massive postpartum hemorrhage—3 after normal spontaneous vaginal deliveries and 4 after cesarean section births. Predisposing diagnoses, when available, included placenta accreta, placental abruption, and traumatic arterial laceration. Knowing there had been a maternal arrest due to hemorrhage, reviewers attempted to identify ways in which the treatment might have been optimized, although it was acknowledged that the size and facilities of the obstetric units involved were varied.

A frequent reviewer impression was that the hemorrhage was so excessive by the time it was diagnosed, it was extremely difficult for the anesthesia provider to “catch up” with the continuing blood loss. Postpartum hemorrhage was not always initially apparent through vaginal bleeding, as it was often primarily internal. The initial presentation was frequently hypotension and/or tachycardia in the

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Respiratory Arrests After Epidural Occurred Within 30 Minutes

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mother, which was usually treated first with intravenous crystalloid and pressors. It was not always clear when continued bleeding should have been suspected as the cause of the maternal vital sign instability.

In some instances, delays in transfusing mothers were related to problems obtaining or transporting blood products from the blood bank, or to an inability to run the blood products through available intravenous lines more rapidly. Some cases involved delays in waiting for crossmatched blood when possibly O-negative or type-specific blood might have been available. Reviewers commented that several patients might have benefited from earlier consideration of additional blood components—including fresh frozen plasma, platelets, or cryoprecipitate.

Laboratory tests of serum hemoglobin and hematocrit, coagulation panels, or disseminated intravascular coagulation (DIC) screens were not always ordered.

Better communication might have facilitated transfusion in some cases. On retrospective reviews, potentially improvable delays were identified in informing blood banks of the need for products, in calling for additional medical assistance, or in notifying obstetricians that postpartum patients were hemorrhaging and that surgical intervention (such as exploration, uterine ligation, or hysterectomy) might be required. Potentially useful equipment, such as central line kits or rapid infusion devices, were sometimes available in the facility, but labor and delivery ward personnel might not have known how or where to obtain them.

General Anesthesia

Included in these maternal arrest cases were 5 general anesthetics and 17 regional blocks. This likely reflects an overall shift toward the use of regional anesthesia in obstetrics. In 3 of the general anesthetics cases, the arrest followed severe postpartum hemorrhage. In those cases, the choice of anesthesia did not likely affect the ultimate outcome significantly. General anesthesia was chosen in 2 cases for postpartum hysterectomy for patients who were already severely bleeding. Only 1 general anesthetic involved a difficult intubation and loss of the airway—traditionally one of the more feared complications of emergency cesarean sections. Interestingly, aspiration of gastric contents, traditionally listed as a leading cause of death in obstetric anesthesia, was not seen in this series of arrests.

Discussion

The physiological changes of pregnancy undoubtedly contribute to the high incidence of anoxic brain damage and death cases after maternal arrests. The size of the full-term uterus decreases functional residual capacity (FRC) in the mother, leading to a much more rapid development of hypoxia during periods of apnea than would be expected in the woman’s non-pregnant state. The increased oxygen demand of pregnancy further shortens the interval of apnea tolerated before arterial desaturation results. Although a pre-oxygenated, non-pregnant woman may sustain a several-minute period of apnea without desaturating, that same patient at 9 months’ gestation breathing room air might not.

Maternal circulation is compromised in the supine position due to compression of the vena cava and aorta by the uterus, decreasing venous return and cardiac output. The necessity of placing an already unstable mother supine, to combat rising spinal levels, to transport her to the operating room, or to manage the airway, may further complicate successful resuscitation.

Monitoring

Since all respiratory arrests after labor epidurals in these cases occurred within the first 30 minutes after catheter insertion, increased monitoring during this time period would seem a worthwhile consideration. This could be visual—with the anesthesia provider, nurse, or a designee in the room with the patient—or through electronic monitoring of pulse oximetry, capnography, or ventilation, with an alarm audible to responsible personnel. Some birthing facilities have labor and delivery rooms equipped with pulse oximeters that read continuously at the nursing stations, yet that is not currently standard. Many of the maternal arrests following labor epidurals occurred on wards in which only fetal monitoring was transmitted continuously to nurses. The outcomes in those cases suggest that by the time hypoxia due to apnea becomes apparent on a fetal tracing, it might already be too late to prevent anoxic brain damage in the mother.

In 4 cases of planned labor epidurals, the anesthesiologist or CRNA observed symptoms or signs consistent with unintentional spinal blockade prior to the arrest (such as positive aspiration for CSF or maternal complaints of sudden headache or difficulty breathing). Since most labor epidural patients in this series arrested after unplanned subarachnoid blocks, patients for whom there are suspicions of “wet tap” may be at increased risk and might benefit from closer observation and/or monitoring.

Case reviews suggest that keeping pulse oximeter or end-tidal carbon dioxide monitor alarms in an audible mode continuously during cesarean sections is advisable, even after delivery of the newborn. As of October 2005, the American Society of Anesthesiologists (ASA) standards for basic anesthesia monitoring include the statement that whenever pulse oximeters or capnrometers are utilized, the low threshold alarms should be audible.

Ventilation

Rapid recognition of maternal respiratory arrest and restoration of oxygenation and ventilation should be key goals. Airway devices such as self-inflating bag/mask systems, oral and nasal airways, laryngeal mask airways (LMAs), and intubation equipment should be immediately available if needed in labor rooms, with all nurses and anesthesia providers acquainted with their location. The recently revised ASA Practice Guidelines for Obstetrical Anesthesia contain more complete lists of potentially useful equipment.

Because an anesthesia provider may not always be the first to arrive on the scene, labor and delivery nurses should also be able to assess the adequacy of ventilation, establish an airway, and begin ventilation if necessary. Supplemental oxygen should be available in the labor room and immediately available in portable tank form, should transportation of an apneic patient become necessary. Since hypoxia will likely develop rapidly in a full-term apneic patient, adequate ventilation and oxygenation of the mother should ideally be established before transporting her to another location.

Circulation

As with any resuscitation, maternal blood pressure and circulation should be evaluated and supported, if necessary, with fluids and pressors. CPR should be started as soon as maternal circulation appears inadequate. Since aortocaval compression and an elevated hemidiaphragm can complicate standard CPR, the American Heart Association suggests displacing the uterus to the left by tilting the patient, and performing chest compressions higher on the sternum (slightly above the center).

Transfusion

Massive hemorrhage on labor and delivery is a rare occurrence, and as a result, many anesthesia providers have little or no experience managing it. Yet, the incidence of major hemorrhage in the obstetric population appears to be increasing over time. The increased rate of repeat cesarean sections, with the associated rise in incidence of placenta previa and placenta accreta, may largely account for this. One New York hospital, after experiencing 2 maternal hemorrhage-related deaths, created a multidisciplinary patient safety team specifically designed to handle labor and delivery patients experiencing major bleeding episodes.

Their obstetric rapid response team includes members of the trauma team, as the individuals identified in that hospital with the most experience in establishing large-bore intravenous lines and massive volume and blood replacement. Efforts were made to identify high-risk patients, who were advised about auto-donation of blood and type and
“Arrest,” From Preceding Page

screened in advance of delivery. A cell saver blood scavenging device was used, when necessary, after the fetus was delivered and after peritoneal lavage.³

With these and other interventions, that hospital was able to significantly decrease the number of maternal deaths, despite an increase in the total number of cases of major obstetrical hemorrhage. This suggests that having a pre-planned and coordinated multi-departmental approach to maternal hemorrhage may well advance patient safety.

Patient Safety

While maternal arrest is, fortunately, a very rare complication, the above cases are a testament to the fact that it still can and does occur—even when currently acceptable anesthesia practices are followed. Anesthesia providers and labor and delivery staff should consider planning their own response to a “worst-case scenario” before it happens to them. A few questions that those providing obstetrical anesthesia may wish to consider:

• If most maternal arrests occur within 30 minutes of the placement of a regional block, how will your patient be monitored during that time period, and who will respond if required?

• If a patient were discovered apneic in a labor and delivery room, where is all potentially necessary airway equipment kept? Would you have access to all the drugs that you might need?

• Are a portable oxygen tank and a bag/mask immediately available for transferring labor patients for crash cesarean sections? Would you need a portable monitor?

• During cesarean sections: As you currently use them, would a monitor alarm notify you if a patient developed apnea at any time?

• How would you and your facility handle an unexpected massive hemorrhage on the labor and delivery ward?

• Who is available to help you with a maternal arrest on labor and delivery, and how would they be notified if needed?

Every case included here was devastating on many levels to the patients, families, and healthcare providers involved. While it is tempting to search for “mistakes” in each individual scenario, the major issues identified were rarely unique. It is hoped that through taking a “systems” approach and focusing instead on the common factors that these cases share, similar occurrences might be prevented and maternal safety improved.

Ann Lofsky, MD is currently a partner in the anesthesia group at Saint John’s Hospital in Santa Monica, CA, and a governor emeritus and anesthesia consultant for The Doctors Company.

References


Intralipid Might Save Lives As a Rescue from Bupivacaine Toxicity

by Robert C. Morell, MD

The intravascular injection or excessive absorption of bupivacaine can lead to cardiac depression, severe arrhythmias, and/or cardiac arrest, from which resuscitation may be difficult, prolonged, and even impossible. A past issue of this Newsletter highlighted the perspective of a patient and her anesthesiologist following a bupivacaine cardiac arrest after a popliteal nerve block.¹ The only reason that the patient survived to tell her story was the heroic and quick action of the anesthesiologist and the resuscitation team at utilizing an available cardiac operating room to institute cardiopulmonary bypass after conventional resuscitative measures were not successful. A new alternative therapy appears to exist. This new and important therapy was emphasized by one of our readers, Dr. Baumgarten, in a Letter to the Editor in the fall 2006 issue of this Newsletter. Several case reports (including recent personal communication) and research data consistently indicate that the intravenous administration of intralipid may facilitate and permit successful resuscitation from bupivacaine cardiotoxicity where conventional advanced cardiac life support protocols may fail. Weinberg and colleagues demonstrated that lipid infusion shifted the dose response to bupivacaine-induced asystole in rats and improved survival of dogs from bupivacaine cardiac toxicity.²³ As Dr. Baumgarten noted, Dr. Rosenblatt and colleagues published a case report of a successful resuscitation using a 20% lipid emulsion (intralipid), after a bupivacaine-induced cardiac arrest.³

Readers should note that other lipid containing medications have not demonstrated such efficacy, and one should be particularly careful not to assume that propofol would be a safe or effective alternative. Propofol has negative inotropic properties that may cause additional cardiac depression in the setting of bupivacaine-induced cardiac decompensation.³

Along with standard resuscitative drugs, it would seem wise to insure the rapid availability of intralipid where regional anesthesia is performed involving the administration of significant quantities of bupivacaine. Certainly, further study is warranted to answer a number of questions including the relationship of intralipid to local anesthetic toxicity caused by agents other than bupivacaine, the optimum dose of lipid emulsion, the potential advantages of lipid infusions vs. bolus dosing, and the optimal interval for redosing.

References


Propofol Safety Review

by Tricia A. Meyer, PharmD

On June 15, 2007, the FDA released a safety alert concerning reports over the past few months of cases of fever, chills, and body aches in several clusters of patients shortly after the administration of propofol. These new cases involved patients undergoing procedures in gastrointestinal suites. The FDA noted that the symptoms were similar to those reported when propofol was first introduced in the US. The postoperative infection in these early cases was attributed to lapses in aseptic technique with risk factors that included “batch” preparation of propofol syringes for use throughout the day, reuse of syringes or infusion pump lines on different patients, use of propofol syrings prepared more than 24 hours in advance, transfer of prepared syringes between operating rooms or facilities, failure to wear gloves during insertion of intravenous catheters, and failure to disinfect the stoppers of the propofol vials. It was also noted that 50-ml and 100-ml vials were used as multi-dose vials. The formulation at that time did not contain preservatives.

In the most recently reported cases, investigators also found use of the single-use vials for multiple patients. To date, tests performed on multiple units of propofol vials and lots by the FDA have not identified any units contaminated with bacteria or endotoxins. Testing of other possible sources such as the lidocaine coadministered with propofol and the instrumenta
tion sterilization systems have not identified any potentially causative agents.

Propofol is marketed as Diprivan® and is also available as a generic disodium edetate. Sodium metabisulfite or benzyl alcohol is added to the propofol to retard the rate of microbial growth. Even though the product contains preservatives, microbial growth is still possible and it is not an antimicrobially preserved product under USP standards. The emulsion is capable of supporting microbial growth in the event of contamination during administration due to the level of soybean oil and egg lecithin or egg yolk phospholipids contained in the product.

Recommendations and considerations by the FDA are:
• Both the vial and prefilled syringe formulation must be used on only 1 patient.
• Administration must commence immediately after the vial or syringe has been opened.
• In general anesthesia or procedural sedation: administration from a single vial or syringe must be completed within 6 hours of opening.
• In ICU sedation: propofol administered directly from a vial must be limited to only 1 patient, must commence immediately on opening the vial and must be completed within 12 hrs of opening the vial.

Package Insert Guidelines:
• Strict aseptic technique must always be used during handling, including hand washing prior to use.
• Propofol should be visually inspected prior to use for:
  – particulate matter
  – discoloration
  – evidence of separation of the phases of the emulsion.
• Do not use if contaminated.
• Prepare for use just prior to administration to each patient.
  - The vial rubber stopper should be disinfected using 70% isopropyl alcohol.
  - Discard unused portions within the required time limits.

The FDA urges individuals to report adverse events to the MedWatch Adverse Event Reporting Program.

Tricia A. Meyer, PharmD, MS, is Director of the Department of Pharmacy and Assistant Professor, Department of Anesthesiology, Scott and White Hospital, Texas A&M Health Science Center, Temple, TX.

General References
We thank Dr. Kempen for his letter highlighting the challenges of caring for patients with coronary drug-eluting stents (DES). We have discussed some of his questions and other issues related to perioperative management of patients with coronary stents with noted national experts in this area from cardiology. Below is a synopsis of the perspective of Cindy L. Grines, MD, FACC, and chair of the 2007 AHA/ACC/SCAI/ACS/ADA Science Advisory committee report on stent management, with her permission.

The purpose of the 2007 AHA/ACC/SCAI/ACS/ADA Science Advisory was to alert both patients and healthcare professionals that stent thrombosis (ST) is a serious medical issue. The guidelines for dual antiplatelet therapy have been changed to say emphatically that patients should receive a minimum of 12 months of dual antiplatelet therapy—and the minimum means, in many cases—physicians may want to go even further than that period of time. There are several patient subsets that would likely benefit much longer than 12 months. These include patients with acute coronary syndromes, long stents, multiple stents, overlapping stents, diabetes, renal failure, all of which are additional risk factors for stent thrombosis. In these patients, indefinite clopidogrel (Plavix) use may be recommended. The guidelines were co-written by the American Heart Association, the American College of Cardiology, as well as the American College of Physicians, Surgeons and Dentistry. The Science Advisory was an attempt to avoid the premature discontinuation of dual antiplatelet therapy; providers must realize stopping antiplatelet therapy in patients with DES without discussing it with their cardiologist could result in their patients having a fatal heart attack. The leading adverse event associated with early discontinuation of antiplatelet therapy is ST. Stent thrombosis occurs in up to 29% of patients who discontinue antiplatelet therapy early. The mortality rate in patients with ST ranges from 20-45%. Premature discontinuation of clopidogrel was associated with a 30-fold greater risk of ST, with >25% of patients who discontinued clopidogrel therapy within the first month suffering ST. In a study of 652 patients treated with sirolimus DES, premature discontinuation of clopidogrel was associated with a 30-fold greater risk of ST, with >25% of patients who discontinued clopidogrel therapy within the first month suffering ST. In a study of 500 patients who received DES after an acute myocardial infarction (MI), the death rate over the next 11 months was 7.5% for those who stopped taking their thienopyridine medication compared with 0.7% in those who had not stopped therapy.

With regard to antithrombin agents, if you look at the studies done on comparing aspirin with warfarin compared to aspirin with thienopyridine, the warfarin is a big loser. I mean, a 5-fold increased risk of ST; so in my mind, I’ve extrapolated other antithrombin agents to the warfarin situation. I tend to lean more in the camp of the antiplatelet agents. But again, I would rather just keep the patient on the aspirin and the clopidogrel because I’m very concerned about the abrupt stopping of the antiplatelet agent, and then at the same time you’re inciting an inflammatory and hypercoagulable state by performing surgery.

Discontinuation of dual antiplatelet therapy with clopidogrel and aspirin does occur because of cost, perceived risk of bleeding, patients and physicians unaware of the benefits and time of therapy required, and the discontinuation of these drugs by physicians, dentists, surgeons, or their staff before surgical procedures. We avoid elective surgery for more than 1 year after DES, more than 3 months after bare metal stents (BMS), as the risk of ST in both stent types remains high during the postoperative period. With more urgent procedures, if any provider—a physician, dentist, or surgeon—feels that stopping the antiplatelet medicines is absolutely necessary, then there should first be a consultation with the patient’s cardiologist. We have changed our practice to never allow the discontinuation of aspirin within the first year of a DES, and would probably extend that to longer duration in stents at high-risk of thrombosis. Importantly, clopidogrel should be restarted as soon as possible. In general, we see more surgeons willing to operate on dual antiplatelet therapies, or at least aspirin. If dual antiplatelet therapy has been discontinued for whatever reason, aspirin should be restarted immediately. Non-enteric coated aspirin (4 baby aspirins) may be given, and the patient should have antplatelet effects within 2 hours.

Drug-eluting stents prevent the tissue growth that causes restenosis and reduce the need for angioplasty or bypass surgery, but it should be noted that the reduced tissue growth means the stent is exposed to blood for a longer time; this increases the risk of clotting. Dual antiplatelet therapy is also important in patients receiving bare metal stents, but the risk of thrombosis in these procedures remains high for only 1 to 3 months. Consideration should be given to using a bare metal stent if patients are noncompliant with medications, or cannot afford to take clopidogrel for the full year, or if they absolutely cannot postpone an elective surgery.

Following is a summary of additional commentary from Deepak Bhatt, MD, FACC, associate director at the Cleveland Clinic Foundation and A. Michael Lincoff, MD, FACC, vice chair of Cardiovascular Medicine at the Cleveland Clinic Foundation.

Although there are no evidence-based data supporting the perioperative use of a short-acting glycoprotein (GP) IIb/IIIa platelet inhibitor ("bridging therapy"), there appears to be a role for this use. There are instances in which the only option perioperatively is fast-acting parenteral antiplatelet inhibition with a GP IIb/IIIa antagonist. There are patients for whom there is increased risk of stent thrombosis (ST); for example, a patient had a complex DES procedure a month ago, and then needed hip surgery after falling and breaking their hip, and the surgeon just absolutely refused to operate. This patient was brought into the hospital and started on a short-acting intravenous IIb/IIIa inhibitor. Though practically speaking it means bringing these patients in hospital, there are many patients for whom that extra 4-day hospitalization is worth it. One has to balance the risks and look at the consequences of thrombosis. In those instances, go ahead and proceed with bridging therapy. Another option is cangrelor, which is being tested in Phase III trials. An intravenous short-acting ADP receptor antagonist, cangrelor may conceptually be a future option in the perioperative period.

We are in agreement with Grines et al.: procedures should only be performed on patients with DES in institutions where 24-hour interventional cardiology coverage is present in the event that immediate percutaneous coronary intervention (PCI) is needed for perioperative ST. Almost all case reports to date have cited ST occurring postoperatively, most commonly in the Post Anesthesia Care Unit, and manifesting as a ST-elevation MI (STEMI). Thus, the importance of having immediate access to a coronary catheterization laboratory must be emphasized. McFadden et al. reported ST and STEMI occurring preoperatively after premature discontinuation of dual antiplatelet therapy, or aspirin, in cases where the patient had completed their prescribed course of clopidogrel. STent thrombosis and its sequelae occur acutely. Therefore, it would be unlikely that a patient with ST would be asymptomatic. However, in all cases, the anesthesiologist (or a member of the anesthesia care team) and surgeon should speak with the patient’s cardiologist in order to reach a consensus as to what the safest course of treatment may be.

We agree with Dr. Kempen that all patients with coronary stents undergo preoperative screening a week
Stents Require a Multidisciplinary Approach

“Stents,” From Preceding Page

before scheduled surgery to ensure that the appropriate care has been coordinated, dual antiplatelet therapy has been appropriately managed, and all appropriate parties are involved in this very complex care.

Ideally, patients who have clopidogrel and aspirin discontinued for more than 5 days prior to a procedure who are asymptomatic should have aspirin reinstituted for 3-5 days to achieve steady-state before proceeding with surgery. We have cancelled a number of cases over the past few months because of premature discontinuation of dual antiplatelet therapy. If aspirin has been discontinued for 3-5 days, we have given 325 mg of non-enteric coated aspirin, and proceeded with surgery later that day to allow platelet inhibition to take effect. Studies have shown that 160 mg of aspirin will inhibit platelet function. The same effect can be achieved with aspirin 75-81 mg over 3-5 days.

We also agree with Dr. Grines that aspirin should never be discontinued in the perioperative period. However, in cases where the surgeon absolutely refuses to operate with the patient on aspirin, then it is imperative that communication occur between the patient’s cardiologist, surgeon, and anesthesia provider, and the risks of ST versus major bleeding be carefully weighed. Again, the risk of ST is 29%, and the mortality rate from ST ranges from 20-45%. The surgeon must be made acutely aware of this when considering whether to operate while the patient remains on aspirin.

The use of platelet infusions intraoperatively should be avoided except in the instance where there is life-threatening bleeding. There are certain states (acute MI, unstable angina, trauma, surgery), in which platelet aggregation and activity are enhanced even without an increase in platelet counts. This phenomenon occurs as a consequence of sympathetic activation and cytokine release. Inflammatory activation from endothelial damage, as in PCI and surgery, exacerbates the prothrombotic state, making the patient highly susceptible for thromboembolic events. Autopsy results have shown this mechanism is responsible for at least half of all perioperative infarctions. Theoretically, apheresis platelets administered to patients with stents who have serum levels of clopidogrel and aspirin may not develop antiplatelet effects to provide adequate protection from ST for hours to days. Also, activation of the transfused platelets may occur, further increasing the risk of ST, MI, and death. Direct and autologous donation of any blood component is being discouraged by blood banks at many institutions, including our own, because of increased cost and no proven safety benefit over homologous donation.

The controversy and concern surrounding coronary artery stents, especially in the case of DES, illustrate the importance of instituting a multidisciplinary approach in the care of these patients.

References

13. Poldermans D, Schouten O, Vidakovic R, et al. A clinical randomized trial to evaluate the safety of a noninvasive approach in high-risk patients undergoing major vascu-
Dear SIRS:

I am a CRNA with 13 years of experience. I never had a problem with a pulse oximeter until I encountered the Datex-Ohmeda Cardiocap 5. I was accustomed to a pulse oximeter alarming loudly anytime it was low or not on the patient. I have had 2 incidences in the last 2 years where the ECG beeped when the pulse oximeter was off, such that one might have thought the pulse oximeter reading was OK when not facing the monitor. While another patient was under monitored anesthesia care, the pulse oximeter initially was working, but ceased to work 3 minutes into the case. Once again the ECG beeped, but without the annoyingly loud alarm from the pulse oximeter; there was a single, short beep about every minute. The probe was not illuminated and had to be switched.

I think it is very dangerous to allow a monitor not to alarm if it is not working. I have worked with many monitors over the course of my career, and feel this is taking a step backward if the software cannot be adjusted. I appreciate any information. Thanks.

Kathleen Piotrowski, MSN, CRNA
Cuyahoga Falls, Ohio

In Response:

Thank you for the opportunity to respond. I’ve reviewed this with our design center in Helsinki, Finland, and have observed the monitor’s behavior in order to provide the most thorough response. First, I would like to provide you with my name and contact information and assure you that you are welcome to contact me directly at any time.

The Cardiocap 5 monitor is designed with a 3-tiered approach to alarm logic where advisory alarms are displayed in white with a single beep, serious alarms are in yellow and provide 3 beeps, and life-threatening alarms display in red and give 5 beeps.

In the situation you describe, I believe the monitor performed according to the specifications. The Cardiocap 5 monitor, by default, sources the heart rate automatically looking for ECG, Pleth, or Invasive Pressure for an available heart rate. When the heart rate is sourced from the ECG, you will hear the beat sound also sourced from the ECG, and the heart rate will be displayed in the same color as the ECG waveform and numeric. If the heart rate is sourced from the Pleth, the beat sound will be sourced from Pleth and will provide an audible tone different from the ECG tone. The heart rate will be displayed in the same color as the Pleth waveform and numeric.

If the current source becomes unavailable, for example the SpO2 probe falls off the patient’s finger, the monitor will automatically search for another heart rate source (either ECG or invasive pressure). When the monitor switches to another source, ECG for example, the tone of the beat sound will change, the numeric on the display will change to match the color and value coming from the ECG, and a white advisory alarm will be displayed noting “SpO2 probe off” or “No SpO2 pulse,” whichever is applicable. After several seconds, the white advisory alarm will escalate to a yellow serious alarm and provide 3 beeps. The yellow alarm remains active until it is either acknowledged, or the alarm event is corrected (i.e., probe returned to the patient’s finger).

Based on the information we have available, I would speculate that the monitor is performing according to specifications. I would be more than happy to discuss this situation further and to engage our Field Service team to complete a more thorough investigation of the monitor to test the performance. Please feel free to contact me at the telephone or email address listed above.

Best regards,
Gina Petry
Product Manager—Perioperative
GE Healthcare Technologies
Madison, Wisconsin

Editor’s Question:

This sounds like the identical mechanism on our Datex-Ohmeda S/5 monitoring system, and it has fooled some of our own clinicians as well. One option your response did not include is to select the heart rate source manually, instead of automatically. At least in the S/5, this would stop the tone, and cause the clinician to look upwards. Is that possible in the Cardiocap 5?

Michael A. Olympio, MD

In Response:

You are correct—it should be the same mechanism as your S/5 monitor. The logic is almost identical throughout the Datex-Ohmeda family of monitors. You can set the heart rate source manually to Pleth, for example. This setting cannot be saved as a default, however. The loss of a pulse from Pleth will result in the loss of the beat sound and a yellow alarm.

Gina Petry
Anesthesia Patient Safety Foundation

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(Texas Society of Anesthesiologists)
In memory of Dr. Oneita M. Hedgecock (Texas Society of Anesthesiologists)
In memory of Laurie A. Noll, MD
(In The Coursin family)
In memory of Bonnie J. Slarsky
(In Texas Society of Anesthesiologists)
In memory of Maurice Chait, MD
(In The Coursin family)
In memory of Dr. Marc Balin (anonymous)

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Wrap Delays Detection of Disconnect

To the Editor:

Accidental disconnection of components of the breathing system during general anesthesia with an endotracheal tube persists as an occasional problem. It seems more likely in face surgery where the tube is in the midst of an active surgical field and not accessible by the anesthesiologist. While the potential for great danger during controlled ventilation or the entrainment of room air and/or rebreathing during spontaneous ventilation still exists, modern electronic monitoring will almost always sound alarms and convey information that leads to rapid discovery and re-connection of the wayward breathing system components. We report an unusual case of breathing system disruption with a misleading presentation in that the capnogram appeared normal and there was no gas irregularity.

A 50-year-old female was undergoing a facelift. After routine anesthesia induction and intubation with a standard 7.5 mm endotracheal tube, the operating room (OR) table was turned 180°. The breathing circuit elbow piece was removed and replaced with a straight connector between the tube adapter and the circuit Y-piece. All connections were snugly pushed together. The patient’s face, neck, endotracheal tube, and distal breathing circuit were prepped into the surgical field. A clear plastic 45 × 60 cm Steri-Drape™ 1010 (3M, Minneapolis, MN) was spirally wrapped around the parts of the endotracheal tube, connector, sample tubing, and circuit that were in the surgical field (see photo).

After approximately 1 hour of surgery, with the patient on controlled ventilation, desflurane at 1 MAC in 1 L/min oxygen, the reservoir bag of the Dräger Apollo anesthesia machine was noted to be completely empty, and, at the same time, the “low volume” alarm of the machine sounded. The capnogram showed a pattern characteristic of spontaneous breathing, with the waveform returning to baseline during each breath. There was no decrease in FiO₂. Oxygen flow was increased from 1 L/min to 10 L/min with no filling of the bag or change in the alarm. Careful inspection revealed that the 15 mm connector had come out of the end of the endotracheal tube. The surgeon quickly grasped the enfolding plastic drape and pushed the enclosed connector back into the endotracheal tube.

Of particular interest in this incident is the fact that the plastic drape wrapped around both the distal circuit tubing and the endotracheal tube prevented significant entrainment of room air and kept the fresh gas flow from completely dissipating away from the patient. There was no CO₂ rebreathing under the drapes as is often seen with disconnects in facial cases. The discontinuity did cause loss of measured expired volume and some pressure, which activated an alarm. The capnograph alarm was not triggered because the capnogram persisted.

Obviously it was necessary and desirable to replace the 15 mm connector into the endotracheal tube, and this was easily accomplished. The unusual placement of the circumferential plastic drape combined with spontaneous ventilation created a unique circumstance that in one way reduced patient danger (fresh gas remained available), but in other ways increased danger in that the characteristic disappearance of the capnogram did not occur with this disconnect.

Anesthesiologists and nurse anesthetists should have heightened awareness of breathing system continuity during major facial surgery and of the potential unusual implications of encasing all the connections in a wrap of sterile plastic drape.

Gregory Rose, MD  
John Eichhorn, MD  
Lexington, KY

Photograph of extensive wrapping of tracheal tube and connection, which delayed detection of the disconnect.
An invited conference sponsored by Cardinal Health Center for Safety and Clinical Excellence was held June 7-8 in San Diego, to review and summarize expert opinion on tight glycemic control (TGC) for acute hospitalized patients. Speakers included Simon Finfer, MBBS (Nice-SUGAR trial, Sydney, Australia) and Philippe Devoe, MD (VISEP/Glucontrol trials, Belgium), with another 45 participants from across the United States and Canada. Thought leaders represented the disciplines of anesthesiology, intensive care, endocrinology, surgery, hospitalist medicine, medical genetics, nutrition, nursing, pharmacy, bio-statistics, and healthcare biotechnology.

The central question, which anchored the conference, was whether ICU patients benefit most from “intensive” or “tight” glycemic control (usually defined as blood glucose in the range of 80-110 mg/dL) or “tighter” control (typically translated as blood glucose in the range of 110-150 mg/dL).

In the meantime, conference presentations yielded these highlights:

- Insulin is the most common drug reported as a medication error to the U.S. Pharmacopeia. Moreover, the error harm rate (categories E, F, H, I) = 9.3%.
- Data from hospitals using “smart” IV pumps documented a high frequency of averted insulin dosing errors in addition to high variability in concentrations and mixed use of weight-based and nonweight-based dosing units.
- The landmark ICU study by Dr. Greet Van den Berghe, Catholic University of Leuven in Belgium, targeted blood glucose of 80-110 mg/dL in the treatment group. She noted decreased mortality and morbidity (less renal failure, surgical wound infections, blood transfusions, ICU ventilator days, etc.) in surgical ICU patients.
- Two recent European glucose control studies—VISEP (488 patients in 17 German Centers) and GluControl (1,101 randomized patients across 21 ICU units in 7 European countries)—were both stopped due to unacceptably high rates of hypoglycemia and lack of beneficial effect.
- The on-going NICE-Sugar open-label, randomized, stratified study in 25 Australian, 19 Canadian, and 2 American hospitals has a planned enrollment of 7,000 patients! This study will compare 2 target ranges for blood glucose (81-108 mg/dL vs. <180 mg/dL). Conference participants expect this to be the pivotal outcome investigation—and one that will likely define the target glucose for future ICU patients. The study is well on its way to 4,000 enrolled patients.
- Current data are insufficient to mandate TGC for patients in the operating room. A recent randomized study in cardiac surgery patients (Ann Int Med 2007;46:235) found no difference in ICU or hospital LOS despite TGC throughout the operative period.
- It is important to note that perioperative hyperglycemia occurring in “non-diabetics” may actually indicate undiagnosed Type II diabetes. Providers should consider hemoglobin A1c determinations in these patients to direct optimal metabolic management.

Additional insights based on the collective experience of participants included:

- Prevalence of diabetes is increasing rapidly.
- TGC requires an interdisciplinary team approach, a culture of safety, and a focus on professional education. Moreover, benchmarks to evaluate effectiveness are needed.
- Current “paper” ICU protocols for TGC achieve target glucose concentrations about 40% of the time.
- Published TGC protocols differ significantly in insulin dosing recommendations.
- Computerized protocols improve the efficacy to 60%, and have the additional benefit of decreasing hypoglycemic episodes.
- bedside glucometers rely on a number of different chemical reagents, and users should be aware of potential confounding variables—even including parameters like hematocrit, Pao2, and so forth. Interfering substances can generate seriously erroneous meter readings.
- Total nursing time for each point-of-care glucose determination varies from 3.5-9 min (median time = 4.7 min). The aggregate time and RN workload of applying TGC is substantial.
- Current continuous glucose monitors (CGM) measure glucose in the interstitial fluid, which lags behind blood concentrations by 3-10 min. Nonetheless, CGM appears to facilitate smoother, timelier titration of insulin infusions, and patients reach target glucose values more quickly. Coordination of this technology with a computerized protocol minimizes the incidence of hypoglycemia.
- Clinical experience suggests minimal risk of a single episode of hypoglycemia (FBS ≤ 40 mg/dL), if diagnosed and managed in a timely fashion.
- Transitions from ICUs to Medical/Surgical care units and from IV to oral feedings are especially problematic in maintaining TGC.
- Intensive insulin therapy and TGC is cost effective, but may be population and protocol sensitive.

The optimal glucose threshold for TGC in ICU patients remains under investigation, and anesthesia providers debate how these principles should apply to patients in the operating room. More data are needed. An independent APSF poll regarding triggers for initiation of insulin therapy is also presented below.

Richard C. Prielipp, MD, MBA, FCCM
Professor and Chair of Anesthesiology
University of Minnesota
Minneapolis, MN

Carol S. Manchester, MSN, APRN, BC-ADM, CDE
Diabetic Clinical Nurse Specialist
UMMC-Fairview
Minneapolis, MN

Timothy W Vanderveen, PharmD, MS
Vice President
Cardinal Health Center for Safety and Clinical Excellence
San Diego, CA

APSF Poll Question:

During general anesthesia in the OR, what is your current upper limit of glucose that triggers (intravenous bolus or infusion) insulin therapy?

<table>
<thead>
<tr>
<th>Upper limit of glucose</th>
<th>that triggers insulin therapy (Percent)</th>
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<tr>
<td>110 mg/dL</td>
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Results of an independent APSF Poll regarding readers' triggers for initiation of insulin therapy.
Letters to the Editor

Are Patients With Obstructive Sleep Apnea Safer at Home?

To the Editor:

I would like to respond to Dr. Weinger’s lead article, published in the 2006-2007 winter issue of the APSF Newsletter, which discusses the dangers of postoperative opioids. My particular interest is in regard to postoperative pain control for the obstructive sleep apnea (OSA) population. It seems much of the data we have related to this safety issue are based on the use of parenteral opioids postoperatively. Specifically, the article mentions Dr. Lofsky’s report on the effect opioids have on the neural efferent system, which is said to be responsible for depression of upper airway patency. The opioid delivery of reference in this discussion was patient-controlled analgesia (PCA). My questions are 1) Has our specialty determined the safety of oral opioid-based analgesics for the ambulatory patient with OSA, and 2) What is the impact of the provision of parenteral opioids as part of the general anesthetic or immediate postoperative pain relief in the OSA patient being discharged to home? I ask these questions in light of the fact that there is an alteration in perioperative sleep that is pronounced in the OSA population and observed in the 24-hour postoperative period. This alteration, which is partly due to the exposure to anesthetics and analgesics, is worsened by the effect of rapid eye movement (REM) sleep rebound and can create a tenuous postoperative period while the patient is home unmonitored.

Drs. Weinger and Morell did provide their personal suggestion that it is likely safer for OSA patients to be discharged home on oral analgesics rather than be admitted and receive parenteral opioids. I can easily agree with this due to all of the potential life-threatening risks of PCA or intermittently dosed opioids when monitoring is substan-

See “OSA,” Next Page

Pipeline Pressure Primer

Dear Q&A,

I have always thought that, in a hospital central gas supply system, the oxygen pipeline should operate at a slightly higher pressure than the air and nitrous oxide lines in order to mitigate the effects of a possible cross connection. I am working at a new hospital and the pipeline person is asking for documentation. Is this just an informal safety measure or is it mandated by code? Thanks for your help.

Samuel Tirer, MD

Dear Dr. Tirer,

The National Fire Protection Association (NFPA) 99 Standard for Health Care Facilities, 2005 Edition, states, “Piping systems, with the exception of nitrogen systems, shall be capable of maintaining 50-55 psig (345-380 kPa gauge) to all outlets at the maximum flow rate.” Reading the NFPA is like reading IRS 1040 instructions, so perhaps there is a qualifier (regarding different oxygen pressure) somewhere else in the document that I missed in my scan. But I have never heard of different wall pressure for O2.

I believe there is not a standard driving this, but a local preference. I have heard of hospitals setting oxygen at the top of the allowable range, such that if a check valve failed somewhere in the system, the oxygen would prevent potentially hypoxic scenarios.

Using the highest pressure for oxygen in a pipeline system is a very old practice for 2 reasons:

1) It allows one to certify that day-to-day running of a mixed pipeline system is “safe” without using an oxygen analyzer on each outlet. In many parts of the world this is the routine safety check. Where gas-mixing devices are used, as with nitrous/oxygen for analgesia, it could be part of the basic design.

2) If there is any sort of link between 2 lines, better that oxygen dilutes the other. I think you’ll find this rule originates in old British standard safe practice that preceded people writing specs.

The APSF Committee on Technology

Dear Dr. Tirer,

The pressure ranges listed in Table 5.1.11 from NFPA 99-2005 for medical air, oxygen, nitrous oxide, helium, and carbon dioxide are the same (50-55 psi). I can find nothing that says one should be greater than the other to avoid cross connections. NFPA 99 also requires stringent initial testing, and specifies testing that is necessary after working on the system.

There are 2 tests acceptable to NFPA to initially verify that there are no cross connections in a system. One is called the Individual Pressurization Test, whereby the system being checked shall be pressurized to 50 psi, while all other disconnected, atmospheric lines are simultaneously checked to determine that test gas is being dispensed only from the outlets/inlets of the piping system being tested.

What some of your contacts may be referring to is the other acceptable method, or Pressure Differential Test. This test does require that the oxygen system and the medical air system (and others) be pressurized and maintained to different, specified psi (50 psi, 60 psi, respectively for oxygen and medical air), after which a pressure test is made at every outlet to check for cross-connections.

NFPA does NOT say that the system needs to be operated during normal use with those pressures—rather only for the verification test.

Mike Mahan, PE
North Carolina Baptist Hospital Engineering
Winston-Salem, NC
Letters to the Editor, continued

"OSA," From Preceding Page

It is certainly a worthwhile goal to care for patients in the perioperative setting, but until these monitors become widely available on the hospital wards, we must be trained to recognize pending opioid toxicity. The APSF is instituting a new standard of care. This would require billions of dollars of equipment that the article acknowledges as being “plagued by false positive . . . and false negative . . . alarms” and thousands of new personnel to monitor the equipment and monitors.

Michelle Laurence, MD
Chicago, Illinois

References

Post-Op Hypoxia Multifactorial and Should Be Treated With Supplemental Oxygen

To the Editor:

In the 2006-07 winter issue of the APSF Newsletter, the suggestion was made that pulse oximetry might be an acceptable monitor to assess and avoid opioid overdose—providing patients breathe only room air. We believe that all post-anesthesia care unit (PACU) patients and those given intravenous and neuraxial opioids should initially be given supplemental oxygen regardless of the monitor used. Hypoxia in the postoperative period is often multifactorial in nature (residual anesthetics, splinting, atelectasis, obesity, fluid overload, opioid medication). Patients can be in pain without significant respiratory depression, yet still be hypoxic. Supplemental oxygen can correct this hypoxia and possibly avoid a catastrophic event. To withhold pain medication from patients because their room air saturations are low would only serve to increase complications relating to the stress response. Patients on oxygen receiving opioids will usually have elevated pCO\textsubscript{2}; however, mild degrees of hypercapnia are well tolerated. It would be ideal to reliably monitor oxygen saturation and expired CO\textsubscript{2} in all patients, but until these monitors become widely available on the hospital wards, we must continue to rely on healthcare providers who are trained to recognize pending opioid toxicity.

Merlin D. Larson, MD
Andrew Itkin, MD
John W. Severinghaus, MD
San Francisco, CA

Reader Has Low Tolerance for Zero Tolerance

To the Editor:

I read with amazement the article “Dangers of Postoperative Opioids” (Vol 21, #4). The article states, “We advocate the use of continuous monitoring of oxygenation (generally pulse oximetry) and of ventilation in non-ventilated patients receiving PCA, neuraxial opioids, or serial doses of parenteral opioids.” Basically the APSF is instituting a new standard of care. This would require billions of dollars of equipment that the article acknowledges as being “plagued by false positive . . . and false negative . . . alarms” and thousands of new personnel to monitor the equipment and monitors.

Robert F. LaPorta, PhD, MD
Glen Cove, NY

Innovative Technology and Pharmaceuticals (ITP)

This column is dedicated to providing our readers with information regarding new and innovative technological or pharmaceutical developments that may directly or indirectly impact patient safety. By virtue of the unique and long-standing relationship between the APSF and industry, it is inevitable that we will, from time to time, discuss or review products, devices, or pharmaceuticals that may be manufactured, sold, or distributed by corporations or entities that have or continue to supply financial or in-kind support to the APSF. We will strive to disclose those relationships as appropriate.

by Joel Saltzman, MD

Establishing vascular access for administration of medications, or to obtain blood for laboratory tests, is stressful for the patient and can be stressful for the practitioner; limiting the number of sticks is beneficial to both. While most practitioners are adept at venipuncture, patients with extremes in age, habits, co-morbidities, and multiple punctures present a challenge to even the most experienced. Not uncommonly, the anesthesia team is called upon to obtain venous access after multiple attempts by others in the hospital. By this time, we may be presented with a patient who is stressed, potentially dehydrated, sore, and angry, and with concerned family members. A new technology has been able to “shine a light” on this problem, a green light.

Experienced practitioners have long been able to access the vascular system provided they can see or feel the vessel, or to attempt a blind stick based on anatomical landmarks. Multiple technologies have tried to assist the practitioner to visualize the target. Ultrasound has assisted, but requires the use of gels and a significant learning curve with specialized training. Transillumination with high-intensity light involves direct patient contact, elimination of ambient light, and may result in heating at the site. One infrared device, VeinViewer by Luminetx, uses near-infrared light to allow the practitioner to visualize the vessel without direct contact, gels, heat, or advanced training. This device projects the image of the vasculature directly onto the patient’s skin, focusing attention on the patient rather than the monitor, and allows both hands to be free to perform the procedure. The practitioner may also visualize arteries as pulsatile structures if they are within the 6-8 mm imaging range of depth.

The near infrared light source is used to differentiate red blood cells from surrounding tissues. The light is reflected back from the surface tissue, but not reflected from the blood in the vessels. The infrared light photons are received by a detector located in the digital video camera; a computer digitizes these photons, produces an image and projects it onto the patient’s skin. The image is displayed in real-time, and veins appear as a black road map on a green field. The non-ionizing energy emitted from the LED light sources is many magnitudes under previously established safety limits.

Whenever a clinician or an institution considers new equipment, safety and cost must be part of the equation. Although the machine is somewhat large, it is self-contained, well-balanced, and relatively easy to move.

This device may help alleviate trips to the operating room for central venous access—offsetting costs and risks that may be deferred by placement of a PICC line or simple peripheral vascular access. Anesthesia, Emergency Room, Radiology, Critical Care, phlebotomists, PICC teams, and others can all utilize this technology throughout the hospital. There is also the potential to update and advance the capabilities of the equipment with software updates imported into the machine via the 2 USB ports. In sum, the VeinViewer can potentially improve patient safety by facilitating intravenous access as an alternative to central venous cannulation, while also reducing patient discomfort.

Dr. Saltzman is Chief of Anesthesiology at Le Bonheur Children’s Medical Center, Memphis, TN.

DISCLOSURES: Luminetx Corporation is a financial contributor to the APSF. Dr. Saltzman has no financial relationship to Luminetx.
Inside This Issue

▲ More About Drug-Eluting Coronary Stents and Late Thrombosis
▲ Perils of Hypotension in the Beach Chair Position
▲ Review of Maternal Arrests
▲ Case Report and Letters to the Editor
Occasionally, ambulatory surgical patients present without an escort for their procedure. This creates a dilemma for caregivers, and allowing patients to drive may have an impact on their safety. The Canadian Medical Protective Association is a mutual defense organization for 95% of Canadian physicians. The national database is a unique and extensive repository of medico-legal data. We scanned this database for malpractice patients who were discharged after an ambulatory surgery procedure and allowed to drive home with a poor outcome. From this database, two malpractice cases of patients who were discharged without an escort after an ambulatory surgical procedure were reported. Both had a car accident and sustained serious injuries. Based on this we do not recommend discharge without an escort after general anesthesia, regional anesthesia, monitored anesthesia or sedation. Driving after ambulatory surgery cannot be considered safe and caregivers need to verify a safe ride home.

(Anesth Analg 2008;106:817–20)

Ambulatory surgery and anesthesia have a remarkable safety record. This success may be due to careful preoperative selection of appropriate patients and thorough evaluation of surgical procedures regarding their suitability as ambulatory surgical procedures.1,2 Modern short-acting anesthetics with a rapid recovery have also contributed to this success. In many countries, anesthetic and surgical associations have developed clear guidelines aiding the selection of patients and procedures.3–5 Appropriate postoperative care has also evolved to maintain this high standard of safety.6 With supporting evidence from audits and research, the limits of what is considered possible and appropriate on an outpatient basis have been extended considerably over recent years.1,2,7 Financial factors and expectations from patients and other doctors may put physicians under pressure to extend these boundaries further.

One study reported that 0.2% of ambulatory surgical patients do not have an escort.8 Another survey indicated that 11% of anesthesiologists would be willing to anesthetize patients without an escort.9 The Canadian Medical Protective Association (CMPA) is a mutual defense organization for physicians who practice in Canada. It is funded and operated on a not-for-profit basis for physicians, by physicians, and its membership of more than 66,000 comprises about 95% of Canadian physicians. The CMPA is uniquely positioned to see practice pitfalls that can result in litigation. The national database is a unique and extensive repository of medico-legal data and information. In a 10-yr case review of litigations in ambulatory surgery, three malpractice cases of car accidents after ambulatory surgery were identified in patients without an escort. One is a case of intranasal midazolam for sedation. This case was settled out of court and did not go to trial. The actual arrangements are not within the public domain. From this national database, we report two malpractice cases of patients who were discharged without an escort after an ambulatory surgical procedure and both had car accidents.

MALPRACTICE CASES

First Malpractice Case

A 44-yr-old man sustained an injury to his right knee. He was a healthy ASA I patient with no medical history, no mental illness, no history of alcohol use or history of a motor vehicle accident. He did have a history of occasional use of marijuana. He was referred to an orthopedic surgeon who diagnosed a tear of the lateral meniscus and recommended an arthroscopy. During the initial consultation, the surgeon informed the patient that he would have to arrange transportation home on the day of the procedure, and that an adult would be required to accompany him home.

On the day of the procedure, the patient presented to the ambulatory surgery unit without an escort, claiming that a friend who had agreed to accompany him was now unavailable. The nursing staff reaffirmed the need for a safe means of transportation home but the patient was anxious to proceed with surgery. The orthopedic surgeon and the anesthesiologist were informed and both physicians decided
that the procedure could be performed under local anesthesia. The patient received an injection of 20 mL lidocaine 1% and 20 mL bupivacaine 0.5% as a local anesthetic. Intraoperatively, he became agitated and required sedation. He was given midazolam 2 mg IV and fentanyl 50 μg IV as well as increments of propofol to a total dose of 50 mg IV. He remained conscious and alert at all times during the procedure.

In the postanesthesia care unit (PACU), he was able to walk and eat and before he was allowed to leave. While eating himself home, the patient had an accident by driving off the road. This accident left him quadriplegic. In court, the patient stated that he stopped off the road to doze for a short period of time and resumed driving shortly before the accident. No other persons or vehicles were involved in the accident. No evidence of alcohol or drug use was noted by the police arriving at the scene. The anesthesiologist was found by the court to be negligent in allowing the patient to drive home after sedation and the orthopedic surgeon was not found guilty.

Second Malpractice Case

A 35-yr-old woman was scheduled to undergo dilation and curettage for an early pregnancy under local anesthesia by a gynecologist. She was a healthy ASA 1 patient with no medical history, no mental illness, no history of alcohol use or history of a motor vehicle accident. On the day of surgery, the prearranged babysitter did not arrive to take care of the young children. As a result, the husband had to stay home to attend to the children. The patient arrived for her ambulatory surgery by herself. She was upset and crying. The gynecologist ordered oral lorazepam 1 mg as a premedication, which was given by the preoperative nurse.

The patient underwent a dilation and curettage under local anesthesia with no other medication. During her stay in the PACU, she was offered a ride home by the PACU nurse who happened to know her personally. The patient refused and drove home alone. Subsequently, she had a car accident with serious injury. She sued the gynecologist and the preoperative nurse who gave her the premedication, not the PACU nurse. Both the gynecologist and the preoperative nurse were found to be negligent for allowing the patient to drive herself home after sedation. A second car was involved in the accident and the injured parties in the second car also sued and were compensated.

DISCUSSION

We describe two malpractice cases in which patients were discharged without an escort after an ambulatory surgical procedure and both had a car accident. The practice of discharging patients without an escort is rare in ambulatory surgery units but does have an impact on patient safety. A study in our institution showed that 0.2% of patients presented without an escort on the day of the procedure.8 Two groups of patients were identified. The first group (n = 24) was comprised of patients who had no escort. The second, a far larger group (n = 36) was comprised of patients who claimed to have an escort and only after the procedure did it become clear that that was not the case.

In a survey of anesthesiologists in Canada, 11% were willing to anesthetize patients who did not have an escort.9 The low rate of major complications after ambulatory procedures is likely to have influenced that decision, but the finding is nevertheless unexpected.

Discharge without an escort is contrary to guidelines issued by professional bodies like the American Society for Anesthesiologists, the Canadian Anesthesiologists’ Society, the Association of Anesthetists of Great Britain and the Australian Day Surgery Council.3–6 These recommendations are supported by the evidence demonstrating that psychomotor impairment and cognitive deficits are common in the postoperative period.10–13 Recovery from ambulatory anesthesia can be divided into three stages. Early recovery refers to the period of awakening and return of vital reflexes. Intermediate recovery refers to the time until home readiness. Criteria for discharge include stable vital signs and the ability to walk.14 Late recovery occurs at home and entails full physiological and psychological recovery. In clinical studies, late phase recovery can be assessed with psychological or psychomotor tests.14 This means that most patients are not fully recovered and back to their normal functional status by the time they meet discharge criteria, even after very short procedures.15–17 Home readiness is not equivalent to street fitness. Furthermore, these national guidelines made no distinctions between sedation, regional anesthesia, and general anesthesia. Patients require escorts to go home regardless of the type of anesthesia.

Driving After Ambulatory Surgery

A major concern for patients without escort is that they will drive home after ambulatory surgery. The Canadian Anesthesiologists’ Society, the Association of Anesthetists of Great Britain, and the Australian Day Surgery Council recommend patients not drive for 24 h, while the American Society for Anesthesiologists guidelines do not comment on the issue of driving. These guidelines are mostly based on older studies investigating longer acting drugs that are no longer commonly used in ambulatory anesthesia.18,19 Several studies investigated the effects of modern, short-acting anesthetic.12,15,20 Thapar et al.15 found significant initial impairment of psychomotor function with various combinations of commonly used sedative drugs (propofol, midazolam, fentanyl). Combinations that included midazolam had the most long-lasting effects, but after 3 h none of the regimens showed any relevant effect.

Sinclair et al.13 were unable to demonstrate significant effects of a balanced general anesthetic, propofol, fentanyl, desflurane, and nitrous oxide on performance in a driving simulator 2 to 24 h after anesthesia. The study was done in volunteers who did not have surgery and did not receive any analgesics or experience pain.

Chung et al.21 compared the driving performance (in a simulator) in patients who had their surgery performed under general anesthesia with healthy, nonanesthetized controls. Under these more realistic circumstances, simulated driving in patients was impaired both pre- and postoperatively. Performance was worst 2 h postoperatively, a critical time, as many patients meet discharge criteria within 2 to 3 h. Within 24 h, driving simulation performance had returned to

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**ANESTHESIA & ANALGESIA**

Case Report

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normal. It is important to note that patients were also impaired preoperatively versus control. This may mean that the stress of surgery or possible lack of sleep may have an influence on driving performance in addition to the effects of the anesthetic. The results of this trial support the current recommendations not to drive for 24 h after ambulatory surgery. The fact that performance levels were at their worst around the time of discharge supports the recommendation to send patients home accompanied by an escort who will drive for them.

Surgery may also impair the ability of the patient to drive. In a study of patients undergoing total knee arthroplasty for osteoarthritis, the brake response time returned to normal at 3 wk after surgery. Most patients undergoing total knee arthroplasty are recommended to return to driving 6 wk after surgery. One of our patients had right knee arthroscopy. The surgery itself, even without the use of sedation, may have affected the patient’s ability to properly use the brake pedal. The degree of functional recovery in patients after surgery may be related to the specific type of surgery as well. This may have a direct influence on the daily function and recovery of the patients in addition to the residual effects of anesthetics. Physical impairment due to pain or residual motor block after local or regional anesthesia will further aggravate this and may contribute to difficulties in performing activities of daily living. Therefore, patients are advised not to drive or operate machinery for a period of time after surgery.

Patient Compliance with Postoperative Instructions

Two surveys assessed patient compliance with postoperative instructions. Correa et al. interviewed 750 patients via a telephone call 24 h after the operation. All had been advised not to drive for 24 h and to have a companion stay with them overnight. Four percent of patients did drive within the 24-h period and 4% of patients were alone overnight despite being escorted home. Cheng et al. surveyed 240 ambulatory patients and found that 1.3% spent the night alone and 4.1% drove within 24 h. These two studies suggest that patient compliance has improved, as previous studies showed that up to 31% went home without an escort and up to 73% of patients drove within 24 h. This encouraging result may reflect the success of improved verbal and written postoperative instructions. Nonetheless, significant numbers of patients still do not follow postoperative instructions. In both studies, 4% of patients drove within 24 h.

While ambulatory surgical units can verify the presence of an escort at discharge, it is impossible to ensure that someone will stay with the patient at home during the night or that recommendations regarding driving are adhered to. Hence, it is important that patients have a clear understanding what the potential hazards are and why they are asked to comply with the recommendations.

Recommendations

These two malpractice cases from the CMPA national database illustrate the potential hazards associated with impaired mental, and possibly physical disability after surgery and anesthesia or sedation.

Many health care professionals may not have realized the potentially disastrous consequences of patients returning home unaccompanied after surgery. Anesthesiologists may wrongly believe that the short-acting anesthetics will have worn off by the time of the discharge or the amount of the sedation is too small to impact the psychomotor function of the patients. Education of surgeons, anesthesiologists and nurses regarding the importance of escorts is essential to the success of the discharge policy.

If no known escort is available before surgery, the elective procedure should be cancelled or patient should be admitted overnight. In the case of an escort not being available after anesthesia is given, elective hospital admission can be arranged. Alternately, volunteers or individuals paid to accompany these patients home or arranged cab rides can be made. It is the obligation of the caregiver not to allow these patients to drive home after anesthesia or sedation. These patients should be escorted to the cabs by a nurse to ensure that they do not drive home themselves. In addition to the cab ride, we recommend that patients sign a waiver of discharge against medical advice. This way, written information is given to the patient explaining why discharge is potentially hazardous and what consequences may arise from leaving without an escort. This is in addition to the written postoperative instructions specific to their procedure that patients receive upon discharge. These instructions should explain what symptoms can be expected after their particular procedure and how to respond should complications occur.

The discharge of patients without an escort after ambulatory surgery is an important issue. Complications can arise after surgery under general anesthesia, regional anesthesia, monitored anesthesia care, or sedation. Discharge without an escort after general anesthesia, regional anesthesia, monitored anesthesia, or sedation is not recommended. From the standpoint of anesthesia societies and the medico-legal system, patients should not receive any anesthesia or sedation and then be allowed to drive home. It is the obligation of the caregiver either to cancel the case, admit the patient to hospital or to arrange for a ride home. Driving after ambulatory surgery cannot be considered safe. As part of quality improvement measures, it is important for hospitals to implement policies that aim to avoid discharge with no escort. This serves to enhance patient safety and ensures that we can provide the best care possible.

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REFERENCES


Anaesthesia for the patient with dementia undergoing outpatient surgery
Kamilia S. Funder, Jacob Steinmetz and Lars S. Rasmussen

Department of Anaesthesia, Centre of Head and Orthopaedics, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark
Correspondence to Lars S. Rasmussen, MD, PhD, Department of Anaesthesia, HOC 4231, Copenhagen University Hospital, Rigshospitalet, DK-2100 Copenhagen, Denmark.
Tel: +45 35 45 34 88; fax: +45 35 45 29 50; e-mail: lsr@rh.dk

Purpose of review
Dementia is common in elderly patients, and anaesthesiologists are increasingly challenged in managing these patients who are especially vulnerable. The aim of this article is to highlight some of the most important perioperative issues relating to demented patients, both regarding anaesthesia and other aspects that should be considered to ensure a quick and uncomplicated recovery.

Recent findings
Demented patients often receive prescribed medication that can interact with various anaesthetic drugs and cause serious side effects. The anaesthesiologist should consider this when choosing the drugs used during surgery and when relieving postoperative pain. Generally, hypnotics, opioids, and inhalational anaesthetics should be administered in lower doses and carefully titrated because of altered pharmacokinetics and pharmacodynamics leading to a great variability, as documented in elderly patients. Neuromuscular blocking agents, and especially rocuronium, display an increased variability in the duration of action, but the new drug sugammadex may reverse the neuromuscular block in a few minutes. Postoperative cognitive decline is more frequent in elderly patients with preexisting cognitive impairment and several preventive measurements can be provided.

Summary
Outpatient surgery for demented patients causes many concerns in relation to anaesthesia. Extensive drug-related problems may arise and restrictive drug usage is recommended to avoid serious complications.

Keywords
anaesthetics, dementia, pain relief, postoperative cognitive dysfunction

Introduction
Because of the population ageing, an increasing number of elderly patients are attending healthcare services, and this quantity is likely to grow in the future [1]. A risk of dementia comes with increasing age, although it also appears in patients below 65 years of age [2]. Dementia is an independent risk factor for experiencing postoperative complications [3]. Anaesthesia for demented patients provides various challenges in the perioperative setting, and this study will highlight some of the important issues.

Definition of dementia
Several classification methods can be used in diagnosing mental disorders, but it is common to adhere to the criteria addressed in the International Classification of Disease-10 manual (WHO) or in the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders [4*]. Dementia is defined as a disturbance of multiple higher cortical functions, including memory, thinking, learning capacity, and judgement. Often, it has occupational and social consequences.

Dementia is one of the most common cerebral disorders and is highly associated with advancing age. The prevalence of dementia is age-specific and doubles with every 5 years of increase in age, and the global prevalence is estimated to be around 4% in people above 60 years of age [5]. Dementia can be classified in different subtypes such as Alzheimer’s dementia (50% of all dementia cases), vascular dementia, and Parkinson’s dementia. [4*,5]. Furthermore, a relatively new group of patients with HIV-associated dementia is increasing [6].

Dementia may be associated with a variety of neuropathological changes such as cerebral atrophy and plaques [7]. Cognitive impairment is not always apparent to those around the patient, and certainly not to the
patient himself [8]. Dementia affects multiple cognitive domains and is eventually manifested in loss of memory, language, and ability to recognize, and identify family members and simple objects. The patient might seem normal at first impression, but the cognitive disability usually becomes obvious when the physician asks for certain details at the preoperative evaluation. It is important to distinguish dementia from other mental disorders, including mild cognitive impairment, depression, and delirium. Information about cognitive status should be obtained not only from the patient but also from an informant close to the patient [8].

**Preoperative evaluation**

Preoperative evaluation for the demented patient undergoing outpatient surgery should include considerations on the following issues to ensure the best possible outcome postoperatively.

**Informed consent**

In the preoperative consultation, the physician should obtain informed consent. First of all, it should be determined whether or not the patient is able to understand, retain, and process the information that is presented before giving consent, and, furthermore, the healthcare personnel should ensure that any sensory deficit the patient might have is corrected, if possible, with sensory aids such as spectacles or hearing aids [9]. In case of significant dementia, a family member or another representative should be sought regarding decisions on treatment.

**Severity of dementia**

The severity of cognitive impairment can be assessed by using the Minimal Mental State Examination (MMSE) [10]. The maximum test score is 30, and a score at or just below 23 points indicates incipient light dementia. Severe dementia corresponds to a MMSE score below 10, but the test has some limitations because the patient must be able to comprehend and perform the tasks in the MMSE and the test is not independent of education or culture.

**Depression**

Depression is another issue that can influence the preoperative assessment of the patient. Demented patients are predisposed to depression and studies show that 30–50% of patients diagnosed with Alzheimer’s disease have symptoms of depression [11]. The two conditions share some of the same features and clinicians need to be aware of the potential confusion between the different syndromes, and carefully establish whether the patient shows signs of real depression, as it might call for alternative preoperative considerations [12].

**Concurrent disease and drug interactions**

Many older people take several prescribed medications and also herbal remedies that can trigger unintended and dangerous interactions when used together with anaesthesia. This is especially a problem with older demented patients as they frequently are not aware of what they are taking and why. For that reason, patients should always be encouraged to either show a list of all medications or bring the drugs to the preoperative consultation. Contrary to the acute setting, outpatient surgery provides the possibility for the clinician to decide whether any prescribed medication should best be avoided preoperatively, thereby reducing the drug-related problems. This is particularly important in patients with Parkinson’s dementia as some anaesthetic drugs can interact with anti-Parkinson drugs, for example opioid-induced muscle rigidity [13].

**Premedication**

Dementia does not indicate a routine use of premedication. However, as irritability, anxiety, and agitation are common symptoms in demented patients [14], it is sometimes necessary to use anxiolytics as these behavioural expressions are best avoided in the operative setting. If this manifestation of dementia is expected, a short-acting benzodiazepine can be administered as premedication. On the contrary, a conservative approach is again preferable due to the side effects of drugs and the potential interactions as previously mentioned. Neuroleptics are best avoided [15], and the administration of preoperative analgesics to demented patients should be similar to other frail elderly, but it should be noted that on rare occasions severe side effects can occur [16].

**Choice of anaesthetics**

Very few recent studies have been conducted concerning demented patients and the evidence is mainly based on investigations, including elderly surgical patients. As a general recommendation, general anaesthetics should be titrated and given in smaller doses in the elderly because of prolongation of onset as well as recovery. This is based on the pharmacodynamic aspect that the elderly, and especially the demented, have an increased sensitivity, and also on changes in pharmacokinetics with a slower distribution and a reduction in clearance. As a result, the elderly may experience a prolonged recovery, and anaesthetic-induced circulatory depression is more common [17]. The prolonged onset time may lead to overdosing induction agents. Depth of anaesthesia monitoring based on electroencephalography may aid in the administration of hypnotics. Such monitoring has been shown to reduce recovery time and drug consumption but the benefit in elderly and demented patients has not been clearly demonstrated yet. However, it should be noted that the baseline bispectral index value of demented patients is
lower than in nondemented elderly patients [18]. Hence, it seems likely that the pattern of depth of anaesthesia changes during surgery in the demented patients might be different.

**Hypnotics**

Increasing age is associated with a substantial decrease in the anaesthetic requirements for induction agents such as thiopental and propofol. In most studies, the adequate dose is 30–50% lower than in young adults. One of the most important factors seems to be that the distribution and the elimination from the central compartment are slower and this probably explains why the thiopental dose should be reduced in the elderly [19,20]. For propofol, a similar reduction in dosage is recommended, and a much lower plasma concentration is needed to achieve the same effect in the elderly ([21*], Fig. 1).

**Opioids**

Opioid potency is increased in the elderly but these drugs cause less circulatory depression. The initial dose should probably be nearly the same in younger adult patients, but subsequent doses should be lower or at least be separated by longer intervals because of reduced clearance. Otherwise, higher plasma concentrations may appear and side effects such as sedation may occur postoperatively [22*]. Remifentanil should be administered at a much lower infusion rate in elderly patients because of a reduction not only in volume of distribution but also in clearance [23,24]. In addition, the sensitivity is much greater, meaning that the same effect can be obtained at a plasma concentration that is 50% lower. The infusion rate in patients above 60–70 years should probably be no more than 30–40% of younger patients as a result of increased drug potency and the decreased elimination rate with advanced age. Bolus doses of remifentanil are generally not recommended in elderly patients for the same reasons. Other opioids should also be carefully titrated due to a pronounced variability in sensitivity.

**Inhalational anaesthetics**

The potency of inhalational anaesthetics is traditionally expressed as the minimum alveolar concentration (MAC), of which one MAC is defined as the concentration that prevents movement in 50% of patients after a painful stimulus such as surgical incision. Increasing age is associated with a reduction in MAC, with a 30% reduction from 20 to 80 years of age for sevoflurane, isoflurane, and desflurane ([25], Fig. 2).

However, it is not entirely predictable, so the dosage must be adjusted individually and this may be easier when administering inhalational anaesthesia – using end-tidal gas concentrations – than with intravenous anaesthesia. In addition, spontaneous ventilation can be maintained, at least for a number of surgical procedures in which neuromuscular block is not needed.

**Neuromuscular blocking agents**

Neuromuscular blocking agents (NMBAs) are useful for providing optimal tracheal intubation conditions. Unfortunately, there is a risk of residual neuromuscular blockade [26,27] and some anaesthesiologists avoid NMBAs, but this practice may be associated with a higher risk of difficult tracheal intubation [28]. In elderly patients, there is a huge variability in the duration of action of several NMBAs, especially rocuronium [29*,30]. A new drug, sugammadex, may allow a very rapid reversal of rocuronium and vecuronium, and full neuromuscular recovery can therefore be obtained in a few minutes after even larger doses of NMBAs [31]. This must, however, be
documented and the most important lesson is that neuro-muscular monitoring should be used when NMBAs are given [26,27].

**Regional anaesthesia**
Patients with preexisting cognitive impairment are at a higher risk of postoperative cognitive deterioration, but none of the numerous randomized trials focusing on cognition have shown a significant advantage of regional anaesthesia beyond the first postoperative week [32]. Early recovery may, however, be improved and another advantage is the opioid sparing that is associated with local anaesthesia, especially if continued postoperatively [33]. The current literature is limited by the fact that demented patients are not enrolled in most scientific studies. Lack of consent is not the only problem in that setting but also the required cooperation of the awake demented patient can be challenging if regional anaesthesia is scheduled.

**Postoperative considerations**
Demented patients undergoing outpatient surgery present the need for specific postoperative concerns, as they are expected to have an early discharge from the hospital, and must, therefore, rely on quick mobilization and uncomplicated rehabilitation.

**Postoperative pain**
One central objective is to relieve postoperative pain, which plays a major part in achieving a successful result following surgery. Pain in general is a common and often neglected condition in older people because age-related factors such as dementia and altered noiceptive pain perception make them highly vulnerable to pain and may challenge assessment [34*]. The experience of pain is very subjective [35], and acute pain is, therefore, often measured by means of self-report and use of visual or numeric scales such as the visual analogue scale and the numeric rating scale [36]. This approach cannot necessarily be used for demented patients because their impaired cognitive function hampers reliable self-reporting. In addition, the lack of communication skills and reduced use of facial expression found in these patients also make it difficult to assess the degree of pain [37*]. Moreover, patients with dementia are less likely to report sensations of pain than cognitively intact patients [35,37*].

In recent years, alternative assessment tools of a more observational character to improve postoperative pain management have been developed. The Mobilization–Observation–Behaviour–Intensity–Dementia pain scale is based on an observation of pain behaviour during rest and physical movement and it has been reported as useful in determining pain in patients with dementia [37*,38]. Therefore, the appropriate strategy for handling postoperative pain is to combine observational reports from the primary caregiver with self-reported standardized pain scales.

**Postoperative complications**
Focus on prevention of postoperative complications is obviously very important for both the patient and the healthcare system. The complications highlighted in this paper are those that most frequently emerge in elderly patients undergoing surgery.

**Delirium and postoperative cognitive dysfunction (POCD)**
Several studies [39*,40–42] have shown that older patients with a preexisting cognitive disorder such as dementia have a higher risk of postoperative cognitive complications than other patients.

Delirium is a common complication following surgery and affects around 40% of the elderly surgical population [39*,40]. Delirium is characterized by a prominent fluctuating change in cognition with major disturbances in attention and thinking, in which the level of consciousness may be affected [43]. Several risk factors other than increasing age and dementia have been identified: drug effects, dehydration, sensory deprivation, and anxiety [40,41]. Postoperative cognitive dysfunction (POCD) is another much more subtle cognitive disorder that is often unnoticed when patients are discharged from the hospital. Symptoms vary amongst patients but usually involve a decline in memory, concentration, and information processing [40,41–43]. The risk of experiencing POCD is lower following minor surgery, but studies on POCD have excluded demented patients so the exact incidence for these patients is still unknown. Delirium and POCD differ significantly in clinical presentation and duration (Table 1), but both are associated with higher mortality and morbidity rates [41,42,44*].

**Sleep disturbance**
Altered sleep patterns are a part of normal ageing but are more conspicuous in people with neurodegenerative

| Table 1 Key differences between delirium and postoperative cognitive dysfunction |
|----------------------------------|---------------------------------|-------------------------------------------------|--------|
| Onset                            | Duration                        | Assessment                                      | Consciousness |
| Delirium                         | Acute, fluctuating              | Days–weeks                                      | Confusion assessment method, Delirium Rating Scale | May be altered |
| POCD                             | Days–weeks                      | Hours–days                                      | Neuropsychological test-battery               | Unaffected    |

POCD, postoperative cognitive dysfunction.
disorders, and the degree of sleep disturbance seems to increase with progressing dementia [45,46]. The lack of sleep can have a profound negative effect on demented patients as it may cause a further decline in cognitive function and potentially evolve into delirium. This can evidently have serious consequences on the duration of the hospital stay and all attempts should be made to promote healthy sleep patterns, preferably supplemented with nonpharmacological therapy to avoid extensive polypharmacy.

Conclusion
Outpatient surgery calls for important preoperative and postoperative considerations in patients with dementia. This group of patients is particularly vulnerable in the perioperative setting and has an overall increased risk of complications including drug interactions, cognitive impairment, and sleep disturbances. Most studies on the effects of anaesthesia have not included patients with dementia, and further research could provide a more thorough understanding of the risks associated with surgery in demented patients that will allow better treatment and preventive methods.

Acknowledgements
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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 (pp. 823–824).


This study describes the classification of mental disorders as well as the dementia subtypes and various comorbidities.


The study provides important recommendations in regard to the assessment of mental capacity in the elderly and in promoting decision-making for patients with dementia.


This paper is published outside the annual period of this review, but is of special interest as it is one of the only studies to describe the altered pharmacodynamic and pharmacokinetic responses seen in the elderly when anaesthetized with propofol.

This excellent study evaluates age-related differences in pharmacokinetics and pharmacodynamics of opioids.


This paper is published outside the annual period of this review, but is of special interest as the study describes the difficulties in predicting the duration of action in elderly patients after administering cisatracurium, vecuronium, and rocuronium.

This excellent study evaluates different approaches used when assessing pain in patients with impaired cognitive function.

The recordings

The 39


The study is concerned with the challenging task of evaluating pain intensity and pain behaviour in patients with increased self-report capacity, using video recordings and observational approaches.


The study describes the cause and identifies risk factors and outcomes associated with postoperative delirium in the elderly.


This follow-up study of patients with POCD shows that these patients have a higher mortality and an increased risk of severe long-term social consequences.


Dexmedetomidine Infusion During Laparoscopic Bariatric Surgery: The Effect on Recovery Outcome Variables

Burcu Tufanogullari, MD*
Paul F. White, PhD, MD*
Mariana P. Peixoto, MD*
Daniel Kianpour, MS*
Thomas Lacour, MD*
James Griffin, MD*
Gary Skrivanek, MD*
Amy Macaluso, MD*
Mary Shah, MD*
David A. Provost, MD†

BACKGROUND: Dexmedetomidine (Dex), an $\alpha_2$ agonist, has well-known anesthetic and analgesic-sparing effects. We designed this prospective, randomized, double-blind, and placebo-controlled dose-ranging study to evaluate the effect of Dex on both early and late recovery after laparoscopic bariatric surgery.

METHODS: Eighty consenting ASA II–III morbidly obese patients were randomly assigned to 1 of 4 treatment groups: (1) control group received a saline infusion during surgery, (2) Dex 0.2 group received an infusion of 0.2 $\mu$g · kg$^{-1}$ · h$^{-1}$ IV, (3) Dex 0.4 group received an infusion of 0.4 $\mu$g · kg$^{-1}$ · h$^{-1}$ IV, and (4) Dex 0.8 group received an infusion of 0.8 $\mu$g · kg$^{-1}$ · h$^{-1}$ IV. Mean arterial blood pressure values were maintained within $\pm$25% of the preinduction baseline values by varying the inspired desflurane concentration. Perioperative hemodynamic variables, postoperative pain scores, and the need for “rescue” analgesics and antiemetics were recorded at specific intervals. Follow-up evaluations were performed on postoperative days (PODs) 1, 2, and 7 to assess severity of pain, analgesic requirements, patient satisfaction with pain management, quality of recovery, as well as resumption of dietary intake and recovery of bowel function.

RESULTS: Dex infusion, 0.2, 0.4, and 0.8 $\mu$g · kg$^{-1}$ · h$^{-1}$, reduced the average end-tidal desflurane concentration by 19, 20, and 22%, respectively. However, it failed to facilitate a significantly faster emergence from anesthesia. Although the intraperioperative hemodynamic values were similar in the four groups, arterial blood pressure values were significantly reduced in the Dex 0.2, 0.4, and 0.8 groups compared with the control group on admission to the PACU (P < 0.05). The length of the PACU stay was significantly reduced in the Dex groups (81 ± 31 to 67 ± 24 vs 104 ± 33 min in the control group, P < 0.05). The amount of rescue fentanyl administered in the PACU was significantly less in the Dex 0.2, 0.4, and 0.8 groups versus control group (113 ± 85, 108 ± 67, and 120 ± 78 vs 187 ± 99 $\mu$g, respectively, P < 0.05). The percentage of patients requiring antiemetic therapy was also reduced in the Dex groups (30, 30, and 10% vs 70% in the control group). However, the patient-controlled analgesia morphine requirements on PODs 1 and 2 were not different among the four groups. Pain scores in the PACU, and on PODs 1, 2, and 7, in the three Dex groups were not different from the control group. Finally, quality of recovery scores and times to recovery of bowel function and hospital discharge did not differ among the four groups.

CONCLUSIONS: Adjunctive use of an intraoperative Dex infusion (0.2–0.8 $\mu$g · kg$^{-1}$ · h$^{-1}$) decreased fentanyl use, antiemetic therapy, and the length of stay in the PACU. However, it failed to facilitate late recovery (e.g., bowel function) or improve the patients’ overall quality of recovery. When used during bariatric surgery, a Dex infusion rate of 0.2 $\mu$g · kg$^{-1}$ · h$^{-1}$ is recommended to minimize the risk of adverse cardiovascular side effects.

From the Departments of *Surgery, †Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas.

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Address correspondence and reprint requests to Dr. Paul F. White, Professor and Holder of the Margaret Milam McDermott Distinguished Chair in Department of Anesthesiology and Pain Management, University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Boulevard, Dallas, TX 75390-9068. Address e-mail to paul.white@utsouthwestern.edu.

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the world. Morbidly obese patients are at an increased risk of developing postoperative obstructive sleep apnea and opioid-induced ventilatory depression. Since Dex possesses an opioid-sparing effect without causing respiratory depression, it has been increasingly used “off-label” during bariatric surgery. However, there is only one study describing the use of an arbitrarily chosen Dex infusion rate in this patient population.

In this prospectively randomized, double-blind, placebo-controlled, dose-ranging study, we tested the hypothesis that Dex infusion would produce dose-related reductions in the anesthetic and analgesic requirements in patients undergoing laparoscopic bariatric surgery. The secondary objectives were to determine if the use of Dex facilitated the recovery process and improved patient outcome.

**METHODS**

After obtaining IRB approval at the University of Texas Southwestern Medical Center at Dallas, and written informed consent, 80 morbidly obese patients, aged 22–66-yr-of-age, scheduled for laparoscopic bariatric surgery (either gastric banding or gastric bypass) were studied according to a randomized, double-blind, placebo-controlled protocol. This investigation was registered with ClinicalTrials.gov (NCT00363935). Patients were excluded if they had: (1) an allergy to \( \alpha_2 \) adrenergic agonist or sulfa drugs, (2) a history of uncontrolled hypertension, (3) heart block greater than first degree, (4) a history of alcohol or drug abuse, (5) clinically significant neurologic, cardiovascular, renal, hepatic, or gastrointestinal diseases, (6) received an opioid analgesic medication within a 24 h period before the operation, (7) were pregnant or breastfeeding, and (8) were unable to speak and read English.

The patients were randomly assigned using a computer-generated random number table to one of the following four treatment groups: (1) control group received saline, (2) Dex 0.2 group received 0.2 \( \mu \text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1} \) IV, (3) Dex 0.4 group received 0.4 \( \mu \text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1} \) IV, and (4) Dex 0.8 group received 0.8 \( \mu \text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1} \) IV.

The study medication was prepared by the operating room (OR) pharmacist in identical 60-mL syringes. Dex 0, 200, 400, or 800 \( \mu \text{g} \) was added to saline to achieve a total volume of 40 mL, resulting in concentrations of 0 \( \mu \text{g} \)/mL (control), 5 \( \mu \text{g} \)/mL, (Dex 0.2), 10 \( \mu \text{g} \)/mL, (Dex 0.4), and 20 \( \mu \text{g} \)/mL, (Dex 0.8), for the 4 study groups. The weight-adjusted doses of all study medications were based on the patient’s actual body weight. The investigators, attending anesthesiologists, OR, recovery and ward nurses, as well as the patients were blinded to the computer-generated randomization schedule.

In the preoperative holding area, the patients used 11-point verbal rating scales (VRS) to assess their baseline pain and nausea levels, with 0 = none to 10 = maximum. Celecoxib, 400 mg orally, was given 30–60 min before induction of anesthesia. Immediately before entering the OR, patients were premedicated with midazolam, 20 \( \mu \text{g} \)/kg IV. Intraoperative monitoring devices included noninvasive arterial blood pressure, electrocardiography, capnography, and pulse oximetry, as well as the cerebral state monitor (Danmeter, Odense, Denmark).

After obtaining baseline measurement of HR and MAP, an infusion of the study medication was started at 0.04 mL · kg\(^{-1} \) · h\(^{-1} \). Anesthesia was induced 3–5 min after starting the study drug infusion with propofol, 1.25 mg/kg IV, in combination with lidocaine, 0.75 mg/kg IV. Rocuronium, 0.6 mg/kg IV, and 4 mL of topical 4% lidocaine were administered before tracheal intubation. Anesthesia was initially maintained with 4% inspired concentration of desflurane in combination with air (1 L/min) and oxygen (1 L/min) mixture.

The intraoperative HR, MAP, end-tidal desflurane concentration, and cerebral state index (CSI) values were recorded at 5 min intervals for 30 min, and subsequently at 10 min intervals until discontinuation of the anesthetic drugs. Hemodynamic values were also recorded at specific end-points (e.g., induction of anesthesia, 1 min after induction, tracheal intubation, 5 min after tracheal intubation, at skin incision, at 5 and 10 min after the skin incision). After induction of anesthesia, MAP values were maintained within ±25% of the baseline values by varying the inspired desflurane concentration. Hypotension (defined as MAP value <25% of the baseline value on two consecutive readings within 2–3 min), not responding to a 2% (vol %) decrease in the inspired desflurane concentration and a 200 mL fluid bolus, was treated with phenylephrine, 100 \( \mu \text{g} \) IV, boluses. The infusion of study medication was discontinued if the hypotension persisted >2 min after these interventions. Upon return of the MAP to ±25% of the baseline value, the study medication infusion was resumed at 50% of the initial infusion rate. In the presence of hypertension (defined as MAP value >25% of the baseline value on two consecutive readings within 2–3 min) and/or tachycardia (defined as HR value >25% of the baseline value > 2 min) despite a 2% (vol %) increase in the inspired desflurane concentration, labetalol, 5 mg IV, boluses were administered. Bradycardia (HR <45) persisting for >2 min was treated with glycopyrrolate, 0.2 mg IV, boluses.

During the operation, patients received similar amounts of IV crystalloid solutions (namely, 25 mL/kg during gastric bypass and 10 mL/kg during gastric banding procedures). Ondansetron, 4 mg IV, was given for prevention of postoperative nausea and vomiting when the laparoscope was withdrawn. Before wound closure, bupivacaine 0.25% was infiltrated at the fascial level of all portals, and residual neuromuscular block was reversed with neostigmine, 40 \( \mu \text{g} \)/kg IV, and glycopyrrolate, 5 \( \mu \text{g} \)/kg IV. The infusion of study medication was discontinued at the start
of the wound closure. Upon completion of wound closure, desflurane was discontinued and the inspired oxygen flow rate was increased to 5 L/min. Times from discontinuation of desflurane to eye opening, obeying simple commands (e.g., open mouth, squeeze hand) and tracheal extubation were recorded. After emergence from anesthesia, patients were administered fentanyl, 25–50 μg IV, boluses to control acute pain in the early postoperative period.

After arrival in the postanesthesia care unit (PACU), patients were connected to a patient-controlled analgesia (PCA) delivery system that was programmed to deliver morphine, 2 mg IV, boluses on demand with a lockout interval of 10 min. When patient’s VRS pain score was <7 and they were judged to be recovered from anesthesia by the PACU staff, they were allowed to self-administer morphine using the PCA delivery system. The parental opioid analgesic requirements were determined in the PACU, as well as on postoperative day (POD) 1 and 2 (with the exception of the patients who had been discharged home on POD 1). Hemodynamic values and VRS pain scores were recorded at 5 min intervals for the first 15 min after arrival in the PACU, and subsequently at 15 min intervals until discharge. The VRS nausea scores and episodes of emesis, as well as the need for rescue antiemetic therapy, were recorded at 30 min intervals until PACU discharge. Patients reporting a VRS nausea score >3 on two consecutive evaluations were administered promethazine, 6.25 mg IV. VRS pain and nausea scores, quality of recovery scores [using a validated 9-item questionnaire13], and patient satisfaction with their pain management (on a 100-point scale with 1 = completely dissatisfied to 100 = completely satisfied) were recorded on PODs 1, 2, and 7. Finally, recovery times from tracheal extubation to ambulation without assistance, tolerating liquids, and passage of flatus were also noted. Patients were asked to note the time they were able to tolerate liquids and their first passage of flatus (“gas”) in a diary.

Data are expressed as mean ± sd, medians (and interquartile ranges), percentages (%), and numbers (n). The statistical analysis was performed using a standard SPSS software package (Chicago, IL). For continuous variables, one-way analysis of variance (ANOVA) and repeated measures of ANOVA (RMANOVA) were used to evaluate changes among the groups. Student’s t-test was used to analyze the parametric data, and discrete (categorical) variables were analyzed using the χ² test, with a P < 0.05 was considered statistically significant. Bonferroni corrections were performed for variables with multiple comparisons over time (i.e., RMANOVA). The group sizes (n = 20) were calculated to detect a >40% reduction in the volatile anesthetic2,8 and/or postoperative opioid analgesic requirement9 with a

Figure 1. (a) Perioperative cerebral state index (CSI) values and (b) end-tidal concentration of desflurane [EtDes (%)] following the start of the study drug infusion. Values are means ± standard deviations. *P < 0.05 versus placebo.

Table 1. Demographic Characteristics, the Type of Laparoscopic Surgical Procedures, Durations of Anesthesia, Surgery, and the Study Medication Infusion

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 20)</th>
<th>Dex 0.2 (n = 20)</th>
<th>Dex 0.4 (n = 20)</th>
<th>Dex 0.8 (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>43 ± 16</td>
<td>47 ± 10</td>
<td>48 ± 9</td>
<td>40 ± 10</td>
</tr>
<tr>
<td>Gender (male/female) (n)</td>
<td>3/17</td>
<td>3/17</td>
<td>4/16</td>
<td>9/11</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>127 ± 25</td>
<td>127 ± 20</td>
<td>138 ± 41</td>
<td>151 ± 36</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>165 ± 12</td>
<td>169 ± 10</td>
<td>169 ± 8</td>
<td>172 ± 13</td>
</tr>
<tr>
<td>ASA (II/III) (n)</td>
<td>6/14</td>
<td>6/14</td>
<td>2/18</td>
<td>4/16</td>
</tr>
<tr>
<td>Type of laparoscopic surgery (n)</td>
<td>12</td>
<td>9</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Gastric banding</td>
<td>8</td>
<td>9</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Gastric bypass</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>116 ± 52</td>
<td>110 ± 62</td>
<td>107 ± 35</td>
<td>111 ± 56</td>
</tr>
<tr>
<td>Duration of anesthesia (min)</td>
<td>153 ± 54</td>
<td>145 ± 63</td>
<td>143 ± 51</td>
<td>145 ± 55</td>
</tr>
<tr>
<td>Duration of infusion (min)</td>
<td>137 ± 53</td>
<td>126 ± 57</td>
<td>124 ± 35</td>
<td>130 ± 55</td>
</tr>
</tbody>
</table>

Data are displayed as means ± standard deviations and numbers (n). No significant differences were noted among the four treatment groups.
Table 2. Perioperative Need for Phenylephrine, β-Blocker and Discontinuation of Study Medication Infusion, Time from Turning Off the Desflurane to Patients’ Extubation, First Spontaneous Eye Opening, Following Simple Commands, Tracheal Extubation, and the Duration of the Postanesthesia Care Unit (PACU) Stay

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 20)</th>
<th>Dex 0.2 (n = 20)</th>
<th>Dex 0.4 (n = 20)</th>
<th>Dex 0.8 (n = 20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rescue phenylephrine [n (%)]</td>
<td>4 (20)</td>
<td>2 (10)</td>
<td>4 (20)</td>
<td>10 (50)*</td>
</tr>
<tr>
<td>Rescue β-blocker [n (%)]</td>
<td>5 (25)</td>
<td>3 (15)</td>
<td>1 (5)</td>
<td>0 (0)*</td>
</tr>
<tr>
<td>Transient discontinuation of study drug [n (%)]</td>
<td>2 (10)</td>
<td>2 (10)</td>
<td>3 (15)</td>
<td>3 (15)</td>
</tr>
<tr>
<td>Time to eye opening (min)</td>
<td>6 ± 3</td>
<td>5 ± 3</td>
<td>6 ± 4</td>
<td>8 ± 6</td>
</tr>
<tr>
<td>Time to follow simple commands (min)</td>
<td>6 ± 3</td>
<td>6 ± 3</td>
<td>6 ± 4</td>
<td>9 ± 6</td>
</tr>
<tr>
<td>Time to tracheal extubation (min)</td>
<td>7 ± 3</td>
<td>5 ± 3</td>
<td>6 ± 4</td>
<td>9 ± 6</td>
</tr>
<tr>
<td>Duration of the PACU stay (min)</td>
<td>104 ± 33</td>
<td>81 ± 31*</td>
<td>82 ± 24*</td>
<td>87 ± 24*</td>
</tr>
</tbody>
</table>

Data are displayed as means ± standard deviations, numbers, and percentages.

* P < 0.05 compared with the control group.

power of 80% [assuming a variability (sd) of ±20%] and a significance level of 0.05.

RESULTS

A total of 125 patients were screened for eligibility to participate in the study, and 80 patients were subsequently enrolled (n = 20 per group). Three patients (one from each of the Dex 0.2, 0.4, and 0.8 groups) were admitted to the intensive care unit from the postsurgical ward because of surgical complications at the gastrointestinal anastomosis site (e.g., bleeding, obstruction) and their postoperative data were excluded from the final analysis. There were no significant differences among the four groups with respect to age, gender, weight, height, ASA physical status, type of laparoscopic bariatric surgery, perioperative CSI values, and the durations of study medication infusion, surgery, and anesthesia times (Table 1 and Fig. 1). Recovery times after discontinuation of the study medication and desflurane to tracheal extubation, spontaneous eye opening, and obeying simple commands did not differ among the four groups (Table 2).

End-tidal concentrations of desflurane during the operation were significantly lower in the Dex 0.2, 0.4, and 0.8 groups compared with the control group during surgery (>30 min after induction) (Fig. 1, P < 0.05). In addition, the percentage of patients who required rescue treatment with phenylephrine for persistent hypotension during surgery was significantly higher in the Dex 0.8 group compared with the control group (50% vs 20%, P < 0.05). The study medication infusion was transiently discontinued (<10 min) in 2 (10%), 2 (10%), 3 (15%), and 3 (15%) patients in the control, Dex 0.2, Dex 0.4, and Dex 0.8 groups, respectively, because of an inability to maintain the MAP values in the desired range (±25% of the baseline values) under the conditions of the study [i.e., ensuring that the patients CSI values were in a range consistent with a “state of unconsciousness” (<60)].

Compared with the control group, MAP values at the time of skin incision were significantly reduced in the Dex 0.2, Dex 0.4, and Dex 0.8 groups (Fig. 2a). However, the HR values were not different (Fig. 2b). Although the MAP values at 70 and 100 min after the start of the study drug infusion were significantly lower in the Dex 0.4 and Dex 0.8 groups compared with the control group (86 ± 15 and 81 ± 16 vs 97 ± 12 and 85 ± 11 and 84 ± 14 vs 96 ± 14, respectively, P < 0.05, Fig. 2c), these minor differences were not clinically significant. However, the MAP values during the first 45 min in the PACU were significantly lower in the Dex 0.2, 0.4, and 0.8 groups compared with the control group (Fig. 3a). The perioperative HR values did not differ among the four study groups (Figs. 2d and 3b).

Pain scores in the PACU, as well as the average pain scores on POD 1, 2, and 7, did not differ significantly among the four groups. However, the amount...
of fentanyl administered in the PACU after emergence from anesthesia was significantly reduced in the Dex 0.2, 0.4, and 0.8 groups compared with the control group (113 ± 85, 108 ± 67, 120 ± 78 vs 187 ± 99 μg, respectively, P < 0.05). The total amount of PCA morphine self-administered on PODs 1 and 2 did not differ among the four treatment groups (Table 3).

The overall incidences of postoperative emetic symptoms during the first 24 h after surgery were reduced in the Dex 0.2, 0.4, and 0.8 groups compared with the control group (25, 30, and 45 vs 65%, respectively). The VRS nausea scores on arrival in the PACU were also significantly lower in the Dex 0.2, 0.4, and 0.8 groups compared with the control group (25, 30, and 45% vs 65%, respectively, P < 0.05). The durations of the emetic drugs in the PACU was significantly reduced in all three Dex groups (Table 4). Similarly, the need for rescue antiemetic therapy in the early postoperative period in this laparoscopic bariatric surgery patient population. However, the anesthetic and analgesic-sparing effects of Dex were not strictly dose-related over the four-fold drug concentration range studied. Although Dex facilitated the early recovery (e.g., PACU stay), later recovery events (e.g., hospital discharge, resumption of oral intake and bowel function) were similar in all four groups. The reduced need for potent opioid analgesics and less severe emetic symptoms in the Dex groups probably contributed to the reduced PACU stay.

Dex is only Food and Drug Administration-approved for sedation of initially intubated and mechanically ventilated patients by continuous infusion for <24 h in the intensive care setting. There are numerous clinical reports describing the “off label” use of Dex infusion as an adjuvant during and/or after surgery.7–12,14–18,19 A previous study evaluated different bolus doses of Dex for premedication20; however, dose-ranging studies are lacking for when the drug is administered as a continuous infusion during surgery. Given the propensity of the drug to produce hypotension and/or bradycardia when it is administered to volunteers or patients,15–17,21–23 it was important to determine an infusion rate that would maximize the anesthetic and analgesic-sparing effect while minimizing the occurrence of adverse cardiovascular side effects requiring therapeutic interventions (e.g., phentylephrine, labetalol). In several reports, Dex infusion rates ranging from 0.4 to 10 μg·kg⁻¹·h⁻¹ have been used during bariatric surgery,10–12 In contrast to the case report19 in which a high-dose infusion (>1 μg·kg⁻¹·h⁻¹) of Dex was administered as the primary drug in a total IV anesthetic technique, we used Dex as an adjuvant to the volatile anesthetic desflurane. Therefore, in our prospective dose-ranging study, we evaluated Dex infusion rates of 0.2, 0.4, and 0.8 μg·kg⁻¹·h⁻¹ during anesthesia. Patients assigned to the control group required more frequent use of antihypertensive rescue medication, and the high-dose Dex group required greater use of cardiovascular medication to treat hypotensive episodes during surgery. Hence, these data would suggest that the selected infusion rates of Dex (0.2–0.8 μg·kg⁻¹·h⁻¹) were in the appropriate therapeutic range when it is used as part of a “balanced” anesthetic technique.10

Analogous to the findings of Feld et al.12 when Dex, 0.4 μg·kg⁻¹·h⁻¹, was administered during bariatric surgery as an alternative to fentanyl, we found statistically significant reductions in the volatile anesthetic requirement and the need for potent opioid analgesics in the PACU. The use of Dex infusion, 0.2–0.8 μg·kg⁻¹·h⁻¹, reduced the end-tidal desflurane concentration by 19%–22% during surgery and the fentanyl requirement by 36%–42% in the PACU, contributing to a reduction in postoperative nausea and in the need for rescue antiemetic therapy in the early postoperative period (Figure 3a).
Postoperative Days (PODs) 1 and 2

Analgesia (PCA) Morphine, and Oral Solution of Hydrocodone-acetaminophen Used on the Day of Surgery, as well as on

Table 3. Pain Scores and the Amounts of “Rescue” Fentanyl Used in Postanesthesia Care Unit (PACU), Patient-controlled

Analgesia (PCA) Morphine, and Oral Solution of Hydrocodone-acetaminophen Used on the Day of Surgery, as well as on

Table 3. Pain Scores and the Amounts of “Rescue” Fentanyl Used in Postanesthesia Care Unit (PACU), Patient-controlled

Their Pain Management in the Four Study Groups

Dex 0.2

Dex 0.4

Dex 0.8

PODs

Control

(n = 20)

Dex 0.2

(n = 19)

Dex 0.4

(n = 19)

Dex 0.8

(n = 19)

Pain scores following arrival in PACU

At 0 min

5 ± 3

5 ± 3

5 ± 3

4 ± 3

At 15 min

7 ± 2

5 ± 2

6 ± 3

5 ± 3

At 30 min

6 ± 2

5 ± 2

6 ± 3

4 ± 3

At 60 min

6 ± 3

5 ± 2

5 ± 3

4 ± 3

At 90 min

5 ± 3

4 ± 3

6 ± 3

6 ± 2

At POD 1

4 ± 3

4 ± 3

5 ± 3

4 ± 3

At POD 2

4 ± 3

2 ± 2

3 ± 3

3 ± 3

At POD 7

3 ± 2

1 ± 1

2 ± 1

3 ± 2

Fentanyl use in PACU (µg)

187 ± 99

113 ± 85*

108 ± 67*

120 ± 78*

Pain medication on POD 1

Morphine (mg) (n)

49 ± 26 (20)

37 ± 26 (19)

38 ± 34 (19)

39 ± 27 (19)

Hydromorphone (2.5 mg/mL)–acetaminophen

(167 mg/mL) (mL) (n)

48 ± 23 (6)

28 ± 23 (8)

35 ± 28 (8)

43 ± 25 (3)

Pain medication on POD 2

Morphine (mg) (n)

16 ± 14 (6)

12 ± 7 (6)

24 ± 37 (4)

24 ± 28 (8)

Hydromorphone (2.5 mg/mL)–acetaminophen

(167 mg/mL) (mL) (n)

36 ± 23 (7)

39 ± 16 (12)

57 ± 33 (8)

39 ± 45 (9)

Data are displayed as means ± standard deviations and numbers.

* Verbal rating scale: 0 = no pain to 10 = maximal pain.

* P < 0.05 compared with the control group.

Table 4. Quality of Recovery (QoR) Scores, Postoperative Nausea and Primary Outcome Variables and Patient Satisfaction with Their Pain Management in the Four Study Groups

<table>
<thead>
<tr>
<th>QoR scores*</th>
<th>Control (n = 20)</th>
<th>Dex 0.2 (n = 19)</th>
<th>Dex 0.4 (n = 19)</th>
<th>Dex 0.8 (n = 19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>POD 1</td>
<td>13 ± 3</td>
<td>14 ± 3</td>
<td>13 ± 3</td>
<td>14 ± 3</td>
</tr>
<tr>
<td>POD 2</td>
<td>13 ± 3</td>
<td>16 ± 3</td>
<td>15 ± 4</td>
<td>16 ± 2</td>
</tr>
<tr>
<td>POD 7</td>
<td>16 ± 2</td>
<td>11 ± 1</td>
<td>17 ± 1</td>
<td>16 ± 2</td>
</tr>
<tr>
<td>Nausea/vomiting in PACU [%]</td>
<td>13/3 (65/15)</td>
<td>5/1 (25/5)*</td>
<td>6/0 (30/0)*</td>
<td>9/2 (45/11)</td>
</tr>
<tr>
<td>Required antiemetic therapy [%]</td>
<td>14,70</td>
<td>6,30*</td>
<td>6,30*</td>
<td>2,10*</td>
</tr>
<tr>
<td>Nausea score*</td>
<td>Upon arrival in PACU</td>
<td>3 ± 3</td>
<td>1 ± 1*</td>
<td>2 ± 3</td>
</tr>
<tr>
<td>At 30 min</td>
<td>3 ± 3</td>
<td>1 ± 2*</td>
<td>1 ± 2*</td>
<td>1 ± 2*</td>
</tr>
<tr>
<td>At 60 min</td>
<td>3 ± 3</td>
<td>2 ± 3</td>
<td>1 ± 2*</td>
<td>1 ± 3</td>
</tr>
<tr>
<td>Time to ambulation (h)</td>
<td>10 ± 7</td>
<td>12 ± 9</td>
<td>8 ± 7</td>
<td>9 ± 6</td>
</tr>
<tr>
<td>Time to oral intake (h)</td>
<td>17 ± 13</td>
<td>13 ± 10</td>
<td>16 ± 12</td>
<td>18 ± 9</td>
</tr>
<tr>
<td>Time to passing flatus (h)</td>
<td>32 ± 22</td>
<td>31 ± 12</td>
<td>41 ± 19</td>
<td>38 ± 20</td>
</tr>
<tr>
<td>Discharged on POD 1 [%]</td>
<td>9 (45)</td>
<td>12 (60)</td>
<td>11 (58)</td>
<td>11 (58)</td>
</tr>
<tr>
<td>Hospital discharge (d) Overall</td>
<td>1.5 (3)</td>
<td>1 (1)</td>
<td>1 (3)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Gastric bypass</td>
<td>2 (3)</td>
<td>2 (1)</td>
<td>2 (1)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Gastric banding</td>
<td>1 (3)</td>
<td>1 (1)</td>
<td>1 (3)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Patient satisfaction with pain management*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>POD 1</td>
<td>89 ± 17</td>
<td>86 ± 20</td>
<td>87 ± 16</td>
<td>86 ± 11</td>
</tr>
<tr>
<td>POD 2</td>
<td>89 ± 16</td>
<td>90 ± 16</td>
<td>92 ± 11</td>
<td>90 ± 13</td>
</tr>
<tr>
<td>POD 7</td>
<td>83 ± 25</td>
<td>97 ± 6</td>
<td>86 ± 23</td>
<td>89 ± 14</td>
</tr>
</tbody>
</table>

Data are shown in mean ± standard deviations, numbers (n), percentages (%), medians, and interquartile ranges.

POD = postoperative day; PACU = postanesthesia care unit.

* QoR score: 0 = worst to 16 = best.

* Verbal rating scale: 0 = no nausea to 10 = severe nausea.

* Verbal rating scale: 1 = completely dissatisfied to 100 = completely satisfied.

* P < 0.05 compared with the control group.

period. The failure of Dex to produce a sustained opioid-sparing effect in the later postoperative periods was probably related to its short elimination half-life of 2 h.2–4 These data also support the findings of Angst et al.,24 which suggested that systemic administration of Dex lacks significant preemptive analgesic activity with respect to minimizing postoperative pain.
Preliminary clinical reports\textsuperscript{10,12} have suggested that a continuous infusion of Dex, 0.4–0.7 μg · kg\textsuperscript{-1} · h\textsuperscript{-1}, may be a useful anesthetic adjunct for morbidly obese patients undergoing bariatric surgery. Our findings would suggest that the modest anesthetic-sparing effect was of little (if any) clinical significance because dexmedetomidine failed to facilitate a faster emergence from desflurane anesthesia after bariatric surgery. Although the intraoperative use of Dex decreased the amount of fentanyl used in the early postoperative period, it only reduced the length of stay in the PACU by an average of 15–25 min. Use of Dex failed to reduce the length of the hospital stay after either gastric bypass or banding procedures. Therefore, the primary benefit of Dex in this study appeared to be related to its ability to reduce emetic sequelae by decreasing the need for the desflurane during the operation and fentanyl immediately after surgery. The anesthetic and opioid-sparing effects of Dex in the early postoperative period may decrease the risk of respiratory depression in the PACU for morbidly obese patients who are at greater risk for obstructive sleep apnea and oxygen desaturation.

This study can be criticized because a constant infusion was used. However, the administration of an initial loading bolus of Dex (0.5 μg/kg IV) resulted in a high incidence of hypotension immediately after tracheal intubation in a “pilot” experience before initiating the current protocol. Although use of a variable-rate infusion may minimize both hypo- and hypertensive responses during surgery, it would have confounded our findings and precluded a direct comparison of the four treatment groups. Another criticism of this study relates to our failure to continue the infusion of the study medication into the postoperative period to achieve a more sustained opioid-sparing effect.\textsuperscript{17} However, the use of a Dex infusion is not recommended outside of closely monitored areas (e.g., intensive care unit). Finally, the use of noninvasive blood pressure (vs intraarterial) monitoring for titrating the volatile anesthetic, and fentanyl for pain control in the early postoperative period before initiating maintenance PCA therapy, were intended to mimic standard clinical practice for this surgical procedure.

It has been suggested that Dex infusion is a useful alternative to opioid analgesics, despite its high cost because it lacks the respiratory-depressant effects produced by opioid compounds.\textsuperscript{12,18} In an editorial by Ebert and Maze,\textsuperscript{25} it was suggested that α\textsubscript{2} adrenergic receptor agonists may also be useful in the perioperative period because of their sedative/hypnotic, anxiolytic, and sympatholytic properties. Although we did not assess Dex’s anxiety-relieving properties, our data would suggest that a pharmacoeconomic analysis of the cost:benefit ratio of Dex in this patient population is clearly needed. Given the growing importance of multimodal analgesia in facilitating the recovery process,\textsuperscript{26,27} Dex may prove to be a cost-effective adjuvant in morbidly obese patients who are at increased risk for respiratory complications in the early postoperative period.

In summary, the anesthetic and analgesic-sparing effects of Dex infusion, 0.2–0.8 μg · kg\textsuperscript{-1} · h\textsuperscript{-1}, facilitated early but not late recovery of morbidly obese patients undergoing bariatric surgery. When using a Dex infusion as an anesthetic adjuvant, an infusion rate of 0.2 μg · kg\textsuperscript{-1} · h\textsuperscript{-1} is recommended to facilitate early recovery while minimizing adverse perioperative cardiovascular side effects.

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24. Angst MS, Ramaswamy B, Davies MF, Maze M. Comparative analgesic and mental effects of increasing plasma concentrations of dexmedetomidine and alfentanil in humans. Anesthesiology 2004;101:744–52

25. Ebert T, Maze M. Dexmedetomidine: another arrow for the clinician’s quiver. Anesthesiology 2004;101:568–70


Dexmedetomidine Infusion for Analgesia and Prevention of Emergence Agitation in Children with Obstructive Sleep Apnea Syndrome Undergoing Tonsillectomy and Adenoidectomy

Anuradha Patel, MD, FRCA,* Melissa Davidson, MD,* Minh C. J. Tran, MD, MPH,* Huma Quraishi, MD,† Catherine Schoenberg, BSN,* Manasee Sant, MD,* Albert Lin, MD,* and Xiuru Sun, MS*

BACKGROUND: Dexmedetomidine, a specific α2 agonist, has an analgesic-sparing effect and reduces emergence agitation. We compared an intraoperative dexmedetomidine infusion with bolus fentanyl to reduce perioperative opioid use and decrease emergence agitation in children with obstructive sleep apnea syndrome undergoing adenotonsillectomy (T&A).

METHODS: One hundred twenty-two patients with obstructive sleep apnea syndrome undergoing T&A, ages 2 to 10 years, completed this prospective, randomized, U.S. Food and Drug Administration–approved study. After mask induction with sevoflurane, group D received IV dexmedetomidine 2 µg · kg⁻¹ over 10 minutes, followed by 0.7 µg · kg⁻¹ · h⁻¹, and group F received IV fentanyl bolus 1 µg · kg⁻¹. Anesthesia was maintained with sevoflurane, oxygen, and nitrous oxide. Fentanyl 0.5 to 1 µg · kg⁻¹ was given to subjects in both groups for an increase in heart rate or systolic blood pressure 30% above preincision values that continued for 5 minutes. Observers in the postanesthesia care unit (PACU) were blinded to treatment groups. Pain was evaluated using the objective pain score in the PACU on arrival, at 5 minutes, at 15 minutes, then every 15 minutes for 120 minutes. Emergence agitation was evaluated at the same intervals by 2 scales: the Pediatric Anesthesia Emergence Delirium scale and a 5-point scale described by Cole. Morphine (0.05 to 0.1 mg · kg⁻¹) was given for pain (score >4) or severe agitation (score 4 or 5) lasting more than 5 minutes.

RESULTS: In group D, 9.8% patients needed intraoperative rescue fentanyl in comparison with 36% in group F (P < 0.001). Mean systolic blood pressure and heart rate were significantly lower in group D (P < 0.05). Minimum alveolar concentration values were significantly different between the 2 groups (P = 0.015). The median objective pain score was 3 for group D and 5 for group F (P = 0.001). In group D, 10 (16.3%) patients required rescue morphine, in comparison with 29 (47.5%) in group F (P = 0.002). The frequency of severe emergence agitation on arrival in the PACU was 18% in group D and 45.9% in group F (P = 0.004); at 5 minutes and at 15 minutes, it was lower in group D (P = 0.028). The duration of agitation on the Cole scale was statistically lower in group D (P = 0.004). In group D, 18% of patients and 40.9% in group F had an episode of SPO2 below 95% (P = 0.01).

CONCLUSIONS: An intraoperative infusion of dexmedetomidine combined with inhalation anesthetics provided satisfactory intraoperative conditions for T&A without adverse hemodynamic effects. Postoperative opioid requirements were significantly reduced, and the incidence and duration of severe emergence agitation was lower with fewer patients having desaturation episodes. (Anesth Analg 2010;111:1004–10)
an intraoperative infusion of Dex combined with general anesthesia would be a safe and effective substitute to opiates intraoperatively, reduce opiate requirements postoperatively, and also be effective in reducing the incidence and severity of EA in children with OSAS undergoing T&A.

METHODS
An Investigational New Drug number (76,041) was obtained from the U.S. Food and Drug Administration. The study was registered at www.clinicaltrials.gov (registration number NCT00468052) and approved by the IRB of the University of Medicine and Dentistry of New Jersey. One hundred thirty-seven children ages 2 to 10 years, ASA physical status II–III, undergoing elective T&A, were enrolled in this investigator-initiated, prospective, randomized, blinded, controlled study. Informed, written consent to participate in the study was obtained from the parent or legal guardian and assent from children older than 7 years of age. All patients had OSAS on the basis of clinical symptoms or diagnostic polysomnography. Clinical grading of OSAS was done by the surgeon on the basis of severity of symptoms such as restless sleep, severe snoring, apnea witnessed by the parents, nocturnal enuresis, stertor, hyperactivity, or failure to thrive. Exclusion criteria were known allergy to α2 agonists, developmental delay, cardiac and craniofacial abnormalities, anxiety disorder, chronic disabilities or pain syndrome, and use of psychotherapeutic medications, β blockers, digoxin, cimetidine, α2 agonists, anticonvulsants, or psychotropic medications. A random number table was used to assign subjects into 1 of 2 treatment groups: Dex infusion (group D) or IV fentanyl (group F). The anesthesiologists and data collectors in the operating room (OR) were not blinded; the subjects, their parents, and observers in the postanesthesia care unit (PACU) were blinded to treatment group.

No premedication was given. Monitoring included pulse oximetry, electrocardiogram, noninvasive arterial blood pressure (NIBP), end-tidal CO2, (ETCO2), and a depth of anesthesia monitor, the Bispectral Index (BIS; Aspect Medical Systems, Natick, Massachusetts). Anesthesia was induced with 8% inspired sevoflurane and 60% nitrous oxide (N2O) in oxygen by facemask. Group D received IV Dex (2 μg·kg⁻¹ over 10 minutes, followed by 0.7 μg·kg⁻¹·h⁻¹ until 5 minutes before the end of the surgery), and group F received IV fentanyl (1 μg·kg⁻¹) as a bolus, as soon as IV access was obtained. A balanced salt solution was administered according to standard fluid administration guidelines. Rocuronium 0.6 mg·kg⁻¹ was used to facilitate tracheal intubation. End-tidal sevoflurane concentration was maintained at 1 minimum alveolar concentration (MAC) with 60% N2O as long as the BIS remained below 60 during surgery. If the BIS reached 60 or more, the sevoflurane concentration was increased to reduce the BIS below 60. All patients received IV dexamethasone 0.5 mg·kg⁻¹ (maximum 10 mg) and rectal acetaminophen 30 to 40 mg·kg⁻¹ up to a maximum of 1000 mg before the start of surgery. The data collector recorded the heart rate (HR), systolic and diastolic blood pressures (NIBP), hemoglobin oxygen saturation (SpO2), ETCO2 tension, MAC, and BIS every 5 minutes during the anesthetic. The values in the holding area for HR and systolic blood pressure were used as baseline. Both groups received fentanyl 0.5 to 1 μg·kg⁻¹ for an increase in HR or systolic NIBP 30% above the value before start of surgery and sustained for 5 minutes. Lactated Ringer’s solution 15 mL/kg was administered as a fluid bolus for a 30% decrease of systolic blood pressure from baseline, which continued for 2 readings and glycopyrrolate 0.01 mg·kg⁻¹ for a 30% decrease in HR. Sevoflurane was discontinued once hemostasis was achieved and muscle relaxation was reversed with neostigmine 0.05 mg·kg⁻¹ and glycopyrrolate 0.01 mg·kg⁻¹. The time to awakening (TA), defined as spontaneous eye opening or on command from end of surgery, and the time to extubation (TE), defined as time from end of surgery to tracheal extubation, were recorded. All patients were observed continuously in the PACU for 2 hours by observers blinded to study group. Pain was evaluated using the objective pain score (OPS) in the PACU on arrival and at 5 minutes, at 15 minutes, and then every 15 minutes for 120 minutes. EA was evaluated at the same intervals by 2 scales: the Pediatric Anesthesia Emergence Delirium (PAED) scale and a 5-point agitation scale described by Cole. Duration of severe EA was noted on the Cole scale. Morphine (0.05 to 0.1 mg·kg⁻¹) was given for pain (score >4) or severe agitation (score 4 or 5) lasting more than 5 minutes. HR, systolic and diastolic NIBP, respiratory rate (RR), and SpO2 were recorded in the PACU every 5 minutes for the first 15 minutes, then at 15-minute intervals for the next 2 hours. Any desaturation episode with SpO2 below 95% was noted.

Statistical Methods
A power analysis indicated that 60 subjects were required per group to show that the number of patients needing intraoperative rescue fentanyl and rescue morphine in the PACU would be 50% lower in the subjects receiving Dex. Sixty subjects were also required per group to determine that treatment with Dex would decrease the incidence of severe EA after surgery by 50% with 80% power (α = 0.05) in comparison with the control group.

Data were analyzed using SPSS software (version 16, Chicago, Illinois), and are presented as number (n) or percentage (%), mean ± SD, or median as appropriate. Student t test was used to compare the mean value of quantitative data between the 2 groups. Two-way repeated-measures analysis of variance (ANOVA) was used for NIBP, HR, SpO2, MAC, and BIS. Student t test was used for the comparisons of intragroup values of intraoperative and postoperative systolic blood pressure and HR. Nonparametric data such as pain score, PAED score, and EA score on the Cole scale were compared between groups with Mann–Whitney U test. Fischer exact test was used for comparison of gender; percentage of patients in each group with a preoperative diagnosis of mild, moderate, or severe OSAS; and number of patients rescued with fentanyl or morphine and those with episodes of severe EA. P value of 0.05 or less was considered statistically significant.

RESULTS
Results are presented for 122 patients. One hundred thirty-seven subjects were enrolled in this study; 15 subjects were eliminated from data analysis for the following reasons:
surgery was cancelled for 2 patients, 1 refused to participate after enrolling, and 1 patient had an intraoperative complication. Eleven subjects who completed the study had deviation from this strictly controlled protocol or incomplete data and were also removed before data analysis.

The 2 groups were comparable in age, gender, baseline HR, systolic NIBP, and diagnosis of OSAS (Table 1). The age range of patients in the study was 2 to 10 years, 90% of patients were 6 years or younger, and 26 patients (46.2%) in each group were 2 to 3 years old.

Intraoperative data are presented in Table 2. In group D, 6 patients (9.8%) needed rescue fentanyl in comparison with 22 (36%) in group F (P = 0.001). Mean HR (P = 0.001) (Fig. 1A) and mean systolic NIBP (Fig. 1B) were significantly lower in group D during the first 60 minutes (P = 0.019). Mean diastolic NIBP was not statistically different in the 2 groups (P = 0.29). During the first 60 minutes of the anesthetic, MAC values of sevoflurane were significantly different between the 2 groups (P = 0.015); MAC was lower in group D, ranging from 5.7% to 41.6%. There was a statistical difference in TA and TE, both lower in group D than in group F (P < 0.05). Duration of surgery was statistically lower in group D (P = 0.041). There was no difference in the average dose of intraoperative fentanyl and dexamethasone between the 2 groups. The dose of acetaminophen was lower in group D. None of the subjects needed glycopyrrolate for bradycardia or fluid bolus for hypotension in the OR.

The variables measured in the PACU are shown in Table 3. In group D 10 (16.3%) patients required rescue morphine, in comparison with 29 (47.5%) in group F (P = 0.002). The median of the maximum OPS was 3 for group D and 5 for group F (P = 0.001). The percentage of patients with an OPS score of 4 and above (Fig. 2A) from arrival (P = 0.001) and at 5 and 15 minutes was statistically lower in group D (P < 0.05). On the Cole scale (5-point scale), severe EA was defined as a score of 4 to 5. The frequency of severe EA is shown in Figure 2B. On arrival in the PACU it was statistically lower, 18% in group D and 45.9% in group F (P = 0.004). At 5 and 15 minutes it was statistically lower in group D (P = 0.028). At 30 minutes none of the patients had severe EA in group D, and 1.6% of patients in group F had severe EA. The duration of agitation on the Cole scale showed statistical significance; it was 6.59 ± 7.4 minutes (mean ± sd) for group D and 11.85 ± 12.0 minutes (mean ± sd) for group F (P = 0.004). There was a statistical difference in the median of the highest score on the Cole scale, 3 for group D and 4 for group F (P = 0.001). The percentage of patients with a score of 10 and above for the PAED (Fig. 2C) was statistically lower in group D at arrival (P = 0.004).

**Table 1. Demographic Data**

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (years)</th>
<th>Gender (M/F)</th>
<th>Weight (kg)</th>
<th>Baseline systolic NIBP (mm Hg)</th>
<th>Baseline HR (beats/minute)</th>
<th>OSAS (% patients)</th>
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</thead>
<tbody>
<tr>
<td>F</td>
<td>3.8 ± 1.5</td>
<td>26/42.6</td>
<td>35/26</td>
<td>101 ± 13.7</td>
<td>105 ± 18</td>
<td>120</td>
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<tr>
<td>D</td>
<td>4.2 ± 2.1</td>
<td>26/42.6</td>
<td>35/26</td>
<td>104 ± 12.6</td>
<td>104 ± 15</td>
<td>120</td>
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**Table 2. Intraoperative Data**

<table>
<thead>
<tr>
<th>Data</th>
<th>Group F (n = 61)</th>
<th>Group D (n = 61)</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td>Rescue by fentanyl, n (%)</td>
<td>22 (36.1)</td>
<td>6 (9.8)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Fentanyl rescue dosage (µg/kg)</td>
<td>1.04 ± 0.67</td>
<td>0.73 ± 0.25</td>
<td>0.312</td>
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<tr>
<td>Time of rescue (minutes)</td>
<td>10.82 ± 12.5</td>
<td>17.6 ± 6.77</td>
<td>0.256</td>
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<tr>
<td>Acetaminophen dosage (mg/kg)</td>
<td>31.51 ± 4.96</td>
<td>28.30 ± 6.59</td>
<td>0.02*</td>
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<tr>
<td>Dexamethasone dosage (mg/kg)</td>
<td>0.30 ± 0.12</td>
<td>0.30 ± 0.14</td>
<td>0.847</td>
</tr>
<tr>
<td>Duration of surgery (minutes)</td>
<td>43.33 ± 17.36</td>
<td>37.54 ± 13.33</td>
<td>0.041*</td>
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<tr>
<td>Duration of anesthesia (minutes)</td>
<td>75.08 ± 24.73</td>
<td>69.80 ± 16.82</td>
<td>0.175</td>
</tr>
<tr>
<td>Time to awake (minutes)</td>
<td>8.75 ± 4.06</td>
<td>7.18 ± 4.05</td>
<td>0.03*</td>
</tr>
<tr>
<td>Time to extubate (minutes)</td>
<td>10.44 ± 4.15</td>
<td>8.59 ± 4.51</td>
<td>0.02*</td>
</tr>
</tbody>
</table>

Data are expressed as n, mean ± SD, and percentage.

Group D = dexmedetomidine group; group F = fentanyl group; HR = heart rate; NIBP = noninvasive arterial blood pressure; OSAS = obstructive sleep apnea syndrome.

* P < 0.05.
Children in group D had statistically lower systolic blood pressure and HR, almost the entire duration of the anesthetic (Fig. 1), but none of the patients needed intervention for bradycardia or hypotension on the basis of study criteria. Hemodynamic data are consistent with reports by other investigators. Mason et al. used higher doses of Dex (2 to 3 μg · kg⁻¹ loading dose and infusion of 1.5 to 2 μg · kg⁻¹ · h⁻¹) as the sole drug for sedation in children and observed a decrease in HR and blood pressure, which were within 20% of awake normal range. In children anesthetized with one MAC sevoflurane or desflurane and given a single, lower dose of Dex (0.5 μg · kg⁻¹), Deutsch et al. found a significant decrease in HR, but neither the systolic nor diastolic blood pressure was statistically lower. The biphasic response usually seen in adults, with an initial increase in systolic blood pressure and a reflex decrease in
Dexmedetomidine Infusion for Adenotonsillectomy

HR followed by stabilization of these variables below baseline, is not observed in children.\textsuperscript{15}

On the basis of routine clinical practice, fentanyl was given in a dose of 1 $\mu$g · kg\textsuperscript{-1} as a bolus to the control group. This lower dose is based on the enhanced analgesic sensitivity to opiates in children with OSAS.\textsuperscript{3} It is noteworthy that in the control group only 36% of patients needed rescue fentanyl, indicating that our technique of low-dose fentanyl is effective in almost two thirds of patients. HR and systolic blood pressure increase was used as the trigger for rescue fentanyl in both groups in response to surgical stimulation. The BIS monitor was used to ensure that patients in group D had an adequate depth of anesthesia because they may not display hemodynamic changes due to the inherent sympatholytic properties of Dex. In an attempt to maintain equivalent depth of anesthesia in both groups, the sevoflurane concentration was titrated to maintain a BIS value below 60. Consistent with studies in adult patients, the concentration of sevoflurane required to maintain the BIS below 60 was smaller in patients receiving Dex (MAC in group D was 5.7% to 41.6% lower). Tufanogullari et al.\textsuperscript{8} found reductions in the average end-tidal desflurane concentration of 19%–22%, depending on the rate of Dex infusion, which ranged from 0.2 to 0.8 $\mu$g · kg\textsuperscript{-1} · h\textsuperscript{-1}. The anesthetic-sparing effect of Dex appears to have an added advantage in facilitating earlier awakening and tracheal extubation. In the present study, TA and TE were statistically lower in group D, despite the high dose used. Most investigators using Dex as a low-dose intraoperative infusion or as a single bolus reported no difference in TA and TE in comparison with placebo.\textsuperscript{6,16} Only 1 study reported that a single dose of 0.5 $\mu$g · kg\textsuperscript{-1} Dex, 5 minutes before the end of surgery significantly prolonged TA and TE in comparison with placebo in patients having T&A.\textsuperscript{7}

Evaluation of postoperative pain is complicated by the difficulty in assessing pain in younger children and by the occurrence of EA. It is often difficult to distinguish between pain and EA because of the overlapping clinical picture, and pain itself can be the source of agitation.\textsuperscript{17} Most investigators have used different assessment tools to try and separate the two, but there is generally overlap in the scales, because a child who is restless or thrashing will score high on both scales. We did find a positive correlation between agitation and pain; group F had higher pain and EA scores than did group D. Results on the OPS, Cole scale, and PAED showed a very similar trend in both groups; scores were highest on arrival in the PACU and decreased over time (Fig. 2, A–C). A significantly smaller number of patients needed rescue morphine in group D, 18% in comparison with 44% in group F. Because it is difficult to separate pain and EA, and the fact that the rescue drug for both agitation and pain in our study was morphine, it is not possible to determine whether the morphine was given for pain or for agitation. On the basis of the effectiveness of smaller doses of intraoperative Dex in adult patients for reducing postoperative morphine consumption for 24 hours,\textsuperscript{8,18} we could assume that an analgesic effect would be present in our study patients in the immediate postoperative period. In children, Guler et al.\textsuperscript{7} found that 23% patients who received a single dose of 0.5 $\mu$g/kg Dex before the end of the procedure (T&A) required opioids for analgesia in the PACU in comparison with 53% in the placebo group. Erdil et al.\textsuperscript{19} compared a single dose of 0.5 $\mu$g · kg\textsuperscript{-1} Dex with 2.5 $\mu$g · kg\textsuperscript{-1} fentanyl in patients undergoing adenoectomy and concluded that Dex provided residual analgesia similar to that of fentanyl.

Pain can be severe after T&A, and it is commonly treated with opioids, despite a known sensitivity of patients with OSAS and recurrent hypoxemia to opiates. Brown et al.\textsuperscript{3} reported enhanced analgesic morphine sensitivity in children with OSAS during T&A and reduced morphine requirements after T&A. Therefore, several nonopioid analgesics such as ketorolac, ketamine, and tramadol have been evaluated for pain management after T&A,\textsuperscript{20–22} but none have gained widespread use or acceptance because of concerns with side effects or inadequate analgesia. A morphine-sparing effect of acetaminophen has been demonstrated in pediatric day-case surgery,\textsuperscript{23} and dexamethasone also reduces post-tonsillectomy pain.\textsuperscript{24} In the present study, all patients were given 30 to 40 mg · kg\textsuperscript{-1} of acetaminophen rectally before start of surgery and intraoperative IV dexamethasone. A multimodal, opioid-sparing, analgesic approach including Dex, such as the one used in our study, is worth considering in this patient population with a high potential for adverse respiratory events. The incidence of nausea or vomiting was extremely low in this study. Only 1 patient needed an antiemetic in the PACU, probably because of the antiemetic effect of dexamethasone.

EA is a complex phenomenon, the etiology of which is multifactorial. The wide variability in the incidence of agitation in the different studies on EA may be due to the criteria used to define this phenomenon and the time in the PACU when EA was measured.\textsuperscript{17} We did repeated measurements at frequent time intervals, because a single measurement may not reflect the true incidence of EA.\textsuperscript{11} Group D had a statistically lower frequency of severe EA than did group F until 30 minutes (Fig. 2B). At 30 minutes there was no incidence of severe EA in group D, and in group F it was 1.6%. Severe EA lasting more than 5 minutes was treated. The incidence of severe EA on arrival in the PACU in group D (18%) was similar to that reported by Guler et al.\textsuperscript{7} (17%), who used a single dose of Dex 5 minutes before the end of the procedure in children undergoing T&A. The occurrence of EA in younger patients and otolaryngologic procedures is reported to be high, although the exact reason for this is not known.\textsuperscript{4} Ninety percent of patients in our study were 6 years old or younger, and 26 patients (46.2%) in each group were 2 to 3 years old. Hyperactivity and attention deficit disorder are frequently seen in children with OSAS, possibly explaining or contributing to a high incidence of EA in our T&A patients. Dexmedetomidine has been used successfully as an infusion (0.2 $\mu$g · kg\textsuperscript{-1} · h\textsuperscript{-1}) continued into the postoperative period for 15 minutes or single dose at the end of surgery (0.5 $\mu$g · kg\textsuperscript{-1}) to prevent or reduce emergence delirium in children.\textsuperscript{6,7,16} It must be noted that these studies compared Dex with placebo, whereas our control group received fentanyl 1 $\mu$g · kg\textsuperscript{-1}, which also reduces EA. However, a higher dose is reported to be effective in patients having painful procedures.\textsuperscript{25} From our study and others, it remains difficult to discern whether the analgesic or sedative effects of $\alpha_2$ agonists are responsible for reducing EA in
children; regardless of the mechanism, Dex appears to be effective in a wide range of doses. The half-life of Dex is reported to be 1.8 hours in children, but there are no data on duration of sedative or analgesic effects after discontinuation of Dex infusion. The HRs were significantly slower in group D until 90 minutes in the PACU. The residual effects on HR of an intraoperative Dex infusion and the potential for an attenuated response to postoperative bleeding in T&A patients may be a concern and a disadvantage of using a Dex infusion.

The risk of respiratory morbidity after T&A in children with OSAS is reported to be about 20%. Sanders et al. reported that although the patients with OSAS were more likely to require supplemental oxygen, oral airway use, or assisted ventilation on emergence, severe complications such as laryngospasm and bronchosperm were uncommon. In the present study, there were no instances of laryngospasm or bronchosperm after extubation. One patient developed intraoperative pulmonary edema and was excluded from the study because she remained intubated overnight. Although not a study variable, we noted that extubation was much smoother with less coughing and breath-holding in patients given Dex. All patients were observed continuously in the PACU for 2 hours, and the observers were asked to record the lowest SpO2 during this period. There was a statistically significant difference in the number of patients with SpO2 below 95% in the PACU between the 2 groups, 11 in group D and 25 in group F. This could be related to the smaller requirement for opiates in the PACU in group D or to the lower incidence and duration of severe EA in group D. The goal of having a child who was settled, comfortable, and less restless, with application of monitors and administration of supplemental oxygen in the PACU, was easier to achieve in patients who received Dex.

A few methodological considerations of this study need to be mentioned. The anesthesiologist and the data recorder in the OR were not blinded to the study group. We believe that knowledge of study group assignment did not bias the conduct of the anesthetic, because the study protocol was tightly controlled, with specific criteria regarding intraoperative rescue fentanyl, sevoflurane concentration, the time to discontinue sevoflurane, extubation criteria, and use of rescue morphine in the PACU.

The PAED is the only validated rating scale for emergence delirium. The investigators who developed the PAED scale rated emergence behavior 10 minutes after the child awakened and remained awake (did not fall back to sleep). Early in the present study, we found this to be a potential problem because children who were asleep were receiving ratings of 4 on the first 3 items of the scale because they could not make eye contact, their actions were not purposeful, and they were not aware of their surroundings. Therefore we had to modify the scoring on the scale and rate these items as zero. Clearly, the children were not agitated if they were sleeping. Because we used a modified version of the PAED, we used a second scale (Cole) to run concomitantly to support the findings with the modified version of the PAED. The 1 to 5 scale described by Cole et al. has been used in several studies of EA. It is not a validated scale, but is easy to use, and defining the categories of mild or severe is clear.

The OPS is not a validated scale, but this scale or some modification of it has been used in several studies in children. Although 2 other studies on EA have used the OPS, it is perhaps not the best scale to use in a study on EA because of considerable overlap on the items being scored. We did not follow patients once they were discharged from the PACU. A future study with overnight pulse oximetry data and use of postoperative analgesics would be worthwhile to perform.

**CONCLUSION**

In children undergoing T&A, the goal is to minimize respiratory and airway compromise and have an awake, settled, comfortable child after the surgery. An opioid-sparing technique is particularly appealing in children with OSAS, when airway obstruction is known to preexist and may persist on the night after surgery. An intraoperative infusion of Dex combined with sevoflurane and N2O provided satisfactory intraoperative conditions for T&A without adverse hemodynamic effects. TA and TE were shorter than they were for the patients receiving fentanyl. Postoperative opioid requirements were significantly reduced, and the incidence and duration of severe EA was lower, resulting in a smooth recovery. We have described a practical, effective, and safe technique for using Dex infusion. A multimodal, opioid-sparing, analgesic approach including Dex, such as the one used in our study, can be useful in children with OSAS undergoing other surgical procedures besides T&A, wherein the advantages of decreased perioperative opioid requirements and a reduced occurrence of EA will be beneficial.

**REFERENCES**

Elimination of Preoperative Testing in Ambulatory Surgery

Frances Chung, FRCPC
Hongbo Yuan, PhD
Ling Yin, MSc
Santhira Vairavanathan, MBBS
David T. Wong, MD

BACKGROUND: Preoperative testing has been criticized as having little impact on perioperative outcomes. We conducted a randomized, single-blind, prospective, controlled pilot study to determine whether indicated preoperative testing can be eliminated without increasing the perioperative incidence of adverse events in selected patients undergoing ambulatory surgery.

METHODS: One thousand sixty-one eligible patients were randomized either to have indicated preoperative testing or no preoperative testing. In the indicated testing group, patients received indicated preoperative testing: a complete blood count, electrolytes, blood glucose, creatinine, electrocardiogram, and chest radiograph according to the Ontario Preoperative Testing Grid as per current practice, whereas in the no testing group, no testing was ordered. The investigators, data collectors, and patient outcome reviewers were blinded to the group assignment. The primary outcome measures were the rate of perioperative adverse events and the rates of adverse events within 7 and 30 days after surgery.

RESULTS: Patients’ age, gender, American Society of Anesthesiologists status, type of surgery, and anesthesia were similar between the two groups. There were no significant differences in the rates of perioperative adverse events and the rates of adverse events within 30 days after surgery between the no testing group and the indicated testing group. Hospital revisits 7 days were higher in the indicated testing group (P < 0.05). None of the adverse events were related to the indicated testing or no testing.

CONCLUSIONS: This pilot study showed that there was no increase in the perioperative adverse events as a result of no preoperative testing in our study population. A larger study is needed to demonstrate that indicated testing may be safely eliminated in selected patients undergoing ambulatory surgery without increasing perioperative complications.

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Ambulatory surgery accounts for 65–70 percent of all surgery. The costs of preoperative testing are substantial. In the United States this is estimated at more than $18 billion.1 The costs saving in health care can be significant if preoperative testing is to be eliminated in ambulatory surgery.

A number of observational studies have been conducted to investigate the effectiveness of preoperative testing in ambulatory surgery.2,3 A retrospective study in Mayo Clinic showed that 4% (160 of 3782) of the patients who underwent ambulatory surgery had abnormal testing results.2 No association was found between postoperative adverse events and any testing abnormality. No change in perioperative care management was attributed to the abnormal testing results. In 2002, the “Practice Advisory” of the American Society of Anesthesiologists (ASA) concluded that “routine” preoperative testing does not make a valuable contribution to preoperative evaluation while “indicated” testing may help perioperative management decision making.4

An indicated test is one that is required by specific clinical features or preexisting medical conditions.4 For patients undergoing ambulatory surgery, even indicated testing may be unnecessary in healthy patients, as suggested by a number of case series studies.2,3,5,6 In 2004, a survey of anesthesiologists showed that the current preoperative testing practices in ambulatory surgery are widely disparate, and 40% of anesthesiologists had no concerns about eliminating preoperative testing.7

In 2000, Schein et al.8 published the results of a multicenter, randomized, controlled trial (RCT) studying the impact of eliminating preoperative testing on postoperative outcome in cataract surgery. There was no difference in postoperative adverse events or death, which were identical at 3.1 per 100 operations in the testing and no testing group. Similar to those underlying cataract surgery, patients undergoing ambulatory surgery may be at low risk of perioperative morbidity and mortality.9–12 Therefore, preoperative

...
testing may be unnecessary not only in cataract surgery but also in ambulatory surgery. However, patients having ambulatory surgery may have higher perioperative risk than those having cataract surgery. Patients with preexisting medical diseases are having many different types of surgery on an ambulatory basis. No RCTs of the effectiveness of indicated preoperative testing in ambulatory surgery have been done. Although Schein et al. showed that adverse outcomes did not increase if preoperative testing in cataract patients was eliminated, it remains unknown whether this finding can be applied to selected patients undergoing ambulatory surgery.8 The hypothesis of this study is that there is no significant difference in the incidence of perioperative adverse outcomes between patients with indicated preoperative testing and no testing.

METHODS
Patients and Randomization
This study was a single blinded, pilot RCT conducted at Toronto Western Hospital, an affiliated hospital of University of Toronto. Inclusion criteria were patients scheduled to undergoing orthopedic, plastic, general, urology, ophthalmologic (excluding cataract), or spinal surgery who were older than 16 yr and were scheduled to be discharged home on the same day. Exclusion criteria were patients undergoing ambulatory cardiovascular, thoracic, neurosurgical or cataract surgery, or any of the following medical conditions: i) myocardial infarction (MI) within 3 mo, previous heart surgery or angioplasty; ii) angina, Canadian Cardiovascular Class (CCS) 3, angina on walking <1 flight of stair or two blocks; CCS 4, angina with activities of daily living, including at rest; iii) dyspnea, CCS 3 shortness of breath <1 flight of stair or two blocks, CCS 4 shortness of breath with activities of daily living, including at rest; iv) arrhythmias; v) history of coagulopathy or blood disorder (leukemia, lymphoma, von Willebrands disease, hemophilia, platelet disorder); vi) history of significant anemia; vii) history of significant liver disease (cirrhosis, acute or chronic hepatitis); viii) history of significant renal disease (chronic renal failure, known renal impairment); ix) any other new or worsening medical condition that would warrant medical testing even if surgery was not planned; x) any preoperative testing during 30 days before enrollment; xi) prior enrollment in this trial. Patients who were foreign residents or who could not speak English were also excluded.

The study was approved by Institutional Ethics Board. A list of patients with scheduled ambulatory surgery was obtained from the surgeon’s office. Within 30 days before surgery, patients were referred to the preoperative clinic for registration of ambulatory surgery. At the preoperative clinic, all patients were screened for their eligibility for the study by a research anesthesiologist (S.V.). Each eligible participant was randomly assigned to the indicated testing or no testing group after written informed consent. A computer-generated randomization list was produced in strata according to age (16–39, 40–59, ≥ 60 yr). Preoperative evaluations were performed by anesthesiologists independent of the study.

In the indicated testing group, patients received part or all of a panel of tests ordered by surgeons strictly according to the Ontario Preoperative Testing Grid (Appendix A)13 which was developed by the Ontario Preoperative Task Force, Guidelines Advisory Committee.13 Hospitals in Ontario have adopted these guidelines for indicated preoperative testing for both inpatient and ambulatory surgery. The preoperative testing in this study included complete blood count (CBC), electrolytes, creatinine, blood glucose, electrocardiogram (ECG), or chest radiograph. In the no testing group, no preoperative testing was performed. The indicated testing that was originally ordered for the patients by the surgeons according to the Ontario Preoperative Testing Grid was cancelled. Sickle cell screening, coagulation tests, and pregnancy tests were not studied in this protocol. For patients with diabetes, blood glucose was measured on the day of surgery, regardless of the group assignment.

Noncompliance, i.e., “crossover,” meant that a patient in the no testing group chose to take some tests (or full tests) after randomization and vice versa; a patient in the indicated testing group chose not to take any test. Crossover might have resulted from either patients or anesthesiologists after randomization to the indicated testing or no testing groups. When the anesthesiologist disagreed with the group assignment for patients to the no testing group, he or she could proceed and order tests based on their own clinical judgment. Crossover status was determined according to the information about preoperative tests that was recorded in the surgical chart on the day of surgery.

Data Collection and Outcomes
Baseline and preoperative patient data were collected with the use of standardized medical history questionnaires at the time of enrollment at the preoperative clinic by the research anesthesiologist (S.V.). In the indicated testing group, patients had testing: CBC, electrolytes, creatinine, blood glucose, ECG, or chest radiograph, according to their specific indications. The indicated preoperative tests of patients who were assigned to the no testing group were cancelled and were not done. Data regarding the perioperative adverse events and treatments were obtained by chart abstraction from the computerized hospital charts. At 7 days after surgery, a telephone interview was conducted to collect data on adverse events during the first week. A research nurse (L.Y.) blinded to study group assignment was responsible for the interview. If initial patient contact failed, subsequent follow-up
was attempted until the patient was successfully interviewed. In the event of loss to follow-up (e.g., out of country), a proxy (e.g., a family member of the patient) was approached. Data on readmission, number of visits to physicians or death within 30 days after surgery were also obtained through computerized hospital records.

The primary outcome measures were severe adverse events occurring within 7 and 30 days after surgery. This included MI, myocardial ischemia, cardiac arrest, congestive heart failure, arrhythmia, hypertension, hypotension, stroke, transient ischemic attack, respiratory failure, hypoglycemia, diabetic ketoacidosis, nonketotic hyperosmolar syndrome, and sudden unexpected death. Standard definitions for these adverse events were provided to the data abstractor (L.Y.) (Appendix B). Other outcomes that were studied are: operation room delays/cancellations, delayed discharge, unanticipated admission and readmission at 7 and 30 days, respectively (Appendix B). The cost of tests, defined as charges by the laboratory, ordered per operation was also documented.

During the study, investigators and data abstractor or patient outcome interviewer were blinded to whether patients received the indicated testing or no testing. When they reported that an event had occurred, the relevant documents were reviewed by two anesthesiologists to determine whether they met the standard definition of adverse event. The two anesthesiologists (F.C., D.W.) were not informed of study group assignment and had no access to preoperative testing data. They made a clinical judgment whether a preoperative test was likely to have affected the probability of the event’s occurrence or its severity.

A literature review indicated that there were three large prospective trials of adverse outcomes in ambulatory surgical patients.14–16 In 6914 ambulatory surgical patients, Duncan et al.14 found an incidence of 3.93% cardiorespiratory events. Osborne and Rudkin15 found a 6.7% incidence of cardiorespiratory events in 6000 ambulatory surgical patients. Chung et al.16 found an incidence of 4.33% cardiorespiratory events in 17,639 ambulatory surgical patients. Based on these three studies, a sample size of 10,000 per arm would have 90% power to reject a 1% increase in rate of adverse outcomes in the no testing group with a Type 1 error of 0.05.

**Statistical Analysis**

Data were analyzed as intention-to-treat. Patients remained in the groups to which they were initially assigned, regardless of tests they actually received. A frequency distribution of sociodemographic characteristics and risk factors were presented in the no testing and indicated testing group. Statistical difference in the distribution was determined using χ² test. Analysis of adverse events rate was performed for each period according to the treatment initially received (no testing versus indicated testing). For a combined rate of severe adverse events, events were counted on a per patient basis. In this case, all the severe events were given the same weight. A 95% confidence interval of the relative risk was calculated to compare the risk of occurring adverse event in the no testing group to the risk in the indicated testing group. All analysis was performed using SAS 9.1 (Cary, NC).

**RESULTS**

**Patient Characteristics**

Patients scheduled to undergo ambulatory surgery (2297) were screened for 2 yr (Fig. 1). Eight hundred twenty-four patients were not eligible (31%). Among the ineligible patients, most did not speak English (25%), had blood work from a family doctor (12%), or MI within 3 mo, angina Grade 3 and 4, or dyspnea Grade 3 and 4 (34%). Eligible patients (1061) were randomly assigned either to the no testing group or the indicated testing group. Twelve patients were withdrawn (no testing versus indicated testing: 8 vs 4) mostly due to a change from ambulatory to inpatient surgery. Four patients in the no testing group were withdrawn by surgeons because of new diseases and one patient in the indicated testing group withdrew from the study himself. A similar number of patients changed their minds and did not proceed with surgery (no testing versus testing: 1.9% vs 2.4%).

Among the enrolled patients, 499 (49%) and 527 (51%) patients were in the no testing group and the indicated testing group, respectively. Nineteen crossover cases occurred by switching from the no testing to the indicated testing group due to the anesthesiologist’s request. ECG was the most common request that was ordered for 18 patients because of age and history...
of hypertension. According to the intention-to-treat analysis, these patients were treated as no testing.

In both groups, 85% of patients were older than 40 years. Most patients were ASA I or II status (no testing versus indicated testing: 88% vs 87%) (Table 1). Twelve percent of patients in each group were ASA III. Sixty-four percent in each group had preexisting diseases. Hypertension and diabetes were the two main preexisting diseases. Orthopedic, general, plastic, and ophthalmologic surgery accounted for 81% of the surgery for both groups. More than 50% of patients had general anesthesia in both groups. There was no statistically significant difference in gender, age, ASA status, preexisting diseases, type of surgery, and anesthesia between the two groups.

**Primary Outcomes**

There were no significant differences in the rates of intraoperative and postoperative adverse events between the indicated testing and the no testing groups before patient discharge. For 30 days after discharge, the rate of revisits, including visiting family doctors, emergency, and readmission to hospitals was not significantly different between the two groups. The rate of 7-day revisits to hospitals was higher in the indicated testing group versus the no testing group (5.1% vs 2.2% \( P < 0.05 \)) (Table 2). There was no readmission to the ward within 7 days. For both groups, readmission accounted for 17% of hospital revisits for 8–30 days.

Intraoperative adverse events were mostly associated with cardiovascular and respiratory diseases, such as dysrhythmia and hypertension (Table 3). More adverse events occurred postoperatively rather than intraoperatively. They were mainly related with prolonged postanesthesia care unit stay, e.g., inadequate pain control, nausea/vomiting or prolonged recovery time.

The main reasons that patients revisited the hospital after discharge were severe pain, infection, and other medical problems (Table 4). For the 7 days for hospital

<table>
<thead>
<tr>
<th>Table 1. Demographic Data</th>
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<tr>
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<tr>
<td>N (499)</td>
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<tr>
<td>Gender</td>
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<tr>
<td>Female:Male</td>
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<tr>
<td>Age group</td>
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<td>≥60</td>
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<td>ASA</td>
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<td>II</td>
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<td>III</td>
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<td>Regional</td>
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<tr>
<td>Spinal</td>
</tr>
<tr>
<td>General + regional</td>
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<tr>
<td>Monitored anesthesia</td>
</tr>
</tbody>
</table>

ASA = American Society of Anesthesiologists; CVA = cerebrovascular accident; TIA = transient ischemic attack; COPD = chronic obstructive pulmonary disease.
revisits, severe pain accounted for 25% in the no testing group versus 53% in the indicated testing group. The other medical problems included allergic reaction, recurrent disk hernia, wound dehiscence, and further surgery.

Table 5 shows the rate of perioperative adverse events before discharge from hospital according to the baseline medical status. There were no significant differences in the rates of adverse events when data were stratified by ASA, or preexisting disease. Hypertension and diabetes were the two most common preexisting diseases related to adverse event (Table 5). The indicated testing and the no testing groups had a similar frequency distribution in surgery delay and cancellation, but none was related to medical reasons.

Among 19 patients who crossed-over, three patients had adverse events. Two patients were admitted because of bleeding at the surgical site. In addition, one patient visited a medical clinic because of severe pain 7 days later.

In the indicated testing group, 11.5% (188 of 1632) of the tests were abnormal, 70 abnormal hematology or biochemistry results, and 118 abnormal ECGs. These abnormal tests were expected because of heart disease or diabetes. No association was found between perioperative adverse events and abnormal testing results. No change in perioperative care was attributed to the abnormal testing results except for one patient with atrial flutter with variable atrioventricular block. He was referred to a cardiologist and no treatment or delay of surgery was needed. In the indicated testing group, five patients had adverse events; two had dysrhythmia, two had a hypertensive period, and one had a hypotensive episode. All five had a normal preoperative ECG.

Costs and Saving

A similar number of preoperative tests were ordered for the no testing group and the indicated

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Table 2. Intraoperative and Postoperative Adverse Events Within 30 Days

<table>
<thead>
<tr>
<th>Event Type</th>
<th>No testing (n = 499)</th>
<th>Testing (n = 527)</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraoperative event</td>
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<td></td>
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<tr>
<td>Postoperative event</td>
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<tr>
<td>Unanticipated admission</td>
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<tr>
<td>Others</td>
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<tr>
<td>Hospital revisits (≤7 d) event</td>
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<td>Readmission</td>
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<tr>
<td>Other visits</td>
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<td></td>
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<tr>
<td>Hospital revisits (8–30 d) event</td>
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<td></td>
</tr>
<tr>
<td>Readmission</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other visits</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Event Type</th>
<th>No testing (499)</th>
<th>Testing (527)</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysrhythmia</td>
<td>1</td>
<td>2</td>
<td>1.0 (0.4–3.0)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
<td>0</td>
<td>0.8 (0.4–1.5)</td>
</tr>
<tr>
<td>Hypotension</td>
<td>0</td>
<td>0</td>
<td>0.6 (0.2–1.6)</td>
</tr>
<tr>
<td>Respiratory/Airway</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypoxemia</td>
<td>0</td>
<td>1</td>
<td>0.4 (0.2–0.9)</td>
</tr>
<tr>
<td>Laryngospasm</td>
<td>2</td>
<td>0</td>
<td>0.4 (0.2–0.9)</td>
</tr>
<tr>
<td>Bronchospasm</td>
<td>1</td>
<td>0</td>
<td>0.4 (0.2–0.9)</td>
</tr>
<tr>
<td>Difficult Intubation/Intubated on arrival</td>
<td>1</td>
<td>3</td>
<td>0.4 (0.2–0.9)</td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inadequate pain control</td>
<td>0</td>
<td>0</td>
<td>0.4 (0.2–0.9)</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>0</td>
<td>0</td>
<td>0.4 (0.2–0.9)</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>0</td>
<td>0</td>
<td>0.4 (0.2–0.9)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>0</td>
<td>0</td>
<td>0.4 (0.2–0.9)</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>0</td>
<td>0</td>
<td>0.4 (0.2–0.9)</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>1</td>
<td>0.4 (0.2–0.9)</td>
</tr>
</tbody>
</table>

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Table 3. Diagnoses Associated with Intraoperative and Postoperative Adverse Events

<table>
<thead>
<tr>
<th>Event Type</th>
<th>No testing (499)</th>
<th>Testing (527)</th>
<th>Relative risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysrhythmia</td>
<td>1</td>
<td>2</td>
<td>1.0 (0.4–3.0)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
<td>0</td>
<td>0.8 (0.4–1.5)</td>
</tr>
<tr>
<td>Hypotension</td>
<td>0</td>
<td>0</td>
<td>0.6 (0.2–1.6)</td>
</tr>
<tr>
<td>Respiratory/Airway</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypoxemia</td>
<td>0</td>
<td>1</td>
<td>0.4 (0.2–0.9)</td>
</tr>
<tr>
<td>Laryngospasm</td>
<td>2</td>
<td>0</td>
<td>0.4 (0.2–0.9)</td>
</tr>
<tr>
<td>Bronchospasm</td>
<td>1</td>
<td>0</td>
<td>0.4 (0.2–0.9)</td>
</tr>
<tr>
<td>Difficult Intubation/Intubated on arrival</td>
<td>1</td>
<td>3</td>
<td>0.4 (0.2–0.9)</td>
</tr>
<tr>
<td>Others</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inadequate pain control</td>
<td>0</td>
<td>0</td>
<td>0.4 (0.2–0.9)</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>0</td>
<td>0</td>
<td>0.4 (0.2–0.9)</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>0</td>
<td>0</td>
<td>0.4 (0.2–0.9)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>0</td>
<td>0</td>
<td>0.4 (0.2–0.9)</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>0</td>
<td>0</td>
<td>0.4 (0.2–0.9)</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>1</td>
<td>0.4 (0.2–0.9)</td>
</tr>
</tbody>
</table>

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testing group (Table 6). Nineteen patients were changed from the no testing to the indicated testing group, and 41 tests were conducted. In the no testing group, 1558 tests were ordered and cancelled for 480 patients resulting in a total saving of Canadian $18,447 or $38.50 per patient.

**DISCUSSION**

No RCT concerning the effectiveness of indicated preoperative testing in ambulatory surgery has been published. A literature review indicated that the studies were mostly retrospective chart reviews or case series of healthy patients.2,3,5,6 In this study, we randomized our ambulatory surgical patients to either indicated testing or no testing. This pilot RCT showed that there were no significant differences in the rates of perioperative adverse events and 30-day hospital revisits between patients who underwent the indicated testing versus those with no preoperative testing before ambulatory surgery. There was no perioperative death. In the no testing group, none of the adverse events was associated with no preoperative testing. The rate of intraoperative adverse events was very low (testing versus no testing: 1.3% vs 1.4%). The rate of postoperative adverse events before discharge was higher (testing versus no testing: 4% vs 3.2%). Most of the adverse events were not serious, and were not related to any significant cardiovascular events, respiratory failure, or life-threatening diseases. Consistent with previous studies, these results demonstrated that ambulatory surgery is low risk.9–11,17

<table>
<thead>
<tr>
<th>Table 4. Reasons for Hospital Revisit&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td></td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Severe pain</td>
</tr>
<tr>
<td>Bleeding</td>
</tr>
<tr>
<td>Infection</td>
</tr>
<tr>
<td>Urine retention</td>
</tr>
<tr>
<td>Other related medical problem</td>
</tr>
</tbody>
</table>

<sup>a</sup> One patient may have more than one reason to visit hospital.

<table>
<thead>
<tr>
<th>Table 5. Rates of Intraoperative and Postoperative Adverse Events According to Baseline Medical Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline medical status</td>
</tr>
<tr>
<td>-------------------------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>ASA</td>
</tr>
<tr>
<td>I</td>
</tr>
<tr>
<td>II</td>
</tr>
<tr>
<td>III</td>
</tr>
<tr>
<td>Preexisting disease&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Hypertension</td>
</tr>
<tr>
<td>TIA-CVA</td>
</tr>
<tr>
<td>COPD/asthma</td>
</tr>
<tr>
<td>Obesity</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Thyroid disease</td>
</tr>
<tr>
<td>Renal disease</td>
</tr>
<tr>
<td>Neurologic disease</td>
</tr>
<tr>
<td>Other disease</td>
</tr>
<tr>
<td>No disease</td>
</tr>
</tbody>
</table>

<sup>a</sup> One event might be associated with more than one preexisting disease.
<sup>b</sup> Denominators are the numbers of operations in each subgroup provided in Table 1.
ASA = American Society of Anesthesiologists; CVA = cerebrovascular accident; TIA = transient ischemic attack; COPD = chronic obstructive pulmonary disease.

<table>
<thead>
<tr>
<th>Table 6. Costs of Preoperative Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tests</td>
</tr>
<tr>
<td>---------------------------------------</td>
</tr>
<tr>
<td>CBC</td>
</tr>
<tr>
<td>Electrolytes</td>
</tr>
<tr>
<td>Creatinine/urea</td>
</tr>
<tr>
<td>Blood glucose</td>
</tr>
<tr>
<td>ECG</td>
</tr>
<tr>
<td>Radiograph</td>
</tr>
<tr>
<td>Total</td>
</tr>
<tr>
<td>Saving/costs</td>
</tr>
</tbody>
</table>

<sup>c</sup> Including 41 tests done by patients who were original in no testing group but were changed to testing group.
CBC = complete blood count; ECG = electrocardiogram.
had preexisting diseases. Hypertension and diabetes are the two coexisting diseases most likely associated with perioperative adverse events. This finding is in agreement with a prospective study of 17,638 ambulatory surgical patients that showed several preexisting diseases such as hypertension, obesity, smoking, asthma, and gastroesophageal reflux were more likely to be associated with perioperative adverse events.16

In the literature, the prevalence of abnormal testing results varied widely, and rarely led to significant changes in perioperative management. It has been shown that an abnormal rate of CBC was less than 3% in surgical patients,18–20 but increased to more than 10% in later studies.21–24 Abnormal findings as high as 75% are common on preoperative ECG.25–27 Abnormal preoperative chest radiographs ranged from 10% to 50%.27–29 However, the results influenced management in <5% of cases. Moreover, 30% to 60% of abnormalities discovered on preoperative testing were never investigated before surgery.30 In general, most patients had testing performed before surgery with little time for correction.23 The lack of correlation between the abnormal results and the clinician’s response suggested that abnormalities reported were minor.22

The decision regarding a patient’s fitness for surgery may be accurately predicted on the basis of history and clinical examination.31–33 In patients with false-positive findings, preoperative testing itself may bring more harm than benefit, leading to a cascade of investigations, cancellation or postponement of the planned surgery.34,35

By eliminating the indicated testing in ambulatory surgery, the economic implications may be substantial. Since the publication of Schein et al.’s8 study suggesting no preoperative testing in cataract surgery, centers have adopted this policy with substantial savings.36 In this study, the saving was Canadian $38.50 per patient. Eliminating preoperative testing in ambulatory surgery could mean large savings in the cost of health care.

One of the limitations of this study was its sample size of 1061 patients. To ensure 90% power to reject a 1% increase in rate of adverse events for the no testing group with a Type 1 error of 0.05, a sample size of 20,000 patients would be needed. From the results of this preliminary study, a large multicenter study is justified to demonstrate that preoperative testing may not be necessary in ambulatory surgical patients. The next important criticism is the use of the Ontario Preoperative testing grid to determine testing. This grid is a local, rather than a globally accepted, tool for determining the appropriate need and type of tests to perform preoperatively in ambulatory surgical patients. It, however, is a reasonable representation of the type of testing done for ambulatory surgical patients. This study had strict exclusion criteria with 22.5% of screened patients excluded due to medical reasons. For example, patients having MI within <3 mo before surgery, or angina CCS 3 and 4 were excluded. Therefore this study is not applicable to all ambulatory surgical patients.

To our knowledge, this is the first report of a RCT concerning eliminating preoperative testing in ambulatory surgical patients. Its strength includes ascertaining perioperative adverse events during the study period. This pilot study showed that there was no increase in perioperative adverse events with no preoperative testing in our study population. A larger study is needed to demonstrate that preoperative testing may be safely eliminated in selected patients undergoing ambulatory surgery without increasing perioperative complications.

ACKNOWLEDGMENTS

We acknowledge the expert advice given by Dr. Murray Krahn and Dr. George Tomlinson, Department of Internal Medicine, University of Toronto.

APPENDIX A: Ontario Preoperative Testing Grid13

<table>
<thead>
<tr>
<th>Test (adapted from GAC)</th>
<th>Criteria for tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete blood counts</td>
<td>Patient &gt;60 yr of age, anemia expected</td>
</tr>
<tr>
<td>Electrolyte/creatinine</td>
<td>Currently taking diuretics, renal disease, diabetes</td>
</tr>
<tr>
<td>Blood glucose</td>
<td>Diabetes</td>
</tr>
<tr>
<td>PT/PTT</td>
<td>Currently on anticoagulants, coagulopathy, chronic liver disease</td>
</tr>
<tr>
<td>Sickle cell screening</td>
<td>Patient of African or Caribbean origin</td>
</tr>
<tr>
<td>ECG</td>
<td>All patients &gt;45 yr of age, cardiac history or hypertension</td>
</tr>
<tr>
<td>Chest radiograph</td>
<td>Pulmonary disease, heavy smokers</td>
</tr>
</tbody>
</table>

Cardiovascular disease includes patients who have or have had:
- Previous heart surgery
- A history of heart problems
- Rheumatic heart disease
- A known heart murmur
- Chest tightness/chest pain/angina/or heart attack
- Heart beat irregularities or arrhythmias
- Congestive heart failure
- High blood pressure
- Peripheral vascular disease (i.e., carotid artery disease, aortic aneurysm, or lower limb arterial disease)
- SOB at two blocks on a flat grade or two flights of stairs

Pulmonary disease includes patients who have or have had:
- Chronic bronchitis or emphysema
- Smoking history of >20 pack years (defined as number of packs × number of years)
- Pulmonary fibrosis
- Pulmonary hypertension or previous pulmonary embolism
- Previous lung cancer—Hx of TB
- Cystic fibrosis or bronchiectasis
- Chest wall or back deformity
- Morbid obesity or sleep apnea
- Asthma only if there is a smoking history of any length
- SOB at two blocks on a flat grade or two flights of stairs

Renal disease includes patients who have or have had:
- Chronic renal failure
- Known renal impairment
- Recurrent urinary tract infections
- Recurrent kidney stones

Liver disease includes patients who have or have had:
- Excessive alcohol intake
- Acute or chronic hepatitis
- Previous history of jaundice or unclear etiology
- Cirrhosis

Vol. 108, No. 2, February 2009
APPENDIX B: Definition of Adverse Events

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction</td>
<td>The evolving changes in the ST-T segment, new Q waves, or both on an electrocardiogram; symptoms of ischemia plus abnormal serum levels of cardiac enzymes; or symptoms of ischemia plus left bundle branch block</td>
</tr>
<tr>
<td>Myocardial ischemia</td>
<td>New or more severe chest pain diagnosed as ischemia and requiring treatment</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>New pulmonary edema on a chest radiograph or a diagnosis of congestive heart failure</td>
</tr>
<tr>
<td>Clinically significant arrhythmia</td>
<td>New or worsening disturbance of heart rhythm requiring new treatment or a change in treatment</td>
</tr>
<tr>
<td>Clinically significant hypertension</td>
<td>Increase in systolic pressure to ( \geq 200 ) mm Hg or diastolic pressure to ( \geq 110 ) mm Hg with new antihypertensive treatment or a change in treatment required</td>
</tr>
<tr>
<td>Clinically significant hypotension</td>
<td>A decrease in systolic pressure (&lt; 90 ) mm Hg with treatment required</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>Abrupt onset of a focal neurologic deficit lasting (&lt; 24 ) h and resulting from cerebrovascular ischemia</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>Need for mechanical ventilation</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>Blood glucose level low enough to require intravenous dextrose</td>
</tr>
<tr>
<td>Diabetic ketoacidosis</td>
<td>Hyperglycemia with an increase in the anion gap, metabolic acidosis, and serum or urinary ketones</td>
</tr>
<tr>
<td>OR delays or cancellations</td>
<td>Delays/cancellations in OR due to false-positive preoperative testing or additional testing required by anesthesiologist in the no testing group</td>
</tr>
<tr>
<td>Unanticipated admission</td>
<td>Ambulatory surgery patient was admitted to the hospital instead of being discharged home. Reasons for unanticipated admission, medical, surgical, anesthesia, and social reasons were collected</td>
</tr>
<tr>
<td>Revisits within 7 d and within 30 d</td>
<td>Revisits include visiting family doctors, emergency, and readmission to hospital within 7 and 30 d of ambulatory surgery. Medical, surgical, and anesthesia reasons are documented</td>
</tr>
<tr>
<td>Other new or worsening medical problem requiring treatment with specific medication or procedure</td>
<td></td>
</tr>
</tbody>
</table>

REFERENCES

10. Fleisher LA, Anderson GF. Perioperative risk: how can we study the influence of provider characteristics? Anesthesiology 2002;96:1039–41
12. Warner MA, Shields SE, Chute CG. Major morbidity and mortality within 1 month of ambulatory surgery and anesthesia. JAMA 1993;270:1437–41
Escort accompanying discharge after ambulatory surgery: a necessity or a luxury?
Hui Yun Vivian Ip and Frances Chung

Introduction
Advances in surgery such as minimally invasive techniques, anesthetics pharmacology and regional anesthesia have revolutionized ambulatory surgical care. Surgeries performed on an ambulatory basis have also become more popular owing to the ever increasing pressure on hospital beds. There is an expansion of inclusion criteria for ambulatory surgery, including elderly and obese patients. This creates a danger in discharging patients without meeting the criterion of requirement of a responsible adult as an escort to accompany the patient home. Is the presence of an escort to accompany a patient home after ambulatory surgery an essential discharge criterion? This review examines the current evidence in the literature on whether an escort is necessary for patient discharge after ambulatory surgery.

Prevalence of no escorts in ambulatory surgical patients
In 1972, a survey conducted showed that 31% of patients journeyed home were unaccompanied by a responsible person, 73% of car owners drove within 24 h of the operation and 9% drove themselves home [1]. More than three decades later, little has changed. In an observational study of 28,391 ambulatory surgical patients, an incidence of 0.2% of patients without an escort was reported and, of these, only 9% had their surgery cancelled [2].

Compliance of patients with instructions may also be an issue as shown by our follow-up study of 750 patients. Four percent of patients drove vehicles within 24 h, 1.8% consumed alcohol and one patient made an important decision [3]. Similar results were found in England. Of 240 patients, 4.1% drove, 1.7% made important decisions and 10% cooked, ironed or looked after children. A total of 13.3% failed to have someone to stay with them for 24 h and 1.3% spent the night alone at home [4].

In a recent survey of anesthesiologists, 11.2% were willing to anesthetize ambulatory surgical patients with the knowledge that they did not have an escort accompanying them home later [5]. Chung et al. [6] demonstrated that 79% of patients proceeded to surgery despite the

Purpose of review
There is a growing demand for greater efficiency in ambulatory surgery. The patient population is increasingly sick which is also undergoing more advanced and complex surgery. This creates a danger in discharging patients without meeting the criterion of requirement of a responsible adult as an escort to accompany the patient home. The purpose of this review is to examine the most recent findings to determine whether an escort for patient discharge is necessary.

Recent findings
Recent studies have outlined the risks of discharging patients without escort after ambulatory anesthesia. There are three aspects that deter discharge of patients without an escort: medication used in general anesthetics or sedation; regional anesthesia; and surgical factors. All these can affect the cognitive, memory and psychomotor function of the patients, deeming them unable to perform normal daily activities such as driving.

Summary
Both clinicians and patients may have underestimated the risks associated with discharging patients without an escort after ambulatory anesthesia. There should be greater awareness of this problem. Patient discharge without an escort after ambulatory surgery under general anesthesia, sedation or premedication can potentially be dangerous and is not recommended.

Keywords
ambulatory anesthesia, ambulatory surgery, escort, patient discharge
knowledge of a lack of escort preoperatively. Also, 50% of patients who did not have an escort claimed that they did. A total of 28.2% of the patients went home without an escort, had no responsible adult staying with them overnight and some of the patients without escorts traveled over 2h alone after their surgery [6]. Ambulatory surgical patients who had no responsible adult overnight ranged from 4 to 28% [3,6]. In addition, Pavlin et al. [7] found the lack of immediate availability of an escort accounting for 53% of system-related delays in discharge.

Why should we have an escort to accompany patients home?
Patients who undergo ambulatory surgery have general anesthesia, or local anesthesia with or without sedation, or regional anesthesia with or without sedation. Sometimes, they have a combination of regional and general anesthesia. Each one of the above can have an effect that precludes patients being discharged alone.

Effect of general anesthetics
Studies have demonstrated a significant impairment to the cognitive and psychomotor performance after various types of anesthesia, namely, general anesthesia and monitored anesthesia care [8–10]. However, the extent and duration of these are undetermined. It becomes difficult to advise patients when they can safely return to normal daily living activities. This is particularly important in ambulatory surgery, as patients are often discharged 2–3h post-operatively. The cognitive failures questionnaire, a subjective test to investigate failures of perception, memory and motor function, has been used to study this issue [11,12]. The questionnaire was conducted 3 days post-operatively on 258 ambulatory surgical patients undergoing general anesthesia and 250 patients who had regional anesthesia without sedation. A statistically significant impairment of cognitive function was found in those patients who received general anesthesia [11]. Anesthetic agents can affect cognitive functions such as memory. By demonstrating a difference in regional cerebral blood flow, Veselis et al. [13] postulated that the episodic memory loss produced by propofol could be due to the interference of the brain region identified with the working memory process.

In 12 healthy volunteers, Thapar et al. [10] demonstrated that sedative or analgesic drug combinations, such as midazolam 2mg and propofol 35mg, produced impairment similar to or greater than that observed with a large dose of alcohol. A combination of midazolam, fentanyl and/or propofol produced a significantly greater degree of impairment than alcohol at a blood alcohol concentration of 0.11%. This alcohol concentration was higher than the recommended safe limit for driving of 0.08–0.1% [10]. Midazolam appeared to be the key drug in producing prolonged psychomotor and subjective impairment. Even at 75min, the psychomotor impairment such as eye–hand coordination, subjective effects and short-term memory remained affected greater than the recommended safe limit of alcohol for driving [10]. However, clinically significant difference of these psychomotor impairment and subjective effects could not be demonstrated at 180 and 240min after midazolam, fentanyl and/or propofol administration. There were several limitations to this study. Only relatively low doses of drugs were used; repeated administration of drug or bolus followed by an infusion drug regimen was not explored. This study used healthy volunteers who did not experience preoperative anxiety, sleep deprivation or postoperative pain which may require analgesia. Furthermore, this could not be extrapolated to the elderly population or different ethnic groups. Nonetheless, this study demonstrated potential prolonged psychomotor and subjective impairment of the sedative or analgesic drugs used in ambulatory anesthesia. On the other hand, using a driving simulator to test vigilance and reaction time, Horiuchi et al. [14*] demonstrated that the driving ability was remarkably impaired at 2h after midazolam bolus compared with propofol administration in healthy individuals. They were also able to show that the plasma propofol concentration 60min after injection of 40–80mg of propofol for a 5–8min procedure was less than 100ng/ml [14*] and the driving ability returned to baseline.

Another prospective cohort study of 10 healthy volunteers was conducted by Grant et al. [15]. They studied the psychomotor performance in terms of choice and secondary reaction time during recovery after a target-controlled infusion of propofol. Their study concluded that reaction time was impaired as the plasma concentration of propofol was increased. Psychomotor performance may not be the most sensitive indicator of drug effect after sedation [9]. Lichtor et al. [9] studied 12 healthy volunteers receiving four common drug combinations: propofol 2.5mg/kg; propofol 2mg/kg and fentanyl 2µg/kg; propofol 2mg/kg and midazolam 2mg/70kg; and midazolam 0.07mg/kg and fentanyl 2µg/kg. Sleep latency and psychomotor performance were assessed at different time intervals. Sleep latency was found to be a better instrument in terms of sensitivity for detecting drug effect after different anesthetic regimens. A combination of midazolam and fentanyl was observed to have shorter sleep latency than other drug combinations. Patients fell asleep sooner 6h after the injection of midazolam and fentanyl. The recommendation was that patients must consider driving and operating heavy machinery unsafe activities up to 8h after an injection of midazolam and fentanyl.

Also, there have been recent studies on the effect of general anesthetics and driving performance. A prospective, randomized within-participant design of three
Table 1 Cognitive and psychomotor impairment similar to alcohol after different combinations of sedatives/anesthetics

<table>
<thead>
<tr>
<th>Different sedative/anesthetic combinations</th>
<th>Duration of effects similar to blood alcohol concentration level exceeding the safe limits for driving in United States:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fentanyl 50 μg and propofol 35 mg</td>
<td>5–30 min</td>
</tr>
<tr>
<td>Fentanyl 50 μg and midazolam 2 mg</td>
<td>5–60 min</td>
</tr>
<tr>
<td>Fentanyl 50 μg, midazolam 2 mg and propofol 35 mg</td>
<td>5–75 min</td>
</tr>
<tr>
<td>Fentanyl 1 μg kg⁻¹, propofol 2.5 mg kg⁻¹, nitrous oxide and desflurane 1 MAC</td>
<td>2 h</td>
</tr>
</tbody>
</table>

MAC, minimum alveolar concentration of anesthetic agent. Reproduced from [10,16].

treatments was as follows: no drug; general anesthetics; and alcohol administered to 12 volunteers. A driving simulator test was performed at 2, 4 and 24 h postanesthesia. No significant effects were found on the performance in a driving simulator compared with the control sessions with a balanced general anesthetic with propofol, fentanyl, desflurane and nitrous oxide at any time interval postoperatively [16]. However, healthy volunteers rather than patients were studied and these volunteers had neither surgery nor postoperative pain medications. Table 1 shows the duration of effect similar to a significant alcohol level after a combination of drugs such as fentanyl and midazolam (Table 1).

In addition, a prospective, comparative study on 20 patients undergoing knee arthroscopic surgery matched to 20 healthy controls was performed [17]. The driving simulation performance, electroencephalographically verified parameters of sleepiness and subjective assessment of sleepiness were measured preoperatively and 2 and 24 h postoperatively. Patients showed attention lapses, lower alertness levels and poor lane accuracy at the preoperative testing versus control. The parameters were worse at 2 h postoperatively, but they returned to normal levels by 24 h.

Horiuchi et al. [18] recently evaluated the safety and effectiveness of nurse-administered low-dose propofol sedation on 10,662 patients for diagnostic esophagogastroduodenoscopy. They concluded that it is a safe practice, but they also suggested that patients may be able to drive themselves home or to their offices after the procedure [18]. This should be interpreted with caution as the study included only American Society of Anesthesiologists (ASA) I and II patients undergoing a 5-min diagnostic esophagogastroduodenoscopy. Also these patients did not require any pain medication or anti-emetics in the postoperative period, which could further affect the cognitive or psychomotor level. In addition, the questionnaire regarding driving was provided to only 400 patients (4%). This may have introduced selection bias.

Therefore, general anesthetic has significant impairment on cognitive, memory and psychomotor function, which in turn affects the ability to carry out normal daily activities like driving. After discharge, the functionality of the patient was assessed by using the recently published user-friendly, 14-item Functional Recovery Index in a cohort of 688 patients [19**].

Effect of regional anesthetics

Regional anesthesia may render a patient’s limb immobile for many hours. Patients undergoing surgery having had regional anesthesia with sedation would be exposed to the pharmacodynamic effects as stated above. Using a Balance Master (NeuroCom International Inc., Clackamas, Oregon, USA), a computerized force platform, patients receiving 5 mg of heavy bupivacaine (7.5%) with 10 μg intrathecal fentanyl were shown to have impairment of functional balance at 150–180 min afterwards [20].

Effect from surgery

Surgery itself may impair the ability of the patient to drive. In a study of patients undergoing total knee arthroplasty, the brake response time returned to normal at 3 weeks after surgery [21]. The degree of functional recovery in patients after surgery may be related to the specific type of surgery. The self-rated quality of recovery score was significantly different between minor and major surgery, not to mention sex and age also had an impact on the degree of perceived functional recovery [22]. The Functional Recovery Index developed by Wong et al. [19**] can be used as a tool to evaluate the recovery of patients after their hospital discharge. Furthermore, there is evidence that unrelied pain may decrease psychomotor cognitive performance [23]. This further aggravates the effect of anesthesia on functional capabilities. Postoperative pain is an important factor which may hinder recovery from surgery. A recent systematic review found four significant predictors of postoperative pain: preoperative pain, anxiety, age and type of surgery [24**]. This may help us recognize those at risk and to implement intervention at an earlier stage.

Criteria for discharge

Patients will be considered fit to be discharged home once the discharge score or criteria are met [8]. Ambulatory surgical patients may not have completely regained the physiological state at discharge. Therefore, discharge home does not necessarily equate to complete recovery of the physiological state and by no means the preoperative functional state.
Compliance
Patients frequently disregard hospital instructions [1]. In the survey of 240 patients by Cheng et al. [4], 25% of the patients were unable to comply with the postoperative instructions in full. Patients often forget verbal instructions or ignore them altogether [25,26]. Another study suggested failure to adhere to written instructions could be related to low health literacy and age [27].

The potential for unnecessary harm from noncompliance with postoperative instruction will always be present [4]. Therefore, it is important that patients understand the implications and the potentially life-threatening consequences of noncompliance.

Role of escort
There are few guidelines for the role of escort. Most units would insist on a responsible adult who is physically fit to come to the aid of the patient. A responsible adult can be defined as a person who has the physical and mental ability to assist the patient, recognize when help is needed and to summon help should the patient be unable to do so. The minimum age of this attendant could range from 16 to 18 years [28]. However, there are no guidelines on how frequently the patient should be checked and how much supervision is required. This is further compounded overnight when a carer in a different room has less chance of detecting problems than one sharing the same bedroom [4].

Furthermore, the escort can relay postoperative information which the patient may have difficulty retaining after hypnotic agents, sedation or opioid. He/she can help the patient administer analgesic or antiemetics at home. The carer can also assist in the normal daily activities such as cooking and making decisions.

Recommendations and legal aspects
In a 10-year case review of litigations in ambulatory surgery by the Canadian Medical Protective Association, three malpractice cases of car accidents after ambulatory surgery in patients without an escort were identified. One was a case of intranasal midazolam for sedation [29**]. Another case was a patient with minimal sedation of midazolam 2mg, fentanyl 50μg and propofol 50mg intravenously (i.v.) being discharged without an escort [29**]. He subsequently drove himself home and had an accident, which left him quadriplegic. Also, sedation as little as 1mg lorazepam as a premedication could also deem a clinician to be negligent for allowing the patient to drive home [29**].

There have also been adverse events in children after discharge postoperatively. In many cases, children may need deeper sedation with higher dosage. The American Academy of Pediatrics (AAP)/American Academy of Pediatric Dentistry (AAPD) have recommended discharge criteria to minimize the likelihood of adverse events following sedation. The guideline suggests that a child transported in a car safety seat should be accompanied by at least two adults upon discharge such that transportation to and from a treatment facility is provided by one of the adults, while the other one can take care of the child [30].

There should be wider recognition among anesthesiologists, surgeons and nursing staff regarding the importance of the presence of an escort after sedation or premedication, as well as general anesthetics. Patients should be made aware of the importance of having an escort on discharge home and overnight, together with written information regarding the functional activities which should be avoided after anesthetics or sedation. This includes driving, operating machinery, riding bicycles or taking a responsible role such as taking care of children. Patient education should ideally take place at the time when the decision for surgery is made or in the preoperative clinic. Written as well as verbal instructions should be provided and an interpreter should it be necessary. The name and contact details of the escort should be ascertained preoperatively.

The Ambulatory Anesthesia guidelines from the ASA state: ‘A licensed physician should be in attendance in the facility or in the case of overnight care, immediately available by telephone at all times during patient treatment and recovery and until the patients are medically discharged’ [31]. It would be the responsibility of the anesthesiologist and surgeon regarding the ‘fitness’ for patients to be discharged home as suggested by the Australian College of Anesthetists [32]. The recommendations from various anesthesia societies are summarized in Table 2 [31–36].

If no known escort is available before surgery, the elective procedure should be cancelled, rescheduled or the patient should be admitted overnight in the 23 h care unit. Patients’ compliance with finding an escort for discharge may increase if the cancellation of the surgery is impressed upon them. If an escort is not available after anesthesia has been administered, elective hospital admission should be arranged. If, however, an escort is available at the patient’s home but is unable to travel to the hospital to accompany the patient home, a form of hospital transport should be arranged. The driver or someone should be able to call for help when necessary during the journey home and the patient should be accompanied all the way into his/her accommodation. Whereas some units allow patients to return home under the care of a taxi driver as long as they have an adult carer.
**Table 2 Recommendations of current guidelines**

<table>
<thead>
<tr>
<th>Anesthesia associations</th>
<th>Summary of recommendations</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Society of Anesthesiologists (2003) [31]</td>
<td>It recommends, in part, that patients who receive other than unsupplemented local anesthesia must be discharged with a responsible adult.</td>
<td>It does not mention about driving.</td>
</tr>
<tr>
<td>Canadian Anesthesiologists’ Society (2008) [33]</td>
<td>It advises patients about the additive effects of alcohol and other sedative drugs, about the danger of driving or the operation of other hazardous machinery in the postoperative period and of the necessity for attention by a competent adult.</td>
<td>It mentions about driving and the use of hazardous machinery. It also states the postoperative period most commonly being 24 h postoperatively.</td>
</tr>
<tr>
<td>Royal College of Anaesthetists (2009) [34]</td>
<td>It recognizes information should be given verbally and in written form upon discharge. It also recommends that a responsible adult needs to remain available for 24 h after surgery.</td>
<td>It has not differentiated between patients undergoing general anesthesia and those who had local anesthesia only.</td>
</tr>
<tr>
<td>Association of Anaesthetists in Great Britain and Ireland (2005) [35]</td>
<td>It advises patients to avoid driving for 24 h, especially after receiving sedation, until pain or immobility from operation allows them to safely control the car.</td>
<td>It is not specific regarding the need for an escort to accompany patients home.</td>
</tr>
<tr>
<td>Royal College of Surgeons of Australia and New Zealand (modified in 2009) [32]</td>
<td>It states that the discharge arrangements are the responsibility of the anesthetist and the surgeon. It advises specifically that patients should not drive until physical and mental recovery is compatible with safe driving.</td>
<td>It states that safe driving could be 24 h or more.</td>
</tr>
<tr>
<td>British Association of Day Surgery [36]</td>
<td>It advises patients to have a responsible adult to take them home and a carer at home for the next 24 h.</td>
<td></td>
</tr>
</tbody>
</table>

Waiting to meet them at the end of the journey [4], others may consider leaving a patient in the ‘care’ of a stranger unsafe, especially as the short-term memory may be affected by anesthetic drugs [13]. If a taxi ride is arranged for the patient to go home, the taxi driver does not necessarily have the obligation to be the responsible adult accompanying the patient en route. There is also an issue of getting from the transport vehicle into the accommodation safely.

It is the obligation of the caregiver to prevent the patient driving home. If the patient insists on driving home within 24 h postoperatively, the police or local authorities should be informed as the patient is endangering himself/
herself as well as the general public [28]. There is a lack of current guidelines and, if they exist, they tend to be nonspecific. In the United Kingdom, the Drivers and Vehicle Licensing Agency (DVLA) [37] suggests that there is no need to advise the DVLA unless the medical condition is likely to affect safe driving for longer than 3 months. The DVLA advises that the decision about the capability to drive should be based upon recovery from anesthetics (sedation and cognitive impairment), the distracting effect of pain, impairment due to analgesia as well as any physical restrictions due to the surgery, but does not offer any specific advice.

If the patient insists on leaving the hospital premises, he/she should sign a self-discharge against medical advice form. This way, written information is given to the patient explaining why discharge is potentially hazardous and what consequences may arise from leaving without an escort. However, another dilemma is introduced: is the patient competent to make an informed decision to sign the self-discharge form? Signing a waiver of discharge against medical advice is by no means the perfect solution, though it is the best available method to deter patients from harming themselves and others. A summary of the recommendation for safe patient discharge is shown in Fig. 1.

Conclusion
Patient discharge without an escort after ambulatory surgery under general anesthesia, sedation or premedication can potentially be dangerous and is not recommended. The role of an escort should be more than merely providing the patient with “the ride home”. Hospital administrators should implement policies to prevent patient discharge without an escort. Surgeons, anesthesiologists and nurses involved in patient care and discharge after ambulatory surgery should be aware of these policies and guidelines. Patients certainly should not be allowed to drive home after administration of any kind of hypnotic, sedative or opioid. This should be a fundamental issue of patient safety and good standard of care in relation to ambulatory anesthesia [8,29**].

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. 822).


14. Horiiuchi A, Nakayama Y, Katsuyma Y, et al. Safety and driving ability following low-dose propofol sedation. Digestion 2008; 78:190–194. This study prospectively assessed the safety of low-dose propofol sedation and compared driving ability following propofol and midazolam sedation for esophago-gastro-duodenoscopy. The authors found that driving ability recovered to the baseline level within 60 min of propofol administration after a bolus of 40–80 mg of propofol over 5–8 min. The psychomotor impairment was much more prolonged with midazolam.
19. Wong J, Tong D, De Silva Y, et al. Development of the functional recovery index for ambulatory surgery and anesthesia. Anesthesiology 2009; 101:596–602. This article described a new Functional Recovery Index to assess the functional recovery of ambulatory surgical patients. It was developed using a cohort of 688 patients and it has been validated and is reliable and user-friendly.

Escort accompanying discharge after surgery Ip and Chung 753
Ambulatory anaesthesia

This article discussed the malpractice cases in which patients were discharged without an escort after ambulatory surgery and had a car accident.

Fast-track anesthetic techniques for ambulatory surgery
Paul F. White and Matthew Eng

Purpose of review
Improving perioperative efficiency and throughput has become increasingly important in facilitating the fast-track recovery process following ambulatory surgery. This review focuses on the important role played by the anesthesiologist as a perioperative physician in fast-track ambulatory surgery.

Recent findings
A literature review of more than 200 peer-reviewed publications was used to develop evidence-based recommendations for optimizing recovery following ambulatory anesthesia. The choice of anesthetic technique should be tailored to the needs of the patient as well as the type of surgical procedure being performed in the ambulatory setting. The anesthetic decisions made by the anesthesiologist, as a key perioperative physician, are of critical importance in developing a successful fast-track ambulatory surgery program.

Summary
The pivotal role played by the anesthesiologist as the key perioperative physician in facilitating the recovery process has assumed increased importance in the current outpatient fast-track recovery environment. The choice of premedication, anesthetic, analgesic and antiemetic drugs, as well as cardiovascular, hormonal and fluid therapies, can all influence the ability to fast-track outpatients after ambulatory surgery.

Keywords
ambulatory anesthesia, fast-track surgery, multidisciplinary team, perioperative care, postoperative side effects

Introduction
The concept of fast-track surgery as an approach to improving perioperative efficiency and throughput was introduced in the early 1990s [1]. Fast-track anesthesia represents an approach to improving perioperative efficiency by providing for rapid recovery from anesthesia; it thereby facilitates early discharge from the hospital and more rapid resumption of normal activities of daily living after ambulatory surgery. The increasing popularity of minimally invasive surgical techniques has allowed patients to undergo increasingly complex surgical procedures on an ambulatory or short-stay basis [2]. Therefore, fast-tracking implies implementation of a perioperative patient care paradigm that reduces the time to discharge home and resumption of activities of daily living after a wide variety of surgical procedures.

The role played by the anesthesiologist has evolved from that of a physician primarily concerned with providing optimal surgical conditions and minimizing pain immediately after the operation, to that of a perioperative physician who is responsible for ensuring that patients with coexisting medical conditions are optimally managed before, during, and after surgery [3,4]. Anesthesiologists play a key role in fast-track surgery through their choice of preoperative medication, anesthetic agents and techniques, their use of prophylactic drugs to minimize side effects (e.g. pain, nausea and vomiting, and dizziness), and their administration of adjunctive drugs to maintain major organ system function during and after surgery. In addition to providing the best possible intraoperative surgical conditions, the abilities to provide for a rapid emergence from anesthesia while avoiding postoperative side effects and early complications are critically important for outpatients to meet the criteria for a fast-track recovery (Table 1).

Preoperative preparation
Optimal preoperative preparation of outpatients makes ambulatory surgery both safer and more acceptable for patients and hospital staff. The preparation process aims to reduce risks inherent in ambulatory surgery, improve patient outcome, and make the experience of undergoing surgery more pleasant for patients and their families.

Preoperative medication
When indicated, minimal amounts of preanesthetic medication are given primarily to provide sedation, reduce anxiety, optimize intraoperative hemodynamic stability, and decrease postoperative side effects without prolonging
Table 1 Fast-track criteria

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Details</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Level of consciousness</td>
<td>Awake and oriented</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Arousable with minimal stimulation</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Responsive only to tactile stimulation</td>
<td>0</td>
</tr>
<tr>
<td>II. Physical activity</td>
<td>Able to move all extremities on command</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Some weakness in movement of extremities</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Unable to voluntarily move extremities</td>
<td>0</td>
</tr>
<tr>
<td>III. Hemodynamic stability</td>
<td>Blood pressure ±15% of baseline</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Blood pressure ±30% of baseline</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Blood pressure ±50% of baseline</td>
<td>0</td>
</tr>
<tr>
<td>IV. Respiratory stability</td>
<td>Able to breathe deeply</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Tachypnea with good cough</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Dyspneic with weak cough</td>
<td>0</td>
</tr>
<tr>
<td>V. Oxygen saturation status</td>
<td>Maintains value &gt;90% on room air</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Requires supplemental oxygen</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Saturation less than 90% with supplemental oxygen</td>
<td>0</td>
</tr>
<tr>
<td>VI. Postoperative pain assessment</td>
<td>None or mild discomfort</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Moderate-to-severe pain controlled with intravenous analgesics</td>
<td>1</td>
</tr>
<tr>
<td>VII. Postoperative emetic symptoms</td>
<td>Persistent severe pain</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>None or mild nausea with no active vomiting</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Transient vomiting or retching</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Persistent moderate-to-severe nausea and vomiting</td>
<td>0</td>
</tr>
<tr>
<td>Maximum fast-track score</td>
<td></td>
<td>14</td>
</tr>
</tbody>
</table>

Shown are proposed fast-track criteria to determine whether outpatients can be transferred directly from the operating room to the step-down (phase II) unit. A minimal score of 12 (with no score <1 in any individual category) would be required for a patient to be fast-tracked (i.e. bypass the postanesthesia care unit) after general anesthesia [8].

 recovery from anesthesia [6]. Benzodiazepines remain the most commonly used premedicants (e.g. midazolam 10–20 μg/kg intravenously) because small doses can improve the perioperative fast-tracking process by reducing anxiety and anxiety-related complications, as well as improving patient comfort and satisfaction [7]. With respect to improving surgical outcome, both the β-blockers and α2-agonists are increasingly popular adjuvants to fast-track anesthetic techniques because of their anesthetic and analgesic-sparing effects [8–11]. Premedication with the α2-agonists clonidine and dexmedetomidine has been associated with a reduction in the use of opioid analgesics, postoperative nausea and vomiting (PONV), and intraoperative blood loss [11–13]. The inhibitory effects of these α2-agonists on sympathoadrenergic and hypothalamo–pituitary stress response [14] facilitate glycemic control in patients with type 2 diabetes [15] and reduce myocardial ischemia after surgery [16].

β-Blockers (e.g. atenolol and esmolol) suppress surgery-induced increases in circulating catecholamines and prevent untoward perioperative cardiovascular events in elderly patients undergoing noncardiac surgery [8]. Evidence suggests that β-blockers are most effective in reducing cardiac events in surgical patients with pre-existing coronary artery disease [17,18]. Perioperative β-blockade improved hemodynamic stability during emergence from anesthesia and during the early postoperative period. The anesthetic and analgesic-sparing effects of β-blockers in the ambulatory setting also leads to faster emergence from anesthesia and reduces postoperative side effects (e.g. PONV).

**Perioperative hydration**

Ambulatory surgery has traditionally been performed after an overnight fast to ensure that the patient’s stomach is empty and to minimize the risk of aspiration during the perioperative period. Many studies, however, have demonstrated that avoiding fasting-induced dehydration (e.g. allowing oral intake of clear liquids up to 2–3 h before surgery and intravenous hydration before induction of anesthesia) is both safe and effective in reducing postoperative side effects [19–22]. Liberal (as opposed to restrictive) fluid administration during laparoscopic surgery also leads to improved patient outcomes [23,24]. Even obese patients without comorbid conditions should be allowed to drink clear liquids until 2 h before elective surgery procedures [20]. Preoperative administration of glucose-containing fluids prevents postoperative insulin resistance and attenuates the catabolic responses to surgery while replacing fluid deficits [25,26]. Effects of glucose-containing solutions on clinical outcomes such as length of hospital stay, incidence of PONV, muscle strength, and subjective well-being remain controversial, however [27–29].

Perioperative hydration includes correction of preoperative dehydration caused by fasting, bowel preparation, replacement of blood loss, and insensible fluid losses during the maintenance period [30]. Liberal intraoperative fluid therapy was found to be associated with reduced postoperative side effects (e.g. pulmonary dysfunction, dizziness, drowsiness, thirst, and nausea and vomiting) and a shorter hospital stay after laparoscopic cholecystectomy [24]. Interestingly, liberal fluid administration
leads to improved pulmonary function and significant hypercoagulability after fast-track knee arthroplasty [31*].

**Metabolic and thermoregulation**

Impaired glucose homeostasis during surgery can result in hyperglycemia [26]. Recent evidence suggests that even moderate increases in blood glucose may be associated with adverse outcomes, particularly in patients with cardiovascular, infectious, and neurologic diseases [32,33]. Use of glucocorticoid steroids (e.g., dexamethasone and methyl prednisolone) as part of a fast-track anesthetic technique to reduce emetic symptoms and improve pain control may lead to transient postoperative hyperglycemia in patients with diabetes [34].

Perioperative hypothermia can have a wide range of detrimental effects that may include increased rates of wound infection, morbid cardiac events and blood loss, and can even prolong the hospital stay [35–38]. Hypothermia can be reduced by using forced-air warming blankets and warming irrigation fluids in outpatients undergoing laparoscopic, arthroscopic, and cystoscopic procedures [39]. In addition, warmed and humidified insufflation gases may decrease postoperative pain and the need for opioid analgesics and antiemetic therapy after laparoscopic surgery [40].

**Fast-tracking anesthetic techniques**

The ideal outpatient anesthetic should have a rapid and smooth onset of action, produce intraoperative amnesia and analgesia, provide good surgical conditions with a short recovery period, and have no adverse effects.

**Local anesthesia**

Infiltration of local anesthetics around a surgical incision should be a component of all fast-track ambulatory anesthetic techniques [41,42]. Local infiltration anesthetics alone provide adequate analgesia for superficial procedures (e.g., inguinal herniorrhaphy, breast and anorectal surgery, shoulder and knee arthroscopy) and is underutilized in clinical practice [43–45]. Patient comfort can be improved if intravenous sedation–analgesia is used to supplement local anesthetic infiltration, particularly when the local anesthetic is not completely effective [43,46]. Use of intravenous adjuvants can also increase side effects (e.g., ventilatory depression and PONV), however [47,48*]. The benefits of local wound infiltration in patients undergoing more invasive surgical procedures have not been as extensively studied. Although there is little evidence that ‘pre-emptive analgesia’ involving local anesthetic injections at the surgical wound reduces the risk for developing persistent postoperative pain syndromes [49*], it does lessen both intraoperative and postoperative opioid requirements, as well as opioid-related side effects [50].

Many studies have demonstrated improved analgesia, greater patient satisfaction with pain management, and reduced PONV and length of hospital stay with infusion of local anesthetic at the surgical incision site [51]. For example, patients receiving a continuous infusion of bupivacaine at the incision site not only experienced improved postoperative pain management but also were able to ambulate earlier [52]. Infiltration of local anesthetic at portal sites and the gallbladder bed improves postoperative analgesia after laparoscopic cholecystectomy [53]. Compared with neuroaxial or general anesthetic techniques, local anesthetic infiltration techniques reduce the risk for postoperative urinary retention associated with anorectal surgery [54] and inguinal herniorrhaphy [48*,55]. When used as the primary anesthetic technique, local anesthesia facilitates postanesthesia care unit (PACU) bypass, thereby reducing recovery costs (Tables 2 and 3) [43,46,48*,54,56]. Therefore, routine use of local analgesia at the surgical incision site(s) and in cavitary spaces is recommended for all ambulatory surgical procedures.

**Regional anesthesia**

Intravenous regional anesthesia, peripheral nerve blocks, and ‘mini-dose’ neuraxial blocks are the most popular regional anesthetic techniques used for fast-track ambulatory surgery. Use of intravenous regional anesthesia for

| Table 2 Comparison of anesthetic techniques for outpatient inguinal herniorrhaphy procedures |
|---------------------------------------------|---------------------------------------------|---------------------------------------------|
| Local anesthesia with sedation | General anesthesia | Spinal anesthesia |
| Age (years) | 42 ± 15 | 36 ± 16 | 29 ± 14 |
| Weight (kg) | 73 ± 9 | 75 ± 10 | 73 ± 14 |
| Surgery time (min) | 109 ± 23 | 119 ± 29 | 116 ± 24 |
| Time to awakening (min) | 2 ± 2 | 5 ± 2* | 0 |
| Time to orientation (min) | 4 ± 4 | 10 ± 5* | 0 |
| Time in the PACU (min) | 0 | 40 ± 13 | 35 ± 22 |
| Time to home readiness (min) | 128 ± 68 | 171 ± 40* | 283 ± 80** |
| Nausea and/or vomiting (%) | 8 | 61* | 13 |
| Maximum pain | 14 ± 13 | 27 ± 22 | 31 ± 30* |
| Highly satisfied with anesthesia (%) | 77 | 36* | 63 |

Values are expressed as mean ± standard error. PACU, postanesthesia care unit.

*P < 0.05 versus local sedation.

**P < 0.01 versus local sedation. Data from Song and Greilich [46].
Ambulatory anaesthesia

Table 3 Comparison of anesthetic techniques on recovery profile after anorectal surgery

<table>
<thead>
<tr>
<th></th>
<th>Local anesthesia with sedation</th>
<th>Spinal anesthesia</th>
<th>General anesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of anesthesia (min)</td>
<td>40 ± 15</td>
<td>72 ± 17</td>
<td>75 ± 19*</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>26 ± 14</td>
<td>26 ± 13</td>
<td>26 ± 15</td>
</tr>
<tr>
<td>Phase 1 stay (min)</td>
<td>0</td>
<td>52 ± 18</td>
<td>44 ± 27</td>
</tr>
<tr>
<td>Phase 2 stay (min)</td>
<td>71 ± 17</td>
<td>136 ± 113</td>
<td>120 ± 52*</td>
</tr>
<tr>
<td>Time to oral intake (min)</td>
<td>12 ± 6</td>
<td>59 ± 18</td>
<td>60 ± 29</td>
</tr>
<tr>
<td>Aldrete score (on arrival in recovery)</td>
<td>10 ± 0</td>
<td>9.1 ± 0.4</td>
<td>8.3 ± 0.7*</td>
</tr>
<tr>
<td>Time to Aldrete score of 10 (min)</td>
<td>0</td>
<td>19 ± 7*</td>
<td>30 ± 19*</td>
</tr>
<tr>
<td>Time to home readiness (min)</td>
<td>76 ± 17</td>
<td>103 ± 112</td>
<td>171 ± 58*</td>
</tr>
<tr>
<td>Duration of hospital stay (min)</td>
<td>116 ± 21</td>
<td>266 ± 112</td>
<td>247 ± 65*</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± standard error.

* $P < 0.05$ versus local anesthesia with sedation.

Hand surgery was associated with faster discharge and lower costs compared with either general anesthesia or peripheral nerve block [56]. As supplements to general anesthesia, peripheral nerve blocks (as opposed to local infiltration) improve postoperative analgesia and reduce opioid-related side effects, thereby facilitating the fast-track recovery process [57]. For example, suprascapular block improves the recovery profile after arthroscopic shoulder surgery performed under general anesthesia [58] but not after ‘open’ surgery with interscalene block [59]. As the primary analgesic technique, peripheral nerve blocks are associated with shorter discharge times, improved analgesia, and fewer side effects compared with general anesthesia for hand [57,60], shoulder [61], anorectal [54], hernia repair [46,62], and knee surgery [63].

Although it is widely assumed that regional anesthesia offers advantages over general anesthesia with respect to speed of recovery [64], a recent meta-analysis suggested that there were no significant differences in ambulatory surgery unit time [65]. Use of continuous perineural catheters to administer local anesthetics, however, can improve pain control and expedite hospital discharge after painful upper [66] and lower extremity [67] surgical procedures. In addition, local analgesia can be continued at home after discharge [66–68]. These beneficial findings were confirmed in a recent multicenter trial that utilized patient-controlled perineural local analgesia as an alternative to intravenous patient-controlled analgesia with morphine [69]. A recent meta-analysis confirmed the advantages of a peripheral catheter technique over a parenteral opioid-based analgesic technique for extirpation surgery [70*].

When central neuroaxis block techniques are used as a part of a fast-track regimen, it is important to select the most appropriate local anesthetic and adjuvant combination to avoid prolonged anesthetic effects that have a negative impact on ‘readiness for discharge’ [45]. For instance, prolonging subarachnoid-induced analgesia with fentanyl rather than epinephrine avoids the prolonged time to micturition [71] and reduces the time to discharge from the hospital [72]. As compared with conventional intrathecal doses of local anesthetics, use of so-called mini-dose lidocaine (10–30 mg), bupivacaine (3.5–7 mg), or ropivacaine (5–10 mg) spinal anesthetic techniques, when combined with a potent opioid analgesic (e.g. fentanyl 10–25 μg or sufentanil 5–10 μg), can result in faster recovery of sensory and motor function [73,74]. Compared with a monitored anesthesia care (MAC) technique for ambulatory knee surgery, a mini-dose spinal technique involving lidocaine and fentanyl achieved comparable recovery times after knee arthroscopy [44]. For outpatient laparoscopic gynecologic surgery, this technique has also been reported to offer significant advantages over both conventional spinal and general anesthetic techniques [74,75]. Surgical conditions may be inadequate for lower abdominal procedures, however, and postoperative side effects (e.g. pruritus and nausea) are increased because of the intrathecal opioid [44].

Given that similar analgesia can be achieved using a perineural catheter technique (e.g. continuous femoral or popliteal nerve blocks) as with epidural local analgesia, but without the attendant risk for epidural-related complications (e.g. hematoma formation, abscesses, and hemodynamic instability), peripheral nerve blocks would appear to be preferable for lower extremity surgery in the ambulatory setting. Therefore, the use of epidural analgesia for minimally invasive ambulatory surgery has been discouraged (e.g. colectomy, nephrectomy, splenectomy, and prostatectomy). Epidural anesthesia and analgesia for major laparoscopic surgery only facilitated recovery of bowel function when a traditional, nonacclerated perioperative care program was used [76]. In a recent study, however, patients undergoing laparoscopy-assisted subtotal gastrectomy under combined epidural/general anesthesia experienced a rapid, early recovery and a low incidence of urinary dysfunction [77]. Future advances in fast-track surgery techniques and perioperative use of peripheral μ-opioid antagonists [78] will probably lessen the role of epidural analgesia. The simplest regional anesthetic technique that provides adequate perioperative analgesia is
the most cost-effective option for regional anesthesia in the ambulatory setting.

**Monitored anesthesia care**

Compared with general endotracheal and central neuroaxis anesthetic techniques for superficial (noncavitary) surgical procedures, MAC-based techniques involving the use of local anesthesia via infiltration or peripheral nerve block in combination with intravenous sedative–analgesic drugs can facilitate fast-track recovery [47]. The simplest local anesthetic technique that provides adequate analgesia is recommended to minimize the risk for side effects and complications [79*].

Use of a MAC technique for inguinal hernia repair, and anorectal and hand surgery, was associated with a decreased incidence and severity of postoperative pain, reduced need for opioid-containing analgesics, and less PONV, constipation, ileus, urinary retention and other opioid-related side effects [46,54,56]. MAC techniques commonly involve the use of local anesthesia infiltration or peripheral nerve blocks using a mixture of lidocaine (2%) and bupivacaine (0.5%) or ropivacaine (0.5%), in combination with small doses of midazolam (1–3 mg intravenous) and a variable-rate propofol infusion (25–100 µg/kg per min) [80]. Increasingly, dexmedetomidine (0.5–1 µg/kg) [81] and ketamine (75–150 µg/kg) [82] are being used as alternatives to opioid analgesics such as fentanyl (0.5–1 µg/kg) [83] and remifentanil (0.25–0.5 µg/kg bolus or 0.025–0.05 µg/kg per min infusion) [84] as part of a MAC anesthetic technique to reduce the ventilatory depression produced when combining a potent opioid analgesic with midazolam and propofol [84]. Respiratory depression caused by oversedation and a lack of vigilance is the leading cause of serious patient injuries during MAC [48*].

Use of MAC techniques can facilitate fast-track recovery after ambulatory surgery because these patients routinely bypass the postanesthesia care unit and can be discharged home earlier because of the low incidence of postoperative side effects. Careful intraoperative vigilance to avoid respiratory complications is mandatory to ensure patient safety in the ambulatory setting, however. This is a major concern when sedation analgesic techniques are used in office-based outpatient plastic surgery [85,86].

**General anesthesia**

Despite the obvious advantages of local, regional, and MAC anesthetic techniques, many patients (and surgeons) still prefer general anesthesia because they are unaware of events during the operation. Propofol (1.5–2.5 mg/kg) is clearly the intravenous induction agent of choice for fast-track anesthesia [87]. The less-soluble volatile anesthetics desflurane (3–6%) and sevoflurane (0.75–1.5%) appear to offer advantages over propofol and isoflurane for maintenance of general anesthesia with respect to facilitating the early recovery process [88–91]. Nitrous oxide (50–70%) remains a popular adjuvant during the maintenance period because of its anesthetic and analgesic-sparing effects, low cost, and favorable pharmacokinetic profile [92]. Remifentanil infusion (0.05–0.20 µg/kg per min) is an increasingly popular alternative to nitrous oxide, however, as an adjuvant to the less-soluble volatile anesthetics [93,94].

The β-blocking drugs (e.g. esmolol and labetalol) can be used as alternatives to short-acting opioid analgesics to control transient, acute autonomic responses during surgery [95–97]. Whenever possible, a laryngeal mask airway should be used as an alternative to a tracheal tube [98]. If intubation is required, then short-acting (e.g. succinylcholine and mivacurium) [99] or intermediate-acting (e.g. cisatracurium, vecuronium, and rocuronium) neuromuscular blocking drugs should be used [100]. A novel cyclodextrin compound, namely sugammadex [101], can facilitate more rapid reversal of steroid-based, nondepolarizing neuromuscular blockers than a combination of either edrophonium-atropine or neostigmine–glycopyrrolate, without anticholinergic side effects [102*]. Use of this reversal agent may also lead to earlier tracheal extubation after surgery and reduce postoperative respiratory complications caused by residual muscle paralysis.

Use of volatile agents (as opposed to propofol) for maintenance of anesthesia will increase PONV during the early postoperative period [103]. For patients receiving volatile anesthetics, the most cost-effective antiemetic prophylaxis technique consists of a combination of low-dose droperidol (0.625–1.25 mg intravenous) and dexamethasone (4–8 mg intravenous) [104,105] or methylprednisolone (125 mg intravenous) [106]. If the patient is at increased risk for developing PONV, then a 5-hydroxytryptamine 3 antagonist (ondansetron 4 mg intravenous) should also be added as part of a multimodal antiemetic regimen [105]. The neurokinin-1 antagonists may play an increasingly important role in the management of emetic symptoms in the future. Use of nonopioid analgesics [e.g. nonsteroidal anti-inflammatory drugs (NSAIDs), cyclooxygenase-2 inhibitors, acetaminophen, α2-agonists, glucocorticoids, ketamine, and local anesthetics] as part of a multimodal analgesic regimen will minimize postoperative pain and opioid-related side effects [50,107].

Use of short-acting anesthetics and prophylactic drugs that minimize postoperative side effects will enhance the ability to fast-track patients after ambulatory surgery under general anesthesia [108,109]. Although a majority of both adults and children can be fast-tracked after ambulatory surgery under general anesthesia, minimizing patient discomfort and anxiety during the perioperative period is critically important in establishing a successful fast-track
surgery program after all types of ambulatory surgery [96,108–110]. Finally, improving the titration of both intravenous and inhaled anesthetics by using cerebral monitoring devices (e.g. bispectral index, entropy, and cerebral state monitors) may also facilitate the fast-tracking process [111–114]. In spontaneously breathing (nonparalyzed) patients, however, the value of cerebral monitoring in facilitating the recovery process is questionable [115*].

Postoperative care
In order to implement a successful fast-track recovery program, it is essential to minimize common side effects such as pain, nausea and vomiting, and dizziness, as well as gastrointestinal and bladder dysfunction. Therefore, preventive (or pre-emptive) approaches are necessary during the perioperative period.

Optimizing pain management
An observational study confirmed that poorly controlled pain and associated nausea and vomiting can delay discharge after ambulatory surgery [116]. Improving postoperative pain control accelerates resumption of activities of daily living, impairment of which may otherwise persist for weeks after an elective operation [117–119]. According to a recent systematic review conducted by Liu and Wu [120], there is ‘insufficient evidence to conclude that analgesic techniques influence postoperative mortality or morbidity’ because of the current low incidences of complications. Excessive reliance upon opioids for perioperative analgesia contributes to acute opioid tolerance and hyperalgesia [121–123], however, as well as dose-related opioid side effects (e.g. hypoventilation, sedation, nausea and vomiting, urinary retention, and ileus) that delay hospital discharge and add to the cost of surgical care [51,122]. Although opioid infusions are frequently utilized both intravenously and epidurally, they do not always improve postoperative pain management because of rapid development of tolerance [123] and increased risk for ventilatory depression. Even if optimal pain control had no beneficial economic or physiologic effects, efforts to ensure optimal pain management may eventually be mandated by accrediting agencies as a basic human right [124*].

Multimodal (or ‘balanced’) analgesia involves the use of more than one modality of pain control to obtain additive (or synergistic) beneficial analgesic effects while reducing drug-related side effects [125]. Early fast-track studies demonstrated that these multimodal analgesic techniques can improve recovery and patient outcomes after ambulatory procedures [126,127]. This approach is currently the standard practice in fast-track clinical care plans [1,128] because reliance on a single nonopioid analgesic modality such as NSAIDs may not suffice to control severe pain, and reliance exclusively on opioids produces many side effects [107]. Use of partial opioid agonists (e.g. tramadol) is associated with increased incidence of side effects and patient dissatisfaction compared with both opioid and nonopioid analgesics [129].

Opioid analgesics will continue to play an important role in the acute treatment of moderate-to-severe pain after surgical procedures. Nonopioid analgesics, however, will likely assume a greater role as ‘preventive’ analgesics as the number of minimally invasive (‘key hole’) surgery cases continues to expand [2,41]. In addition to local anesthetics, NSAIDs and cyclo oxygenase-2 inhibitors, drugs such as acetaminophen, ketamine, dextromethorphan, α2-agonists, gabapentin, pregabalin, and even magnesium will probably be more frequently utilized as adjuncts in the multimodal management of postoperative pain [50]. Interestingly, nonanalgesics such as the antieptic droperidol [134] and the glucocorticoid steroids dexamethasone [135], betamethasone [136], and methylprednisolone [137] appear to provide multiple beneficial effects with respect to controlling side effects in the
postoperative period. Novel compounds such as capsicum (the active ingredient in chili peppers) have been found to produce analgesic effects because of their ability to alter nociceptive input at peripheral nerve endings [138]. Other nonpharmacologic approaches involving a variety of acustimulation techniques may also be utilized more extensively as analgesic adjuvants in the future [139*].

Rather than advocating more aggressive use of opioid analgesics [124*,140], use of analgesic drug combinations with different mechanisms of action as part of a multimodal regimen will provide additive (or even synergistic) effects with respect to improving pain control, reducing the need for opioid analgesics, and facilitating the recovery process [130*]. In a recently published critical assessment of multimodal analgesic regimens for laparoscopic surgery Bisgaard [141] recommended that ‘opioids should only be used when these other nonopioid analgesic techniques fail’. Although so-called ‘pre-emptive’ analgesic techniques have been postulated to provide superior analgesia by preventing the establishment of central sensitization [140], this approach does not appear to offer any clinically significant advantages over common preventive multimodal regimens administered after the surgical procedure [142]. Safer, simpler, and less costly analgesic drug delivery systems will still be needed to provide cost-effective pain relief during the postdischarge period as more major surgery is being performed on an ambulatory basis [2]. A more aggressive multimodal strategy involving anesthesiologists, surgeons, and nurses must be employed if we are to improve surgical outcomes for our patients in the future [1]. Newer nonopioid analgesics (e.g. NSAIDs, long-acting local anesthetics, and capsacin) and delivery systems (e.g. infusion systems on Q/I flow) may further improve our ability to prevent moderate-to-severe pain and the need for opioid analgesics [140,143,144].

Ideally, multiple nonopioids (e.g. NSAIDs, cyclo o*nase-2 inhibitors, and gabapentin) could be combined to achieve superior pain relief and perhaps, ultimately, an ‘opioid-free’ environment [50,107]. Multimodal analgesia represents a key element for successful fast-track surgery by minimizing postoperative pain and opioid-related organ dysfunction, and facilitating the recovery process from anesthesia. Newer fast-tracking criteria recognize the importance of controlling pain and opioid-related side effects (e.g. PONV) [5].

**Postoperative nausea and vomiting**

Despite the introduction of many new antiemetic thera-pies, the incidence of PONV remains high, occurring in up to 30% of all surgical cases (including both cardiac and neurosurgery) because of patient, anesthesia, and surgery-related factors [145]. The major risk factors for PONV include female sex, nonsmoker status, history of PONV or motion sickness, intraoperative use of volatile anesthetics and high-dose opioid techniques, as well as postoperative opioid analgesic use [146]. In adults, a multidrug antiemetic prophylaxis strategy consisting of droperidol, dexamethasone [147,148], and a 5-hydroxytryptamine 3 antagonist (ondansetron) is recommended for patients who present with two or more risk factors [149].

Recent studies suggest that nontraditional therapies (e.g. transdermal nicotine and topical capsacin) may be useful additions to the traditional antiemetic drug therapies [150,151]. In addition to the administration of antiemetic drugs, multimodal strategies to reduce the risk for PONV include use of propofol and local anesthetic-based analgesic techniques, and adequate hydration, as well as minimizing perioperative opioid use [152]. Use of cardiovascular drugs (e.g. β-blockers and α₂-agonists) to control transient acute autonomic responses to noxious surgical stimuli and nonopioid analgesics to reduce postoperative pain will minimize emetic symptoms [50,96,97]. In fact, a recent study demonstrated advantages of the NSAID ketorolac as compared with the glucocorticoid steroids with respect to preventing PONV [153]. Nonpharmacologic techniques (e.g. acupuncture, acupressure, and transcutaneous electrical nerve stimulation) can be useful adjuvants to standard antiemetic drugs when used after surgery [154–156]. Therefore, replacing fluid deficits, minimizing use of volatile anesthetics and nitrous oxide, opioid analgesics and reversal drugs, and utilizing propo-fol, multimodal antiemetic prophylaxis and nonopioid analgesic techniques are all important factors in preventing PONV [107]. In the future, practitioners should also consider incorporating alternative medical therapies into their treatment plan [131].

**Postoperative ileus and constipation**

Postoperative ileus can cause discomfort and delay oral food intake, thereby prolonging convalescence and the length of the hospital stay [157]. The key elements in a multimodal fast-track strategy for preventing postoperative ileus include use of minimally invasive surgical techniques, use of a peripherally acting μ-opioid receptor antagonist (e.g. alvimopan and methylaltrexone), avoidance of a nasogastric tube, early oral feeding and ambula-tion, and opioid-sparing analgesic regimens [158]. Rehabilitation paradigms that combine multimodal analgesia with oral feeding and mobilization have been found to decrease the duration of ileus [159]. In addition, there is evidence that reduced perioperative sodium administration and avoidance of fluid excess are associ-ated with earlier return of bowel function after abdominal surgery [160] and a decrease in the duration of the hospital stay [161]. The results of recent clinical trials indicate that use of a peripheral μ-opioid receptor antagonist (i.e. alvimopan or methylaltrexone) can
facilitate the recovery of postoperative bowel activity and may reduce the time to hospital discharge after major surgical procedures [78,162,163]. Importantly, minimizing the use of opioid-containing oral analgesics after discharge reduces both constipation and PONV [164].

Implementing a multidisciplinary approach for fast-track recovery

A common experience at ambulatory centers implementing fast-track surgery has been the challenge of changing longstanding surgical nursing care principles [165,166], and this represents a major component of the ‘total care’ package [167]. An intensified nurse-based preoperative patient education program is a crucial adjunct to improved fast-track anesthetic and surgical care [109]. These programs need to focus on what is expected from the patient as an active participant in the recovery and rehabilitation process [168]. The provision of daily nurse care (i.e. clinical pathway) charts remains an important element in the fast-track recovery process. It is essential to secure daily tasks and to establish programs to facilitate education of new personnel because every aspect of care must be carefully explained. Therefore, multidisciplinary team meetings before and after implementing fast-track ambulatory surgery are crucial to the overall success of the program [109].

Conclusion

Anesthesiologists play an important role in the implementation of fast-track ambulatory surgery programs as a result of their decisions regarding perioperative care (Table 4). Understanding the importance of coexisting diseases and taking appropriate steps to minimize postoperative complications through appropriate use of preoperative medications, selection of the optimal anesthetic and analgesic techniques, and maintaining normal organ system function will lead to improved patient care at reduced cost [169]. As more information becomes available, it should be possible to make recommendations for each of these steps on a procedure-specific basis, as has been achieved for postoperative pain management [1,50]. Inadequately controlled pain is among the major factors that contribute to delayed discharge and unanticipated hospital admissions after ambulatory surgery (Table 5). Despite increased attention to minimizing pain and preventing PONV, these remain significant impediments to a fast-track recovery after ambulatory surgery [170,171].

Future advances in fast-track surgery will require interdisciplinary collaborations involving anesthetic, surgery, and nursing care [172]. Anesthesiologists, however, are the ones who make the decisions regarding premedica-

<table>
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<th>Period</th>
<th>Details</th>
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<tbody>
<tr>
<td>I. Preoperative period</td>
<td>Stabilize coexisting diseases (e.g. hypertension or diabetes) and encourage prehabilitation exercise program and smoking cessation. Optimize patient comfort by minimizing anxiety and discomfort. Ensure adequate rehydration by replacing fluid deficits. Appropriate use of prophylactic therapies to prevent postoperative complications (e.g. nausea, vomiting, pain, and ileus).</td>
</tr>
<tr>
<td>II. Intraoperative period</td>
<td>Utilize anesthetic techniques that optimize surgical conditions while ensuring rapid recovery with minimal side effects. Administer local analgesia via peripheral nerve blocks, wound infiltration, and/or instillation. Apply multimodal analgesia and antiemetic prophylaxis (including use of glucocorticoid steroids). Minimize use of nasogastric tubes and avoid excessive fluid administration.</td>
</tr>
<tr>
<td>III. Postoperative period</td>
<td>Allow patients who meet discharge criteria to be fast-tracked (i.e. discharged earlier from recovery units). Ensure adequate pain control during the postdischarge period, utilizing nonopioid analgesics to minimize need for opioid-containing analgesics. Encourage early ambulation and resumption of normal activities of daily living.</td>
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Table 4 Key elements of the perioperative anesthetic management for facilitating fast-track recovery after elective ambulatory surgery

<table>
<thead>
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<th>Period</th>
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<tr>
<td>I. Preoperative period</td>
<td>Female sex</td>
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<tr>
<td>Intraoperative period</td>
<td>Congestive heart failure</td>
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<tr>
<td>Postoperative period</td>
<td>Long duration of surgery</td>
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<td></td>
<td>General anesthesia</td>
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<td></td>
<td>Spinal anesthesia</td>
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<td></td>
<td>PONV</td>
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<td>Unanticipated admissions</td>
<td>Moderate-to-severe pain</td>
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<td>Pain</td>
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<td>Bleeding</td>
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<td></td>
<td>Excessive drowsiness</td>
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<td>No escort</td>
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Table 5 Factors alleged to delay discharge and lead to unanticipated admissions after ambulatory surgery

<table>
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<tr>
<th>Period/type of admission</th>
<th>Factors</th>
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<tr>
<td>Delayed discharge</td>
<td>Female sex</td>
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<td></td>
<td>Increasing age</td>
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<td></td>
<td>Congestive heart failure</td>
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<td>Long duration of surgery</td>
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<td>Excessive drowsiness</td>
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<tr>
<td></td>
<td>Pain</td>
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<td></td>
<td>Bleeding</td>
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<td>Surgical complications</td>
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<td>Abdominal surgery</td>
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<td>Otorhinolaryngology</td>
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<td></td>
<td>and urology surgery</td>
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<tr>
<td></td>
<td>Nausea and vomiting</td>
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<tr>
<td></td>
<td>Somnolence</td>
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<td></td>
<td>Aspiration</td>
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<td>No escort</td>
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<tr>
<td></td>
<td>Diabetes mellitus</td>
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<td></td>
<td>Ischemic heart disease</td>
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<td>Sleep apnea</td>
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</table>

PONV, postoperative nausea and vomiting. Data from Awad and Chung [173].
tion, fluid management, anesthetic and adjuvant drugs, treatment of side effects, and pain management during the early postoperative period. Interventions to modify surgical stress responses are also performed by anesthe-
siologists and include perioperative use of β-blockers, glucocorticoid steroids and administration of fluids, as well as control of stress-induced hyperglycemia by administering insulin [29,50,172]. The effective control of stress responses will probably prove to be advantageous with respect to improving patient outcome. Furthermore, expansion of the anesthesiologists’ interventions beyond the operating and recovery rooms may also be necessary in the future.

Perioperative anesthetic care should be viewed as a multidisciplinary strategy to improve the management and outcome of patients undergoing surgery, rather than as a subspeciality limited to one medical profession [174]. As a member of the multidisciplinary team, the decisions of the anesthesiologist have a direct impact on the ability to achieve a fast-track recovery after ambulatory surgery. It was recently reported that an anesthesiologist-led management team improved operating room efficiency (resulting in a 48% reduction in ‘gap time’ between cases in the same operating room) when defined scheduling policies were supported by surgeons, nurses, and hospital administrators [175]. In addition, the implementation of a multidisciplinary approach to minimizing common postoperative side effects can lead to reduced recovery room and hospital stays, as well as better pain control and patient satisfaction after surgery [173].

In summary, anesthesiologists directly contribute to the fast-track process through their choice of appropriate anesthetic techniques for a given ambulatory surgical procedure. By encouraging the optimal use of multimodal analgesia, as well as by implementing novel techniques that can minimize side effects (e.g. PONV and ileus) after hospital discharge, anesthesiologists can play an important role in helping patients to resume their activities of daily living more rapidly after ambulatory surgery [2,68,135,163]. The time is right for anesthesiologists to become more actively involved as perioperative physicians in facilitating the recovery process after ambulatory surgery.

Acknowledgements
Parts of this article were adapted from a review article by White et al. [130].

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 (pp. 608–609).


Ambulatory anaesthesia


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Fast-track anesthetic techniques

White and Eng 555


124 White PF, Kehlet H. Improving pain management: are we jumping from the frying pan into the fire? Anesth Analg 2007; 105:10–12.

This editorial describes the importance of a ‘balanced’ approach to acute and chronic pain management, with an emphasis on opioid-sparing techniques for facilitating postoperative recovery and rehabilitation.


130 White PF, Kehlet H, Neal JM, et al. Role of the anesthesiologist in fast-track surgery: From multimodal analgesia to perioperative medical care. Anesth Analg 2007; 104:1380–1396. This paper discusses the important role of the anesthesiologist as the key perioperative physician in the surgical care team in terms of developing a successful fast-track ambulatory surgery program by optimizing preoperative preparation, choosing the optimal anesthetic technique, and minimizing postoperative complications.


165 Alvimopan, a peripherally acting mu-opioid receptor antagonist, compared with placebo in postoperative ileus after major abdominal surgery. Results of a randomized, double-blind, controlled study. Surg Endosc 2006; 20:84–70.


A Retrospective Study of Intraoperative Awareness with Methodological Implications

George A. Mashour, MD, PhD
Luke Y.-J. Wang, MD
Christopher R. Turner, MD, PhD, MBA
John C. Vandervest, BS
Amy Shanks, MS
Kevin K. Tremper, PhD, MD

BACKGROUND: Awareness during general anesthesia is a problem receiving increased attention from physicians and patients. Large multicenter studies have established an accepted incidence of awareness during general anesthesia as approximately 1–2 per 1000 cases or 0.15%. More recent retrospective data, however, suggest that the actual incidence may be as low as 0.0068%.

METHODS: To assess the incidence of awareness at our institution, we conducted a review of adult patients undergoing surgical procedures over a 3-year period. Information on awareness came from entries of “Intraoperative Awareness” captured during our standard evaluations on postoperative day one in our perioperative information system. Patients were not questioned specifically about awareness.

RESULTS: We reviewed 116,478 charts; 65,061 patients received general anesthesia and 51,417 received other types of anesthesia. Of the patients receiving general anesthesia, 44,006 had complete postoperative documentation. The reported incidence of undesired intraoperative awareness in this population was 10/44,006 (1/4401 or 0.023%). Of the patients who received other anesthetic modalities, 22,885 had complete postoperative documentation. Undesired intraoperative awareness was reported in 7/22,885 patients who did not receive general anesthesia (1/3269 or 0.03%). The reported incidence of intraoperative awareness was not statistically different between the two groups (P = 0.54). Relative risk of intraoperative awareness during a general anesthetic compared with a nongeneral anesthetic was 0.74, with 95% confidence interval [0.28, 2.0].

CONCLUSION: Using a retrospective methodology, reports of intraoperative awareness are not statistically different in patients who received general anesthesia compared with those who did not. These results suggest that, despite success with other rare perioperative events, the resolution of retrospective database analyses may be too low to study intraoperative awareness.

(Anesth Analg 2009;108:521-6)

Awareness during general anesthesia, which denotes both awareness and subsequent explicit recall of intraoperative events, is a problem receiving increased attention by both patients and clinicians. A proportion of patients experiencing awareness may subsequently develop serious psychological sequelae, including posttraumatic stress disorder (PTSD). In 2004, the Joint Commission on Accreditation of Hospital Organizations issued a Sentinel Alert to promote greater attention to the problem. Despite recent attention by the medical community and the lay press, the incidence of intraoperative awareness—and hence the magnitude of the problem—remains uncertain. A multicenter study in the United States by Sebel et al. estimated an incidence of awareness with explicit recall of approximately 0.13%, a rate consistent with large European studies demonstrating awareness in 1–2/1000 cases. In contrast, a recent study of awareness in a regional medical system by Pollard et al. reported a much lower incidence of 1 episode of awareness/14,560 cases, or 0.0068%.

Establishing the validity of the retrospective study of awareness is necessary if we are to adjudicate between these disparate reports. Retrospective analyses of data derived from an electronic perioperative information system have been successfully used at our institution to study rare events such as impossible mask ventilation and postoperative renal failure. To compare the incidence of undesired awareness at our institution with the disparate rates in the literature, as well as explore the use of electronic databases for the study of intraoperative awareness, we conducted a review of more than 100,000 cases over a 5-year period.

METHODS

With IRB approval, a retrospective electronic chart review was conducted on adult patients receiving...
anesthesia at the University of Michigan Health System between January 1, 2004 and February 20, 2007. Information regarding awareness was obtained from patient interview on postoperative day 1. Inpatients were interviewed directly by residents. Nurses called outpatients by phone. All patients were asked if they experienced any problems related to anesthesia. If they discussed intraoperative awareness, these data were entered into a perioperative clinical information system (Centricity™ from General Electric Healthcare, Waukesha, WI) by selecting the category of “Intraoperative Awareness” in the postoperative documentation window. Patients were not interviewed using a Brice et al9 or modified Brice interview, i.e., they were not asked specifically about awareness.

The electronic charts were queried for postoperative documentation of “Intraoperative Awareness.” After the initial query, all charts with reports of “Intraoperative Awareness” were reviewed and correlated with existing Quality Assurance data regarding awareness. The intraoperative record was analyzed for anesthetic technique and anesthetic drugs, as well as the use of benzodiazepines, opioids, and neuromuscular blocking drugs. No electroencephalographic devices were used for the detection of intraoperative awareness during this time period examined. Statistical comparison was performed using a χ² test, as well as assessing relative odds ratios. A P value of <0.05 was considered significant.

RESULTS

We reviewed 116,478 charts between January 1, 2004 and February 20, 2007; 65,061 patients received general anesthesia and 51,417 received other anesthetic modalities. Of the patients receiving general anesthesia, 44,006 had complete postoperative documentation, for a compliance rate of 67%. Of the 44,006 patients who received general anesthesia and had complete postoperative documentation during the time period of study, 10 complained of some degree of awareness (Table 1), an incidence of 1/4401 or 0.023%. Demographic data for this patient cohort are shown in Table 2. Analysis of the general anesthetics for the time period of study indicates that 90% of cases were performed using inhaled anesthetics, whereas 10% used total IV anesthesia (TIVA).

Of the 10 patients who complained of awareness in this group, five were men and five were women. There were no consistent findings regarding anesthetic choice, use of benzodiazepines, or use of opioids. All 10 patients had received neuromuscular blocking drugs at some time. Of the 10 cases of awareness, two patients were in the high-risk category: one was undergoing an emergent cesarean delivery, and the other was undergoing a heart transplant. One patient had a confirmed awareness event during TIVA after the discontinuation of nitrous oxide (patient 10). Figures 1A and B depict the anesthetic regimen for each case. Several cases documented insufficient anesthesia on the electronic record that correlated with complaints of awareness. For patient 1, awareness at the end of the procedure was likely due to low levels of isoflurane documented at minute 210 of the case. Patient 2 had low sevoflurane concentrations and insufficient IV anesthesia at the start of surgery (“S”), when he reported awareness. Patient 4 reported awareness at the beginning of the case, around the time a vaporizer leak was noted in the

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>ASA</th>
<th>Surgery</th>
<th>Awareness report</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>73</td>
<td>F</td>
<td>4</td>
<td>Abdominal abscess drainage</td>
<td>Aware for approximately 15 min at the end of the case with 10/10 pain</td>
</tr>
<tr>
<td>2</td>
<td>82</td>
<td>M</td>
<td>3</td>
<td>Nissen</td>
<td>Aware of pain on incision</td>
</tr>
<tr>
<td>3</td>
<td>68</td>
<td>F</td>
<td>3</td>
<td>Cardiac ablation</td>
<td>Vague recall of intubation</td>
</tr>
<tr>
<td>4</td>
<td>49</td>
<td>M</td>
<td>2</td>
<td>Tibial plateau fracture repair</td>
<td>Aware of leg manipulation and paralysis at beginning of surgery</td>
</tr>
<tr>
<td>5</td>
<td>33</td>
<td>F</td>
<td>2E</td>
<td>Emergent cesarean delivery</td>
<td>Experience of paralysis and pain</td>
</tr>
<tr>
<td>6</td>
<td>47</td>
<td>F</td>
<td>3</td>
<td>Incisional hernia repair</td>
<td>Aware at some point during surgery, but unconcerned</td>
</tr>
<tr>
<td>7</td>
<td>60</td>
<td>M</td>
<td>4</td>
<td>Heart transplantation</td>
<td>Heard intraoperative conversations, but unconcerned</td>
</tr>
<tr>
<td>8</td>
<td>65</td>
<td>M</td>
<td>3</td>
<td>Carotid endarterectomy</td>
<td>Heard voices, felt endotracheal tube and unable to move</td>
</tr>
<tr>
<td>9</td>
<td>84</td>
<td>M</td>
<td>3</td>
<td>Colectomy</td>
<td>Heard voices, thought he was dead</td>
</tr>
<tr>
<td>10</td>
<td>49</td>
<td>F</td>
<td>3</td>
<td>Diskectomy</td>
<td>Aware and paralyzed for a portion of the case [after intravenous line became disconnected during TIVA]</td>
</tr>
</tbody>
</table>

Table 1. Perioperative Data of Patients Experiencing Awareness During General Anesthesia

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>65,061</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA</td>
<td>2.27</td>
</tr>
<tr>
<td>Age</td>
<td>49 (± 18)</td>
</tr>
<tr>
<td>Men</td>
<td>30,774</td>
</tr>
<tr>
<td>Women</td>
<td>34,287</td>
</tr>
</tbody>
</table>

Table 2. Demographic Data of Patient Cohort Analyzed for Awareness During General Anesthesia

Pt. = patient; ASA = American Society of Anesthesiologists Classification; TIVA = total intravenous anesthesia.
chart. Finally, patient 10 experienced awareness after nitrous oxide was discontinued and an IV line infiltration was recorded in the record. It was not possible to identify the temporal location of awareness in the remaining cases.

An additional 51,427 patients underwent procedures during the time period of study, but did not receive general anesthesia. Of the patients who received other anesthetic modalities, 22,885 had complete postoperative documentation for a compliance of 45%. Of this cohort, seven patients complained of being aware during the case, an incidence of 1/3269 or 0.03%. These patients had been managed with a variety of anesthetic modalities (Table 3). Of the seven patients complaining of awareness in this population, six were women. In the case of the one male patient, the report of awareness was given by his daughter. This was the only patient in the study who did not report intraoperative awareness independently.

There was no statistically significant difference between the incidence of awareness in the general anesthesia (0.023%) and nongeneral anesthesia (0.03%) populations at our institution ($P = 0.54$). Relative risk of undesired intraoperative awareness during a general anesthetic compared with a nongeneral anesthetic was 0.74, with 95% confidence interval [0.28, 2.0].

**DISCUSSION**

Awareness during general anesthesia is a problem that has captured the attention of clinicians, patients, and the general public. Although awareness is a significant source of fear for many patients undergoing surgery, the actual incidence and sequelae of awareness remain a matter of controversy. This is highlighted by recent studies reporting rates of awareness and subsequent PTSD that were lower than previously thought.$^{2,6}$

In this retrospective study, we found the incidence of complaints of intraoperative awareness during general anesthesia to be 1/4401 or 0.023%. We acknowledge that these data likely represent an under-estimate of the actual incidence of awareness in the population studied. As Sebel et al.$^4$ noted: “A single short postoperative visit by an anesthesiologist without use of a structured interview is unlikely to elicit many cases of awareness,” an effect also noted by Moerman et al.$^{10}$ Sandin et al. and Sebel et al. found considerably increased reports of awareness during the second interview at 1 wk postoperatively.$^{1,5}$ Indeed, our data were obtained retrospectively, our patients did not receive a Brice interview or other technique of specifically assessing awareness, and our patients were interviewed on postoperative day 1, all of which might result in an under-estimation of the true incidence.

Even with suboptimal conditions for detection of awareness, our rate of undesired awareness was still more than three times that of 0.0068% reported by Pollard et al.$^6$ in which a structured interview was used. It is important to note that the structured interview in the Pollard et al. study omitted a question specifically assessing recall that is present in the standard Brice interview. Our demographic data appeared comparable, with an average ASA classification of 2.27 (vs 2.37 in Pollard et al.), an average age of 49 ± 18 years (vs 46 ± 16), and a male:female ratio of 1:1.1 (vs 1:1.3). Although data reported in the Pollard et al. study were gathered, in part, at an academic medical center, no resident or nurse trainees were identified as being involved in patient care. Since resident physicians are routinely involved in patient care at our institution, this may account for some disparity in outcome.

Another possible difference relates to the use of TIVA at our institution. The centers in the Pollard et al. study “rarely used” IV drugs as the sole anesthetic; in our study, 1 of the 10 patients who complained of awareness during general anesthesia experienced the event during a failed TIVA. Given the large number of cases analyzed, it is difficult to establish the precise number of anesthetics in which TIVA was used at some point. We have established, however, that approximately 9/10 cases used an inhaled anesthetic. Thus, the rate of awareness during known TIVA (1/10) is comparable to the overall use of TIVA in the study population (1/10).

Although our incidence of 0.023% was considerably less than that reported by Myles et al.$^{11}$ and Sebel et al.$^4$ (which ranged from approximately 0.10% to 0.20%), this disparity is likely mitigated by our lack of a structured interview and a 1 wk postoperative interview. Although not in perfect agreement with either study, it is easier to reconcile our data with that of Sebel et al.$^3$ than Pollard et al.$^6$

All patients who have postoperative complaints receive follow-up phone calls. Those reporting intraoperative awareness are offered psychiatric counseling. Of the 17 patients reporting undesired intraoperative awareness, only one requested psychiatric care (patient 10 receiving general anesthesia, described in Table 1). Although formal postawareness psychiatric evaluation was not systematically performed on all patients, it would appear that the occurrence of sustained psychiatric sequelae in our population was likely closer to that reported by Samuelsson et al.$^2$ rather than Osterman et al.$^1$ It must be noted, of course, that patients afflicted with PTSD often avoid health care professionals and clinical settings because they can serve as triggers that evoke traumatic memories.$^{12}$

The most surprising finding of the present study is that the incidence of intraoperative awareness in patients who did not undergo general anesthesia (0.03%, $n = 22,885$) was not statistically different compared with those who did (0.023%, $n = 44,006$) ($P = 0.54$). There are several possible interpretations of this finding. We could postulate that, since sedation also suppresses consciousness and memory, perhaps the incidence was truly the same in anesthetized and sedated patients. This is, however, an absurd conclusion. Sedated patients are often very aware of their
surroundings, as well as talking with the anesthesiologist and surgical team during the procedure. We therefore reject this interpretation. The more likely interpretation is that the resolution of this retrospective study of more than 100,000 anesthetics at a single institution was too low to capture the incidence with

Figure 1. Graphical representation of the anesthetic regimen for the 10 cases of intraoperative awareness during general anesthesia Cases 1–5 (A), Cases 6–10 (B). Data from cases 1–2, 4–9 were taken directly from the electronic record and were based on end-tidal gas concentrations; data for case 3 were taken from a paper record and were based on vaporizer gas concentrations.
accuracy. Thus, the current study suggests critical methodological limitations to retrospective analyses, despite large sample sizes, and supports prospective approaches to assessing intraoperative awareness.

The finding of awareness complaints in patients not receiving general anesthesia is provocative. It is important to note that it was not simply awareness of pain, but awareness itself that was a source of distress. Several patients reported that they heard conversations during their procedure, indicating that this level of consciousness was inconsistent with their expectations. Furthermore, although 5/7 patients in this group reported pain, it was not the sole complaint. For example, patient 3 (Table 3) had a functioning spinal anesthetic but was distraught at hearing conversations, seeing bright lights, and feeling as if she had died. Although the significance is unclear, complaints of intraoperative awareness in patients receiving general anesthesia had a 1:1 male:female ratio, whereas this ratio was 1:6 in patients who did not have general anesthesia. Undesired intraoperative awareness in patients not receiving general anesthesia indicates the potential for disparity between the expectations of the patient and those of the anesthesiologist. We must also recognize that prior patient conversations with our surgical colleagues may establish expectations (e.g., complete unconsciousness) that are not met during the procedure itself. Unmet expectations, rather than events in themselves, may contribute to patient distress.

In conclusion, the incidence of undesired awareness during general anesthesia at our institution was more than three times as high as that recently reported by Pollard et al., despite the fact that no formal awareness interview was used. The self-
reported incidence of intraoperative awareness was not statistically different in patients receiving general anesthesia and those who did not. These results suggest that large retrospective analyses are probably inadequate to study intraoperative awareness. Furthermore, the dissatisfaction with awareness during nongeneral anesthetics suggests that prospective studies should evaluate the relationship between patient’s pre-procedure expectations and post-procedure perceptions of anesthetic adequacy.

REFERENCES

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Table 3. Complaints of Awareness from Patients not Receiving General Anesthesia

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>ASA</th>
<th>Surgery</th>
<th>Anesthetic technique</th>
<th>Awareness report</th>
</tr>
</thead>
<tbody>
<tr>
<td>1’</td>
<td>54</td>
<td>F</td>
<td>3</td>
<td>Femoral-popliteal bypass</td>
<td>Spinal</td>
<td>Complained of awareness during the case.</td>
</tr>
<tr>
<td>2’</td>
<td>56</td>
<td>F</td>
<td>3</td>
<td>Incisional hernia repair</td>
<td>Awake fiber optic</td>
<td>Complained of awareness during intubation. [After induction and failed airway management, the patient was awakened for fiber optic intubation. She was informed of this possibility preoperatively.]</td>
</tr>
<tr>
<td>3’</td>
<td>32</td>
<td>F</td>
<td>2</td>
<td>cesarean delivery</td>
<td>Spinal</td>
<td>Complained of hearing conversations, seeing bright lights, feeling as though she were underwater, feeling as though she were dead.</td>
</tr>
<tr>
<td>4’</td>
<td>33</td>
<td>F</td>
<td>2</td>
<td>Excisional breast biopsy</td>
<td>Monitored anesthesia care</td>
<td>Patient was very upset in the recovery room because she was aware during the case and sometimes felt pain.</td>
</tr>
<tr>
<td>5’</td>
<td>66</td>
<td>F</td>
<td>3</td>
<td>Right medial rectus recession</td>
<td>Retrobulbar block</td>
<td>Patient reported conversations, pain and recall of the doctor trying to give her more drugs.</td>
</tr>
<tr>
<td>6’</td>
<td>36</td>
<td>F</td>
<td>2E</td>
<td>Emergent cesarean delivery</td>
<td>Epidural</td>
<td>Patient reported awareness of incision, but was unconscious for the rest of the case. [In this case, the epidural anesthesia was not sufficient and general anesthesia was then induced.]</td>
</tr>
<tr>
<td>7’</td>
<td>54</td>
<td>M</td>
<td>3</td>
<td>Resection of back melanoma</td>
<td>Spinal</td>
<td>Reported pain at the end of the case and reported hearing conversations between anesthesiologist and surgeon. Patient was then given intravenous sedative-hypnotic.</td>
</tr>
</tbody>
</table>

ASA = American Society of Anesthesiologists Classification.
Day surgery: how far can we go and are there still any limits?
Nusrath Qadir and Ian Smith

Purpose of review
Day surgery continues to be a popular form of care, and patients and procedures of ever-increasing complexity are now being considered. As previous restrictions are regularly swept away, it is reasonable to ask where the new limits are and whether there are still any absolute contraindications to day surgery.

Recent findings
Recent evidence provides confirmation that some of the more complex, minimally invasive surgical procedures, such as laparoscopic nephrectomy, can safely and successfully be undertaken on a day-case basis. This transformation is clearly dependent on the development of appropriate technologies, but also involves a realistic assessment of when complications will occur and whether or not these will be prevented by an overnight hospital stay. A similar approach can be applied to the impact of various medical comorbidities, with current evidence suggesting that many predict intraoperative, but not postoperative, complications. The interactions of various factors – medical and surgical – however, may be more important.

Summary
Day surgery has clearly expanded beyond its previous limits, but some absolute contraindications still remain. A great deal is possible, but not everything that can be done necessarily benefits patients and some cases may only be feasible in expert hands and in ideal conditions.

Keywords
ambulatory anaesthesia, postoperative complications, preoperative assessment, selection criteria

Introduction
Day surgery is now an established speciality, which makes up a major portion of elective care in North America, Europe and much of the developing world. Although there is considerable variation in day surgery rates between (and even within) individual countries, it continues to expand in popularity, encompassing an ever-growing range of surgical procedures and patients of increasing medical complexity. Where day surgery was once seen as a highly specialized form of care, suitable for only the simplest of procedures and carefully selected fit patients, it is now seen as the treatment of choice for many operations with patients only excluded if there are convincing reasons.

As traditional limits on day surgery are regularly being surpassed, it is pertinent to ask how much further day surgery can be expanded and whether there are any finite boundaries. This expansion is being driven on two main fronts. New technologies and surgical developments are constantly refining operative practice such that a greater range of procedures become possible on an ambulatory basis. Furthermore, a better understanding of the nature and timing of surgical complications is also reducing the need for prolonged hospitalization. In parallel, improved anaesthetic drugs, techniques and perioperative care, combined with an improved understanding of the interaction of various comorbidities with postoperative outcome, have all increased the number of patients who can safely be discharged on the day of surgery. The present review will attempt to illustrate some of these developments using examples from the recent literature.

Surgical limits
Minimally invasive techniques have dramatically reduced tissue trauma, blood loss, pain and surgical morbidity after a wide range of procedures. This impact is well illustrated by laparoscopic cholecystectomy, which reduced the postoperative stay from 5–6 days for the traditional open operation to only 1–2 days. Surgeons were initially concerned that same-day discharge would delay the detection of bleeding or bile leaks, but subsequent experience shows these occur early, where they are detectable before discharge, or after several days, when even inpatients would have been discharged [1]. Early discharge may still be delayed by severe pain or surgical complications, but these are difficult to predict. Current advice is to manage all patients – including acute presentations – on a common pathway, which incorporates preassessment, day of surgery admission and same-day discharge if feasible [1]. The application of laparoscopic surgery has
Reduced the length of stay for numerous other operations and only relatively minor developments are then required to transfer the procedure into the day surgery arena, although this final step may take some time. For example, laparoscopic nephrectomy was first performed in 1991, but the world’s first day case nephrectomy was not undertaken until 2006 [2]. Yet achieving this milestone required little more than application of standard day surgery anaesthetic and analgesic protocols and giving careful thought to the size and location of the extraction port. The success of this first procedure has been reproduced in a small series [3\textsuperscript{**}] and also extended from simple to radical nephrectomy as well as pyeloplasty and adrenalectomy.

Endoscopic and interventional radiological procedures are also developing with extreme rapidity, and most appear suitable for day surgery. The need to prevent haemorrhage from the femoral arterial access site and the prolonged administration of platelet inhibitors to prevent abrupt vessel closure after percutaneous coronary interventions [4\textsuperscript{**}], however, mean that these patients are rarely discharged the same day. Arguing that the transradial route is safer and that a single bolus of the glycoprotein IIb–IIIa inhibitor abciximab is as effective as an overnight infusion, Bertrand and colleagues [4\textsuperscript{**}] randomized 1005 patients who had undergone uncomplicated percutaneous implantation of coronary artery stents to same-day discharge or a conventional overnight stay. Of the 504 patients randomized to day surgery, 88% were successfully discharged the same day. There were no significant differences in the incidence of major cardiac events – such as death, myocardial infarction and the need for further revascularization – or in major bleeding, access site complications and readmission rates.

The routine practice of many vascular surgeons is also to admit patients for overnight observation after endovascular interventions. This practice, however, has recently been challenged by an observational study of 112 interventions in 97 patients with intermittent claudication [5\textsuperscript{**}]. Only 8% of patients required hospital admission, and this was obvious within 2 h in all cases. No significant complications occurred following discharge in any of the other patients [5\textsuperscript{**}].

Defining surgical limits

The above incidents are good examples of novel day surgical procedures and many more are potentially possible. Is it practical to define some limits or guidelines? One possibility is to make a list of procedures that have been performed as day surgery, ideally accompanied by evidence of good practice; an approach taken by the British Association of Day Surgery. The Association’s Directory of Procedures [6] initially suggested target rates for day-case and short-stay surgery for 160 different operations. Updating such a list is necessary as experience evolves, however, and the latest (2007) version of the British Association of Day Surgery Directory contains several new procedures and a number of revised targets.

An alternative is to develop a set of a-priori criteria to guide clinicians as to which type of procedure may be suitable for day surgery. One American approach suggested using ‘maximum anaesthetic complexity’, with more complex procedures excluded from day surgery [7]. An obvious advantage, at least in North America, is the published American Society of Anesthesiologists’ ‘Relative Value Guide’ (ASA RVG), which is updated every year to reflect changing surgical practice. The ASA RVG assigns numerical units to measure the typical amount of anaesthesia work in providing care for a given procedure. For example, knee arthroscopy scores 3, laparoscopic cholecystectomy and prostatectomy each score 7 while heart transplantation scores 20. The authors [7] advocated that only cases with an ASA RVG of 7 or below should be done as day cases. This strategy is still dependent on regular updates, but also suffers from several other limitations [8\textsuperscript{*}]. The ASA RVG is based on American procedural codes and does not readily map to more internationally recognized coding systems, such as ICD-9-CM. A number of common day-case procedures are missing and only those performed relatively frequently have been analysed in detail. Fundamentally more limiting is the fact that several relatively high risk or painful procedures are associated with a rather low anaesthetic workload and therefore low ASA RVG scores [8\textsuperscript{*}].

The anaesthetic workload is also likely to reflect predominantly the intraoperative complexity of a given case. A patient may be difficult to manage during (or shortly after) a procedure – for surgical or anaesthetic reasons – but this need not preclude same-day discharge, provided these problems have resolved in sufficient time. The notion that day surgery should be confined to ‘simple’ or ‘nonchallenging’ cases is outdated. Day surgery limits are better governed by the invasiveness of the procedure, considering the extent of blood loss, postoperative pain and the degree (and duration) of physiological disturbance. These are all likely to be considerable after large open operations on body cavities, while surgical procedures that require circulatory support are also not eligible for day surgery because of a high mortality risk.

One Swiss group [8\textsuperscript{*}] developed an algorithm based on the means of surgical access, size of the organ involved and overall invasiveness of the procedure to decide which cases could be treated as day cases. Using general principles means that the model can be applied to any operation, but it was further refined by including procedures performed as a day case on more than 10 occasions, as this implied any potential complications could be managed outside hospital [8\textsuperscript{*}].
Facilitating surgical expansion

There are many surgical procedures that lead to minor postoperative complications, although most can be managed without hospitalization. Telephone support following discharge is common, but any advice is naturally dependent on what the patient reports. A group from Spain came up with a system based on mobile phones with cameras that can be used to send pictures and pulse oximetry readings to a hospital server, enabling the health professionals to manage their patients more effectively [11**]. The availability of images modified treatment in nine cases (18%), and avoided a return visit to hospital in all but one of these. Although the study numbers were small, this does show a way for future development in this field.

The incidence of several surgical complications, and thus the success of day surgery, may be influenced by the anaesthetic technique. Local anaesthesia, in particular, may have several advantages. Although usually performed under general anaesthesia, 1025 patients (61% of all cases) underwent thyroidectomy under local anaesthesia supplemented by sedation over a 16-year period by a single surgical team [10]. The proportion of local anaesthesia cases increased progressively over the course of the series, as did the proportion discharged within 6 h. Overall, 80% of local anaesthetic thyroidectomies were discharged within 6 h, with only 4% needing to stay more than 1 day [10]. Interestingly, in a procedure with a significant risk of bleeding, the authors preferentially used nonsteroidal anti-inflammatories for pain relief and routinely avoided opioid analgesia to minimize nausea, vomiting and sedation [10].

In a randomized controlled trial comparing local and general anaesthesia for thyroidectomy, day surgery was successful in almost 90% of patients in both groups, with no difference in postoperative complications or admissions [11**]. Local anaesthesia was associated with a faster recovery, however, and the proportion of cases performed under local anaesthesia and as day surgery both increased significantly after the study was completed [11*].

Local, and especially regional, anaesthesia can be extremely beneficial in facilitating major orthopaedic surgery. Using a catheter technique, continuous infusions of local anaesthesia can provide excellent pain relief in situations where oral analgesia alone is insufficient. One example is lower extremity surgery, where continuous peripheral nerve blocks provide sustained and effective analgesia while enhancing rehabilitation and patient satisfaction [12]. Similarly, major shoulder surgery is notoriously painful, but interscalene brachial plexus block can provide highly effective analgesia [13**]. Using a disposable elastomeric pump, five patients achieved excellent analgesia at home following day-case shoulder surgery, the value of the technique being highlighted in one patient who had to return to hospital for pain management after their interscalene catheter became dislodged [13**].

The benefits of local and regional anaesthesia are less clear in other types of day surgery. Advantages such as improved analgesia and reduced nausea are not consistently observed [14] and may be dependent on the skill of the individual anaesthetist and the use of an appropriate technique, such as low-dose spinal anaesthesia [15]. Choice of drug is also important: 2-chlorprocaine resulted in more rapid recovery of sensory and motor function after spinal anaesthesia and avoided the transient neurological symptoms associated with lidocaine [16**]. Local anaesthesia is undoubtedly a less expensive option than either regional or general anaesthesia for some operations, such as hernia repair [17], but more importantly local anaesthesia frequently makes day surgery possible for patients who have medical conditions that might preclude same-day discharge after general anaesthesia.

Medical limits

In the early days of day surgery there were numerous arbitrary limits, such as age, American Society of Anesthesiologists status and body mass index (BMI). The intention was to exclude those with comorbidities in the belief that risks and complications would be reduced by inpatient management. Subsequent experience showed the overall risks of day surgery to be very low and many of these limits, such as age, have been abandoned while others have been substantially relaxed. Medical selection criteria were extensively reviewed recently [18] and it was noted that unanticipated admission after day surgery remains uncommon, with an incidence ranging from 0.28% to 1.42%, with less than 20% of these cases being for medical reasons. While a number of medical factors – such as increasing age – do predict increased perioperative adverse events, they are not predictive of adverse postoperative events or of an increased likelihood of hospital admission or readmission. It is, however, important that preexisting conditions are optimally controlled, acute exacerbations of illness are avoided and, ideally, patients with chronic respiratory diseases abstain from smoking for a period of 4 weeks [18].

Obesity

While obesity is associated with numerous perioperative problems, the evidence suggests that most occur within the intraoperative or early postoperative period [19] and should logically not contraindicate same-day discharge. Furthermore, the level of risk is better known and modern anaesthetic drugs and techniques can be effectively applied to the obese patient [19]. Where day surgery was once restricted to patients with a BMI of 30 kg/m² or less, these limits have been greatly relaxed and a BMI of 40 kg/m² [20] or even a BMI of 50 kg/m² or more [21] is now considered acceptable.
Obesity is a rapidly increasing problem in the western world with surgical treatment being more commonly performed, increasingly on a day-case basis. One series of 343 consecutive day-case laparoscopic gastric bandings was performed on patients with an average BMI of 44.5 kg/m², ranging to as high as 62.7 kg/m² in the most extreme case [22]. Only three patients required hospital admission. A recent randomized trial confirmed the possibility of day-case gastric banding [23], with 76% of patients being satisfactorily discharged on the day of surgery. The day-case patients appeared to experience more pain, however, and one-half would have preferred an overnight admission.

Obesity may also be associated with obstructive sleep apnoea. Good evidence on the safety of day surgery in obstructive sleep apnoea is lacking [18], but expert opinion [24] suggests that superficial surgery is safe if performed under local or regional anaesthesia and may be acceptable with general anaesthesia, whereas airway and laparoscopic surgery are inadvisable.

Are there still limits?

While there are still some absolute surgical limits, minimally invasive techniques are finding ways around these limits and some very adventurous procedures are now being undertaken. Absolute social limits also exist, such as the absence of a competent carer or living in a remote location, but arrangements with friends and relatives (or even a paid carer) and hospital hotels can circumvent these too.

The association between comorbidities and adverse outcome is far from clear and many conditions predict only intraoperative complications that can still be managed in a day-case setting. These complications, however, can be more difficult to manage in an isolated environment and stricter limits may be needed for free-standing day surgery centres. More attention should be focused on possible interactions, since the presence of multiple comorbidities makes postoperative hospital admission far more likely; scoring all factors together in a risk index may be the best way to predict this outcome [25].

Interactions between the patient and the procedure are also important. Ambitious surgery is possible in relatively healthy day cases, while the more severely compromised can safely undergo simple surgery. Complex surgery in patients with multiple morbidity, however, is best reserved for inpatients.

Conclusion

Although an ever-increasing range of medical and surgical complexity is now possible in day surgery, achieving this sometimes requires some highly specialist skills, techniques and equipment. A distinction must be made between what is technically possible and that which is actually desirable. It is vital that further developments in day surgery are driven by what best enhances the patient’s outcome and experience, rather than just a desire to cut costs.

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. 607):

1 NHS Institute for Innovation and Improvement. Focus on: cholecystectomy. [Available from enquiries@institute.nhs.uk.]

A common pathway for the care of all patients undergoing laparoscopic cholecystectomy is proposed, based on expert opinion and best practice. Elective patients undergo targeted investigations before specialist referral and concurrent preassessment with subsequent day of surgery admission. Emergency cases should be rapidly investigated, preassessed and undergo surgery during the acute admission. Any patient meeting discharge criteria should be discharged on the day of surgery.


The authors describe how they have extended their experience with the world’s first true day-case laparoscopic simple nephrectomy, and have now performed a successful series of transperitoneal advanced urological laparoscopic procedures. The series includes six nephrectomies (including one radical nephrectomy), six pyeloplasties and four adrenalectomies for Conn’s syndrome. Operative times ranged from 1.3 to 3 h with no major immediate or delayed complications. Pain was manageable with oral analgesia and patient satisfaction was good. Subsequently, the team have successfully performed at least one further day-case radical nephrectomy (I. Smith, A. Golash, personal communication).


A total of 1005 patients undergoing uncomplicated transradial percutaneous coronary artery stent implantation were pretreated with aspirin and clopidogrel and a single bolus of 0.25 mg/kg abciximab. Then 501 patients were randomized to receive a standard 12 h infusion of abciximab and an overnight stay; the remaining 504 patients received no infusion and were discharged after an observation period of 4–6 h without any detriment in terms of all major outcomes.


During 27 months, 97 patients with intermittent claudication underwent 112 peripheral angioplasty interventions by a single vascular surgeon. Almost one-half involved the superficial femoral artery and 24% were multiple. Patients were mobilized in 1.4 ± 1.3 h and were discharged within 2 ± 1.2 h. Only 8% of interventions resulted in admission; the need for which was apparent within 1 h. The were no deaths or readmissions and costs were reduced from $1800 to $320 per patient.


An algorithm based on surgical access (endoscopic or open), organ size and invasiveness identified operations suitable for day surgery according to basic principles. Expert review suggested that only a relatively small number of the identified procedures needed to be reclassified (from day case to inpatient or vice versa) based on more specific factors. The model could be useful in identifying the potential to move inpatient procedures to day surgery in various countries and the associated cost savings.
Day surgery: are there still limits? Qadir and Smith


Fifty-four day-case patients were discharged with mobile camera phones over a 5-month period. In eight patients (14%) with blood-stained wound dressings, the images showed a haematoma that was diagnosed as normal and a return hospital visit was avoided. The additional information also modified the management of one further patient. Patients were highly satisfied with the additional security and attention afforded by the system.


Fifty-eight patients undergoing thyroidectomy were randomized in equal numbers to receive general anaesthesia or an anterior local anaesthetic field block (without regional cervical block) supplemented with sedation. The surgical time, complications and patient satisfaction did not differ between the groups. Eighty-six per cent of the general anaesthesia group and 90% of the local anaesthesia group were successfully discharged as day cases, although the local anaesthesia group had a significantly shorter postoperative stay.


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Continuous interscalene brachial plexus block was assessed in a pilot study of 10 patients undergoing major shoulder surgery. The first five stayed overnight to assess the effectiveness of the analgesia but the next five patients were discharged on the day of surgery following rotator cuff repair, subacromial decompression or shoulder arthroplasty. Pain relief was good in all cases, but was compromised by pump failure in three cases in phase 1 (after which portable electronic pumps were replaced by disposable elastomeric pumps) and by catheter displacement in one of the day cases.


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Knee arthroscopy patients were randomized to spinal anaesthesia with 50 mg either plain 1% lidocaine or plain 1% preservative-free 2-chloroprocaine. Motor function recovered in a median (range) of 60 (45–120) min after 2-chloroprocaine compared with 100 (60–140) min with lidocaine, while median time to unassisted ambulation was also faster, occurring in 103 (70–191) min compared with 152 (100–185) min with lidocaine. Lidocaine was associated with a 33% incidence of transient neurological symptoms that were not observed with 2-chloroprocaine.


Obstructive sleep apnoea is not always formally diagnosed but should be suspected when frequent sleep disturbance is associated with daytime somnolence. Opioid analgesia should be avoided where possible, and if the patient has a continuous positive airway pressure device this should be used before and after surgery.


The authors combined a number of risk factors to produce an outpatient surgery admission index to help identify day-case patients at higher risk of immediate hospital admission.
Nerve Injury After Peripheral Regional Block

Michael Bishop, M.D.
Clinical Professor of Anesthesiology
UCSD Hillcrest Medical Center
Case Presentation
Case Presentation

• Planned ulnar nerve transposition
• 71 y/o female patient with hypertension
• Axillary block via transarterial technique
• Uneventful block with good surgical anesthesia
• Tourniquet time 2 hours
• Returns 10 days later with numbness and weakness of hand on surgical side
• Complains of severe shooting pains in hand
Nerve Anatomy

From: Payne Jr., S.H.: Nerve Repair and Grafting in the Upper Extremity
Wallerian Degeneration

- Follows neural injury with axonal interruption
- The nerve fiber distal to the site of injury undergoes a predictable anterograde degenerative process known as Wallerian Degeneration
- This calcium-mediated process begins within hours of injury and results in fragmentation and phagocytosis of the axon and myelin sheath
- The process typically is completed within 5-8 weeks and results in an endoneurial sheath containing only Schwann cells
- The nerve fiber proximal to the site of injury may show no or only mild degeneration, however in severe trauma the degenerative process may proceed in the retrograde fashion to include the nerve cell body.
Wallerian Degeneration
Classification and Pathophysiology of Nerve Injury

• The Seddon Classification published in 1943

• Three grades of nerve injury
  – Neuropraxia
  – Axonotmesis
  – Neurotmesis
  – Clinically useful in predicting functional outcome.
Neuropraxia

- Mildest grade of injury
- Defined as a reduction or complete block of conduction across a nerve segment without disruption of axonal continuity
- The symptoms are thought to be due to ion-induced conduction block and in some cases damage to myelin in the injured segment.
- No Wallerian degeneration occurs.
- Functional loss is transient and full recovery is the rule.
- Symptoms may last from hours to weeks.
Neuropraxia
Axonotmesis

• Results from more severe injury and causing interruption of the axon and myelin sheath.
• The neural connective tissue, including endoneurium, perineurium, epineurium and other supporting tissues, remains intact and provides a conduit to guide regrowing axons to the target tissues.
• Distal Wallerian degeneration occurs.
• Prognosis for functional recovery is good
Axonotmesis

- Duration of symptoms depends on the location of the lesion; proximal lesions require a longer time period for regrowth of the axons to the target tissues.
- Axon regrowth occurs at approximately 1 inch per month and there is a period of maturation preceding functional recovery. Thus, resolution of symptoms typically can require months.
- Return of function is not dependent on perfect recovery of preinjury nerve structure.
- With very proximal lesions recovery of function may not be complete. This occurs if atrophy of motor end plates or sensory receptors occurs before the axon can regrow to reinnervate these structures.
Axonotmesis
Neurotmesis

- Most severe grade of injury
- Occurs when there is complete transection of the axon and all supporting neural connective tissue or when, in addition to axonal interruption, the neural connective tissue is so damaged that severe internal fibrosis occurs within the nerve
- Without surgical intervention functional recovery is poor because resulting scar tissue prevents axonal regrowth to the target tissues
Neurotmesis
Causes of Nerve Injury

• **Mechanical Trauma** due to puncture of the nerve by the nerve block needle has long been thought to be a primary cause of nerve injury.

• Bigeleisen (2006) investigated this possibility
Mechanical Trauma

- Twenty six patients underwent axillary block with ultrasound assistance using a 22 ga B bevel needle
- Musculocutaneous, median, ulnar and radial nerves identified using ultrasound
- Each nerve localized by elicitation of a paresthesia or feeling a “pop” as the needle pierced the fascia surrounding the nerve.
Mechanical Trauma

• 2-3 ml of the local anesthetic solution was injected
• If the injection appeared intraneural, the needle was withdrawn and an additional 2-3 ml was injected around the nerve
• If a halo appeared on initial injection an additional 2-3 ml was injected around the nerve
• All blocks were successful and no patients required analgesia in the PACU
Mechanical Trauma

- Twenty two of 26 patients (72 of 104 nerves) had puncture of at least one nerve as determined by ultrasound.
- Puncture of a nerve did not always result in paresthesia or dysesthesia.
- If paresthesia or dysesthesia did occur on nerve puncture, it variably increased or decreased during injection.
Mechanical Trauma

• No patients had residual neural injury following the blocks as determined by 6 month follow up.

• This suggested that “neural puncture and or injection *per se* are not the immediate or most likely cause of nerve injury after nerve block using the techniques described in this study”.
Mechanical Trauma

- Baciarello et al. (2007) suggested that, while intraneural injections may not necessarily cause nerve injury, intrafascicular injections almost invariably do cause nerve injury.
- Kapur et al. (2007) found that epineural injections of dog sciatic nerve *in vivo* with 4 ml of 2% lidocaine resulted in nerve injury only when the injection pressure exceeded 12 psi. This suggests that the intraneural pressure may be the causative factor in nerve injury following intraneural puncture and injection.
Ischemia

• This can occur with high intraneural pressure due to:
  – Intraneural injection
  – Vascular compromise due to tourniquet use or patient positioning.

• Large myelinated fibers appear to be more sensitive to ischemia than smaller nonmyelinated fibers.
Ischemia

• Greensmith and Murray (2006) cite an investigation into the effect of epinephrine containing injectate in resulting nerve injury.
• Rabbit sciatic nerves *in vivo* were subjected to topical endoneurial or intrafascicular injections with various concentrations of bupivacaine with or without 5 mcg/ml epinephrine.
• Intrafascicular injections were always associated with nerve injury while the endoneurial applications were associated with nerve injury only in the presence of epinephrine.
• This suggests that epinephrine may play a contributing role in the development of nerve injury after nerve block.
Compression

• May result in injury independent of ischemia

• Studies with pressure cuffs demonstrated conduction block associated with:
  – Focal demyelization after displacement of axoplasm and myelin internodes
  – Associated with obliteration of nodes of Ranvier.
Nerve Stretch

- Normal nerves can stretch up to 10-20% before injury occurs.
- One study found 17 nerve injuries attributed to traction in 417 total shoulder arthroplasties performed under general anesthesia.
- Traction using greater than 7 kg has also been associated with a higher risk of nerve injury.
Patient Positioning

- The effect of wrist extension for intra-arterial puncture on nerve injury was studied in awake healthy volunteers.
- All were found to have conduction block involving the median nerve after 30-60 minutes of wrist extension.
Local Anesthetic Toxicity

• Uncertain significance in the etiology of nerve injury after nerve block
• High concentrations of local anesthetic applied directly to nerve fibers may result in irreversible conduction loss in experimental preparations
• The significance of this factor in daily practice is less clear
Unknown factors

- Also account for some clinical postoperative nerve injuries
- The incidence of nerve injury following general anesthesia, in the absence of nerve block, is said to be 1/300 for the ulnar nerve and 1/1000 for all other peripheral nerves (Ridgeway and Herrick 2006)
Magnitude of the Problem
Magnitude of the Problem

• Brul et al. (2007)
• Retrospective study
• Reviewed all English language studies from January 1995-December 2005 found on MEDLINE search
• Total of > 65,000 peripheral nerve blocks
• Overall incidence of nerve injury < 3%
Magnitude of the Problem

• Permanent nerve injury defined as an injury with symptoms lasting >12 months after the block

• Studies that followed patients for that period of time demonstrated only **one** permanent injury in a patient who had a femoral nerve block

• Self reported data may have underestimated true incidence of injury
Magnitude of the Problem

- Recent review by Sorenson (2008) cites:
- Incidence of nerve injury of 10-15% in prospective studies
- 95% of deficits resolve in 4-6 weeks
- 99% of deficits resolve within 1 year
Summary

• Nerve injury after peripheral regional block is uncommon and usually due to neuropraxia with relatively rapid resolution
• Permanent injury is rare
Diagnosis of Nerve injury

"I’m stumped. We’ll have to wait for the autopsy."
Diagnosis of Nerve Injury

• Careful Physical Examination with specific neurological focus would appear to be the first and foremost activity to be undertaken when a patient presents with potential nerve injury after nerve block

• Motor and sensory deficits should be carefully documented
Diagnosis of Nerve Injury

• EMG/NCS studies can:
  – Help localize a nerve injury to a specific root, trunk, cord or peripheral nerve
  – Determine if the lesion involves motor, sensory or both types of nerve fibers
  – Help determine if there is preexisting nerve pathology
Diagnosis of Nerve Injury

• Electromyography (EMG)
• Involves the direct examination of skeletal muscles by placement of a small needle electrode
• Normal muscle at rest is electrically silent
• Axonotmesis/Neurotmesis injury patterns include:
  – fibrillation, positive sharp wave discharge at rest
  – abnormal recruitment pattern
• Changes are best seen 2-3 weeks after initial injury
  – use of the EMG in the acute injury phase may show complete loss of recruitment suggestive of acute injury
  – may show evidence of an old pre-existing injury.
Diagnosis of Nerve Injury

• **Nerve Conduction Study (NCS)** involves the measurement of the ability of peripheral nerves to conduct electrical activity after stimulation.

• Latency, distance travelled and nerve conduction velocity are all measured.

• The hallmark of Neuropraxia is slowed or blocked conduction across a nerve segment.

• In the immediate post injury phase, NCS may show decreased recruitment pattern in either Neuropraxia or Axonotmesis.
Diagnosis of Nerve Injury

- **Imaging Studies** such as MRI and CT scan may also be helpful in the evaluation of a nerve injury.

- Both MRI and CT have limitations in distinguishing nerves from the surrounding soft tissues:
  - MRI and especially MRN (magnetic resonance neurography) is superior to CT.
  - MRI of muscles can reveal signal changes in denervated (Axonotmesis/Neurotmesis) muscle as early as 4 days post injury.
  - Normal STIR/T2 weighted images are consistent with Neuropraxia.
Clinical Pathway Summary

• Borgeat 2005
• Careful examination with documentation of motor and sensory deficits.
• Neurological Consultation
• If compression by hematoma or other external influence is suspected, perform MRI/CT
• EMG in 1-3 days. If normal repeat in 3-4 weeks. If abnormal repeat in 6 months
• NCS in 1-3 days. If normal follow clinically. If abnormal repeat in 6 months.
Clinical Pathway Summary

• ASRA Practice Advisory 2008
  – Complete or progressive neural deficits should prompt urgent evaluation by a neurologist or neurosurgeon
  – Incomplete lesions with evidence of moderate or severe defect are an indication for early neurological consultation and consideration of neurophysiologic testing
  – Mild and/or resolving symptoms without objective evidence of neural deficit require only patient reassurance
Clinical Pathway Summary

• Consider adopting a team approach
  – Anesthesiologist
  – Surgeon
  – Neurologist/ Neurophysiologist
  – Physical Therapist

• Have team in place before it is needed
• Involve members early after suspected injury
• Make sure everyone is telling the patient the same thing to avoid confusion
Treatment of Nerve Injury
Treatment of Nerve Injury

• Dictated by the results of the work up
• Rarely is surgical intervention warranted
• Detailed discussion with patient as to:
  – Nature of injury
  – Expected prognosis including low likelihood of permanence of symptoms
  – Time course of expected recovery
• Physical therapy to maintain mobility
• Careful follow up
Prevention of Nerve injury
or How to Stay Out of Tiger Country
Prevention of Nerve Injury

• Patient should be awake or lightly sedated
  – Pain on needle placement or injection is not absolutely predictive of nerve injury, it seems prudent to utilize this important feedback
  – Special care with interscalene blocks

• Use care with Needle Placement
  – It seems obvious that careful needle placement and use of a B bevel needle should help to minimize the likelihood of injury
Prevention of Nerve Injury

• Cautious use of Epinephrine
• Use volume over concentration with respect to local anesthetic
• Careful positioning during and after the block
• Document the block carefully including any untoward occurrences
Prevention of Nerve Injury

• **Nerve Stimulation Technique Criteria**
  (Ridgway and Herrick 2006)
  – Obtain loss of twitch at or above 0.2 MA (if using a stimulator with 0.1ms pulse width)
  – Instant loss of twitch with initial 0.5ml injected
  – Low resistance to injection
  – Painless injection
Prevention of Nerve Injury

- Ultrasound guided needle placement is becoming the gold standard for regional anesthesia.
- There is no clear evidence that technique of nerve block (paresthesia, nerve stimulator, ultrasound guided) has a better safety profile with respect to nerve injury.
- Ultrasound guidance certainly seems to have “face validity“ if nothing else. What can compare to actually seeing your needle and injection in real time?
Prevention of Nerve Injury

• Use caution in patients with known or suspected preexisting neurological disease
  – Diabetes mellitus
  – Chemotherapy induced
  – Scheduled surgery on a nerve in the distribution of the planned block
Finish of Case Presentation

• On exam patient had a tender cord in the axilla at the site of the axillary block
• Positive Tinel’s sign over the cord
• CT scan showed organized hematoma in the region of the axillary artery compressing the ulnar nerve
• Surgical consultant declined exploration citing duration of symptoms
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Obstructive Sleep Apnea
A Clinical Approach

Michael Bishop, M.D.
What is Obstructive Sleep Apnea? (OSA)
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- Disorder characterized by disruption of sleep
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- Repeated episodes of partial or complete obstruction of the upper airway
What is Obstructive Sleep Apnea? (OSA)

• Disorder characterized by disruption of sleep
• Repeated episodes of partial or complete obstruction of the upper airway
• Symptoms
  – Snoring
  – Episodic hypopnea/apnea
  – Arterial oxygen desaturation
  – Hypercarbia
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- Repeated episodes of partial or complete obstruction of the upper airway
- Symptoms
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  - Episodic hypopnea/apnea
  - Arterial oxygen desaturation
  - Hypercarbia
- Increased sympathetic nervous system tone
Secondary Effects of Sleep Fragmentation

• Daytime somnolence
Secondary Effects of Sleep Fragmentation

- Daytime somnolence
- Memory loss
Secondary Effects of Sleep Fragmentation

- Daytime somnolence
- Memory loss
- Distractive or aggressive behavior
Secondary Effects of Sleep Fragmentation

- Daytime somnolence
- Memory loss
- Distractive or aggressive behavior
- Increased risk of automobile or other accident
Physiological Effects

• Pulmonary hypertension
Physiological Effects

- Pulmonary hypertension
- Cor pulmonale
Physiological Effects

- Pulmonary hypertension
- Cor pulmonale
- Systemic hypertension
Physiological Effects

- Pulmonary hypertension
- Cor pulmonale
- Systemic hypertension
- Cardiac arrhythmias
Physiological Effects

- Pulmonary hypertension
- Cor pulmonale
- Systemic hypertension
- Cardiac arrhythmias
- Myocardial Infarction
Physiological Effects

- Pulmonary hypertension
- Cor pulmonale
- Systemic hypertension
- Cardiac arrhythmias
- Myocardial Infarction
- Cerebrovascular disease
Physiological Effects

- Pulmonary hypertension
- Cor pulmonale
- Systemic hypertension
- Cardiac arrhythmias
- Myocardial Infarction
- Cerebrovascular disease
- Insulin resistance
Up to 38,000 deaths per year may be caused by cardiovascular disease attributable to sleep related breathing disorders.
Prevalence of OSA

- Overall prevalence in the U.S.- 5% to 10%
Prevalence of OSA

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• Up to 24% in men and 9% in women
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- In obese individuals: up to 50% in men and 40% in women
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Prevalence of OSA

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- Up to 24% in men and 9% in women
- In obese individuals: up to 50% in men and 40% in women
- Up to 82% of men and 93% of women with OSA have not yet been diagnosed
- Prevalence in surgical patients higher than that in the general population
Diagnosis of Sleep Apnea

- Classically made on the basis of sleep laboratory polysomnography
  - Complex
  - Expensive
  - Requires an overnight stay
  - Significant wait to schedule
Diagnosis of Sleep Apnea

• Now there are a number of portable alternatives
  – Convenient
  – Does not decrease the sensitivity of diagnosis
Diagnostic Criteria

- Sleep study detects the number of apneic and hypopnic episodes
Diagnostic Criteria

- Sleep study detects the number of apneic and hypopnic episodes
- Grading scale based on the number of episodes per hour
Diagnostic Criteria

• Sleep study detects the number of apneic and hypopnic episodes
• Grading scale based on the number of episodes per hour
• Results in apnea/hypopnea index
Grading of OSA

• Grading criteria vary between laboratories
Grading of OSA

• Grading criteria vary between laboratories
• ASA guidelines grading
Grading of OSA

- Grading criteria vary between laboratories
- ASA guidelines grading
  - AHI 6-20 Mild OSA
  - AHI 21-40 Moderate OSA
  - AHI > 40 Severe OSA
Problems With AHI

• The AHI may vary depending on:
  – Study center
  – Anxiety
  – Sleep deprivation
  – Opiates

• The severity of the AHI number does not necessarily correlate with:
  – The magnitude of the desaturation
  – Adequacy of the ventilation recovery
Why Do We Care?

• Patients with OSA have:
Why Do We Care?

• Patients with OSA may have:
  – Higher incidence of difficult intubation and ventilation
Why Do We Care?

• Patients with OSA may have:
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  – Higher incidence of postoperative complications; primarily respiratory, resulting in arterial oxygen desaturation
Why Do We Care?

• Patients with OSA may have:
  – Higher incidence of difficult intubation and ventilation
  – Higher incidence of postoperative complications; primarily respiratory resulting in arterial oxygen desaturation

• The rate of complication varies in direct proportion to the increasing severity of OSA
Why Do We Care?

• Postoperative deaths have been attributed to apnea in these patients
Why Do We Care?

Unpublished data from UCSD Medical Center suggests that the proximate cause of cardiac arrest is obstructive apnea/hypopnea in up to 51% of patients

Davis, 2008
Questionnaires to Determine Risk of OSA

- Many published questionnaires seeking to identify patients at risk for OSA
  - Berlin Questionnaire
  - Flemons Questionnaire
  - ASA Checklist
  - STOP Questionnaire
  - STOP-BANG Questionnaire
OSA Questionnaires Rely On

- Patient self reporting
  - Snoring
  - Apneic episodes
  - Arousals from sleep
  - Daytime somnolence

- Physical Data
  - Hypertension
  - Gender/Age
  - BMI
  - Neck and waist circumference
  - Airway anomalies
Statistical Considerations

Sensitivity: The ability of a test to identify people who truly have the disease

False positive: People without the disease who test positive

Specificity: The ability of a test to identify people who truly don’t have the disease

False Negative: People with the disease who test negative
Sensitivity of the Questionnaires

• Sensitivity ranges from 54-100%
Sensitivity of the Questionnaires

• Sensitivity ranges from 54-100%
• Varies with the population being tested and the measured AHI index used for comparison (patients with more severe OSA are easier to identify)
Sensitivity of the Questionnaires

- Sensitivity ranges from 54-100%
- Varies with the population being tested and the measured AHI index used for comparison (patients with more severe OSA are easier to identify)
- Sensitivity generally increases with increasing OSA severity
Importance of Sensitivity

• Ideally we want to identify EVERY patient with OSA preoperatively
Importance of Sensitivity

• Ideally we want to identify EVERY patient with OSA preoperatively
• A missed OSA diagnosis can lead to tragedy
Importance of Sensitivity

• Ideally we want to identify EVERY patient with OSA preoperatively

• A missed OSA diagnosis can lead to tragedy

• Once a patient with OSA is identified perioperative patient care can be modified accordingly
Specificity of the Questionnaires

- Specificity is much less, ranging from 38-60%
Specificity of the Questionnaires

- Specificity is much less, ranging from 38-60%
- Specificity generally decreases as the AHI increases
Specificity of the Questionnaires

• Specificity is much less, ranging from 38-60%
• Specificity generally decreases as the AHI increases
• Chung et al. (2008) found that the specificity of the Berlin and STOP questionnaires and the ASA Checklist did not differ significantly from chance
Specificity of the Questionnaires

- Specificity is much less, ranging from 38-60%
- Specificity generally decreases as the AHI increases
- Chung et al. (2008) found that the specificity of the Berlin and STOP questionnaires and the ASA Checklist did not differ significantly from chance
- Thus all have many false positives
Importance of Specificity

• The cost of identifying and appropriately caring for the OSA patient is substantial
Importance of Specificity

• The cost of identifying and appropriately caring for the OSA patient is substantial

• ASA Taskforce on OSA estimates the annual cost of implementing their guidelines as:
Importance of Specificity

- The cost of identifying and appropriately caring for the OSA patient is substantial.
- ASA Taskforce on OSA estimates the annual cost of implementing their guidelines as:
  - $80,000
  - Additional $50,000 for an outpatient facility.
Bottom Line

• A test with high sensitivity and low specificity will have many false positives resulting in diminished cost effectiveness.

• A test with low sensitivity and high specificity will fail to identify patients requiring special treatment.
The Ideal Screening Test

• Has excellent sensitivity when used in a low risk population
The Ideal Screening Test

• Has excellent sensitivity when used in a low risk population
• Has a false negative rate of 0%
The Ideal Screening Test

• Has excellent sensitivity when used in a low risk population
• Has a false negative rate of 0%
• Minimally intrusive
The Ideal Screening Test

• Has excellent sensitivity when used in a low risk population
• Has a false negative rate of 0%
• Minimally intrusive
• Relatively inexpensive
The Ideal Screening Test

- Has excellent sensitivity when used in a low risk population
- Has a false negative rate of 0%
- Minimally intrusive
- Relatively inexpensive
- Reliable
The Ideal Screening Test

- Has excellent sensitivity when used in a low risk population
- Has a false negative rate of 0%
- Minimally intrusive
- Relatively inexpensive
- Reliable
- Unfortunately doesn’t yet exist

Ramachandran et al. (2009)
What to Do?
What to Do?

Consider other factors?
Factors to be Considered

- Do PACU respiratory events predict post PACU oxygen desaturation episodes in hospitalized patients with and without OSA?

Gali et al. (2007)
PACU Events Studied

- Bradypnea < 8 respirations per minute
- Apnea > 9 seconds
- Desaturation < 90% on 4 L/M nasal cannula
- Inability to wean from nasal cannula
- Pain sedation mismatch (high concurrent pain and sedation scores)
Results

• Incidence of postoperative desaturation episodes increased from 37% to 57% comparing OSA patients with and without PACU episodes (NS)
• Statistically significant increase in post PACU desaturation episodes comparing the OSA and non OSA groups as a whole
• Indicated the importance of postoperative monitoring in OSA patients
Repeat Study

• Gali et al. (2009)
  – 693 patients
  – Screened for OSA with Flemons Questionnaire
  – Monitored PACU events as before
  – Four groups
    • OSA: low vs. high risk
    • Recurrent PACU events: yes vs. no
  – Looked for postop respiratory and cardiovascular events
  – Calculated postop oxygen desaturation index (ODI) measuring number of desaturations per hour
Results

• High risk OSA group had a higher risk of:
  – recurrent PACU events
  – postop respiratory complications
• Patients with recurrent PACU events had:
  – higher mean ODI overall
  – larger number of pts with ODI > 10
  – higher risk of postop respiratory complications
Results

• Rate of postoperative respiratory complication by group

  – Low OSA/ Low PACU: < 1%
  – High OSA/Low PACU: 2%
  – Low OSA/ High PACU: 11%
  – High OSA/ High PACU: 33%
Bottom Line

• Institutional Program should consist of:
  – Robust Screening Tool for OSA
  – Careful monitoring for recurrent respiratory events in the PACU
Initial UCSD Approach

• UCSD Hillcrest Medical Center OSA Taskforce decided to use the STOP Questionnaire
  – Simplicity of use
  – Felt to have an acceptable sensitivity: 65.6 – 79.5% based on AHI index used (AHI 5, 15, 30 cutoffs)
STOP Questionnaire

1. Do you **Snore** loudly? (louder than talking or loud enough to be heard through closed doors)

2. Do you often feel **Tired**, fatigued or sleepy during the daytime?

3. Has anyone **Observed** you stop breathing during your sleep?

6. Do you have or are you being treated for high blood **Pressure** or have you been advised to be treated for high blood pressure?

High risk of OSA: Yes to 2 or more questions
Low risk of OSA: Yes to fewer than 2 questions
UCSD Experience With STOP

• Initial 1459 questionnaires in Preop Clinic
• 969 completed (66%)
• Considering only completed questionnaires:
  – Pts with prediagnosed OSA: 72 (7.4%)
  – Pts at high risk of OSA by STOP: 117 (12%)
  – Total # OSA pts: 72 + 117 = 189 (19.5%)
• Thus 117 pts were identified who may have been missed!
PACU Event Monitoring

• Also considered PACU Events when deciding patient disposition
  – Home
  – Floor
  – IMU/ICU
Outcome

No known significant post PACU respiratory problems or deaths related to respiratory problems
Problems Identified

• Low completion rate:
  – may have missed some pts with OSA
  – need to improve completion rate

• Sensitivity of STOP may be too low
  – Ramachandran et al. (2009)
  – Meta-analysis of OSA screening tools
  – STOP graded as: ”No preoperative value, unacceptable FN rate”
Consider Use of STOP-BANG Questionnaire

- Do you **s**nore loudly? (louder than talking or loud enough to be heard through closed doors)
- Do you often feel **t**ired, fatigued or sleepy during the daytime?
- Has anyone **o**bserved you stop breathing during your sleep?
- Do you have or are you being treated for high blood **p**ressure or have you been advised to be treated for high blood pressure?

**Additional data gathered added to STOP**

- **BMI** > 35 kg/m²
- **Age** > 50
- **Neck circumference** > 40 CM
- **Male** **g**ender

High risk of OSA: Yes answer to 3 or more questions
Low risk of OSA: Yes answer to less than 3 questions
Advantages and disadvantages of STOP - BANG

- Sensitivity of 83.6, 92.9 and 100% depending on AHI index used
- Graded by Ramachandran as: “Excellent screening test for severe OSA, unacceptable FN rate for diagnosis of OSA”
- Decreased specificity as compared to STOP
- More cumbersome to administer
So Where Did This Leave Us?

Current UCSD OSA Algorithm
Disclaimer

As stated in the ASA guidelines, “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 recommendations that are supported by analysis of the current literature and by synthesis of expert opinion, open forum and clinical feasibility data.”
Preoperative Preparation

- Assessment of OSA risk: STOP vs. STOP-BANG
Preoperative Preparation

• Assessment of OSA risk: STOP vs. STOP-BANG
• Further OSA testing?
  – Should all questionnaire positive pts receive a formal sleep test
  – Polysomnogram or home study
Preoperative Preparation

• Assessment of OSA risk: STOP vs. STOP-BANG

• Further OSA testing?
  – Should all questionnaire positive pts receive a formal sleep test
  – Polysomnogram or home study

• Consider anesthetic technique
  – Local/MAC vs. Regional vs. general
  – Limit narcotic use
  – Steroid use to decrease airway swelling? (esp. upper airway surgery)
Additional Preoperative Preparation

• Is preop CPAP beneficial?
• Corda et al. (2009)
• Ten obese pts with mean AHI 55
• Applied CPAP for 6 months and tested upper airway caliber and collapsibility at baseline, 1 week and 6 months
Results

• Significant improvement in airway caliber after 1 week but no additional change over 6 months
• Significant reduction in collapsibility after 6 months
• Subgroup of 5 patients retested 1 week after withdrawal of CPAP showed:
  – Rapid reduction in airway caliber
  – Continued reduction in collapsibility
• Possible benefit of CPAP for 1 week preop
• But did not recheck AHI after CPAP
History, physical exam and result of OSA questionnaire → High probability of OSA → Consider modification of anesthetic technique → Sleep study referral → Consider preop CPAP
Intraoperative events

- Difficult Airway
Intraoperative events

- Difficult Airway
- Airway Trauma
Intraoperative events

- Difficult Airway
- Airway Trauma
- Airway Swelling
Intraoperative events

- Difficult Airway
- Airway Trauma
- Airway Swelling
- Sensitivity to Narcotics
History, physical exam and result of OSA questionnaire

High probability of OSA

Consider modification of anesthetic technique

OR events
- Difficult airway
- Airway swelling

Sleep study referral
- Preop vs. postop

Consider preop CPAP
PACU Respiratory Events
History, physical exam and result of OSA questionnaire

High probability of OSA

Consider modification of anesthetic technique

Sleep study referral
Preop vs. postop

Consider preop CPAP

OR events
Difficult airway
Airway swelling

No respiratory events in PACU
Room air SPO2 normal in quiet environment with pain controlled

Respiratory events in PACU
Bradypnea <8 respirations/min
Apnea > 9 sec
Desaturation <90% on 4 L/M nasal cannula
Inability to wean from nasal cannula
Pain sedation score mismatch (high concurrent pain and sedation scores)
PACU Care

• Observe for respiratory events and treat as needed
• Consider starting CPAP/BIPAP therapy
• Observe for an extended time period per ASA OSA Taskforce guidelines
History, physical exam and result of OSA questionnaire → High probability of OSA

→ Consider modification of anesthetic technique
→ Sleep study referral
→ Preop vs. postop OR events

Difficult airway
Airway swelling

No respiratory events in PACU
Room air SPO2 normal in quiet environment with pain controlled

→ Keep in PACU up to 3 hrs longer than non OSA patient

Respiratory events in PACU
Bradypnea <8 respirations/min
Apnea > 9 sec
Desaturation <90% on 4 L/M nasal cannula
Inability to wean from nasal cannula
Pain sedation score mismatch (high concurrent pain and sedation scores)

Consider initiation of CPAP/BIPAP in PACU

→ Observe for up to 7 hrs after last event until room air SPO2 is normal in a quiet environment with pain controlled

Consider preop CPAP
Respiratory Events Don’t Resolve

- Admit patient for continuous observed SPO2/CO2 monitoring
- Initiate or continue CPAP/BIPAP therapy
History, physical exam and result of OSA questionnaire

High probability of OSA

Consider modification of anesthetic technique

Sleep study referral
Preop vs. postop

Consider preop CPAP

OR events
Difficult airway
Airway swelling

Respiratory events in PACU
Bradypnea <8 respirations/min
Apnea > 9 sec
Desaturation <90% on 4 L/M nasal cannula
Inability to wean from nasal cannula
Pain sedation score mismatch (high concurrent pain and sedation scores)

Consider initiation of CPAP/BIPAP in PACU

Observe for up to 7 hrs after last event until room air SPO2 is normal in a quiet environment with pain controlled

Respiratory events not resolved

Admit for continuous SPO2/CO2 monitoring
Possible CPAP/BIPAP

No respiratory events in PACU
Room air SPO2 normal in quiet environment with pain controlled

Keep in PACU up to 3 hrs longer than non OSA patient
Respiratory Events Resolve

• Assess patient risk for post PACU desaturation events
Respiratory Events Resolve

- Assess patient risk for post PACU desaturation events
  - Type of anesthesia
Respiratory Events Resolve

- Assess patient risk for post PACU desaturation events
  - Type of anesthesia
  - Type of surgery
Respiratory Events Resolve

• Assess patient risk for post PACU desaturation events
  – Type of anesthesia
  – Type of surgery
  – Type of postoperative narcotics
Respiratory Events Resolve

• Assess patient risk for post PACU desaturation events
  – Type of anesthesia
  – Type of surgery
  – Type of postoperative narcotics
  – Patient age
Respiratory Events Resolve

• Assess patient risk for post PACU desaturation events
  – Type of anesthesia
  – Type of surgery
  – Type of postoperative narcotics
  – Patient age
  – Sophistication of home support
Risk Assessment

• High risk
  – Admit for continuous SPO2/CO2 monitoring and possible CPAP/BIPAP
Risk Assessment

• High risk
  – Admit for continuous SPO2/CO2 monitoring and possible CPAP/BIPAP

• Low risk
  – Possible additional PACU stay
  – Discharge home or to floor with caution
History, physical exam and result of OSA questionnaire

High probability of OSA

Consider modification of anesthetic technique

Sleep study referral
Preop vs. postop

Consider preop CPAP

OR events
Difficult airway
Airway swelling

Respiratory events in PACU
Bradypnea <8 respirations/min
Apnea > 9 sec
Desaturation <90% on 4 L/M nasal cannula
Inability to wean from nasal cannula
Pain sedation score mismatch (high concurrent pain and sedation scores)

Consider initiation of CPAP/BIPAP in PACU

Observe for up to 7 hrs after last event until room air SPO2 is normal in a quiet environment with pain controlled

Respiratory events resolved

Clinician assessment as high risk

Admit for continuous SPO2/CO2 monitoring
Possible CPAP/BIPAP

Respiratory events not resolved

Clinician assessment as low risk

Discharge home or to floor

No respiratory events in PACU
Room air SPO2 normal in quiet environment with pain controlled

Keep in PACU up to 3 hrs longer than non OSA patient

Assess risk based on
Type of anesthesia
Type of surgery
Expected postop pain
Type of postoperative narcotic prescribed
Patient age
Sophistication of home support

Clinician assessment as low risk
Patient With Low Risk of OSA

It is important to emphasize that one limb of the flow sheet has been omitted for clarity; that being the patients who are considered to be at low risk of OSA, based on the preoperative evaluation. Since no evaluation tool is 100% sensitive in all groups, any patient who evidences concerning respiratory patterns in the PACU should be carefully observed and discharged to an unmonitored area with caution.
Continuous SPO2/CO2 Monitoring

If the decision is made to admit the patient for respiratory monitoring, it is critical that the results of this monitoring are continuously observed.

It is of no use to place a patient on a pulse oximeter in a bed at the far end of the hall where the alarm cannot be heard.

Traditionally these patients have been observed in an ICU or IMU setting with “hard-wired” monitors.
Newer Monitoring Modalities

There are newer modalities of pulse oximetry/carbon dioxide monitoring whereby the data from a bedside monitor are continuously streamed wirelessly to a central observation station.

Potentially allows OSA patients to be cared for postoperatively on a surgical floor. This may have important consequences for facilities where ICU/IMU beds are at a premium.
Nellcor Oxinet
Does CPAP/BIPAP Use Obviate Continuous Monitoring?

• Bolden *et al.* (2007)
  – CPAP did not reliably prevent desaturation episodes in the first 24 postoperative hours in OSA patients

• Personal opinion
  – In the post operative period, the effects of residual anesthesia and/or pain medication may result in confusion or an abnormal sleep state during which the patient may somehow disable or remove the CPAP, rendering it ineffective.
  – If anything, the preoperative use of CPAP should make it even more compelling to observe the patient overnight in the hospital.
Additional Concern

• Recent work by Frances Chung at the University of Toronto
• AHI and ODI showed worsening after either general or neuraxial anesthesia
  – Peaked at postop day 3
  – Did not return to baseline until day 7
Inpatient vs. Outpatient Facility

• I see no significant difference in the type of care that should be expected from a freestanding outpatient facility as compared to an inpatient facility when treating patients with OSA.

• All the pertinent information discussed here has equal relevance for both facilities.

• When the practitioner considers whether a patient with OSA is a candidate for surgery at their free standing center, they must be absolutely sure that they can provide not only the appropriate surgical care but also the appropriate postoperative care and monitoring.
The position statement of the ASA Task Force on Perioperative Management of Patients with Obstructive Sleep Apnea is reproduced below

“Factors to be considered in determining whether outpatient care is appropriate include (1) sleep apnea status, (2) anatomical and physiological 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.”
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Pain management after ambulatory surgery
Stephan A. Schug\textsuperscript{a,b,c} and Chui Chong\textsuperscript{b}

\textsuperscript{a}Pharmacology and Anaesthesiology Unit, School of Medicine and Pharmacology, University of Western Australia. \textsuperscript{b}Department of Anaesthesia and Pain Medicine, Royal Perth Hospital, Perth, Australia. \textsuperscript{c}Department of Anaesthesiology and Intensive Care Medicine, University of Muenster, Muenster, Germany

Correspondence to Professor Stephan A. Schug MD, FANZCA FFPMANZCA, UWA Anaesthesia, Level 2 MRP Building G Block, Royal Perth Hospital, GPO Box X2913, Perth WA 6847, Australia. Tel: +61 8 9224 0201; fax: +61 8 9224 0279; e-mail: stephan.schug@uwa.edu.au

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Purpose of review
Poor pain management has been a problem after ambulatory surgery. This review examines the current situation and recent advances in the area.

Recent findings
Despite significant scientific advances in the management of postoperative pain, surveys continue to show poor pain control in the routine clinical setting of day-case surgery. Causes are poor implementation of the progress and lack of adherence to established guidelines with too much reliance on opioids and lack of continuation of analgesic techniques into the postoperative period. The current literature with regard to systemic analgesia supports the concept of multimodal analgesia with an emphasis on the widespread use of appropriate nonopioids including NSAIDs or cyclo-oxygenase-2 inhibitors. The other mainstay of pain management after ambulatory surgery should be local anaesthetics, either used single shot, but with appropriate adjuvants, or by continuous peripheral nerve blocks. The latter techniques show increasingly promising results with a good safety record and are reviewed extensively.

Summary
Multimodal analgesia and local anaesthetic techniques are the avenues to improve the still disappointing quality of analgesia after ambulatory surgery.

Keywords
ambulatory surgery, local anaesthetics, multimodal analgesia, non opioids, postoperative analgesia

Introduction
Previous studies have shown that a high percentage of discharged ambulatory surgical patients suffer from moderate-to-severe pain during the first 24–48 h postoperatively [1–3]. The question remains if this unsatisfactory situation with regard to pain management after ambulatory surgery has improved over time; this review will address recent articles relating to the issues around pain after ambulatory surgery and effective analgesic regimen for its management.

How much progress has been made recently with regard to pain management after ambulatory surgery?
A number of recent surveys in a variety of settings and countries continue to identify a high incidence of postoperative pain in the setting of ambulatory surgery. Even in a dedicated day-surgery unit, severe pain was reported in 10% of 4046 patients [4]. Twenty-four hours after laparoscopic day-case cholecystectomy, 65% of patients reported moderate and 23% severe pain [5*]. Pain was also the most frequent problem identified among 4185 patients undergoing ambulatory urological surgery [6]. Similarly, only 60% of patients after ambulatory gynecologic surgery were satisfied with their postoperative pain control [7]. These disappointing results have been replicated in two Swedish nation-wide surveys of ambulatory surgery; pain was here again the most common problem at follow-up after discharge in a general [8**] and a paediatric population [9**]. Pain was also the most common reason for unplanned hospital admission in a large prospective cohort study across 14 day-surgery units in Finland [10*].

A German survey identified only partial adherence to guidelines for acute pain therapy as a potential cause of the lack of improvement in this area [11]. This observation is in line with the views expressed by White [12**] in a recent editorial; he criticizes the ‘disconnect’ between the significant scientific advances in the area of multimodal analgesia and the lack of implementation of these concepts into routine clinical practice. This
The concept of multimodal analgesia
Multimodal or balanced analgesia, involving the use of more than one analgesic compound or modality of pain control to achieve an opioid-sparing effect, obtain additive (or even synergistic) pain relief while minimizing adverse effects, has become the gold standard for postoperative pain management [13]. Surprisingly, despite the widespread clinical use of such combinations, there are limited studies that examine their effectiveness in combination. A review in 2007 summarized the clinical evidence for addition of selected second drugs to an opioid or NSAID/cyclo-oxygenase-2 (COX-2) inhibitor [14]. There is strong evidence to suggest that opioids in combination with either NSAIDs/COX-2 inhibitors or local anaesthetics or both provide improved analgesia or a reduction in opioid consumption/ adverse effects or both. These combinations should be considered for every patient unless contraindicated. Favourable evidence, but insufficient to warrant consideration of the drug for every patient, existed for combining opioids with paracetamol, α2-agonists (clonidine, dexmedetomidine), antiepileptics (including gabapentin), glucocorticoids and N-methyl-D-aspartate (NMDA) antagonists.

The recent and unprecedented retraction of 21 articles by Dr Scott Reuben, a leading investigator in perioperative analgesia, has caused concerns regarding the validity of concepts of multimodal analgesia among many practitioners [15,16]. This has prompted a cursory review in the form of an editorial of both the retracted and unpimpeached literature [17**]. The authors conclude that postoperative administration of COX-2 inhibitors has consistently improved analgesia, reduced opioid-related side effects and improved quality of patient recovery in the early and intermediate postoperative period. The preemptive effect of NSAIDs and COX-2 inhibitors, their ability to prevent chronic pain after major orthopaedic surgery and their effect on bone healing are now concepts that require further investigation.

Overall, use of multimodal analgesia with an emphasis on nonopioids and local anaesthetics is a promising concept, in particular, after ambulatory surgery. Adverse effects of opioids such as nausea and vomiting can influence time to discharge and readmission rates unfavourably; in ambulatory surgery, adverse effects from opioids are the second leading cause for rehospitalization of patients after incomplete pain relief [18]. In a recent double-blind study involving 216 day-surgery patients, perioperative use of 1 μg/kg of fentanyl exacerbated postoperative nausea and vomiting without an improvement in postoperative pain and led to increased respiratory depression, hypotension and bradycardia [19*]. Another double-blind randomized controlled trial which involved 145 patients undergoing ambulatory abdominal surgery emphasized the benefits of avoiding even codeine; patients on combination of acetaminophen and ibuprofen were more satisfied with their analgesia, had fewer side effects and comparable pain intensity when compared with patients receiving acetaminophen and codeine and caffeine [20*].

Nonopioid analgesics
Nonopioid analgesics can be used on their own or in combination for pain of mild or moderate intensity [21]. Their use in ambulatory surgery is widespread; in the Swedish survey, paracetamol was used in 95% of patients to initiate analgesia, followed by NSAIDs in 73% and COX-2 inhibitors in 15% [8**]. Similarly in the German survey, novaminsulfone in 34% and NSAIDs in 28% were used perioperatively, and 58% received NSAIDs and 32% novaminsulfone for home [11].

Even paracetamol on its own has a role in pain relief after ambulatory surgery as shown in an open prospective study [22]. Intravenous administration of 1 g paracetamol 30 min before the planned end of minor knee, gynaecological or varicose vein surgery in 601 American Society of Anesthesiologists (ASA) I or II ambulatory patients provided very good or good analgesic efficacy in 82% of patients. Some outpatient procedures such as fractional curettage might result in more mild pain that paracetamol cannot make a difference here [23*]. This reinforces the concept that analgesic interventions have procedure-specific efficacy, a notion shown for paracetamol [24].

With regard to analgesics with an anti-inflammatory effect, nonselective NSAIDs and selective COX-2 inhibitors have comparable efficacy in acute pain with NNT50 in the range of 2–3 [25–27,28*]. In this context, it is surprising that a recent study in ambulatory gynaecological surgery found the preoperative administration of the nonselective NSAID ketorolac superior to the COX-2 inhibitor etoricoxib [29*]. The authors speculate about reasons for these findings contradicting the meta-analyses quoted above.

The adverse effect profiles of COX-2 inhibitors offer advantages over NSAIDs in the perioperative setting [30]: the rate of gastroduodenal ulceration is comparable to placebo (versus 20–40% even with short-term use
NSAIDs in at-risk populations); reduced blood loss as COX-2 inhibitors have no effect on platelet function; COX-2 inhibitors do not trigger bronchospasm in aspirin-sensitive patients. The issue of thrombotic cardiovascular events caused by COX-2 inhibitors has been discussed extensively in the wake of the rofecoxib withdrawal. In the largest pooled posthoc analysis to date, short-term perioperative use of parecoxib and valdecoxib were not found to increase the risk of cardiovascular adverse events after noncardiac surgery [31**]. However, renal adverse effects of nonselective NSAIDs and COX-2 inhibitors are most likely comparable.

**Gabapentinoids**

The effects of the anticonvulsants gabapentin and pregabalin in the postoperative pain setting have been rather promising. In a number of careful meta-analyses, they reduced postoperative pain, opioid consumption and opioid adverse effects significantly [32]. They caused only minor adverse effects such as sedation and dizziness, though these might have implications for discharge in an ambulatory setting.

The results of the limited number of trials in this setting have been less clear. For arthroscopic shoulder surgery, 800 mg gabapentin did not improve analgesia provided by a brachial plexus block, possibly due to the excellent analgesia and prevention of early central sensitization achieved by the nerve block [33]. Similarly, 100 mg pregabalin did not have beneficial effects in patients having minor gynaecological surgery to the uterus only [34]. On the other hand, 150 mg pregabalin improved analgesia without reducing analgesic requirements after ambulatory laparoscopic gynaecological surgery [35]. In a comparative trial, 1200–1600 mg gabapentin provided better pain relief than 15 mg meloxicam after ambulatory laparoscopic cholecystectomy [36**]; combining both did not offer advantages and shows that it might not always be useful to combine multiple modalities.

**Local anaesthetics**

As outlined above, local anaesthetics on their own or in combination with systemic analgesics can provide excellent analgesia and are very useful in an ambulatory setting. Even simple infiltration with local anaesthetics can be very effective. This has been repeatedly demonstrated with use of trocar site infiltration in laparoscopic cholecystectomy [37] whereby preincisional infiltration seemed superior to the postoperative one. However, intraperitoneal nebulization of 100 mg of ropivacaine in gynaecologic laparoscopic surgery had no analgesic effect [38].

Multiple studies have looked at the addition of various compounds to local anaesthetics in a number of settings. Intravenous regional anaesthesia (IVRA) in particular has very limited postoperative analgesic effects. However, addition of 30 mg ketorolac, especially when combined with 8 mg dexamethasone, to lidocaine for IVRA after ambulatory hand surgery provided improved longer lasting analgesia and reduced rescue analgesia requirements when compared with lidocaine on its own [39*]. With regard to intraarticular administration, the addition of sufentanil to ropivacaine and clonidine did not provide additional analgesic benefits after arthroscopic cruciate ligament repair [40]. The addition of 100 mg tramadol to 0.25% bupivacaine for arthroscopic meniscectomy prolonged analgesia and led to reduced rescue analgesic consumption, earlier discharge and unassisted ambulation [41*]. This is consistent with previous studies showing a peripheral effect of tramadol [42–44] and is a promising outcome for this adjuvant.

**Continuous peripheral nerve blocks**

Postoperative analgesia after single-injection regional nerve blocks even with long-lasting local anaesthetics is limited to a duration of maximum of 12–16 h. There is now increasing interest in continuous peripheral nerve blocks (CPNBs) to provide longer-lasting analgesia at home after ambulatory surgery. These techniques are most commonly used after orthopaedic surgeries and have been reviewed recently [45*,46,47*]. CPNBs have been used at various locations, including paravertebral, interscalene, intersterneolomastoid, infraclavicular, axillary, psoas compartment, femoral, fascia iliaca, sciatic/Labat, sciatic/popliteal and tibial nerve placement. Overall, compared with patients discharged home with oral analgesia, patients with CPNBs reported less insomnia, dramatically less opioid consumption with fewer opioid-related side effects and higher satisfaction [48].

Issues of infusion rate and concentration of local anaesthetics are particularly important in the outpatient setting with limitations of reservoir volume and concerns about patient safety. The relative effects of concentration and volume were investigated recently. A study compared the effects of 0.2% (basal 8 ml/h, bolus 4 ml) vs. 0.4% (basal 4 ml/h, bolus 2 ml) ropivacaine in continuous popliteal-sciatic nerve blocks of ambulatory patients undergoing moderately painful orthopaedic surgery at or distal to the ankle [49*]. Surprisingly, patients given 0.2% ropivacaine experienced an insensate limb (thought to make the limb prone to accidental injury) significantly more often than those receiving 0.4% ropivacaine, whereas there were minimal differences between the two groups for pain scores, supplemental oral opioids consumption and
patient satisfaction scores. In a similar study of the same regimen via an infraclavicular catheter in patients undergoing moderately painful orthopaedic surgery distal to the elbow, the opposite was found [50*]; patients given 0.4% ropivacaine experienced an insensate limb significantly more often than those receiving 0.2% ropivacaine. Although analgesia was similar, satisfaction with postoperative analgesia was higher in the 0.2% ropivacaine group. The same infusion regimen via interscalene catheters led to inconclusive results with regard to insensate limbs but showed better analgesia with the lower concentration [51*]. These findings suggest that the relationship between ropivacaine concentration and effect is opposite for continuous popliteal-sciatic and interscalene nerve blocks and might be block-specific. Surgical procedure, catheter location, physical therapy regimen and specific local anaesthetic infused are likely confounding factors that affect the optimal regimen.

With regard to the routine use of CPNBs in an ambulatory setting, Fredrickson et al. [52**] reported a case series of 300 patients with continuous interscalene analgesia for shoulder surgery. Thirteen patients experienced inadequate pain relief after leaving the postanaesthesia care unit (PACU). Of these, five were rescued with additional ropivacaine, three had the catheter effectively reinserted, and five were managed with oral opioids. One patient required antibiotics treatment for catheter site infection. Three patients had neurological sequelae which all resolved by 6 months. In another case series involving 400 continuous popliteal-sciatic nerve blocks for postoperative analgesia, the incidence of severe neuropathy or infection complications was 0.5 and 0.25%, respectively [53]. These results are in line with previous case series [54,55]. Even in children, CPNBs can be used safely in an outpatient setting, as confirmed in a recent audit of 108 paediatric patients [56].

In one of the case series quoted above, duration of infusion was found to be an independent risk factor for infectious complications in CPNBs [55], leading to recent reviews of the risk of infection with use of CPNBs [57**,58]. Although these complications are rare, severe infectious complications have been reported. Other risk factors include omission of alcohol-based skin disinfection, poor surgical aseptic conditions, lack of antibiotic prophylaxis, site of catheters insertion (groin and axilla have higher risk) and frequent change of dressing [57**]. The specific issue of infusion contamination is addressed in the other review that recommends use of premanufactured sterile products or compounding by pharmacy and a ‘hang-time’ of 72 h in view of the risk of contamination with more frequent reservoir changes [58*].

**Conclusion**

Postoperative pain management aims not only to decrease pain intensity, but also to increase patient comfort and to improve postoperative outcomes. This is particularly important in ambulatory surgery. Regrettably, despite the theoretical progress made in the management of postoperative pain, the results in clinical practice continue to disappoint. Concepts of multimodal analgesia with avoidance or reduction of opioid use and more widespread use of local anaesthetic techniques, as simple infiltrations or by continuous peripheral nerve block techniques, should be used more widely.

**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 (pp. 822–823).

6. This prospective study supports the importance of follow-up of day-case surgery patients after discharge to identify problems, in particular, with analgesia.
10. This article presents valuable insights into the perioperative management of day-case surgical patients on the basis of a nation-wide survey identifying pain as the most common complaint.
12. This is an identical survey to that in [8**], however, in a paediatric population, with similar results.
14. By a different methodology, this study confirms the results of the two surveys quoted above in another Scandinavian county.
17. An excellent editorial highlighting the issues and causes of poor pain management after ambulatory surgery.
An interesting study showing superiority of gabapentin over an NSAID with regard to analgesia in the perioperative setting with no further benefit by combining both medications.

The above article shows that the poor postoperative analgesia provided by IVRA can be improved by adding anti-inflammatory compounds.

The above article shows interesting and promising results on the intraarticular use of tramadol.

The above article shows a useful review of the use of these techniques in the ambulatory setting.

The above article shows addressing the issues of concentration versus volume of local anesthetics in CPNBs.

The above article addresses the issues of concentration versus volume of local anesthetics in CPNBs.

The above article addresses the issues of concentration versus volume of local anesthetics in CPNBs.

A valuable survey of routine clinical practice in a ‘real world setting’ confirming the efficacy and safety of CPNBs for ambulatory surgery.


A ‘must read’ review for every anaesthesiologist performing CPNBs on this really important issue.


A review of a specific topic related to the overall issue discussed in [57**].
Postoperative Pain Management After Ambulatory Surgery: Role of Multimodal Analgesia

Ofelia Loani Elvir-Lazo, MDa, Paul F. White, PhD, MD, FANZCAb,c,d,e,f,*

KEYWORDS
• Ambulatory surgery • Multimodal analgesia • Opioid analgesics • Nonopioid analgesics

Postoperative pain remains a challenging problem, which requires a proactive approach using a variety of treatment modalities to obtain an optimal outcome with respect to enhancing patient comfort and facilitating the recovery process. Multimodal (or balanced) analgesia represents an increasingly popular approach to preventing postoperative pain. The approach involves administering a combination of opioid and nonopioid analgesics that act at different sites within the central and peripheral nervous systems in an effort to improve pain control while eliminating opioid-related side effects.1–5 The adaptation of multimodal (or balanced) analgesic techniques as the standard approach for the prevention of pain in the ambulatory setting is one of the keys to improving the recovery process after day-case surgery.1,6

Poorly controlled pain is a major factor contributing to a delayed discharge after ambulatory surgery.2,4 Improving postoperative pain control accelerates the ability of patients to resume their activities of daily living.5 Many patients undergoing ambulatory surgery continue to experience unacceptably high levels of pain after their operation.2–4 Despite recent advances in our knowledge of multimodal analgesic therapies1 and progress in our understanding of the pathophysiologic basis of acute pain, there remains a need for clinicians to implement evidence-based, procedure-specific
multimodal analgesic protocols, which are modified to meet the needs of individual patients and to enhance the quality of postoperative pain management.\textsuperscript{6}

The armamentarium of analgesic drugs and techniques for the management of postoperative pain continues to grow at a rapid rate. However, there seems to be a significant disconnect between the publication of analgesic studies in the peer-reviewed literature, demonstrating approaches to improving acute pain management and the application of these concepts in clinical practice. A part of the problem relates to the increasing number and complexity of elective operations that are being performed on an ambulatory (or short-stay) basis in which the use of conventional opioid-based intravenous patient controlled analgesia and central neuraxial (spinal and epidural) analgesia techniques are simply not practical for acute pain management. This rapidly expanding patient population requires an aggressive perioperative analgesic regimen that provides effective pain relief, has minimal side effects, is intrinsically safe, and can be managed by the patient and their family members away from a hospital or surgical center.

One of the most important factors in determining when a patient can be safely discharged from a surgical facility, and that also has a major influence on the patient’s ability to resume their normal activities of daily living, is the adequacy of postoperative pain control.\textsuperscript{3,7} Perioperative analgesia has traditionally been provided using potent opioid (narcotic) analgesics. However, extensive reliance on opioid medication for acute pain management is associated with a variety of perioperative complications (eg, drowsiness and sedation, postoperative nausea and vomiting (PONV), pruritus, urinary retention, ileus, constipation, ventilatory depression), which can contribute to a delayed hospital discharge and resumption of normal activities of daily living.\textsuperscript{8} Anesthesiologists are increasingly using a combination of nonopioid analgesic medications as the first line of therapy for the prevention of pain in the postoperative period. However, opioid analgesics will likely remain the primary treatment option for patients who require rescue analgesic therapy in the postoperative period until more potent and rapid-acting nonopioid analgesics become available for routine clinical use.

In 2000, the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) introduced new standards that mandated pain assessment and treatment as part of routine patient care in an attempt to improve control of acute pain. Many medical institutions have misinterpreted this mandate as requiring that the treatment of pain must be guided by patient reports of pain intensity indexed to a numerical pain scale.\textsuperscript{5} After the implementation of a routine numeric pain scoring system in the recovery room, Frasco and colleagues\textsuperscript{9} reported a significant increase in the use of opioid analgesics. Vila and colleagues\textsuperscript{10} reported that as a result of the JCAHO-mandated policy for pain management, the incidence of opioid-related adverse reactions increased from 11 to 25 per 100,000 inpatient days at their medical center. Most adverse drug reactions were preceded by a documented decrease in the patient’s level of consciousness due to opioid-related sedation. In the ambulatory setting, the primary factor responsible for postdischarge nausea and vomiting is the use of oral opioid-containing analgesics.\textsuperscript{11} Raeder and colleagues\textsuperscript{12} reported that the use of ibuprofen after ambulatory surgery was associated with fewer gastrointestinal side effects (eg, PONV, constipation) when compared with the use of an oral combination of acetaminophen and codeine.

Early studies evaluating approaches to facilitating the recovery process have demonstrated that the use of multimodal analgesic techniques can improve early recovery as well as other clinically meaningful outcomes after ambulatory surgery.\textsuperscript{13,14} These benefits have been confirmed in more recent studies\textsuperscript{15,16} and are currently the recommended practice in most fast-track clinical care plans.\textsuperscript{5} It is clear that the
reliance on a single nonopioid analgesic modality (eg, local analgesics, nonsteroidal antiinflammatory drugs [NSAIDs], and/or acetaminophen) will not suffice to control moderate to severe postoperative pain, and excessive reliance on opioid analgesics produces undesirable side effects. The short- and long-term benefits of using multimodal analgesia regimens to reduce opioid-related side effects remain controversial, because the definition of multimodal analgesia is not uniform in the anesthesia and surgery literature. In some contexts, multimodal analgesia refers to systemic administration of analgesic drugs with different mechanisms of action, whereas in other situations it refers to concurrent application of analgesic pharmacotherapy in combination with regional analgesia.

A deficiency in the design of many of the published studies involving multimodal analgesic therapies is that the drug regimens were not continued into the postdischarge period. For example, only immediate pre- and postoperative administration of the cyclooxygenase 2 (COX-2) inhibitor rofecoxib as part of a multimodal analgesic regimen in outpatients undergoing inguinal hernia repair provided limited benefits beyond the early postoperative period. However, when the COX-2 inhibitors are administered for 3 to 5 days after ambulatory surgery, the greater benefits were achieved with respect to clinically relevant patient outcomes (eg, resumption of normal activities) and improvements in pain control. While opioid analgesics continue to play an important role in the acute treatment of moderate to severe pain in the early postoperative period, nonopioid analgesics will likely assume a greater role as preventative analgesics in the future as the number of minimally invasive (keyhole) surgery cases continues to expand.

Nonopioid analgesics are increasingly being used as adjuvants before, during, and after surgery to facilitate the recovery process after ambulatory surgery because of their anesthetic- and analgesic-sparing effects and their ability to reduce postoperative pain (with movement), opioid analgesic requirement, and side effects, thereby shortening the duration of the hospital stay. The use of traditional NSAIDs, COX-2 inhibitors, acetaminophen, ketamine, dexametomidine, dextromethorphan, alpha2-agonists, gabapentin, pregabalin, β-blockers, and glucocorticoid steroids can provide beneficial effects when administered in appropriate doses as part of a multimodal analgesic regimen in the perioperative setting. Dexamethasone when used as an adjuvant decreases oxycodone consumption and helps to reduce postoperative pain. Recent studies have confirmed that a rational combination of different nonopioid analgesics when given as part of multimodal analgesia reduces postoperative pain.

The potential beneficial effects of administering local anesthetics via alternative routes of administration for improving the perioperative outcomes continue to be investigated. The administration of intranasal lidocaine in combination with naphazoline decreased both intra- and postoperative pain and reduced rescue analgesic requirements in the postoperative period. Although intra-abdominal administration of levobupivacaine was alleged to produce satisfactory analgesia in patients undergoing abdominal hysterectomy procedures, the study was flawed due to the failure to include a placebo control group. However, other studies have demonstrated the effectiveness of the intravenous infusion of lidocaine in reducing postoperative pain and facilitating the recovery process. Yardeni and colleagues suggested that perioperative administration of intravenous lidocaine could improve early postoperative pain control and reduce surgery-induced immune alterations.

The use of continuous local anesthetic techniques (eg, for perineural blocks or wound infiltration) has become increasingly popular due to their ability to control moderate to severe pain after major ambulatory orthopedic surgery procedures. The availability
of disposable local anesthetic infusion systems and the encouraging results from these early studies have led to the increasing popularity of these techniques for pain control in the postdischarge period. However, the clear benefits of these approaches for managing pain after ambulatory surgery must be balanced against the cost of the equipment and the resources needed to safely manage these systems outside the hospital environment.

Topical capsicum has also been found to produce prolonged analgesic effects because of its ability to alter nociceptive input at the peripheral nerve ending. The use of transcutaneous electrical nerve stimulation and acupoint stimulation has also been reported to improve postoperative pain management. Because these techniques cause no adverse effects, their use as an adjunct to conventional pharmaceutical approaches could be considered, particularly for patients in whom conventional analgesic techniques fail and/or are accompanied by severe medication-related adverse events.

Preemptive analgesic techniques have been postulated to provide superior analgesia by preventing the establishment of central sensitization. However, this approach does not seem to offer any clinically significant advantages over so-called preventative multimodal analgesic regimens when an effective pro-active approach to pain management is initiated in the early postoperative period and extended into the postdischarge period.

Of importance for improving the quality of pain control and facilitating recovery in the future is the need to educate patients and their family members (caregivers) about the importance of continuing their analgesic medications after the patient leaves the hospital or day-surgery center. It is also important to emphasize the need for collaboration between the various health care providers involved in the patient’s perioperative care (eg, anesthesiologists, surgeons, nurses, and physiotherapists) to integrate improved perioperative pain management strategies with the recently described fast-track recovery paradigms. This type of multi-disciplinary approach has been documented to improve the quality of the recovery process and reduce the hospital stay and postoperative morbidity, leading to a shorter period of convalescence after surgery.

A critical assessment of the peer-reviewed literature regarding the optimal analgesic therapies for outpatient laparoscopic cholecystectomy by Bisgaard concluded that a multimodal analgesic regimen consisting of a preoperative single dose of dexamethasone, incisional local anesthetics (at the beginning and/or end of surgery), and continuous treatment with NSAIDs (or COX-2 inhibitors) during the first 3 to 4 days provided the best clinical outcome. It was further suggested that elimination of opioid-based analgesia would be highly desirable in the future. These important findings have been confirmed by White and colleagues. In a prospective, placebo-controlled study, involving the administration of celecoxib on the day of surgery and subsequently for 3 days after outpatient laparoscopic surgery as part of a multimodal analgesic regimen, it was found that celecoxib-treated patients not only experienced less pain and reduced need for opioid-containing oral analgesics but also (more importantly) were able to resume normal activities of daily living 1 to 2 days earlier.

With the more widespread use of multimodal perioperative analgesic regimens, involving both opioid and nonopioid analgesic therapies, physicians and nurses are becoming increasingly aware of the important role that these techniques play in facilitating the recovery process and improving patient satisfaction. Although many factors, in addition to pain, must be carefully controlled to minimize postoperative morbidity and facilitate the recovery process after elective surgery (eg, PONV,
hydration status), the adequacy of pain control should remain a major focus of health care providers, caring for patients undergoing ambulatory surgical procedures.\textsuperscript{17,19}

With the changes in health care dictated by economic pressures, there has been a realization that the duration of the hospital stay can be reduced without compromising the quality of patient care. Advances in surgical technology and anesthetic drugs and techniques have made an impact on the way perioperative care is currently being delivered to patients undergoing ambulatory surgery. Multidisciplinary fast-track or accelerated recovery processes encompass many aspects of anesthesia and analgesic care,\textsuperscript{5} optimizing not only the preoperative preparation and prehabilitation but also the intraoperative attenuation of surgical stress and postoperative pain control and rehabilitation procedures.\textsuperscript{65}

Current evidence suggests that these improvements in patient outcome related to pain control can best be achieved by using a combination of preventative analgesic techniques involving both central and peripheral-acting analgesic drugs as well as novel approaches to administering drugs in locations remote from the hospital setting. It is of critical importance for clinical investigators to return to the hard work of performing prospective, randomized clinical trials on a procedure-specific basis to evaluate the use of different analgesic combinations as part of multimodal analgesic treatment regimens in the postoperative period.\textsuperscript{63,66} Improving recovery after ambulatory surgery by optimizing anesthetic and analgesic techniques will benefit patients, health care providers, and society-at-large in the future.\textsuperscript{67}

REFERENCES


Patient satisfaction following day surgery

Paulo Lemos MD (Clinical Chief of Anesthesiology)a,⁎
Ana Pinto MD ( Resident in Oncology)a,
Gustavo Morais MD ( Resident in Cardiology)a,
José Pereira MD ( Resident in Neuroradiology)a,
Rui Loureiro MD ( Resident in Internal Medicine)a,
Sofia Teixeira MD ( Resident in Endocrinology)a,
Catarina S. Nunes PhD ( Assistant Professor)b

aDepartment of Anesthesia, Hospital Geral de Santo António, 4099-001 Porto, Portugal
bSciences Faculty, Department of Applied Mathematics, University of Porto, 4169-007 Porto, Portugal

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Day surgery;
Health care: quality indicators;
Patient satisfaction

Abstract

Study Objective: To evaluate patient satisfaction at discharge and 30 days after day surgery, and to identify predictive factors of patient satisfaction.

Design: Observational, prospective study.

Setting: Day surgery unit of a university hospital.

Patients: 251 consecutive patients, aged 43 ± 15 years (56.6% women), scheduled for day surgery.

Interventions: Patients were asked to answer a questionnaire.

Measurements: Patients’ level of satisfaction was recorded in relation to different variables, using questions of demographics, logistics, and those relating to surgery.

Main Results: Over 95% of patients were satisfied with their care at both interviews; 74.5% of patients were completely satisfied at the discharge time; and only 62.4% had the same opinion 30 days after the surgery (P < 0.01). Postoperative pain control [odds ratio (OR) = 1.6], waiting time for surgery (OR = 1.4), and patient changing room conditions (OR = 1.3) were the most important factors influencing patient satisfaction at the time of discharge. Clinical outcome (OR = 3.2), clinical information (OR = 1.6), and postoperative pain control (OR = 1.3) were the main factors affecting patient satisfaction 30 days after surgery.

Conclusions: Overall satisfaction following day surgery was at least 95% at discharge and at 30 days. However, complete satisfaction was present only in 75% at discharge and decreased to 62% at 30 days. Clinical outcome was strongly related to patient satisfaction at 30 days after surgery. Factors directly controlled by anesthesiologists such as postoperative pain and information provided, also had a significant impact on patient satisfaction.

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1. Introduction

Day surgery accounts for more than 50% of all elective surgery performed in many countries in North America, Europe, and Oceania [1]. Clinical, economic, and social advantages [2] associated with excellent safety and low morbidity rates [3,4] have made day surgery popular in many countries. High levels of patient satisfaction have been achieved [5,6], even when frequent and uncomfortable post-discharge symptoms were found [7,8]. The aim of the present study was to prospectively assess patient satisfaction rates following day surgery: at the time of discharge and 30 days after surgery. A secondary goal was to identify any possible predictive factors of patient satisfaction.

2. Materials and methods

After receiving approval by the Hospital Geral Santo António Institutional Ethics Committee, we performed a prospective, observational study at the Day Surgery Unit (DSU) of Hospital Geral Santo António, Porto, Portugal, from December 2004 to March 2005. Written and verbal informed consent was obtained from all patients. Patients had to be over 15 years of age. Assessment was undertaken using anonymous questionnaires filled in by an interviewer who was a medical student. No health care providers were used as interviewers so as to assure neutrality and independence in the gathering of the answers. Questionnaires were completed at two interviews: the first at the time of discharge on the day of surgery (P0) and the second 30 days after surgery (P30). The second interview was undertaken by telephone. For each patient, the interviewer was the same for both interviews. A maximum of three attempts was made to try to reach the patients for the telephone interview. If we failed to reach a patient following the third attempt, data for that patient consisted only of the results obtained in the first interview.

We investigated demographic variables (age, gender, and education), and variables related to anesthetic technique and surgery. We looked at three different anesthetic techniques: general anesthesia, regional anesthesia, and sedation with local anesthesia. Surgery-related variables were: surgical speciality (general surgery, vascular surgery, orthopedic surgery, gynecology, urology, and neurosurgery), surgical procedure (e.g., laparoscopic cholecystectomy, carpal tunnel release, hemorrhoidectomy, pilonidal cyst excision, varicose vein surgery, circumcision, inguinal hernia repair, laparoscopic tubal sterilization, thyroid lobectomy), and previous DSU experience. At the first interview, patients were asked if they considered themselves ready for discharge and were willing to go home.

Level of literacy was classified according to a 1 to 6 point numerical scale: 1 = illiterate, 2 = primary school educated (4 yrs), 3 = secondary school (9 yrs), 4 = high school (12 yrs), 5 = college degree, and 6 = some graduate school beyond college.

Other variables analyzed at P0: ease in locating the DSU, comfort in the waiting room, changing room conditions, operating room comfort, recovery area comfort, waiting time for surgery, sufficient postoperative information provided by the surgeon or anesthesiologist, and empathy of the staff. These variables were classified using a 1 to 6 point numerical scale: 1 = totally dissatisfied; 2 = moderately dissatisfied; 3 = slightly dissatisfied; 4 = slightly satisfied; 5 = moderately satisfied; and 6 = completely satisfied. Due to the low percentage of answers below 4 in the numerical scale, which made statistical analysis difficult to perform, this variable was redefined in the following terms: the “totally satisfied group” corresponded to the completely satisfied ones = 6, and the “not totally satisfied group” referred to the remaining choices, i.e., 1, 2, 3, 4, and 5.

Data were processed in Microsoft Excel and analyzed in SPSS for Windows (version 11.0.1; SPSS, Inc., Chicago, IL). Data are means + SD and were evaluated by Wilcoxon signed ranks, chi-square analysis, and Kruskal-Wallis test. Differences were considered significant when \( P < 0.05 \). Logistic regression through a multivariate analysis was used to identify the strength association of the different variables analyzed.

3. Results

A total of 251 consecutive patients who met the inclusion criteria were enrolled in the study. Patients were 43 ± 15 years old and 56.6% were women. All of the enrolled patients participated in the first interview. Demographic data are shown in Table 1. At 30 days after surgery, 30 patients
was 51.6 ± 30.2 minutes and ranged from 5 to 185 minutes. Almost 60% of the patients had no more than 4 years of schooling.

For 84.1% (n = 221) of patients, this surgery was their first experience in the DSU. Nevertheless, only 18 of the 221 patients (8.1%) declared at P30 that they would not like to be operated on again on a day-surgery basis. All but 4 patients (1.6%) interviewed at P0 considered themselves ready for discharge home. These 4 patients expressed a desire to be operated on again on a day-surgery basis. All but 4 patients (8.1%) declared at P30 that they would not like to be discharged home. These 4 patients expressed a desire to be discharged on the day of surgery. All patients interviewed at P30 confirmed that they were medically discharged on the day of surgery.

Overall patient satisfaction scores are shown in Table 2. Sixty-four (25.5%) and 83 patients (37.6%) were not totally satisfied at P0 and P30, respectively. A significant difference was observed between satisfaction scores at P0 and P30 (P < 0.01), as noted via Wilcoxon signed rank test.

No statistical difference was found between level of satisfaction with respect to gender or previous experience. However, differences (P = 0.002) existed for age. The mean age for the “not totally satisfied” group was 37.86 years [95% confidence intervals (CI 95%); 34.45-41.27] compared with the “totally satisfied” group, whose mean age was 44.42 years (CI 95%; 42.20-46.64). Differences were also noted in patients’ education levels (P = 0.007). The mean value for the “totally satisfied” group was 2.64 (CI 95%; 2.47-2.81) while 3.06 was the mean value found for the “not totally satisfied” group (CI 95%; 2.74-3.38).

Postoperative pain intensity [odds ratio (OR) = 1.6], waiting time for surgery (odds ratio = 1.4), and changing room conditions (OR = 1.3) were the only factors significantly influencing patient satisfaction level at discharge time (P0) when logistic regression was used (Table 3).

The information provided by the anesthesiologist did not seem to influence patient satisfaction levels. However, patients who visited the anesthesia clinics before the surgical procedure did score higher in patient satisfaction (P = 0.023) than those who did not make this visit.

There was no statistical difference between patient satisfaction and several variables analyzed at P30: surgical speciality, anesthesia clinics, anesthetic technique, and need for unanticipated emergency health care. Patients in the “totally satisfied” group reported better postoperative clinical information (P < 0.001), less postoperative pain (P < 0.001), less infection and/or inflammation (P = 0.007), and a better final outcome (P < 0.001; Table 4) than did those in the “not completely satisfied” group. Nevertheless, final outcome (OR = 3.2), clinical information (OR = 1.6), and postoperative pain intensity (OR = 1.3) were the only factors influencing patient satisfaction at P30 when logistic regression was used (Table 4).

Thirty-seven patients (16.7%) required unanticipated emergency health care. The main reasons related to surgical wound complications (eg, surgical hemorrhage, problems related to suture, infection), postoperative pain, doubts concerning postoperative medication prescription, or lack of information. One patient had a corneal ulcer after general anesthesia. At P30, the majority of patients reported being in

### Table 1

<table>
<thead>
<tr>
<th>Variables studied</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Education</td>
<td></td>
</tr>
<tr>
<td>Illiterate</td>
<td>16 (6.4)</td>
</tr>
<tr>
<td>Primary school (4 yrs)</td>
<td>131 (52.2)</td>
</tr>
<tr>
<td>Secondary school (9 yrs)</td>
<td>41 (16.3)</td>
</tr>
<tr>
<td>High school (12 yrs)</td>
<td>38 (15.1)</td>
</tr>
<tr>
<td>College degree</td>
<td>14 (5.6)</td>
</tr>
<tr>
<td>More than college degree</td>
<td>11 (4.4)</td>
</tr>
<tr>
<td>Anesthetic Technique</td>
<td></td>
</tr>
<tr>
<td>General anesthesia</td>
<td>177 (70.5)</td>
</tr>
<tr>
<td>Sedation with local anesthesia</td>
<td>46 (18.3)</td>
</tr>
<tr>
<td>Loco-regional anesthesia</td>
<td>28 (11.2)</td>
</tr>
<tr>
<td>Surgical specialty</td>
<td></td>
</tr>
<tr>
<td>General surgery</td>
<td>132 (52.6)</td>
</tr>
<tr>
<td>Vascular surgery</td>
<td>35 (13.9)</td>
</tr>
<tr>
<td>Orthopedic surgery</td>
<td>32 (12.7)</td>
</tr>
<tr>
<td>Urology</td>
<td>25 (10.0)</td>
</tr>
<tr>
<td>Gynecology</td>
<td>22 (8.8)</td>
</tr>
<tr>
<td>Neurosurgery</td>
<td>5 (2.0)</td>
</tr>
<tr>
<td>Surgical procedure</td>
<td></td>
</tr>
<tr>
<td>Varicose vein surgery</td>
<td>36 (14.3)</td>
</tr>
<tr>
<td>Pilonidal cyst excision</td>
<td>33 (13.1)</td>
</tr>
<tr>
<td>Carpal tunnel release</td>
<td>25 (10.0)</td>
</tr>
<tr>
<td>Ingual hernia repair</td>
<td>20 (7.9)</td>
</tr>
<tr>
<td>Laparoscopic tubal sterilization</td>
<td>18 (7.2)</td>
</tr>
<tr>
<td>Other hernia repair</td>
<td>16 (6.4)</td>
</tr>
<tr>
<td>Hemorrhoidectomy</td>
<td>14 (5.6)</td>
</tr>
<tr>
<td>Thyroid lobectomy</td>
<td>11 (4.4)</td>
</tr>
<tr>
<td>Circumcision</td>
<td>9 (3.6)</td>
</tr>
<tr>
<td>Laparoscopic cholecystectomy</td>
<td>8 (3.2)</td>
</tr>
<tr>
<td>Varicocelectomy</td>
<td>7 (2.8)</td>
</tr>
<tr>
<td>Local excision of breast</td>
<td>6 (2.4)</td>
</tr>
<tr>
<td>Anal sphincterotomy</td>
<td>5 (2.0)</td>
</tr>
<tr>
<td>Hydrocelectomy</td>
<td>5 (2.0)</td>
</tr>
<tr>
<td>Lumbar disc repair</td>
<td>3 (1.2)</td>
</tr>
<tr>
<td>Orchidectomy</td>
<td>3 (1.2)</td>
</tr>
<tr>
<td>Fistulectomy</td>
<td>3 (1.2)</td>
</tr>
<tr>
<td>Other</td>
<td>29 (11.5)</td>
</tr>
</tbody>
</table>

### Table 2

Overall patient satisfaction level at discharge time (P0) and 30 days after surgery (P30)

<table>
<thead>
<tr>
<th>Patient Satisfaction</th>
<th>Degree</th>
<th>P0 * N</th>
<th>%</th>
<th>P30 b N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completely dissatisfied</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Moderately dissatisfied</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>1.8</td>
</tr>
<tr>
<td>Slightly dissatisfied</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>1.4</td>
</tr>
<tr>
<td>Slightly satisfied</td>
<td>4</td>
<td>13</td>
<td>5.2</td>
<td>19</td>
<td>8.6</td>
</tr>
<tr>
<td>Moderately satisfied</td>
<td>5</td>
<td>51</td>
<td>20.3</td>
<td>57</td>
<td>25.8</td>
</tr>
<tr>
<td>Completely satisfied</td>
<td>6</td>
<td>187</td>
<td>74.5</td>
<td>138</td>
<td>62.4</td>
</tr>
</tbody>
</table>

* Interview at P0.

b Interview by telephone at P30.
a convalescence phase (59.5%), 36.9% declared being cured, and only 3.6% reported a recurrence of the original problem. Nevertheless, 64.4% of patients had already resumed professional activity.

4. Discussion

Our study found that over 95% of patients had some degree of satisfaction after surgery both at discharge and at 30 days (100% and 96.8% of pts, respectively). Similar studies have reported slightly lower levels of satisfaction. Bain et al. found an overall satisfaction rate of 85% among 3,438 day surgery patients in a multicentric Scottish survey [5]. Beverly Philip evaluated overall satisfaction in a questionnaire returned by 1,511 patients, in which 97% would choose day surgery again [6].

Our study did not look just at overall satisfaction. We also carefully evaluated data from the patients who reported being totally satisfied with their experience. As expected, the number of totally satisfied patients was less than the number of overall satisfied. Our finding of 75% of patients who were totally satisfied cannot be compared to data from other centers. The decrease in totally satisfied patients to 62% at 30 days is an important result. It shows that information obtained at discharge does not reflect longer term patient satisfaction. The answers provided by patients at discharge (through personal interview vs. telephone interview 30 days later) may have been influenced by the fear of suffering “retaliation” from the health staff involved and jeopardizing future care [9]. Thirty days after surgery, many patients felt completely cured and were at home. This situation allowed them the freedom to express their true satisfaction level without any constraint. A bias could also partly explain the reduction in percentage of patients in the totally satisfied group between the time of discharge and 30 days after surgery. Our study attempted to minimize this type of bias by enrolling medical students as interviewers [10]. Moreover, at discharge, patients could only evaluate the perioperative

### Table 3  Factors associated with patient satisfaction at discharge time (P0), comparing those patients completely satisfied (totally satisfied group) with the patients in the other levels of satisfaction (not totally satisfied group)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Not totally satisfied group (n = 64) Mean (CI 95%)</th>
<th>Totally satisfied group (n = 187) Mean (CI 95%)</th>
<th>P-value&lt;sup&gt;a&lt;/sup&gt;</th>
<th>P-value&lt;sup&gt;b&lt;/sup&gt; OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ease in locating the DSU</td>
<td>5.47 (5.26–5.68)</td>
<td>5.66 (5.53–5.79)</td>
<td>0.004</td>
<td>NS</td>
</tr>
<tr>
<td>Waiting room comfort</td>
<td>4.30 (3.91–4.69)</td>
<td>4.95 (4.76–5.14)</td>
<td>0.001</td>
<td>1.262</td>
</tr>
<tr>
<td>Changing room comfort</td>
<td>4.25 (3.87–4.63)</td>
<td>4.99 (4.80–5.18)</td>
<td>0.001</td>
<td>1.262</td>
</tr>
<tr>
<td>Operating room comfort</td>
<td>5.56 (5.33–5.78)</td>
<td>5.78 (5.70–5.87)</td>
<td>0.006</td>
<td>NS</td>
</tr>
<tr>
<td>Recovery area comfort</td>
<td>5.17 (4.89–5.46)</td>
<td>5.59 (5.47–5.72)</td>
<td>0.003</td>
<td>NS</td>
</tr>
<tr>
<td>Waiting time for surgery</td>
<td>3.81 (3.27–4.35)</td>
<td>4.88 (4.64–5.13)</td>
<td>0.008</td>
<td>1.348</td>
</tr>
<tr>
<td>Information from the surgeon</td>
<td>4.17 (3.67–4.68)</td>
<td>4.82 (4.55–5.08)</td>
<td>0.008</td>
<td>NS</td>
</tr>
<tr>
<td>Information from the anesthetist</td>
<td>4.84 (4.40–5.28)</td>
<td>4.97 (4.72–5.22)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Friendly staff</td>
<td>5.86 (5.75–5.97)</td>
<td>5.96 (5.92–5.99)</td>
<td>0.019</td>
<td>NS</td>
</tr>
<tr>
<td>Postoperative pain</td>
<td>4.66 (4.31–5.00)</td>
<td>5.29 (5.14–5.45)</td>
<td>0.001</td>
<td>1.557</td>
</tr>
<tr>
<td>Postoperative nausea and vomiting</td>
<td>5.92 (5.85–5.99)</td>
<td>5.91 (5.85–5.96)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Postoperative haemorrhage</td>
<td>5.69 (5.49–5.89)</td>
<td>5.99 (5.00–6.99)</td>
<td>0.019</td>
<td>NS</td>
</tr>
</tbody>
</table>

CI = Confidence interval, OR = odds ratio, NS = not statistically significant, DSU = day surgery unit.
<sup>a</sup> P-value of the Kruskal-Wallis Test (univariate analysis).
<sup>b</sup> P-value of the Logistic Regression (multivariate analysis).

### Table 4  Factors associated with patient satisfaction 30 days after surgery (P30), comparing those patients completely satisfied (totally satisfied group) with the patients in the other levels of satisfaction (not totally satisfied group)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Not totally satisfied group (n = 64) Mean (CI 95%)</th>
<th>Totally satisfied group (n = 187) Mean (CI 95%)</th>
<th>P-value&lt;sup&gt;a&lt;/sup&gt;</th>
<th>P-value&lt;sup&gt;b&lt;/sup&gt; OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postop clinical information</td>
<td>4.77 (4.40–5.15)</td>
<td>5.69 (5.54–5.84)</td>
<td>&lt;0.001</td>
<td>1.609</td>
</tr>
<tr>
<td>Postop pain</td>
<td>3.94 (3.59–4.28)</td>
<td>4.86 (4.66–5.06)</td>
<td>&lt;0.001</td>
<td>1.343</td>
</tr>
<tr>
<td>PONV</td>
<td>5.78 (5.62–5.94)</td>
<td>5.89 (5.82–5.96)</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>Wound infection/inflammation</td>
<td>2.72 (2.58–2.86)</td>
<td>2.91 (2.85–2.98)</td>
<td>0.007</td>
<td>NS</td>
</tr>
<tr>
<td>Final outcome&lt;sup&gt;c&lt;/sup&gt;</td>
<td>2.10 (1.98–2.22)</td>
<td>2.48 (2.39–2.56)</td>
<td>&lt;0.001</td>
<td>3.153</td>
</tr>
</tbody>
</table>

CI = confidence interval, OR = odds ratio, Postop = postoperative, PONV = postoperative nausea and vomiting, NS = not statistically significant.
<sup>a</sup> P-value of the Kruskal-Wallis Test (univariate analysis).
<sup>b</sup> P-value of the Logistic Regression (multivariate analysis).
<sup>c</sup> The numerical scale used was 1 to 3.
Postoperative pain intensity was a decisive factor in patient satisfaction following day surgery in several studies [5,9,11,13,23-25]. Both at discharge and 30 days after surgery, patients with lower postoperative pain scores were also the ones who reported higher satisfaction levels. Effective postoperative pain control allows not only a faster postoperative recovery period and associated lower morbidity, but also in higher patient satisfaction scores. Improving pain control may be one of the major investments that health professionals should seriously consider in the field of day surgery. However, Rawal et al. found that patients with significant side effects such as moderate to severe pain often did not report dissatisfaction with their care if they felt that their caregivers were concerned [26].

Interestingly, we did not find any influence of postoperative nausea and vomiting (PONV) on patient satisfaction. In contrast, other studies have noted that the occurrence of PONV is a very strong predictor of patient satisfaction [9,11,27,28]. It is likely that the low frequency of PONV among the patients in our DSU, as a result of an antiemetic prophylaxis protocol, might explain these results [29].

The response rate obtained in our study can be regarded as satisfactory when compared with that of other studies. Nevertheless, the data may be skewed by the absence of data from those patients who could not be contacted, or by the acquiescence bias that may occur in telephone interviews [30]. The fact that our questionnaire has not been validated may be seen as a limitation.

We found multiple factors that individually influence patient satisfaction levels. Some of these do so independently and others do not. For this reason, we applied logistic regression to identify the strength association of the different variables studied.

The widespread development of day-surgery programs, the significant improvements in surgical techniques, and the introduction of newer anesthetic agents and devices, lead all health professionals to face new challenges in an increasingly demanding society. Non-traditional patient-oriented outcome measures such as functional health status and patient satisfaction are currently employed for quality evaluation of day surgery. For success in quality improvement, thorough study of the target population becomes an essential step for meeting the requirements and expectations of individual patients.

In conclusion, the results of our study show that patient satisfaction following day surgery should be evaluated not just at discharge, but also some time later. Our results also suggest that improving outcomes, controlling postoperative pain, increasing the information provided to patients and relatives, and reducing the waiting time for surgery, may increase patient satisfaction following day surgery. These may be predictive factors of patient satisfaction.
Acknowledgment

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References

Challenges in Pediatric Ambulatory Anesthesia: Kids are Different

Corey E. Collins, DO\textsuperscript{a,b}, Lucinda L. Everett, MD\textsuperscript{b,c,*}

The care of the child having ambulatory surgery presents a specific set of challenges to the anesthesia provider. This review focuses on areas of clinical distinction that support the additional attention children often require, and on clinical controversies that require providers to have up to date information to guide practice and address parental concerns.

Specifically, this article addresses various categories of risk as applied to children presenting for ambulatory surgery (cardiovascular and respiratory risk, as well as the potential for neurocognitive dysfunction in the very young). The authors consider the role of perioperative anxiety and agitation, the influence these phenomena have on the experience of pediatric patients and their families, and potential strategies to minimize these outcomes. Considering the preponderance of head and neck surgery for pediatric ambulatory surgery, the authors focus on issues that complicate ear, nose, and throat (ENT) cases, including surgical risk, issues related to sleep-disordered breathing, and postoperative nausea and vomiting (PONV). This article discusses guidelines for pediatric anesthesia care and possible future implications for credentialing providers.

RISK IN PEDIATRIC AMBULATORY ANESTHESIA

Many pediatric anesthetics are done on an outpatient basis; although these are minor cases, they may present significant challenges to the clinician. In 2006, the most

\textsuperscript{a} Department of Anesthesiology, Pediatric Anesthesia, Massachusetts Eye and Ear Infirmary, 243 Charles Street, Boston, MA 02114, USA
\textsuperscript{b} Harvard Medical School, 25 Shattuck Street, Boston, MA 02115, USA
\textsuperscript{c} Department of Anesthesiology, Critical Care and Pain Management, Pediatric Anesthesia, Massachusetts General Hospital, 55 Fruit Street, GRB-444, Boston, MA 02114, USA
\textsuperscript{*} Corresponding author. Department of Anesthesiology, Critical Care, and Pain Management, Pediatric Anesthesia, Massachusetts General Hospital, 55 Fruit Street, GRB-444, Boston, MA 02114.

E-mail address: leverett@partners.org

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common cases in children less than 15 years of age were myringotomy with tube insertion (667,000), tonsillectomy with or without adenoidectomy (530,000), and adenoidectomy alone (132,000).1

Information about risk comes from several types of data. Large descriptive series give an overall picture of pediatric anesthesia outcomes, but may be limited in the type and amount of detail, and often come from a single institution; most of these are not specific to outpatients. Incident-reporting studies such as the American Society of Anesthesiologists (ASA) Closed Claims study give more detail on individual serious adverse events, but do not have denominator data to describe the population. Clinical registries gather data prospectively about a given population or problem; the Pediatric Perioperative Cardiac Arrest (POCA) registry has provided valuable information about anesthetic-related cardiac arrest, and in the future more and larger registry efforts should yield more precise outcomes data.

Risk factors associated with serious adverse events in pediatric anesthesia include young age (most frequently <12 months), coexisting disease as reflected by higher ASA status (particularly congenital heart disease), and emergency surgery.2 A recent large study from France reflects the modern era of anesthetic drugs and monitoring and shows a low overall rate of major morbidity related to anesthesia.3 In outpatient outcome studies, Fleisher and colleagues4 analyzed data of 783,558 surgical admissions in New York State, but no pediatric-specific risks were identified. A retrospective survey of outpatient-procedure–related death in Massachusetts between 1995 and 1999 did not report any pediatric deaths.5 Smaller series of pediatric ambulatory cases primarily detail unanticipated admission rates (0.9%–2%, usually for extensive surgery or protracted vomiting) and the rates of minor complications such as vomiting, cough/croup, and somnolence.6–8

The ASA Closed Claims Project reviews claims against anesthesiologists after the cases have reached some conclusion in the legal system. Analysis of patterns of injury from these cases has identified several situations in which anesthesiologists can recognize and decrease risk, such as cardiac arrest in adults having spinal anesthesia. Comparison of pediatric with adult claims in the early era of the Closed Claims Project showed that claims in pediatric patients were more likely to have been precipitated by a respiratory event, and more often deemed preventable by reviewers.9 Analysis of the more recent pediatric cases in the Closed Claims database found a relative reduction in claims for death/brain damage and for respiratory events, particularly inadequate ventilation and oxygenation. This improvement may be related to the adoption of pulse oximetry and capnography as standards in the early 1990s.10 Again, younger age and higher ASA status correlated with risk; half of the claims involved patients less than 3 years of age, and one-fifth were ASA 3 to 5.

Cardiac Risk

After the observations in the early Closed Claims series relating cardiac arrest to respiratory events, the POCA Registry was established to study anesthetic-related cardiac arrest in children. The initial results showed a cardiac arrest rate of 1.4 per million anesthetics, with the highest incidence in children less than 1 year of age and ASA 3 to 5. Cardiac arrests described in healthy children were primarily related to respiratory difficulty (laryngospasm or anatomic airway obstruction) and to relative anesthetic overdose (primarily with halothane), the latter accounting for nearly half of cardiac arrests in patients who were ASA 1 to 2.11 The POCA group published a follow-up analysis in 2008 that showed a significant decline in cardiac arrest related to volatile anesthetic overdose, but a constant proportion of respiratory causes, with laryngospasm still prominent.12 The other causes of pediatric cardiac arrest identified in
healthy patients (hypovolemia from blood loss and hyperkalemia from transfusion of stored blood) are unlikely to be seen in the ambulatory population. There was only 1 cardiac arrest in the 2000 POCA report related to hyperkalemia from succinylcholine in a patient with unrecognized myopathy; case reports of this clinical scenario from the early 1990s resulted in a US Food and Drug Administration (FDA) warning against the routine use of succinylcholine in pediatric patients.13

Respiratory Risk

As noted earlier, perioperative respiratory adverse events (PRAE) in children may precipitate serious adverse outcomes. Respiratory events are common in studies of pediatric anesthesia complications; in evaluating these studies, it is important to consider the definitions used, which are frequently not consistent (eg, selection of an oxygen saturation of 95% as the threshold to describe a complication will result in a higher incidence than a threshold of 90% saturation). It is also important to consider the patient population, case type, and anesthetic technique; for example, a series of children with indwelling central venous catheters having propofol anesthetics for diagnostic and therapeutic procedures described a significantly lower incidence of laryngospasm than was seen in many other series.14

In a large series of pediatric patients, Murat and colleagues3 found that respiratory events represented 53% of all intraoperative events, and were more frequent in ENT surgery, with ASA physical classification status 3 to 5, and with tracheal intubation. Mamie and colleagues15 described an overall 1.57 relative risk increase for PRAE in any child having ENT surgical procedures. Other risks for PRAE included provider experience, younger age, and upper respiratory infection. Although data suggest low overall risks for brief procedures such as myringotomy and ventilation tube (M&T) placement,12,16 the clinician must consider the risk of upper respiratory infection, potentially difficult mask ventilation, and comorbidities. In 1990, Markowitz-Spence and colleagues17 reported their experience with 510 children having M&T with 12% minor PRAE and 1.4% serious PRAE. In 2002, Hoffman and colleagues18 reported a similar series of 3198 children with a 9% adverse-event rate and 1.9% major PRAE. All patients received inhalation induction with halothane, and therefore it is unclear whether the data are applicable to today’s practice. Their data included 19/1005 cases of laryngospasm, airway obstruction, or significant desaturation.18 These investigators and others report that significant comorbidities and concurrent illness, including acute or recent respiratory infection, predicted increase PRAE.19–21 Both of these series represent data from a pediatric specialty center, and applicability to a general anesthesia practice should be made with caution; available data make it impossible to quantify whether risks are different in other settings. Because most M&T patients are less than 6 years of age, with peak incidence during infancy, an effort should be made to optimize the timing of the procedure and perioperative care to minimize risk.

Neurocognitive Outcomes

Although there is generally a focus on immediate risk in the perioperative period, a growing concern among parents relates to the possibility of adverse neurocognitive outcomes in very young children after anesthesia. In the last several years, the lay press has picked up on some animal and preliminary clinical studies that raise these questions. The initial animal studies involved chronic exposure of pregnant rats to subanesthetic concentrations of halothane, and showed behavioral abnormalities in the rat pups produced. Subsequent studies designed more specifically to study the effects on the brain have found neural degeneration, usually apoptosis (programmed
cell death) in a diffuse pattern. Multiple studies have shown this effect, although some have not. Almost all classes of anesthetic and sedative medications have been shown to have adverse effects in laboratory animals (volatile anesthetics, nitrous oxide, benzodiazepines, propofol, barbiturates, ketamine). Opioids generally show minimal effects, and there is some suggestion of mitigation of adverse effects of isoflurane by dexmedetomidine. Some animal data suggest that the adverse effects on neuronal development occur to a more significant extent in the absence of a painful stimulus, and so would be more relevant to sedation/anesthesia for intensive care unit (ICU) care or prolonged procedures. There remains much to learn about the mechanism of the tissue changes seen in animals, as well as how the experimental factors apply to humans (developmental age, duration of exposure and dosages, animal species, and anesthetic management).

Epidemiologic information from human studies has only recently become available. A study from the Mayo Clinic used an existing birth cohort for learning disability, and found that children who had received 2 or more anesthetics before the age of 4 years were at increased risk to develop learning disability. This was a retrospective study and impossible to discern whether this was a causal association or whether anesthesia was a marker for other factors which might cause learning disability; the anesthetics involved also occurred in children born between 1976 and 1982, before the availability of current drugs or monitoring modalities. A retrospective pilot study found more behavioral disturbances in children who had anesthesia/urologic surgery before 24 months of age. Most recently, a twin study showed no differences in learning ability in twin pairs in which 1 was exposed to anesthesia before the age of 3 and 1 was not; these investigators concluded that anesthesia at an early age is a marker of vulnerability for learning disability rather than a causative factor. Several large prospective studies are being designed or are in process to attempt to find a more definitive answer to this question, but conclusive data are likely to be several years away. However, it seems that, if risk for postanesthetic neurocognitive dysfunction exists in human infants, it is greatest in the very premature infant, for prolonged anesthesia/sedation and possibly at very high doses, and in the absence of painful stimuli. All of this should be reassuring to parents of children coming for brief ambulatory procedures.

Preoperative Anxiety and Postoperative Agitation

Predicting and managing anxiety in the child and parents is an important part of creating a safe and pleasant anesthetic experience for the pediatric outpatient. Studies confirm some of our clinical impressions: risk factors for high anxiety at induction include younger age, behavioral problems with previous health care attendances, longer duration of procedure, having more than 5 previous hospital admissions, and anxious parents. Kain and colleagues have published on several aspects of this issue, showing that midazolam premedication or parental presence decreases anxiety and improves acceptance of a mask induction, with midazolam somewhat more effective than parental presence, but that parental presence does not add to the benefit of premedication. Detailed analysis shows that children who benefit most from parental presence are somewhat older, have lower levels of anxiety at baseline, and have calmer parents who value preparation and coping skills for medical situations. A calm parent did benefit anxious children, whereas overly anxious parents did not confer any benefit. A comprehensive patient preparation program decreased anxiety and improved the quality of induction to a similar degree compared with midazolam, but patients in the preparation program also had decreased incidence of emergence delirium, lower requirements for opioids in the recovery area,
and a shorter time to discharge compared with premedication or parent-present induction alone.\textsuperscript{31}

Emergence agitation or delirium is a troublesome and poorly understood entity. It occurs most often in children aged 2 to 5 years, and an association has been found between preoperative anxiety in the child and parent, emergence delirium, and maladaptive behaviors (sleep disturbances, and so forth) after discharge.\textsuperscript{32} Agitation is more common after volatile anesthetics than after propofol. Although the clinical opinion of many recovery nurses is that delirium is more common after the shorter-acting volatile anesthetics than after halothane or isoflurane, the literature does not strongly support this\textsuperscript{33,34}, the occurrence in the early postoperative period with these shorter acting medications may lead to this impression. The rate of emergence does not seem to be responsible for the agitation itself, as comparison between sevoflurane and propofol showed that children emerged at the same rate but there was significantly higher agitation with sevoflurane.\textsuperscript{35} Midazolam premedication does not seem to decrease the incidence of emergence agitation, whereas several studies have suggested that ketamine has a favorable effect, perhaps related to duration of sedation. Small doses of propofol or dexmedetomidine near the end of anesthesia have been effective in reducing agitation.\textsuperscript{36,37}

In true emergence delirium, children are agitated, unaware of their surroundings, and inconsolable.\textsuperscript{38} Several clinical scales have been developed to attempt to quantify the severity of emergence delirium. The clinician faced with such a child needs to determine whether pain is, or could be, a component, in which case analgesics should be titrated if there is no contraindication. For nonpainful procedures, or if pain is believed to have been treated adequately, sedative drugs may be administered. In a monitored setting with appropriate staffing, a small dose of propofol may be used. Some agitation is self-limited; the anesthesia team should assess the need for treatment, weighing the potential for patient injury against risks such as respiratory depression, nausea/vomiting, and delayed discharge.

**CHALLENGES IN AMBULATORY ENT ANESTHESIA**

As noted earlier, rates of mortality or significant morbidity are low in pediatric ambulatory anesthesia. ENT surgery is routinely cited as the highest-risk surgical area for pediatric outpatients,\textsuperscript{3,11,12,39} and anesthetic-related decisions can affect length of stay (LOS), total costs, patient satisfaction, and secondary morbidity.\textsuperscript{40,41} Favorable results are reported in many series of outpatient ENT surgery with careful preoperative screening and intraoperative management; Gravningsbråten and colleagues\textsuperscript{42} reported an office-based practice of ENT surgery in 1126 children with 90 minutes or less of observation time with 1 reintubation for atelectasis (0.1% immediate complication rate).

Tonsillectomy with or without adenoidectomy confers some specific risks resulting from a shared airway, a surgical site in the pediatric airway, and sequelae from the necessary depth of anesthesia. Bleeding, pain control, oral intake, and oxygenation are the primary early complications following elective pediatric tonsillectomy.\textsuperscript{43–45} Most sources support the safety of tonsillectomy as an outpatient procedure in older children who are ASA 1 to 2 at general hospitals,\textsuperscript{19,41,44–46} but some literature reports an increase in complications among children less than 3 years of age.\textsuperscript{47,48} Other reports recommend application of clinical indicators to recommend safe discharge, even in younger children.\textsuperscript{19,48,49} Same-day discharge may be more costly than admission because of increased recovery-room LOS in children less than 3 years of age.\textsuperscript{50} Children with obstructive sleep apnea (OSA) may require overnight monitoring, as is discussed in more detail later.
Despite the overall low morbidity associated with ambulatory tonsillectomy in children, there are important rare and ominous risks. In a 2008 review of closed claims in New York State, awards against anesthesiologists were higher than against surgeons ($5 million vs $839,650) and often involved airway complications. The presenting indications for many children undergoing tonsillectomy may include comorbidities that increase risk, such as OSA, obesity, central sleep apnea, or syndromes associated with facial dysmorphisms (eg, trisomy 21 syndrome, CHARGE syndrome). Post-tonsillectomy hemorrhage (PTH) can result in death. Windfuhr and colleagues reported survey data on lethal and near-lethal hemorrhage and concluded that delay in return to the operating room, repeated hemorrhage episodes, and aspiration of blood contributed to mortality. They also concluded that admission status did not affect morbidity. These investigators urge aggressive airway management to prevent the secondary sequelae of aspiration and inability to intubate when faced with significant PTH; immediate volume resuscitation, and transfusion, if indicated, are also important components of care.

Direct vascular injuries can occur, most often during adenoidectomy. Significant vascular branches of the external carotid artery (tonsillectomy) or the facial and maxillary arteries (adenoidectomy) may be injured during surgery and may require proximal carotid control for repair. Other rare complications include atlantoaxial subluxation, mandible condyle fracture, infection, and eustachian tube injury. Myringotomy and tube placement can also be complicated by significant vascular events (intrapetrous internal carotid artery puncture leading to pseudoaneurysm formation or arterial hemorrhage requiring endovascular intervention; profuse venous hemorrhage from injury to an anomalous jugular bulb).

Surgical technique may affect the quality of recovery, with techniques such as radiofrequency ablation of tonsillar tissue having less pain than standard cold tonsillectomy; dissection with electrocautery seems to be associated with the highest degree of postoperative pain. Injection of local anesthesia after tonsillectomy seems to confer a modest reduction in pain, but systematic review suggests that equivalent results can be obtained by topical application using swabs. Rare serious events are reported related to local anesthetic injection (cervical osteomyelitis, Horner syndrome, and airway obstruction due to vocal cord paralysis).

Anesthetic management can also affect the perioperative course. Intubation without muscle relaxant has become more common in pediatric anesthesia because of a lack of appropriately short nondepolarizing muscle relaxants; although adequate depth must be ensured to avoid laryngospasm, this obviates any possible emetogenic effects of reversal agents and the risk of residual muscle weakness. A propofol-based technique offers advantages in minimizing PONV and may be associated with less bleeding during tonsillectomy.

Supraglottic airways are used enthusiastically in tonsillectomy by some providers but are not widely embraced; providers in the United Kingdom report the use of an endotracheal tube in 79% of cases, despite the continued trend to avoid paralytics and the availability of reinforced supraglottic devices. Conversely, a recent Norse report documented 1126 cases of office-based tonsillectomy and adenoidectomy with a supraglottic airway; 0.6% required conversion to endotracheal tube. A letter in response from Xue and colleagues presented a thorough argument for a reinforced supraglottic airway with specific attention to the implications of kinking and dislodgment from the intraoral surgical gag, the mechanical impediment tonsillar hyperplasia can create, and the risk of PRAE without adequate anesthetic depth. Clearly, safe airway management can include a spectrum of techniques, and further study is needed to confirm whether any specific technique is superior.
The implications of sleep-disordered breathing, OSA, or central sleep apnea are significant and can introduce predictable risk in the care of the pediatric patient. As Lerman\textsuperscript{61} states in a 2009 review, there are important pathophysiological, anatomic, and pharmacological considerations and important distinctions between the child with this disease and the adult.\textsuperscript{49} In children, this disease affects both genders equally, is associated with all body types, and is primarily a surgically treated entity; in adults, incidence in men exceeds women, obesity is often present, and nonsurgical interventions are first-line therapy (continuous positive airway pressure [CPAP], weight loss). Children and adults can suffer cardiovascular sequelae such as cor pulmonale and pulmonary hypertension. Cognitive impairment, learning disorders, and behavioral problems can complicate both populations.\textsuperscript{60} Although children with OSA are recognized as being at increased risk perioperatively, the provider must consider whether extensive preoperative testing (echocardiogram, electrocardiogram, complete blood count, nocturnal somnography) will contribute to decision making about management or plans for admission.\textsuperscript{61,62}

A review of adenotonsillectomy for OSA in young children found a significantly higher incidence of respiratory complications before the age of 3 years, and recommended routine admission for those patients.\textsuperscript{63} In a survey of anesthesiologists in the United Kingdom, only 36% of respondents considered children for same day discharge after tonsillectomy with adenoidectomy, especially with a history of OSA.\textsuperscript{59} Sanders and colleagues\textsuperscript{64} documented increased complications after tonsillectomy with adenoidectomy in children with OSA versus those without, but found no effect on LOS.

Several articles have documented enhanced sensitivity to opioids in children with OSA. Brown and colleagues\textsuperscript{65} calculated that sleep somnography can predict the risk of sensitivity to parenteral morphine: if the pulse oximetry nadir was less than 85%, a subject requires roughly 50% of the postoperative dose of morphine for analgesia. Hullett and colleagues\textsuperscript{66} described equivalent analgesia with less respiratory depression using tramadol compared with morphine in nonobese children with OSA after tonsillectomy with adenoidectomy.

Obesity

Obesity is an important confounder for ambulatory risk. An estimated 16% of the children in the USA meet the definition of obesity. Tait and colleagues\textsuperscript{67} reported that obese children are significantly more likely to present for surgery with complicating comorbidities such as asthma, reflux disease, type II diabetes mellitus, and OSA. Obesity increased the risk of complication during anesthesia including higher incidence of difficult mask ventilation, airway obstruction, and PRAE. Four-hundred and two of 1147 subjects underwent ENT surgery. The obese children had significantly less PONV (4.8% vs 16.8%).\textsuperscript{67} Ye and colleagues\textsuperscript{68} reported an 11.2% PRAE rate following tonsillectomy for OSA; obesity (as well as young age and higher apnea-hypopnea indexes) was identified as a significant risk factor. Nafiu and colleagues\textsuperscript{62} correlated obesity with increased risks for PRAE after tonsillectomy, including intraoperative desaturation, difficult laryngoscopy, and airway obstruction in the operating room and the recovery room. A correlation between body mass index (BMI) and LOS was documented.

Outcomes after surgery may be variable. In an article comparing tonsillectomy with tonsillotomy, de la Chaux and colleagues\textsuperscript{69} reported complete surgical cure of OSA (apnea-hypopnea index [AHI] 14.9 preoperative to 1.1 postoperative) with significantly less pain and lower PTH rates after CO\textsubscript{2} laser tonsillotomy. Shine and colleagues\textsuperscript{70} found a less dramatic effect with tonsilloadenoidectomy in morbidly obese children.
with OSA; although all subjects benefited from surgery (AHI 20.7 preoperatively to 7.3 postoperatively), only 8 of 18 children no longer needed CPAP management after surgery. They were unable to assign variables for responders to nonresponders to surgery. A 2009 meta-analysis further documented the incomplete benefit of surgery in obese children with OSA. In 2004, Shatz investigated the effectiveness of adenoidectomy in 24 infants with OSA symptoms and reported curative results with no morbidity.

**PONV and Pain Management in Tonsillectomy**

PONV can be troublesome to patients and families, and is known to delay discharge. General risk factors for PONV in children include age more than 3 years, duration of surgery more than 30 minutes, strabismus surgery, and history of postoperative vomiting in the child or PONV in the parents. PONV after tonsillectomy occurs at rates as high as 50% to 89%, which is believed to be related to swallowed blood, pharyngeal stimulation, and the need for opioid analgesics. Blacoe and colleagues reported their experience with unplanned admissions after ambulatory surgery and found PONV to be the most common reason for admission. General surgery cases were significantly more likely to result in PONV than ENT cases (24% vs 15%). Edler and colleagues studied LOS data after tonsillectomy with adenoidectomy in 2008 and found PONV to be the most significant factor in delayed discharge readiness. Each PONV/retching episode increased LOS by 30 minutes (as did a single SpO2<95%). Prophylaxis is generally recommended using 1 or more agents including dexamethasone, 5-hydroxytryptamine-3 (5-HT3) antagonists, droperidol, or promethazine. Dexamethasone, frequently used by the otolaryngologist to decrease swelling and improve oral intake, is also effective in reducing PONV. The usual dose is 0.5 mg/kg, although a prospective dose-response study showed no difference within the range of 0.0625 to 1.0 mg/kg in the outcomes of pain, vomiting, time to oral intake, or voice change. Dexamethasone at 0.5 mg/kg has recently been linked to increased PTH.

Nonsteroidal antiinflammatory drugs (NSAIDS) are used infrequently in tonsillectomy in the United States because of concern for bleeding, but a Cochrane Review concluded that their use significantly decreased PONV without significant effect on PTH. A recent survey of pediatric anesthetists in the United Kingdom revealed that 77% use NSAIDs in the perioperative care of children having tonsillectomy. Acetaminophen is effective when effective loading doses are used, although rectal administration has a slow and variable onset; intravenous propacetamol (not available in the United States at the time of writing) may offer further advantage. Other non-opioid analgesics such as ketamine, tramadol, and dexmedetomidine have shown efficacy and opioid-sparing effects in small studies. Although codeine is frequently prescribed for post-tonsillectomy analgesia, newer understanding of the pharmacogenetic basis of variability of codeine activity and reports of respiratory depression after discharge suggest that a uniformly safe and effective analgesic regimen has yet to be identified.

Although no data currently document the variability in practice among American anesthesia providers, it seems prudent to recommend a tonsillectomy technique that uses dexamethasone and 5-HT3 antagonists, minimizes opioid doses possibly (including a revisitation of the American acceptance of NSAID use), and uses propofol as a main component of the anesthetic. Cost analysis also supports the use of propofol and multimodal PONV prophylaxis. Several groups have described low incidence of complication in outpatient tonsillectomy with appropriate patient selection and clinical protocols designed to manage postoperative pain and decrease PONV. Unlike adult patients, there is a requirement to consider the ability of the
parent or guardian to understand the discharge risks and instructions, proximity, and potential causes for delay should return to hospital become indicated, and the overall clinical assessment of the surgical team before discharge. Each institution should consider these issues in formulating specific discharge criteria.

**CREDENTIALING IN PEDIATRIC ANESTHESIA**

Credentialing continues to be an area of controversy in pediatric anesthesia; which patient requires a pediatric anesthesiologist? What is the definition of a pediatric anesthesiologist? There is general consensus that high-risk procedures should not be undertaken on an infrequent basis, but specifics are less clear on what numbers are required for ongoing competency and what situations require specialized care. There is some evidence that adverse events are less common in the hands of experienced pediatric anesthesiologists. The 1989 conclusion of the National Confidential Enquiry into Perioperative Deaths recommended that surgeons and anesthetists in the United Kingdom not undertake occasional pediatric practice; in the United Kingdom, specialists care for children younger than 5 years of age, and in Scandinavia, the age is 2 years.

Training programs are accredited by the Accreditation Council for Graduate Medical Education (ACGME); pediatric anesthesia was the first operating room (OR) subspecialty of anesthesiology to have accreditation for fellowship training, beginning in 1997. Anesthesiologists receive board certification through the American Board of Anesthesiology (ABA); at present, subspecialty board certification does not exist for any OR subspecialty of anesthesiology, although it does exist for Pain Management and Critical Care. The Society for Pediatric Anesthesia has proposed “subspecialty certification in advanced pediatric anesthesiology” as part of a tiered system to provide excellent care to high-risk pediatric patients, but, at the time of writing, this proposal remains with the Board of Directors of the ABA.

Until formal requirements, if any, are developed for pediatric anesthesia care, institutions and anesthesiologists should consider their individual practice settings and competencies, and guidelines from several professional organizations. The American Academy of Pediatrics (AAP) Section on Anesthesiology has published Guidelines for the Pediatric Perioperative Anesthesia Environment, which suggest that each facility define the spectrum of pediatric patients and cases for which it will provide care, and the number of cases of each required for the facility to maintain its competence. These guidelines also suggest that the institution define which pediatric patients are considered to be at increased risk, and that their anesthesia care should be provided by anesthesiologists who are fellowship trained in pediatric anesthesia or have equivalent experience. Similar recommendations have been made by the ASA and the Society for Pediatric Anesthesia. Some states have also instituted or considered requirements to have anesthesiologists caring for children (of some defined age) meet certain minimal case numbers. The AAP guidelines also include recommendations for appropriately sized airway and monitoring equipment, child-friendly spaces including separate preoperative area for children/families, and age-specific competencies and resuscitation skills for OR and recovery staff.

**SUMMARY**

Careful patient screening and selection help to minimize the risk of adverse outcomes in pediatric ambulatory surgery, and the overall rates of serious morbidity in the United States remain low. Errors in medication doses and effects, airway management, malfunctioning equipment or alarms, distraction, inexperience, or other human-related
issues contribute to many preventable events. The unique physiologic, anatomic, and pharmacologic state of children of various ages challenges the anesthesia provider to remain vigilant during surgery; knowledge of potential complications in common pediatric ENT procedures may help avoid risk. Each institution should continuously review admission criteria, staffing decisions, postoperative management resources, and quality-improvement methods to moderate risk and respond to crises.

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The present guidelines were compiled by a multidisciplinary international panel of individuals with interest and expertise in postoperative nausea and vomiting (PONV) under the auspices of The Society of Ambulatory Anesthesia. The panel critically evaluated the current medical literature on PONV to provide an evidence-based reference tool for the management of adults and children who are undergoing surgery and are at increased risk for PONV. In brief, these guidelines identify risk factors for PONV in adults and children; recommend approaches for reducing baseline risks for PONV; identify the most effective antiemetic monotherapy and combination therapy regimens for PONV prophylaxis; recommend approaches for treatment of PONV when it occurs; and provide an algorithm for the management of individuals at increased risk for PONV.

general surgical population and in up to 70%–80% of high-risk surgical patients (2–4). The adverse effects of PONV range from patient-related distress to postoperative morbidity. PONV associated with ambulatory surgery increases health care costs due to hospital admission and accounts for 0.1%–0.2% of these unanticipated admissions, which is significant in the United States where more than 31 million patients undergo ambulatory surgery each year (1,5–7).

The present guidelines were developed under the auspices of the Society of Ambulatory Anesthesia (SAMBA). The panel reviewed new literature since a previous consensus guideline on PONV was published in 2003 (8). A Medline search revealed that an additional 250 comparative antiemetic trials were published since February 2002, when the medical literature was last reviewed. These guidelines provide up-to-date information to practicing physicians and other health care providers about strategies to prevent and treat PONV.

Establishment of Expert Guidelines

To produce the SAMBA guidelines for the management of PONV, an unrestricted educational grant was provided by Baxter (transdermal scopolamine), GSK (ondansetron), Merck (aprepitant), MGI Pharma (palonosetron) and Roche, Inc. (granisetron). The primary author was requested to form a multidisciplinary international panel of individuals (anesthesiologists, surgeon, pharmacist, nurse anesthetist, perianesthesia nurse, and a biostatistican). Members from the first PONV consensus panel (8) were contacted. Additional experts were sought from Europe, Australasia, and from other health care disciplines. The panel selections were based on significant expertise in this area of research and representation in professional societies with an interest in the management of PONV. Sponsoring pharmaceutical companies did not play any role in the selection of the panel or topics. Panel members were asked to review the medical literature on PONV (from November 2005). Members, working in pairs, undertook a topic to research and presented the evidence-based data to the group, who discussed the evidence and reached consensus on its inclusion in the guidelines. When full agreement could not be obtained, the majority view was presented and the lack of full agreement was stated. Members of SAMBA also had an opportunity to review and comment on the consensus statements prior to publication. A draft of the consensus guidelines was presented to an audience at the 2006 SAMBA midyear meeting and was subsequently posted on the website for 4 wk from November 1 to November 29, 2006, for SAMBA member comments. The members’ comments were sent by e-mail to the Chair of the SAMBA Scientific Committee, who anonymized them and sent them to the guidelines panel for review and discussion. A consensus was reached on each item submitted to either incorporate it in the guidelines or reject it based on the presence of adequate published data.

Goals of Guidelines

The panel defined the following goals for the guidelines: 1) Identify the primary risk factors for PONV in adults and postoperative vomiting (POV) in children; 2) Establish factors that reduce the baseline risks for PONV; 3) Determine the most effective antiemetic monotherapies and combination therapy regimens for PONV/POV prophylaxis, including pharmacologic and nonpharmacologic approaches; 4) Ascertain the optimal approach to treatment of PONV with or without PONV prophylaxis; 5) Determine the optimal dosing and timing of antiemetic prophylaxis; 6) Evaluate the cost-effectiveness (C/E) of various PONV management strategies using incremental C/E ratio (cost of treatment A – cost of treatment B)/(success of treatment A – success of treatment B); 7) Create an algorithm to identify individuals at increased risk for PONV and to suggest effective treatment strategies.

Strength of Evidence

A variety of grading systems has been proposed to document the strength of evidence of randomized and observational studies supporting a treatment. The panel decided not to grade the included literature but to base its recommendations exclusively on valid studies with a minimal risk of bias. Thus, recommendations were made only if they were supported by randomized trials and systematic reviews of randomized trials that documented efficacy and harm of antiemetic interventions, and by nonrandomized studies that used logistic regression to identify risk factors of PONV.

Guideline 1: Identify Patients’ Risk for PONV

Risk factors for PONV in adults are shown in Table 1 and Figure 1.

Risk factors for POV in children are shown in Figure 2.

Estimating an individual’s risk for PONV can indicate who will most likely benefit from prophylactic antiemetic therapy. In adults, only a few baseline risk factors occur with enough consistency to be considered independent predictors for PONV (3,9–12,21–31). Female gender, nonsmoking, and the history of PONV or motion sickness are among the most important and prevalent patient-specific predictors. Some studies also reported migraine, young age, anxiety, and patients with a low ASA risk classification as independent predictors for PONV, although the strength of these factors varies from study to study (12,32). Anesthesia-related independent predictors are general anesthesia with volatile anesthetics, nitrous oxide, and
Table 1. Risk Factors for Postoperative Nausea and Vomiting (PONV) in Adults

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Points</th>
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<tbody>
<tr>
<td>Female gender</td>
<td>1</td>
</tr>
<tr>
<td>Non-smoker</td>
<td>1</td>
</tr>
<tr>
<td>History of PONV</td>
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<tr>
<td>Postoperative opioids</td>
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</table>

| Sum = | 0 ... 4 |

Risk Factors Points

Risk Factors

<table>
<thead>
<tr>
<th># of Risk Factors</th>
<th>PONV Risk</th>
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<tbody>
<tr>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>1</td>
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<tr>
<td>2</td>
<td>40%</td>
</tr>
<tr>
<td>3</td>
<td>60%</td>
</tr>
<tr>
<td>4</td>
<td>80%</td>
</tr>
</tbody>
</table>

Figure 1. Simplified risk score for PONV in adults (3). Simplified risk score from Apfel et al. (3) to predict the patients risk for PONV. When 0, 1, 2, 3, or 4 of the depicted independent predictors are present, the corresponding risk for PONV is approximately 10%, 20%, 40%, 60%, or 80%.

Risk Factors

<table>
<thead>
<tr>
<th># of Risk Factors</th>
<th>POV Risk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>1</td>
<td>20%</td>
</tr>
<tr>
<td>2</td>
<td>40%</td>
</tr>
<tr>
<td>3</td>
<td>60%</td>
</tr>
<tr>
<td>4</td>
<td>80%</td>
</tr>
</tbody>
</table>

Figure 2. Simplified risk score for POV in children (39). Simplified risk score from Eberhart et al. (39) to predict the risk for POV in children. Four independent predictors of POV were identified, including duration of surgery ≥30 min, age ≥3 yr, strabismus surgery, and a positive history of PONV in the patient, parent or sibling. They demonstrated that the risk for POV was 9%, 10%, 30%, 55%, and 70% when 0, 1, 2, 3, or 4 of those independent predictors were present.

It is appreciated that some types of surgery are associated with a higher incidence of PONV than others. However, no agreement could be reached about whether the association between type of surgery and increased PONV risk is causal. Numerous studies suggest that the higher incidences are due to other independent risk factors associated with the type of surgery (3,10,14,22,26,27,32), while other analyses suggest that certain types of surgery are independent risk factors (4,9,11,12,23,28,30) (Table 1).

Many factors commonly believed to augment risk are not actually independent factors. These include obesity, anxiety, antagonizing neuromuscular blockade (10,22,26,30,32–35). However, no single patient- or anesthetic-related risk factor is sufficiently sensitive or specific enough to provide a useful risk assessment for PONV. Several risk models have therefore been developed (30). The simplified models of Apfel et al. and Koivuranta et al. have shown some usefulness for the prediction of the PONV baseline risk in a variety of situations (10,24,27,28). It is important to note that no risk model can accurately predict the likelihood of an individual having PONV; risk models only allow clinicians to estimate the risk for PONV among patient groups (32).

In children, a number of papers have been published citing a variety of risk factors associated with POV (36–38). However, evidence is lacking to support these associations. More recently, Eberhart et al. (39) published a study of a large series of pediatric patients in which a multivariable analysis was applied to identify pov risk factors in children. Four independent predictors of POV were identified, including duration of surgery ≥30 min, age ≥3 yr, strabismus surgery, and a positive history of PONV in the patient, parent or sibling. They demonstrated that the risk for POV was 9%, 10%, 30%, 55%, and 70% when 0, 1, 2, 3, or 4 of those independent predictors were present.

Use of prophylactic antiemetics should be based on valid assessment of the patient’s risk for POV or PONV. In other words, antiemetic prophylaxis should be used only when the patient’s individual risk is sufficiently high. This can be estimated by multiplying the expected incidence (baseline risk) by the relative risk reduction resulting from prophylaxis. This approach produces a clinically meaningful decrease in the risk of PONV (2,40). However, more liberal prophylaxis is appropriate for patients in whom vomiting poses a particular medical risk, including those with wired jaws, increased intracranial pressure, gastric or esophageal surgery, and when the anesthesia care provider determines the need or the patient has a strong preference to avoid PONV.

Guideline 2: Reduce Baseline Risk Factors for PONV

Approaches for decreasing baseline risk factors are presented in Table 2.
Table 2. Strategies to Reduce Baseline Risk

- Avoidance of general anesthesia by the use of regional anesthesia (11,16) (randomized, controlled trial, RCT)
- Use of propofol for induction and maintenance of anesthesia (4,14,41,42) (RCT/systematic review, SR)
- Avoidance of nitrous oxide (3,4,43,44) (RCT/SR)
- Avoidance of volatile anesthetics (15,28) (RCT)
- Minimization of intraoperative (SR) and postoperative opioids (3,13,15,17,18,20,28,43) (RCT/SR)
- Minimization of neostigmine (19,45) (SR)
- Adequate hydration (46) (RCT)

Discussion

Reducing baseline risk factors can significantly decrease the incidence of PONV. Use of regional anesthesia is associated with a lower incidence of PONV than general anesthesia in both children and adults (11,16). Sinclair et al. (11) found the risk for PONV is nine times less among patients receiving regional anesthesia than those receiving general anesthesia. When general anesthesia is required, use of propofol for induction and maintenance of anesthesia decreases the incidence of early PONV (occurring within the first 6 h; number-needed-to-treat [NNT] = 5) (47). The IMPACT study evaluated several strategies to reduce PONV in 5199 high risk patients (4). The study reported a 59% incidence of PONV in patients treated with a volatile anesthetic or nitrous oxide. Use of propofol reduced PONV risk by 19%. Avoiding nitrous oxide reduced PONV risk by 12%. The combination of propofol and air/oxygen (total IV anesthesia) had additive effects, reducing PONV risk by approximately 25% (4). These findings are supported by two meta-analyses demonstrating that avoiding nitrous oxide reduces PONV risk (43,44) and a randomized, placebo-controlled trial showing that volatile anesthetics are the primary cause of early PONV (0–2 h), but that they do not have an impact on delayed PONV (2–24 h) (15). However, nitrous oxide has little impact when the incidence of PONV is low (44). Baseline risk for PONV can also be reduced by minimizing intraoperative and postoperative opioids (3,13,15,17,18,28,43,48). To achieve satisfactory analgesia without opioids, alternate modalities of pain management may be used. Randomized controlled trials and meta-analyses show that perioperative nonsteroidal antiinflammatory drugs and cyclooxygenase-2 inhibitors (49–51), and, less so, intraoperative ketamine (52), may have a morphine-sparing effect in the postoperative period. Theoretically, this decrease in opioid consumption could lead to a decrease in the incidence of opioid-related nausea and vomiting. Reducing the dose or avoiding neostigmine has been studied as a means for reducing baseline risk for PONV. Meta-analyses demonstrate that high-dose neostigmine (>2.5 mg) is associated with increased PONV and that reducing the dose can decrease PONV risk (19,45). However, the clinical importance of neostigmine’s effects on PONV has been questioned (35).

Systematic reviews of randomized controlled trials show that supplemental oxygen has no effect on nausea or overall vomiting, although it may reduce the risk of early vomiting (53,54). As a result, supplemental oxygen is not recommended in these guidelines.

Guideline 3: Administer PONV Prophylaxis Using One to Two Interventions in Adults at Moderate Risk for PONV

Prophylactic doses and timing for administration of antiemetics in adults are shown in Table 3. A treatment algorithm is presented in Figure 3.
prophylaxis, although a systematic review shows that some of the data on granisetron may be less reliable than others (61,68–70,80–83). Tropisetron, 2 mg IV, shows significant efficacy for reducing risk for nausea and vomiting and is recommended for PONV prophylaxis (79,84). The 5-HT3 antagonists have a favorable side effect profile and are considered equally safe. The number-needed-to-harm (NNH) with a single dose of

Table 3. Antiemetic Doses and Timing for Prevention of Postoperative Nausea and Vomiting (PONV) in Adults

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Dose</th>
<th>Evidence</th>
<th>Timing</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexamethasone</td>
<td>4–5 mg IV</td>
<td>SR (55–57)</td>
<td>At induction</td>
<td>RCT (57)</td>
</tr>
<tr>
<td>Dimenhydrinate</td>
<td>1 mg/kg IV</td>
<td>SR (58) RCT (59,60)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dolasetron</td>
<td>12.5 mg IV</td>
<td>RCT (61)</td>
<td>End of surgery; timing may not affect efficacy</td>
<td>RCT (61)</td>
</tr>
<tr>
<td>Droperidola</td>
<td>0.625–1.25 mg IV</td>
<td>RCT (62,63)</td>
<td>End of surgery</td>
<td>SR (64)</td>
</tr>
<tr>
<td>Ephedrine</td>
<td>0.5 mg/kg IM</td>
<td>RCT (65,66)</td>
<td>End of surgery</td>
<td>RCT (65,66)</td>
</tr>
<tr>
<td>Granisetron</td>
<td>0.35–1.5 mg IV</td>
<td>RCT (67–71)</td>
<td>End of surgery</td>
<td>RCT (68–70)</td>
</tr>
<tr>
<td>Haloperidol</td>
<td>0.5–2 mg IM/IV</td>
<td>SR (72)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prochlorperazine</td>
<td>5–10 mg IM/IV</td>
<td>RCT (73)</td>
<td>End of surgery</td>
<td>RCT (73)</td>
</tr>
<tr>
<td>Promethazineb</td>
<td>6.25–25 mg IV</td>
<td>RCT (74,75)</td>
<td>At induction</td>
<td>RCT (74,75)</td>
</tr>
<tr>
<td>Ondansetron</td>
<td>4 mg IV</td>
<td>RCT (76)</td>
<td>End of surgery</td>
<td>SR (67)</td>
</tr>
<tr>
<td>Scopolamine Transdermal patch</td>
<td>SR (77,78)</td>
<td>Prior evening or 4 h before surgery</td>
<td>RCT (78)</td>
<td></td>
</tr>
<tr>
<td>Tropisetron</td>
<td>2 mg IV</td>
<td>RCT (79)</td>
<td>End of surgery</td>
<td>Expert opinion</td>
</tr>
</tbody>
</table>

Note: These recommendations are evidence-based and not all the drugs have a FDA indication for PONV.

Drugs are listed alphabetically.

-a See Food and Drug Administration (FDA) "black box" warning.

-b FDA Alert: Should not be used in children less than 2 years old.

RCT = randomized, controlled trial; SR = systematic review.

Figure 3. Algorithm for management of postoperative nausea and vomiting (PONV).
Butyrophenones

Prophylactic doses of droperidol, 0.625–1.25 mg IV, are effective for the prevention of PONV (62,63). The efficacy of droperidol is equivalent to that of ondansetron for PONV prophylaxis, with an NNT of approximately 5 for prevention of nausea and vomiting (0–24 h) (2,4). Droperidol is most effective when administered at the end of surgery (64). It also effectively reduces the risk for opioid-induced nausea and vomiting, with a NNT of approximately 3, when given concomitantly with patient-controlled analgesia (PCA) (86,87). Many physicians have stopped using droperidol due to the FDA “black box” restrictions on its use. However, the droperidol doses used for the management of PONV are extremely low, and at these dosing levels droperidol is unlikely to be associated with significant cardiovascular events (88–90). The panel expressed considerable concern about the quality and quantity of evidence and the validity of the FDA conclusion. If it were not for the black-box warning, droperidol would have been the panel’s overwhelming first choice for PONV prophylaxis.

Haloperidol, which has antiemetic properties when used in low doses, has been investigated as an alternative to droperidol (72,91). A meta-analysis of published and unpublished randomized trials suggests that at doses much lower than those used to treat psychiatric disorders, 0.5–2 mg IM or IV, haloperidol effectively reduces PONV risk with a NNT of between 4 and 6 (72). At these doses, sedation did not occur, and cardiac arrhythmias were not reported. Of 806 patients exposed to haloperidol, 1 (0.1%) had extrapyramidal symptoms with 4 mg. There are no reports in the medical literature about optimal timing of haloperidol administration. Haloperidol carries a risk of QTc prolongation in its label and thus it is not recommended as first-line therapy. However, it can be considered as an alternative to droperidol if the black box warning precludes use of that drug.

Dexamethasone

The corticosteroid, dexamethasone, effectively prevents nausea and vomiting (55,56). It is recommended at a prophylactic dose of 4–5 mg IV (depending on the dosage formulation in different countries) for patients at increased risk for PONV. For PONV prophylaxis, the efficacy of dexamethasone 4 mg IV seems to be similar to that of ondansetron 4 mg IV and droperidol 1.25 mg IV (4). The recommended timing for administration is at induction of anesthesia rather than at the end of surgery (57). Adverse events have not been noted after a single bolus dose of dexamethasone (55).

Dimenhydrinate

Dimenhydrinate is an antihistamine with antiemetic effects. Data from placebo-controlled trials suggest that its degree of antiemetic efficacy may be similar to the 5-HT₃ receptor antagonists, dexamethasone, and droperidol (58). The recommended dose is 1 mg/kg IV (58–60). However, not enough data are available to establish the optimal timing and dose response for dimenhydrinate administration or its side effect profile. Direct comparisons with other antiemetic drugs are lacking.

Transdermal Scopolamine

A systematic review of transdermal scopolamine shows that it is useful as an adjunct to other antiemetic therapies (77). The patch effectively prevents nausea and vomiting postoperatively (NNT = 6). It is applied the evening before surgery or 4 h before the end of anesthesia due to its 2–4 h onset of effect, which may be problematic in some centers (78). Adverse events associated with transdermal scopolamine are generally mild; the most common being visual disturbances (NNH = 5.6), dry mouth (NNH = 13), and dizziness (NNH = 50) (77). Transdermal scopolamine has been found useful for control of nausea in the setting of PCA (92,93).

Combination Therapy

Adults at moderate risk for PONV should receive combination therapy with one or more prophylactic drugs from different classes. In general, combination therapy has superior efficacy compared with monotherapy for PONV prophylaxis (94,95). Drugs with different mechanisms of action should be used in combination to optimize efficacy. The 5-HT₃ antagonists, which have better antivomiting than antinausea efficacy (yet are associated with headache), can be used in combination with droperidol, which has greater antinausea efficacy and a protective effect against headache (96). The 5-HT₃ antagonists can also be effectively combined with dexamethasone (55). One study found no difference in efficacy for preventing PONV when low-dose granisetron (0.1 mg) in combination with dexamethasone 8 mg was compared with ondansetron 4 mg plus dexamethasone 8 mg (97). In a single study, the combination of a 5-HT₃ antagonist and promethazine significantly reduced both the frequency and severity of nausea and vomiting (74). Optimal antiemetic dosing with combination therapy needs to be established. Combination therapy regimens using ondansetron with either droperidol or dexamethasone are the most widely studied. It has been suggested that, with combination therapy, dexamethasone doses should not exceed 10 mg IV and that droperidol doses should not exceed 1 mg IV (96). When used in combination with another drug, ondansetron doses in adults typically should not exceed 4 mg, and can be much lower (96).
Lack or Limited Evidence of Effect

Some therapies have proven ineffective for PONV prophylaxis. These include metoclopramide when used in standard clinical doses (10 mg IV), ginger root, and cannabinoids (nabilone, tetra-hydrocannabinol) which, although promising in the control of chemotherapy-induced sickness, are not effective in PONV (98–102). In two randomized trials, the phenothiazines, promethazine, 12.5–25 mg IV, administered at the induction of surgery, and prochlorperazine, 5–10 mg IV, given at the end of surgery were shown to have some antiemetic efficacy (73,74). Similarly, it was suggested that the phenylethylamine, ephedrine, 0.5 mg/kg IM, may have an antiemetic effect when administered at the end of surgery (65,66). Due to a paucity of data, evidence is not as strong as for the other, well documented antiemetic drugs; therefore, further research is warranted before these drugs can be recommended as first-line therapy. There is inadequate evidence to suggest that hypnosis is a promising modality for PONV prophylaxis.

Nonpharmacologic Prophylaxis

A meta-analysis of nonpharmacologic PONV prophylaxis demonstrated antiemetic efficacy with acupuncture, transcutaneous electrical nerve stimulation, acupoint stimulation, and acupressure (NNT \(\geq 6\) h after surgery) \(\approx 5\) (103). A systematic review of 26 trials by Lee and Done (104) showed that stimulation of the P6 acupuncture point reduced the incidence of nausea, vomiting, and need for rescue medication. In a randomized, controlled trial, P6 electro-acupoint stimulation led to a complete response rate as high as that of ondansetron when compared with controls (\(P = 0.006\)) (105). P6 stimulation was particularly effective at reducing the incidence and severity of nausea (19%) compared with ondansetron (40%) and placebo (79%). Stimulation of Korean hand acupoints proved effective in preventing PONV as well, reducing the incidence of postoperative vomiting in two randomized controlled trials by approximately half (106,107).

Cost Effectiveness

The C/E of therapy is one of the primary considerations in determining whether to use PONV prophylaxis. However studies assessing C/E of PONV interventions have several drawbacks; they use variable methodologies, they are often too small to be reliable, and many are not specifically designed for that purpose. This panel recommends that future C/E studies be conducted according to established guidelines (108–111). Such guidelines address components of the numerator and denominator of a C/E ratio. The numerator should measure resource use and the denominator should provide a value of health consequences.

Willingness to pay is a recommended measure in cost benefit analyses. Gan et al. determined that patients are willing to pay approximately $100 to prevent experiencing PONV and Diez found parents are willing to spend approximately $80 to prevent PONV in their children (112,113). Reducing baseline risk can be a cost-effective strategy. For example, it is more cost-effective to use a propofol/isoflurane regimen, which is associated with the lowest cost per episode of PONV avoided, than either propofol/sevoflurane or sevoflurane/sevoflurane (114). C/E assessments for PONV prophylaxis are more difficult and depend on the specific model and assumptions chosen. It is estimated that each episode of emesis delays discharge from the postanesthesia care unit (PACU) by approximately 20 min (115). However, in a retrospective study of patients who underwent ambulatory surgery, Dexter and Tinker (116) demonstrated that if PONV could have been eliminated in patients who suffered this complication, the length of PACU stay for all patients would only have been reduced by <5%. Hill et al. (117) found prophylaxis in high-risk patients was more cost-effective than placebo due to increased costs associated with nausea and vomiting. The additional costs associated with PONV in placebo patients were up to 100 times higher compared with prophylaxis with a generic antiemetic and the cost of treating vomiting was three times more than the cost of treating nausea. Similarly, a study evaluating dolasetron, droperidol, or no prophylaxis in high-risk patients found that prophylaxis with either of the two antiemetics was more cost-effective than no prophylaxis and subsequent rescue therapy (118). On the other hand, in a study that did not assess C/E but evaluated factors affecting cost, there was no difference in the time to discharge, rate of unanticipated admission, or time to return to normal activity between the prophylaxis and treatment groups in an ambulatory setting, apart from the highest risk group (female patients with a history of motion sickness or PONV who were undergoing highly emetogenic procedures) who reported high patient satisfaction when prophylaxis was given (119). It has been suggested that PONV prophylaxis is cost-effective with the older, less expensive drugs when patients have a 10% or more risk of emesis (120). In another model, treatment of PONV with ondansetron was more cost-effective than prevention in both a low (30%) and a high (60%) risk setting (121). This was due to the high success rate of treating established PONV, even with low doses of ondansetron (1 mg). When using a willingness-to-pay rate of $100 per case avoided, PONV prophylaxis proved cost-effective in groups with a 40% risk of PONV. Lower drug acquisition costs support PONV prophylaxis in patient groups at a lower risk for PONV (122). The decision about whether or not to use PONV prophylaxis, or to treat patients with established symptoms, not only depends on the efficacy of the drug but also on the baseline risk for PONV, adverse effects of the antiemetics, and drug acquisition costs, which will vary from one setting to another. For instance, anesthesiologists may be more likely to administer prophylaxis with an inexpensive...
Table 4. Pharmacologic Combination Therapy for Adults and Children

<table>
<thead>
<tr>
<th>Adults</th>
<th>5-HT&lt;sub&gt;3&lt;/sub&gt; receptor antagonist + dexamethasone (4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(4,55,95,97,130,131)</td>
</tr>
<tr>
<td></td>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt; receptor antagonist + droperidol (4,64,95,130,131)</td>
</tr>
<tr>
<td></td>
<td>5-HT&lt;sub&gt;3&lt;/sub&gt; receptor antagonist + dexamethasone + droperidol (4)</td>
</tr>
<tr>
<td>Combinations in children</td>
<td>Ondansetron, 0.05 mg/kg, + dexamethasone, 0.015 mg/kg (132,133)</td>
</tr>
<tr>
<td></td>
<td>Ondansetron, 0.1 mg/kg, + droperidol, 0.015 mg/kg (134)</td>
</tr>
<tr>
<td></td>
<td>Tropisetron, 0.1 mg/kg, + dexamethasone, 0.5 mg/kg (135)</td>
</tr>
</tbody>
</table>

See Table 5 for maximum doses for children.

generic antiemetic even if the baseline risk is low and, consequently, many patients must be treated prophylactically for one to benefit.

**Novel Therapies**

Preliminary data on novel therapies for PONV prophylaxis and treatment show promising results with opioid antagonists and neurokinin-1 (NK<sub>1</sub>) receptor antagonists, suggesting that confirmatory studies are warranted. Low-dose naloxone, 0.25 μg·kg<sup>-1</sup>·h<sup>-1</sup>, reduced nausea and vomiting and decreased the need for rescue medication compared with placebo in adult patients (123), and significantly reduced opioid-related side effects including nausea in children and adolescents (124). Another opioid antagonist, nalmeprine, proved effective in reducing opioid-induced nausea, vomiting, and need for rescue medication in patients receiving PCA (125). Alvimopan, 6 mg, an opioid antagonist that does not cross the blood–brain barrier effectively reduced nausea and vomiting in patients undergoing abdominal surgery compared with placebo (126). An alternative therapy, the NK<sub>1</sub> receptor antagonist, CP-122,721, significantly reduced emesis over a 24-h period, both alone and in combination with ondansetron, compared with ondansetron alone (127). Another NK<sub>1</sub> receptor antagonist, GR205171, significantly controlled emesis (P < 0.01) and reduced nausea in established PONV compared with placebo (128). The NK<sub>1</sub> antagonist, aprepitant 40 mg PO, was equivalent to ondansetron 4 mg IV in the incidence of nausea and reducing the need for rescue in the initial 24 h postoperatively, but was significantly better than ondansetron for preventing vomiting in the 24 and 48 h after surgery (P < 0.001) (129).

**Guideline 4: Administer Prophylactic Therapy with Combination (≥2) Interventions/Multimodal Therapy in Patients at High Risk for PONV**

Recommended combination therapy is shown in Table 4.

A treatment algorithm is presented in Figure 3.

**Discussion**

Patients who are at high risk for PONV should receive prophylaxis with combination therapy or a multimodal approach that includes two or more interventions. Regional anesthesia should be considered for patients at high risk for PONV. If general anesthesia is used, baseline risk factors should be reduced when possible. Nonpharmacologic therapies should be considered as adjuncts to pharmacologic therapy. Antiemetics recommended for prophylaxis in adults and children are shown in Tables 3 and 5. When used in combination, drugs from different classes should be selected to optimize their effects.

For PONV prophylaxis, the efficacy of dexamethasone 4 mg IV, ondansetron 4 mg IV, and droperidol 1.25 mg IV appear to be similar (4). Systematic reviews addressing specific therapeutic combinations have shown the combination of a 5-HT<sub>3</sub> receptor antagonist and either dexamethasone or droperidol is more effective than monotherapy with any of the drugs (4,55,95,130,131). Similarly, droperidol combined with dexamethasone is more effective than either drug alone (4). When the different combinations were compared, no differences were found between 5-HT<sub>3</sub> receptor antagonist plus droperidol; 5-HT<sub>3</sub> receptor antagonist plus dexamethasone; and droperidol plus dexamethasone (4,130). Combinations involving metoclopramide were not found to reduce PONV to a greater extent than monotherapy (94,136,137).

A multimodal approach to minimize PONV combines nonpharmacologic and pharmacologic prophylaxis as well as interventions that reduce baseline risk (46,88). Scuderi et al. (46) tested the efficacy of a multimodal approach to reducing PONV. Their multimodal approach consisted of preoperative anxiolysis and aggressive hydration; oxygen; propylactic antiemetics (droperidol and dexamethasone at induction and ondansetron at end of surgery); total IV anesthesia with propofol and remifentanil; and ketorolac. No nitrous oxide or neuromuscular blockade was used. Patients who received multimodal therapy had a 98% complete response rate compared with a 76% response rate among patients receiving antiemetic monotherapy and a 59% response rate among those receiving routine anesthetic plus saline placebo.

**Guideline 5: Administer Prophylactic Antiemetic Therapy to Children at Increased Risk for POV; as in Adults, Use of Combination Therapy Is Most Effective**

The prophylactic antiemetic doses recommended for children at risk for POV are shown in Table 5. Recommended combination therapy is shown in Table 4.

**Discussion**

In children, the POV rate can be twice as high as in adults, which suggests a greater need for POV prophylaxis in this population (145). The prophylactic antiemetics recommended for children are shown in...
Table 5. Antiemetic Doses for Prophylaxis of Postoperative Vomiting (POV) in Children

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose</th>
<th>Evidence</th>
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</thead>
<tbody>
<tr>
<td>Dexamethasone</td>
<td>150 μg/kg up to 5 mg SR (55,138,139)</td>
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</tr>
<tr>
<td>Dimenhydrinate</td>
<td>0.5 mg/kg up to 25 mg SR (58,140)</td>
<td></td>
</tr>
<tr>
<td>Dolasetron</td>
<td>350 μg/kg up to 12.5 mg RCT (141,142)</td>
<td></td>
</tr>
<tr>
<td>Droperidol†</td>
<td>10–15 μg/kg up to 1.25 mg SR (64)</td>
<td></td>
</tr>
<tr>
<td>Granisetron</td>
<td>40 μg/kg up to 0.6 mg RCT (71)</td>
<td></td>
</tr>
<tr>
<td>Ondansetron†</td>
<td>50–100 μg/kg up to 4 mg SR (81,146)</td>
<td></td>
</tr>
<tr>
<td>Perphenazine‡</td>
<td>70 μg/kg up to 5 mg RCT (143,144)</td>
<td></td>
</tr>
<tr>
<td>Tropisetron</td>
<td>0.1 mg/kg up to 2 mg SR (84)</td>
<td></td>
</tr>
</tbody>
</table>

Note: These recommendations are evidence-based and not all the drugs have an FDA indication for postoperative nausea and vomiting (PONV).

Drugs are listed alphabetically.

† See Food and Drug Administration (FDA) “black box” warning. Recommended doses 10 to 15 μg/kg.
‡ Approved for POV in pediatric patients aged one month and older.
§ N formulation of perphenazine is no longer available in the United States, only oral formulation.

RCT = randomized, controlled trial; SR = systematic review.

Table 5. Children who are at moderate or high risk for POV should receive combination therapy with two or three prophylactic drugs from different classes.

Ondansetron has been studied extensively for POV prophylaxis in children and has recently been approved for use in children as young as one-month-old (76,146). It is recommended at a dose range of 50–100 μg/kg (76). Compared with placebo, the NNT to prevent early (0–6 h) and late (0–24 h) vomiting is between 2 and 3 (76). Ondansetron is the only 5-HT3 antagonist that has been approved for a pediatric (age <2) indication. Dolasetron is also recommended for POV prophylaxis, but only in children aged 2 yr and older. The optimal dose of dolasetron for POV prophylaxis is 350 μg/kg (20,141,142,147).

Granisetron at a dose of 40 μg/kg and tropisetron at a dose of 0.1 mg/kg have significantly reduced the incidence of POV in children (71,84). However, the data available about use of these 5-HT3 antagonists in the pediatric population are slim. Because the 5-HT3 antagonists as a group have greater efficacy for the prevention of vomiting than nausea, they are the drugs of first choice for prophylaxis in children.

Studies of PONV in children have been limited to the measurement of vomiting, as the reliable, effective evaluation of nausea in nonverbal children is difficult. This methodological limitation may explain some of the reported differences in efficacy of interventions in children and adults. Meta-analyses and single studies have shown that the 5-HT3 antagonists are superior to droperidol and metoclopramide for the prophylaxis of POV in children. Therefore, the panel recommends the use of 5-HT3 antagonists as the first choice for prophylaxis of POV in children. However, no pediatric study has demonstrated superior efficacy of any one 5-HT3 antagonist over another for the prophylaxis of POV.

Dexamethasone has been used in children at a dose of 150 μg/kg, with a NNT to prevent early and late vomiting of about four (55,138,139). A systematic review of dimenhydrinate demonstrates an antiemetic efficacy in children at a dose of 0.5 mg/kg (58). When given at a dose of 70 μg/kg, perphenazine demonstrated antiemetic efficacy in children, although only the oral formulation can be used as the IV formulation is no longer available in the United States (143,144). Droperidol can also be used for the prophylaxis of POV and is administered in a dose range of 50–75 μg/kg. Although these doses correspond to the officially tested doses, the panel considered them too high in a child. If we assume that the pediatric doses on a per kg body weight basis may be extrapolated from adult doses (i.e., 0.625–1.25 mg), the dose range in children should correspond to 10–15 μg/kg. The NNT for prevention of early vomiting is approximately 5 and is between 4 and 5 for prevention of late vomiting (64). Due to the potential increased risk for extrapyramidal symptoms and high levels of sedation found with droperidol, the panel recommended that this drug be reserved for pediatric patients who have failed all other therapies and are being admitted to the hospital.

Numerous, small randomized trials have compared the efficacy of combination therapy with monotherapy for POV prophylaxis. Most have found combination therapy more effective (132–135). Many of the studies that did not find combination therapy superior to monotherapy were under-powered to adequately show a difference between treatment groups (148–150). Combinations that showed efficacy for reducing POV are shown in Table 4. It has been suggested that, with combination therapy in children, dexamethasone doses should not exceed 150 μg/kg and droperidol doses should not exceed 50 μg/kg (96). (See comments above regarding droperidol dosing.) When used in combination with another drug, ondansetron doses should not exceed 50 μg/kg. Combinations with metoclopramide proved no better outcomes than monotherapy alone (151,152).

Guideline 6. Provide Antiemetic Treatment to Patients with PONV Who Did Not Receive Prophylaxis or in Whom Prophylaxis Failed

A treatment algorithm is presented in Figure 3.

Discussion

When PONV occurs postoperatively, treatment should be administered with an antiemetic from a pharmacologic class that is different from the prophylactic drug initially given, or, if no prophylaxis was given, the recommended treatment is a low-dose 5-HT3 antagonist (85,153). The 5-HT3 antagonists are the only drugs that have been adequately studied for the treatment of existing PONV (85,154). The doses of 5-HT3 antagonists used for treatment are smaller than those used for prophylaxis: ondansetron 1.0 mg; dolasetron 12.5 mg; granisetron 0.1 mg; and tropisetron 0.5 mg (NNT = 4–5) (85,76). Smaller doses of dolasetron have not been studied. Alternative treatments
for established PONV include dexamethasone, 2–4 mg IV, droperidol, 0.625 mg IV, or promethazine 6.25–12.5 mg IV (75,153,155). Propofol, 20 mg as needed, can be considered for rescue therapy in patients still in the PACU and has been found as effective as ondansetron (156–158). However, the antiemetic effect with low doses of propofol is probably brief (159).

One-third of patients who are treated with opioids for postoperative pain will have nausea or vomiting (87). In this group of patients, the addition of droperidol, 2.5 mg, to every 100 mg morphine in a PCA device was effective for reducing PONV (87). Ondansetron, 8 mg, also proved more effective than metoclopramide for controlling opioid-induced emesis and nausea in this population (160).

Repeating the medication given for PONV prophylaxis within the first 6 h after the patient has left the PACU confers no additional benefit (156). If more than 6 h has elapsed, it may be possible to achieve some effect with a second dose of a 5-HT<sub>3</sub> antagonist or butyrophenone (droperidol or haloperidol), but this has not been demonstrated in clinical trials and should only be attempted if triple therapy has been used for prophylaxis and if no alternatives are available for rescue that have not been used for prophylaxis. Readministration of dexamethasone or transdermal scopolamine is not recommended.

The attempt at rescue should be initiated when the patient complains of PONV and, at the same time, an evaluation should be performed to exclude an inciting medication or mechanical factor for nausea and/or vomiting. Contributing factors might include a morphine PCA, blood draining down the throat, or an abdominal obstruction.

**Postdischarge Nausea and Vomiting**

After ambulatory surgery, approximately one-third of patients experience PONV, many of whom did not experience PONV prior to discharge (161,162). Such patients often do not have access to treatment for their postdischarge nausea and vomiting (PDNV). A systematic review of all studies assessing PDNV after outpatient surgery found that, on discharge, 17% of patients experience nausea (range, 0%–55%) and 8% have vomiting (range, 0%–16%) (163). Administration of prophylactic antiemetics may be warranted in patients at high risk for PDNV; however, many of the available antiemetics have a short half-life and may not be suitable for this purpose. A meta-analysis assessing prophylactic therapy for PDNV after ambulatory surgery found a NNT of approximately 5 with combination therapy versus a NNT of approximately 12–13 for ondansetron, 4 mg, or dexamethasone, 4–10 mg alone (161). Droperidol was ineffective at preventing PDNV at a dose <1 mg, and there was insufficient evidence to evaluate droperidol >1 mg. A systematic review of 58 articles demonstrated that use of propofol versus inhaled anesthesia also reduced the incidence of PDNV (P < 0.05) (164). Small randomized controlled trials have demonstrated efficacy in preventing PDNV with orally disintegrating ondansetron tablets, acupuncture stimulation of P6, and transdermal scopolamine (78,165,166).

**CONCLUSION**

These guidelines provide a comprehensive, evidence-based reference tool for the management of patients undergoing surgical procedures who may be at risk for PONV. Not all surgical patients will benefit from antiemetic prophylaxis; thus identification of patients who are at increased risk leads to the most effective use of therapy and the greatest cost-efficacy. Although antiemetic prophylaxis can not eliminate the risk for PONV, it can significantly reduce the incidence. When developing a management strategy for each individual patient, the choice should be based on patient preference, C/E, and level of PONV risk.

Among the interventions considered, a reduction in baseline risk factors and use of nonpharmacologic therapy are least likely to cause adverse events. PONV prophylaxis should be considered for patients at moderate to high risk for PONV. Depending upon the level of risk, prophylaxis should be initiated with monotherapy or combination therapy using interventions that reduce baseline risk, nonpharmacologic approaches, and antiemetics. Antiemetic combinations are recommended for patients at high risk for PONV. All prophylaxis in children at moderate or high risk for PONV should include combination therapy using a 5-HT<sub>3</sub> antagonist and a second drug. Because the effects of interventions from different drug classes are additive, combining interventions has an additive effect in risk reduction.

When rescue therapy is required, the antiemetic should be chosen from a different therapeutic class than the drugs used for prophylaxis. If PONV occurs within 6 h postoperatively, patients should not receive a repeat dose of the prophylactic antiemetic. An emetic episode more than 6 h postoperatively can be treated with any of the drugs used for prophylaxis except dexamethasone and transdermal scopolamine.

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Update on the Management of Postoperative Nausea and Vomiting and Postdischarge Nausea and Vomiting in Ambulatory Surgery

Tina P. Le, BS, Tong Joo Gan, MD, FRCA*

Over the past several decades, as the risk of major mortality due to surgery has decreased, attention has shifted to addressing factors that negatively influence patient morbidity and patient satisfaction, such as postoperative nausea and vomiting (PONV). Since the previous article on PONV in this publication,1 several developments have aided in the prevention and management of this complication of surgical anesthesia. The 5-hydroxytryptamine type 3 (5-HT3) receptor antagonists continue to be the mainstay of antiemetic therapy, but newer approaches, such as neurokinin-1 antagonists, a longer-acting serotonin receptor antagonist, multimodal management, and novel techniques for managing high-risk patients, are gaining prominence.

PONV continues to be one of the most common complaints following surgery, occurring in more than 30% of surgeries, or as high as 70% to 80% in certain high-risk populations without prophylaxis.2 Though generally nonfatal and self-limited, PONV may lead to rare but serious medical consequences, including dehydration and electrolyte imbalance, venous hypertension, bleeding, hematoma formation, suture dehiscence, esophageal rupture,3,4,5 blindness,6 and aspiration.7 PONV also has a profound impact on patient satisfaction, quality of life, and estimated health

Department of Anesthesiology, Duke University Medical Center, Duke University School of Medicine, Box 3094, Durham, NC 27710, USA
* Corresponding author.
E-mail address: gan00001@mc.duke.edu
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care costs as a result of delayed discharge, prolonged nursing care, and unanticipated hospital admissions. PONV is often cited as one of the postsurgical complications patients would most like to avoid, and patients have reported being willing to pay between $56 and $100 out of pocket for an effective antiemetic.

Nausea and vomiting due to surgery may also occur beyond the immediate postoperative period. Although not as well studied as PONV, the related problem of postdischarge nausea and vomiting (PDNV) has received increasing attention from health care providers, especially because patients who experience no PONV immediately after surgery may develop PDNV after discharge. In one study, approximately 36% of patients who experience PDNV had not experienced any nausea or vomiting before discharge. Surveys of patients following ambulatory surgery have found PDNV to range between approximately 20% and 50%, resulting in increased difficulty in performing activities of daily living and longer recovery times before resuming normal activity.

The issues of PONV and PDNV are especially significant in the context of ambulatory surgeries, which comprise more than 60% of the combined 56.4 million ambulatory and inpatient surgery visits in the United States. Although the incidence of PONV and PDNV in ambulatory surgeries may be slightly lower than that of inpatient surgeries, it is believed to be underreported, given the limited amount of time that ambulatory surgery patients spend under direct medical care. Yet because of this relatively brief period that ambulatory patients spend in health care facilities, it is particularly important to prevent and treat PONV and PDNV swiftly and effectively.

**MECHANISM OF EMESIS**

Much of our current understanding of the basic neuroanatomy and physiology of emesis comes from the work of Wang and Borison in the 1950s. The central coordinating site for nausea and vomiting is located in an ill-defined area of the lateral reticular formation in the brainstem (Fig. 1). This “vomiting center,” as it is traditionally called, is not so much a discrete center of emetic activity as it is a “central pattern generator” (CPG) that sets off a specific sequence of neuronal activities throughout the medulla to result in vomiting. Multiple inputs may arrive from areas such as

![Fig. 1. Mechanism of nausea and vomiting.](image-url)
the higher cortical centers, cerebellum, vestibular apparatus, vagal, and glossopharyngeal nerve afferents to trigger the complex motor response of emesis; direct electrical stimulation of the CPG also causes emesis. A particularly important afferent is the chemoreceptor trigger zone (CTZ), located at the base of the fourth ventricle in the area postrema and outside the blood-brain barrier, which plays a role in detecting emetogenic agents in the blood and cerebrospinal fluid (CSF). Although direct electrical stimulation of the CTZ does not cause vomiting, the CTZ communicates with the adjacent nucleus tractus solitarius (NTS), which in turn projects into the CPG. Signals between these anatomic areas are mediated through a variety of neurotransmitter receptor systems, including serotonergic, dopaminergic, histaminergic, cholinergic, and neurokininergic; antiemetic prophylaxis or therapies block one or more of the associated receptors, including serotonin 5-HT₃, dopamine D₂, histamine H₁, muscarinic cholinergic, and neurokinin NK₁.

RISK FACTORS AND PROTECTIVE FACTORS FOR PONV AND PDNV

Assessment of patient risk factors is a key component in guiding antiemetic prevention and management strategies. A variety of surgical, anesthetic, and patient factors have been investigated as predictors of patient risk for PONV, the most significant of which are listed in Table 1. However, according to the 2007 Society for Ambulatory Anesthesia (SAMBA) Guidelines for the Management of PONV, only a few baseline risk factors occur with enough consistency to be validated as independent predictors for PONV. Several predictive models have been developed to stratify risk for PONV, but a simplified scoring system by Apfel and colleagues continues to be one of the most popular and compares favorably against other scoring systems. In a 2-center inpatient study, Apfel and colleagues identified 4 highly predictive risk factors for PONV: female gender, history of motion sickness or PONV, nonsmoker, and use of perioperative opioids. The presence of 0, 1, 2, 3, or 4 of these factors corresponded to a PONV incidence of 10%, 21%, 39%, 61%, and 79%, respectively. The Apfel score may be used to guide antiemetic strategies for high-risk patients, and in at least 2 studies, prophylaxis based on Apfel scores has led to a significant decrease the incidence of PONV.

The use of risk scores in predicting postoperative vomiting (POV) has also been extended to the pediatric population with the POstoperative VOmiting in Children score (POVOC score). The incidence of POV in pediatric patients is estimated to

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Risk factors for PONV and PDNV</th>
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<tbody>
<tr>
<td><strong>Patient Factors</strong></td>
<td><strong>Anesthetic Factors</strong></td>
</tr>
<tr>
<td>Female</td>
<td>Use of perioperative opioids</td>
</tr>
<tr>
<td>Nonsmoker</td>
<td>Use of volatile anesthetics</td>
</tr>
<tr>
<td>History of motion sickness or previous PONV</td>
<td>Nitrous oxide</td>
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<tr>
<td>Family history of motion sickness or PONV (pediatric)</td>
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<tr>
<td>Age ≥ 3 y (pediatric)</td>
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be about between 9% and 42% overall, and as high as 80% for specific types of surgery. However, it should be noted that nausea is often not recorded, as it is often difficult to assess in this younger patient population. To develop the POVOC score, Eberhart and colleagues compiled data from 1257 pediatric surgeries at 4 institutions and identified 4 independent risk factors for POV: duration of surgery 30 minutes or longer, age 3 years or older, strabismus surgery, and a positive history of POV in the child or POV/PONV in relatives (mother, father, or siblings). Similar to the Apfel score, the incidence of POV was 9%, 10%, 30%, 55%, and 70% for 0, 1, 2, 3, and 4 risk factors present, respectively. To date, there has only been one external validation study, which found that a modified POVOC score (excluding strabismus surgery) accurately predicted POV in pediatric patients, at a level comparable to the Apfel score for adults.

The 1999 study by Sinclair and colleagues, spanning 3 years and involving more than 17,000 patients, continues to be the most comprehensive examination of PONV risk factors specifically in ambulatory surgery patients. In addition to the 4 factors identified by Apfel and colleagues, duration of anesthesia longer than 30 minutes, general anesthesia, and type of surgery were also cited as independent predictors of PONV. However, it should be noted that while certain types of surgeries (particularly plastic, ophthalmologic, and orthopedic surgeries) appear to be correlated with higher rates of PONV, there is conflicting evidence as to whether other independent risk factors associated with type of surgery are actually responsible for the increased rates of PONV. Other studies, not confined specifically to ambulatory surgery patients, have also pointed to the use of volatile anesthetics, use of nitrous oxide, and administration of intraoperative and postoperative opioids as significant risk factors for PONV.

Risk factors for PDNV have mainly been studied in the context of risk factors for PONV. However, a recent study by White and colleagues suggests that while higher Apfel scores correlate to a greater incidence of PONV symptoms in the early (0–24 hours) postoperative period, it appears to have little predictive value for emetic symptoms occurring in the late (24–72 hours) postoperative/postdischarge period. Nevertheless, the few studies attempting to identify specific PDNV risk factors have found them to be similar to those typically associated with PONV. Mattila and colleagues evaluated postdischarge symptoms in 2754 adult and pediatric ambulatory surgery patients, and found that the odds ratios (ORs) of postdischarge vomiting were 0.23 and 0.26 for local and spinal anesthesia, respectively, when compared with general anesthesia. Female gender was also a risk factor for PDNV, with ORs of 2.74 and 2.79 for nausea and vomiting, respectively. Duration of surgery longer than 30 minutes increased the risk for nausea only, with a 56% increase in incidence of postdischarge nausea for surgeries 30 to 59 minutes’ duration, and a 64% increase for surgeries 60 minutes or longer. However, type of surgical procedure had no impact.

In the same study, no specific risk factors for postdischarge vomiting could be identified in the pediatric population, although use of general anesthesia, age 3 years or older, and duration of surgery 30 minutes or longer correlated with an increased risk of postdischarge nausea. Other studies have suggested that PDNV in children may be correlated to factors such as emetic symptoms prior to discharge, increased age, duration of journey home after discharge, pain at home, and use of postoperative opioids, but these associations need further study.

### ANTIEMETICS IN CLINICAL PRACTICE

Most antiemetic agents act on one or more of the neurotransmitter receptor types found in the anatomic sites responsible for emesis. To date, no single agent has
been found to block all receptor types, nor is there any single drug that is completely effective against PONV in all cases. Thus, appropriate prevention and management of PONV and PDNV require familiarity with a broad range of drug classes. In comparing various antiemetics and the evidence for or against them, it is helpful to determine the number needed to treat (NNT), or the number of patients that must be exposed to a particular intervention in order for one patient to benefit over receiving placebo or no treatment. The number needed to harm (NNH) is an estimate of the frequency of drug-related adverse effects. A list of common antiemetics, typical dosages, and NNT are listed in Table 2.

**Serotonin Antagonists**

Since their introduction in the early 1990s to treat chemotherapy-induced nausea and vomiting, serotonin antagonists have become one of the cornerstones of modern antiemetic prophylaxis and therapy, particularly in the setting of PONV. Serotonin is found in high levels in the enterochromaffin cells of the gastrointestinal tract, as well as in the central nervous system, and may be released to stimulate either the vagal afferent neurons or the CTZ to activate the vomiting center. Although there are multiple serotonin receptor types, the 5-HT$_3$ subtype appears in its greatest concentration in the NTS, area postrema, and the dorsal motor nucleus of the vagus nerve, which all play a significant role in coordinating the vomiting reflex. The 5-HT$_3$ receptor antagonists (5-HT$_3$ RAs), which include ondansetron, granisetron, dolasetron, ramosetron, tropisetron, and most recently palonosetron, act by inhibiting the action of serotonin in 5-HT$_3$ receptor-rich areas of the brain.

Ondansetron (Zofran), granisetron (Kytril), dolasetron (Anzemet), and palonosetron (Aloxi) are all approved for use in PONV by the Food and Drug Administration (FDA) (ramosetron and tropisetron are not available in the United States). In general, all of the 5-HT$_3$ RAs are safe, effective, and have similar side effect profiles. Side effects are usually short term and of mild to moderate intensity, with the most common being headache, dizziness, constipation, and diarrhea. However, the differing chemical

<table>
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<tr>
<th>Agent or Strategies</th>
<th>NNT</th>
<th>NNT</th>
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<tbody>
<tr>
<td>Ondansetron 4 mg IV$^{53}$</td>
<td>4.6</td>
<td>6.4</td>
<td>4.4</td>
</tr>
<tr>
<td>Dexamethasone 8 mg IV or 10 mg PO (adults)$^{75}$</td>
<td>Early 5.0</td>
<td>Early 3.6</td>
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<td></td>
<td>Late 4.3</td>
<td>Late 4.3</td>
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<tr>
<td>Dexamethasone 1–1.5 mg/kg IV (children)$^{75}$</td>
<td>Early 10</td>
<td>Late 3.1</td>
<td></td>
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<tr>
<td>Transdermal scopolamine 1.5 mg patch$^{82}$</td>
<td>4.3</td>
<td>5.6</td>
<td>3.8</td>
</tr>
<tr>
<td>Droperidol 0.625–1.25 mg IV$^{85}$</td>
<td>5</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Haloperidol 0.5–4 mg IM/IV$^{82}$</td>
<td>3.2–4.5</td>
<td>3.9–5.1</td>
<td></td>
</tr>
<tr>
<td>Metoclopramide 10 mg IV$^{100}$</td>
<td>No significant effect</td>
<td>Early 9.1</td>
<td></td>
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<tr>
<td></td>
<td>Late 10</td>
<td></td>
<td></td>
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<tr>
<td>Propofol infusion$^{105}$</td>
<td>8.6 (Postdischarge 12.5)</td>
<td>11.2 (Postdischarge 10.3)</td>
<td></td>
</tr>
<tr>
<td>Acupuncture$^{123}$</td>
<td>30% baseline risk 11</td>
<td>30% baseline risk 11</td>
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<td>70% baseline risk 5</td>
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structures of each drug may explain slight differences in receptor binding affinity, dose response, and duration of action.\textsuperscript{23} Most available data suggest that 5-HT\textsubscript{3} RAs are most effective when administered at the end of surgery,\textsuperscript{48–50} but at least one study has suggested that dolasetron may be administered around the time of induction of anesthesia, with little effect on efficacy.\textsuperscript{51}

All of the 5-HT\textsubscript{3} RAs are equally effective for the treatment of PONV.\textsuperscript{52} Ondansetron, as the prototypical 5-HT\textsubscript{3} RA, has been the most studied. In a quantitative systematic review of placebo-controlled trials of ondansetron, Trame`r and colleagues\textsuperscript{53} found that ondansetron, 4 mg had an NNT of about 4.6 for the prevention of vomiting, 6.4 for the prevention of nausea, and 4.4 for the prevention of both in the first 48 hours postoperatively. Risk of severe side effects was generally low, with an NNH of 36 for headache, 31 for elevated liver enzymes, and 23 for constipation. This study and others have also suggested that ondansetron is slightly more effective against vomiting than nausea.\textsuperscript{52,53} However, a recent study by Jokela and colleagues\textsuperscript{54} found that 4 mg ondansetron reduced the incidence of nausea by 26% over placebo, and vomiting by 33%, a difference that the investigators concluded was not of statistical significance. While not commenting on the antinausea versus antiemetic properties of ondansetron, a Cochrane systematic review found that ondansetron reduces the relative risk of nausea and vomiting by 32% and 45% over placebo, respectively.\textsuperscript{55} The review also evaluated 5 studies of ondansetron and reported no evidence that the risk of PONV differed for groups based on timing of administration. Controversy also exists as to whether ondansetron offers greater benefit for PONV prophylaxis greater than 4 mg,\textsuperscript{56–59} and a study in ferrets has found that the dose-response curve for ondansetron is unique in that it has better antiemetic efficacy at low (<50 \textmu g/kg subcutaneously) and high (>100 \textmu g/kg subcutaneously) doses.\textsuperscript{60} However, for the purposes of clinical practice the usual recommended dose of ondansetron in humans is 4 mg intravenously (IV), administered at the end of surgery.\textsuperscript{24}

Unlike ondansetron, the other 5-HT\textsubscript{3} RAs exhibit linear dose-response curves, with increasing doses achieving greater clinical effect until the maximal effective dose is reached.\textsuperscript{61} The dose recommended for PONV prophylaxis with granisetron is 0.35 to 1.5 mg IV (5–20 \textmu g/kg).\textsuperscript{24,62,63} In a multicenter, dose-ranging study, Taylor and colleagues\textsuperscript{64} found that intravenous doses as low as 0.1 mg given at the first symptoms of nausea or vomiting were effective in increasing the percentage of patients experiencing no vomiting in the first 24 hours to 38%, compared to 20% of patients with no vomiting on placebo. The recommended dose for dolasetron is 12.5 mg IV,\textsuperscript{24} based on a trial demonstrating that single-dose dolasetron 12.5 mg administered before the end of surgery resulted in a greater than 50% increase in complete response (CR; no emesis and no rescue medication for 24 hours) over placebo, with no significant increase in CR at 25- or 50-mg doses.\textsuperscript{65}

Palonosetron is the newest 5-HT\textsubscript{3} RA and has recently been approved in the United States for PONV. Unlike other drugs in its class, which exhibit simple bimolecular binding, palonosetron exhibits positive cooperativity in binding to its receptor; moreover, its molecular structure does not mimic that of serotonin and it therefore does not bind at the serotonin binding site of the 5-HT\textsubscript{3} receptor.\textsuperscript{66} As a result, palonosetron may bind more tightly to the receptor, allow multiple palonosetron molecules to bind to a single receptor, and make it less likely to be displaced by serotonin molecules.\textsuperscript{67} Furthermore, some data suggest that palonosetron may promote internalization of the 5-HT\textsubscript{3} receptor as an inverse agonist (similar to some G-protein coupled receptor antagonists), decreasing the function of the receptor in the absence of
agonist exposure. Thus, receptor internalization may contribute to palonosetron’s relatively long duration of action.

A large, randomized, placebo-controlled study by Candiotti and colleagues found that 43% of patients given palonosetron 0.075 mg before induction exhibited CR in the 0 to 24 hours postoperatively, compared with 20% of patients who received placebo. Moreover, patients receiving palonosetron reported less severe nausea and decreased interference in postoperative function due to PONV. A separate study of European patients by Kovac and colleagues found similar results for palonosetron, 0.075 mg in increasing CR rates, and the investigators also noted continued efficacy of palonosetron over placebo for 24 to 72 hours. It has been suggested that the long half-life of palonosetron may confer an antiemetic effect for several days after administration, which would be particularly useful in minimizing PDNV following ambulatory surgery; however, further studies are necessary to confirm any advantage over other serotonin antagonists.

Few studies have examined 5-HT3 RAs for the prevention of PDNV. A systematic review by Gupta and colleagues found that ondansetron 4 mg resulted in a relative risk reduction of 23% and 37% for postdischarge nausea and vomiting, respectively. However, it should be noted that the NNT was 12.9 for nausea and 13.6 for vomiting. Ondansetron, granisetron, and dolasetron are available as intravenous medications or oral tablets; palonosetron is currently only available as an intravenous medication. Ondansetron is also available as an orally disintegrating tablet (ODT), which seems to be as effective as the intravenous form. Some studies suggest that providing patients with the ODT before discharge may be particularly helpful in reducing the incidence of PDNV at home. In a study of pediatric patients, Davis and colleagues found that only 14.5% of children who received 5 at-home doses of ondansetron ODT experienced postdischarge vomiting, compared with 32% of children receiving placebo. A small study by Gan and colleagues found a decreased incidence of PDNV and PDNV severity in patients receiving ondansetron ODT following ambulatory surgery.

A relatively new but growing field in 5-HT3 RA research is that of pharmacogenomics. The 5-HT3 RAs are metabolized by cytochrome P450 in the liver, and differences in the activity or levels of the CYP2D6 isoform of the enzyme appear to have an effect on the pharmacokinetics and clinical efficacy of the drug in certain individuals. Candiotti and colleagues have reported that patients with 3 copies of the CYP2D6 gene or who have certain genetic polymorphisms in the CYP2D6 gene are ultrarapid metabolizers of ondansetron and are more likely to experience ondansetron failure for POV. Another recent study by Rueffert and colleagues analyzed DNA from 95 patients who had suffered from POV and matched them with 94 controls. The researchers found that variations in the genes of the serotonin receptor subunits, HTR3A and HTR3B, were associated with increased individual risk of developing POV. Although pharmacogenomic research is still in its early stages and it is currently of limited use in actual clinical practice, it may provide greater insights into assessing individual patient risk for PONV in the future.

### Steroids

Dexamethasone has been shown to be useful in the management of PONV. The mechanism of its antiemetic activity has not been fully elucidated, but it is believed that corticosteroids act centrally to inhibit prostaglandin synthesis or to control endorphin release. Dexamethasone may also be particularly effective when used in
combination with 5-HT₃ receptor antagonists, as it may (1) reduce levels of serotonin by depleting its precursor tryptophan, (2) prevent release of serotonin in the gut, and (3) sensitize the 5-HT₃ receptor to other antiemetics.⁷⁵

According to a study by Wang and colleagues,⁷⁶ dexamethasone is most effective for PONV prophylaxis when administered at induction rather than at the end of surgery. A systematic review and meta-analysis of 17 trials by Karanicolas and colleagues⁷⁷ found that dexamethasone reduced the incidence of postoperative nausea (PON) by 41%, POV by 59%, and nausea or vomiting by 45% relative to placebo, with the incidences of headache and dizziness being similar between the 2 groups. These results are similar to an earlier quantitative systematic review, which reported an NNT of 7.1 for the prevention of early vomiting in adults and children, and 3.8 for the prevention of late vomiting.⁷⁵ Karanicolas and colleagues⁷⁷ also reported that doses of 8 to 16 mg were significantly more effective at reducing PONV than doses of 2 to 5 mg, consistent with an earlier study by Elhakim and colleagues concluding that a dose of 8 mg dexamethasone provided maximal PONV prophylaxis when combined with ondansetron.⁷⁸ However, the SAMBA guidelines recommend a prophylactic dose of dexamethasone 4 to 5 mg IV at induction, which seems to be as effective as ondansetron 4 mg IV in preventing PONV.²⁴

**Cholinergic Antagonists**

The anticholinergic agents are among the oldest antiemetics. Both scopolamine (hyoscine) and atropine block muscarinic cholinergic emetic receptors in the cerebral cortex and the pons.⁷⁹ However, atropine has weaker antiemetic effects than scopolamine⁸⁰ and is generally not used in the postoperative period because of its cardiovascular effects.¹

Most studies of scopolamine for use in PONV have investigated transdermal scopolamine (TDS) patch, designed to release 1.5 mg of scopolamine over 3 days. In a double-blind sham and placebo-controlled study of 150 patients, White and colleagues⁸¹ compared preoperative transdermal scopolamine (TDS) 1.5 mg patch to intravenous ondansetron 4 mg or droperidol 1.25 mg administered before the end of surgery. The investigators found that premedication with TDS was as effective as ondansetron or droperidol in the prevention of both early and late PONV/PDVN, but also noted that TDS was associated with a greater risk of dry mouth. These findings correlate with an earlier quantitative systematic review by Kranke and colleagues,⁸² which found that although TDS is an effective antiemetic and has an NNT of 5.6 for the prevention of POV, the NNH is 5.6 for visual disturbances, 12.5 for dry mouth, and 50 for dizziness. Thus, the high rate of anticholinergic side effects of scopolamine may limit its use as a stand-alone antiemetic agent.

Scopolamine may be most useful as an adjunct to other antiemetics. In a trial of outpatient plastic surgery patients at high risk for PONV, Sah and colleagues⁸³ found that those who received a preoperative TDS patch in addition to intraoperative ondansetron had a statistically significant reduction in PON between 8 and 24 hours in comparison with those who received a placebo patch and ondansetron only. However, a similar, larger, multicenter trial found that a combination TDS and ondansetron reduced PONV as compared with ondansetron alone 24 hours after surgery, but not at 48 hours.⁸⁴ This study also noted that the incidence of adverse effects, including anticholinergic effects was not statistically different between the 2 groups, while patient satisfaction in the TDS group was significantly higher, suggesting that scopolamine might be a safe and effective adjunct in the management of PONV, especially when used in combination with ondansetron.
Dopamine Antagonists

The dopamine receptor antagonists act at the D₂ receptors in the CTZ and area postrema to suppress nausea and vomiting. There are 3 types of dopamine antagonists commonly used as antiemetics: butyrophenones, benzamides, and phenothiazines.

Butyrophenones

In addition to their strong D₂ receptor antagonism, the butyrophenones are α-blockers, contributing to their adverse effects of sedation and extrapyramidal symptoms, although the latter are rare at the low doses given for PONV. The 2 primary antiemetic agents in this group are haloperidol and droperidol. The clinical efficacy of droperidol 0.625 to 1.25 mg IV before the end of surgery has been well established, and until recently it had been widely used in the prevention and management of PONV as a cost-effective antiemetic. The IMPACT trial, a factorial trial of more than 5000 patients, found that droperidol is as effective as ondansetron and dexamethasone in reducing the risk of PONV. A meta-analysis by Leslie and Gan examining the safety of the 5-HT₃ antagonists with dexamethasone or droperidol found that all were generally well tolerated and had comparable safety profiles, even when used in combination.

However, in 2001 the FDA issued a “black box” warning for droperidol, citing reports of severe cardiac arrhythmias (eg, torsades de pointes) and rare cases of sudden cardiac death associated with the use of droperidol. Although the use of droperidol has declined precipitously since then, many experts and anesthesia providers still believe that the warning was not justified, and that droperidol remains a safe, effective, and economical antiemetic. Nevertheless, the warning, along with the FDA’s recommendation that all elective surgery patients receiving droperidol be placed on continuous electrocardiographic monitoring for 2 to 3 hours following administration, has limited its use in the ambulatory setting.

Accordingly, there has been an increased interest in haloperidol as an antiemetic. Haloperidol has been used primarily as a potent antipsychotic since the 1960s. Haloperidol has a faster onset of antiemetic action and has a longer half-life than droperidol, but its effect does not last as long, most likely because it has a weaker binding affinity than droperidol for the D₂ receptors in the CTZ and area postrema. In a meta-analysis of published and unpublished trials from 1962 to 1988, Buttner and colleagues found that haloperidol 0.5 to 4 mg was effective for established PONV over placebo, with an NNT of 3.2 to 5.1 over the first 24 hours postoperatively, although some of the trials included had flaws in design or data reporting. A small study of 90 nonsmoking, female patients in Taiwan found that haloperidol 2 mg IV was as effective as ondansetron 4 mg IV in preventing PONV for the first 24 hours, with no QTc prolongation observed. A similar study also did not observe QTc prolongation and found that haloperidol 1 mg IV was similar to ondansetron 4 mg IV, but both medications were only effective antiemetics relative to placebo in the early postoperative phase (0–2 hours). More recent studies by Rosow and colleagues have demonstrated the antiemetic efficacy of haloperidol over placebo and increased efficacy of haloperidol with ondansetron over ondansetron alone. However, additional studies are necessary to determine optimal dosing, timing, and safety profile before haloperidol may be used in regular clinical practice, either as prophylaxis or treatment.

Phenothiazines

The phenothiazines, which include promethazine, chlorpromazine, prochlorperazine, perphenazine, and thiethylperazine, are some of the most commonly used antiemetics in the world. However, their use has fallen out of favor due to their high incidence of...
adverse effects, such as sedation, restlessness, diarrhea, agitation, and central nervous system depression, and more rarely, extrapyramidal effects, hypotension, neuroleptic syndrome, and supraventricular tachycardia. Promethazine 12.5 to 25 mg IV given at the induction of surgery, and prochlorperazine 5 to 10 mg IV given at the end of surgery have both been shown to have antiemetic efficacy when combined with ondansetron. A retrospective review has also suggested that promethazine 6.25 mg, a dose low enough to limit most adverse effects, may be more effective than ondansetron for treating PONV in patients who have failed previous ondansetron prophylaxis. However, strong data are lacking and phenothiazines are currently not recommended as first-line antiemetic agents.

**Benzamides**

The most commonly used antiemetic in this group is metoclopramide, a procainimide derivative that blocks D2 receptors both centrally at the CTZ and area postrema, and peripherally in the gastrointestinal tract. Metoclopramide increases lower esophageal tone and promotes gastric motility, which may make it useful in preventing the delayed gastric emptying caused by opioids. A quantitative systematic review of 66 studies using various regimens of metoclopramide found no significant antinausea effect, an NNT of 9.1 to prevent early vomiting in adults, and an NNT of 10 to prevent late vomiting in the same population. In children, the NNT to prevent early vomiting was 5.8, with no significant late antivomiting effect. The review also noted that the best documented doses of metoclopramide were 10 mg IV for adults and 0.25 mg/kg IV for children. A more recent double-blind study in children undergoing tonsillectomy failed to show equivalence between metoclopramide 0.5 mg/kg and ondansetron 0.1 mg/kg, and in fact showed that ondansetron was superior for control of PONV. Given the lack of evidence showing antiemetic efficacy, metoclopramide is not recommended for PONV at this time.

**Antihistamines**

The antiemetic properties of antihistamines such as diphenhydramine, dimenhydrinate, cyclizine, doxylamine, and promethazine are derived from their blockade of the histamine H1 receptor in the NTS, at the vomiting center, and vestibular system; they have little or no direct action at the CTZ. However, their anticholinergic activity is responsible for their most common side effects of sedation, dry mouth, blurred vision, and urinary retention. Although generally inexpensive and readily available, the use of antihistamines in PONV has not been well studied. In a meta-analysis of 18 controlled trials, Kranke and colleagues reported that prophylactic dimenhydrinate (classified there to include both dimenhydrinate and the related diphenhydramine) reduces PONV in adults and children up to 48 hours after surgery, with a recommended dose of 1 mg/kg IV. There have been few studies of dimenhydrinate that specifically compare it with other antiemetics, and dose, timing, and side effect profiles have not been fully established. Doxylamine in combination with pyridoxine (Diclectin) has been shown to reduce the incidence of PONV in women undergoing laparoscopic tubal ligation. Although doxylamine is available in the United States, the combination with pyridoxine is only approved in Canada.

**Propofol**

The mechanism of antiemetic activity using propofol is unclear, but it has been observed that patients who receive propofol for induction tend to have less PONV. This observation has been supported by several meta-analyses, including one that examined postoperative outcomes under inhaled and intravenous anesthetic
Gupta and colleagues found that maintenance with a propofol infusion resulted in a decreased incidence of PONV and PDNV over inhaled anesthetics, with an NNT of 8.6 and 11.2 for PON and POV, respectively, and an NNT of 12.5 and 10.3 for postdischarge nausea and vomiting, respectively. A clinical trial of 2010 surgical patients in the Netherlands found that propofol total intravenous anesthesia (TIVA) resulted in a significant reduction of PONV compared with isoflurane-nitrous oxide anesthesia, with an NNT of 6.

Recent studies have suggested that TIVA alone may not be an optimal strategy for PONV prophylaxis. In a small randomized trial, White and colleagues found that although there were no significant differences in early PONV outcomes between patients given dolasetron prophylaxis and those given propofol-based TIVA, PDNV was significantly more common for patients in the TIVA group. The investigators suggest that although TIVA may be similar in efficacy to dolasetron for early PONV, its effects may be too short-lived to offer protection against PDNV.

Over the past several years, particularly as experience with the technique has increased and costs have decreased, the use of TIVA with propofol has become more popular for ambulatory surgery. One of the greatest limiting factors for increased use of TIVA continues to be cost, as economic analyses have suggested that routine use of TIVA for PONV prophylaxis is generally not cost-effective. Nevertheless, propofol-based TIVA is still a reasonable option for high-risk patients, especially as part of a multimodal management strategy (see Combination Therapies and Multimodal Prevention, below).

**NOVEL ANTIEMETIC THERAPIES**

**Neurokinin-1 Antagonists**

The neurokinin-1 receptor antagonists (NK₁ RAs) are a new class of antiemetic drugs that competitively inhibit the binding of substance P, a neuropeptide released from enterochromaffin cells. Substance P plays an important role in emesis as a ligand for neurokinin-1 receptors, which are located in the gastrointestinal tract and the area postrema. The NK₁ RAs are believed to suppress nausea and vomiting by acting centrally on the neurotransmission between the NTS and CPG. These agents may also act peripherally to block NK₁ receptors in the vagal terminals of the gut to decrease the intensity of the emetogenic signals sent to the CPG.

The first NK₁ RA to be approved by the FDA was aprepitant (Emend), for chemotherapy-induced nausea and vomiting. The first clinical trial to study the efficacy of aprepitant in PONV was a multicenter, double-blind study of 805 patients conducted by Gan and colleagues, who found that preoperative aprepitant, both 40 mg and 125 mg orally were equivalent to preoperative ondansetron 4 mg IV in terms of CR rates, nausea control, and use of rescue antiemetics. However, the study also found that aprepitant was superior for prevention of vomiting in the first 24 and 48 hours, with no vomiting in 90% of patients in the aprepitant 40 mg group, 95% of the aprepitant 125 mg group, and 74% of the ondansetron group in the first 24 hours. A follow-up study by the same group in an international population confirmed that aprepitant was superior to ondansetron for incidences of no vomiting in the first 24 and 48 hours, and also found that peak nausea scores were lower in patients receiving either dose of aprepitant. A post hoc analysis of the pooled data from both studies found that in the 24 hours after surgery, aprepitant 40 mg was slightly more effective than ondansetron in terms of no significant nausea (56.4% vs 48.1%), no nausea (39.6% vs 33.1%), no vomiting (86.7% vs 72.4%), no nausea and no vomiting
(38.3% vs 31.4%), and no nausea, vomiting, and no use of rescue antiemetics (37.9% vs 31.2%). The study group also noted that the 125-mg dose was similar or even slightly less effective than the lower dose, leading to the recommended and approved preoperative dose of 40 mg for PONV prophylaxis.

NK₁ RAs are safe and well tolerated, with the most common side effects being asthenia, diarrhea, dizziness, and hiccups. Although further studies are needed to establish their place in clinical practice, the NK₁ RAs offer many potential benefits for the management of PONV, especially as an alternative to patients who have failed treatment or prophylaxis with antiemetics in other classes. Aprepitant may be particularly useful in the ambulatory setting, as it comes in both a convenient oral form and a recently approved intravenous form (fosaprepitant) that may be useful for established PONV, although clinical trials with the intravenous formulation have not been conducted in the PONV setting.

**Opioid Antagonists**

Perioperative opioid use has long been known to increase the risk of PONV by decreasing gastric motility and delaying gastric emptying via the inhibition of central μ-opioid receptors. Thus, the use of centrally acting opioid receptor antagonists, such as naloxone, may have antiemetic efficacy. Preliminary studies have found that low-dose naloxone (0.25 μg/kg/h) is effective in reducing the incidence of PONV compared with placebo in both adults and children. A recent small study of 50 patients undergoing knee replacement surgery found that epidural sufentanil containing low-dose naloxone was effective in reducing PONV compared with sufentanil without naloxone. However, there is a paucity of clinical data about the use of opioid receptor antagonists in PONV, and further study is necessary.

**NONPHARMACOLOGIC TECHNIQUES**

Given that no single pharmacologic therapy is completely effective for PONV prophylaxis, nonpharmacologic techniques have become a reasonable adjunct to antiemetic drugs. Of all the nonpharmacologic techniques, acupuncture is one of the most well studied and accepted forms of treatment of PONV. The mechanism of acupuncture in the prevention of nausea and vomiting is not entirely clear; it may activate A-β and A-δ fibers to influence neurotransmission in the dorsal horn or other centers, influence the release of endogenous opioids, or inhibit gastric acid secretion and normalize gastric dysrhythmia.

Most data about acupuncture in PONV have examined the use of the acupuncture point pericardium 6, or P6, located 4 cm proximal from the wrist crease between the tendons of the palmaris longus and flexor carpi radialis muscles. A recently revised Cochrane database review of 40 randomized controlled trials determined that acupuncture stimulation of P6 is effective in the prevention of PONV, with few side effects. The NNTs were reported based on the baseline risk of nausea. At a control event rate of 30% (the estimated overall incidence of PONV), the NNT was 11 for both nausea and vomiting. At a baseline risk of 70% (estimate for high-risk populations), the NNT was 5 for both nausea and vomiting.

There are several comparable variations on traditional acupuncture, including acupressure and acupressure wristbands, acustimulation using transcutaneous electrical stimulation, acupuncture injections, and electroacupuncture. These techniques may be of particular benefit in the ambulatory setting, as many of them can be performed rapidly and do not require special training. Another benefit of acupuncture is its favorable side effect profile compared with pharmacologic techniques,
making it a reasonable adjunct to antiemetic drugs. In a large prospective survey of doctors and physiotherapists, there were no serious adverse events due to acupuncture and the risk of adverse events was 14 per 10,000 treatments, with the most common being mild, including fainting, exacerbation of symptoms, and lost or forgotten needle.124

**THERAPIES LACKING SUFFICIENT EVIDENCE**

In addition to some of the antiemetic agents mentioned previously, several other therapies that have been previously explored lack sufficient evidence or fail to demonstrate significant effect to be recommended for routine use in the management of PONV and PDNV.

Although earlier studies reported on the use of supplemental oxygen to reduce the incidence of PONV,125,126 their findings have not been confirmed by subsequent studies. A systematic review of 10 trials by Orhan-Sungur and colleagues127 reported that the relative risk of overall PONV in patients receiving 80% FiO2 was 0.91, and concluded that supplemental oxygen did not reduce the incidence of PONV. Another recent randomized trial of 304 women receiving ambulatory gynecologic laparoscopy found that there were no significant differences in PONV or antiemetic use between women receiving 80% supplemental oxygen and those in the 30% oxygen control group.128

The use of cannabinoids, including dronabinol, tetrahydrocannabinol, and nabilone, in PONV has not been well studied, and clinical data are lacking. Tramer and colleagues129 conducted a systematic review of 30 trials evaluating cannabinoids in the setting of chemotherapy-induced nausea and vomiting, and found that dronabinol had superior antiemetic activity to phenothiazines. However, the analysis failed to demonstrate statistically significant improvement in antiemetic efficacy between dronabinol and placebo, and between nabilone and phenothiazines, although the investigators did cite a “clinically significant difference” in favor of the cannabinoids and urged further study. Nevertheless, given the common and often unpleasant side effects of most cannabinoids, which include dysphoria, depression, and hallucinations, they are unlikely to be used in regular clinical practice.129

Despite its long history of use in traditional Chinese and Indian medicine, ginger (*Zingiber officinale*) does not appear to be effective for PONV. A systematic review of 6 randomized controlled trials by Ernst and Pittler was unable to draw a conclusion about the efficacy of ginger.130 Since then, there have been few additional studies, with one placebo-controlled trial of 180 patients finding that ginger failed to reduce the incidence of PONV after gynecologic laparoscopy.131

**MANAGEMENT STRATEGY**

As no single intervention can completely prevent or treat PONV, it is important to formulate multimodal approaches to maximize clinical efficacy while minimizing risks to the patient. While there is no clear formula for the prevention and management of PONV, an effective management strategy should consider (1) assessment of risk for developing PONV and baseline risk reduction, (2) prophylaxis and cost-effectiveness, (3) combination therapy, and (4) rescue treatment. Fig. 2 shows a recommended management strategy based on patient risk.

**Assessment of Risk and Baseline Risk Reduction**

As discussed earlier, the Apfel score may be a useful clinical tool in assessing patient risk. After taking these patient factors into consideration along with the surgical risk
factors for PONV, the patient’s overall risk for PONV should be determined, and the anesthesia technique should be tailored to minimize the patient’s baseline risk.

When appropriate, the use of regional anesthesia over general anesthesia can significantly reduce a patient’s risk of PONV. In high-risk patients, avoidance of volatile anesthetics and nitrous oxide through the use of TIVA with propofol may be appropriate. Two meta-analyses by Tramér and colleagues have found that avoidance of nitrous oxide reduces the risk of PONV, with an NNT of 13 to prevent early and late vomiting. It should be noted, however, that in studies with higher than average baseline risks of PONV, the investigators found that the NNT was about 5, whereas in studies in which the risk was lower than average, omitting nitrous oxide had no effect on outcome. This observation emphasizes the importance of assessing a patient’s individual risk factors before formulating an approach for the management of PONV. A separate systematic review by Tramér and Fuchs-Buder found that high-dose neostigmine (>2.5 mg) is associated with increased risk of PONV, suggesting reduction or avoidance of neostigmine as another strategy to decrease PONV risk. Baseline risk reduction may also be achieved by minimizing the use of intraoperative and postoperative opioids with nonopioid adjuncts, such as nonsteroidal anti-inflammatory drugs, cyclooxygenase-2 inhibitors, and local anesthetics.

**Prophylaxis and Cost-Effectiveness**

The cost-effectiveness of PONV prophylaxis is an important consideration in formulating a management strategy. Unfortunately, it is often difficult to gauge and compare
the cost-effectiveness of many antiemetic therapies, as cost-effectiveness analyses vary widely in terms of the antiemetic regimens they choose to evaluate, the costs they take into account, and the criteria they use in drawing a conclusion. A cost-effectiveness study by Hill and colleagues\textsuperscript{9} compared ondansetron 4 mg, droperidol 0.625 mg, droperidol 1.25 mg, and placebo, and determined that the use of antiemetic prophylaxis was more cost-effective and achieved higher satisfaction rates compared with placebo in high-risk patients. Frighetto and colleagues\textsuperscript{135} used a decision-analysis model to determine that prophylactic antiemetic therapy with dolasetron or droperidol was more cost-effective than no prophylaxis followed by subsequent rescue therapy. However, other studies have suggested that treatment of PONV may be more cost-effective than prophylaxis for patients at both low (30\%) and high (60\%) risk, due to the high efficacy of ondansetron for the treatment of established PONV.\textsuperscript{136}

Despite these conflicting data, it seems that studies comparing antiemetic therapy with placebo tend to find that using an antiemetic is more effective than placebo and preferable to no prophylaxis.\textsuperscript{137} Still, it remains unclear which antiemetic therapies are most cost-effective, what doses of medication are most cost-effective, and whether PONV prophylaxis is cost-effective for all patients or only for those at higher risk. Future studies have been encouraged to follow established guidelines for cost-effectiveness studies, such as reporting cost-effectiveness as a ratio of resource use to value of health consequences.\textsuperscript{138–140}

\textbf{Combination Therapies and Multimodal Prevention}

Because there are no single antiemetic agents that are completely effective in preventing or treating PONV, the concept of combination therapy using multiple agents has become particularly appealing. As noted earlier, the IMPACT trial found that ondansetron 4 mg IV, dexamethasone 4 mg IV, and droperidol 1.25 mg IV are equally effective as single agents for the prevention of PONV.\textsuperscript{2} Due to their established efficacy and widespread use, these 3 agents are the most commonly studied antiemetics used in combination therapy. The IMPACT trial examined the effect of various combinations of the 3 therapies, and determined that each of the 3 antiemetics acted independently, such that combinations of any 2 or 3 of them would reduce the risk of PONV in an additive manner. These findings are similar to those of various meta-analyses and systematic reviews, which have reported that combinations of 5-HT\textsubscript{3} RAs and either droperidol or dexamethasone are equally safe and effective in reducing PONV.\textsuperscript{75,87,141} A cost-effectiveness analysis by Pueyo and colleagues\textsuperscript{142} compared each of the possible 2-drug combinations of ondansetron, droperidol, and dexamethasone. The investigators found that ondansetron and droperidol is less expensive than, and as effective as, ondansetron and dexamethasone, while being more effective than droperidol and dexamethasone—albeit at a slightly increased cost. Regardless, the evidence would suggest that combination therapy using any of these 3 drugs would be a reasonable strategy for decreasing PONV risk.\textsuperscript{24}

In general, combination therapy is recommended for patients at moderate risk for PONV. For patients at high risk of PONV, combination antiemetic therapy can be used in conjunction with other pharmacologic and nonpharmacological techniques to further reduce the risk of PONV. This approach is often labeled “multimodal management” or “balanced antiemesis,” as it combines multiple therapeutic options to maximize antiemetic efficacy. Scuderi and colleagues\textsuperscript{143} reported on the use of a multimodal approach that included preoperative anxiolysis, aggressive hydration, supplemental oxygen, droperidol and dexamethasone at induction, ondansetron at the end of surgery, TIVA with propofol and remifentanil, and ketorolac, with no use of nitrous oxide or neuromuscular blockade. The multimodal approach achieved
a 98% CR rate, compared with 76% with antiemetic monotherapy using ondansetron 4 mg, and a 59% CR rate on placebo. However, the researchers did note that patient satisfaction scores were similar between the multimodal approach and monotherapy, although they were both higher than those for patients receiving placebo and rescue antiemetic therapy only.

Habib and colleagues\textsuperscript{144} have compared 3 regimens: a multimodal management strategy, which included TIVA with propofol, ondansetron, and droperidol; a combination therapy with ondansetron and droperidol, and receiving isoflurane and nitrous oxide (no TIVA); and TIVA with propofol only. The CR rates at 24 hours were 80% for the multimodal approach, 63% for the combination therapy group, and 43% for the TIVA-only group. In slight contrast to the study by Scuderi and colleagues, patient satisfaction scores were found to be highest for the multimodal approach, over both combination therapy with inhaled anesthetics or TIVA only.

**Rescue Treatment and Management of PDNV**

Even with baseline risk reduction and antiemetic prophylaxis, some patients will inevitably experience PONV or PDNV.\textsuperscript{16} Before initiating rescue antiemetic drugs, other factors that may contribute to PONV should be considered and addressed, such as pain, concomitant use of opioids or other medications, or mechanical reasons (eg, blood in the throat, abdominal obstruction, and so forth). In general, patients who have not previously received antiemetic prophylaxis should be given a 5-HT\textsubscript{3} RA, while patients who have already received prophylaxis should be given a rescue antiemetic from a different treatment class than the prophylactic drug.\textsuperscript{24} Unlike PONV prophylaxis, there are relatively few trials that have studied treatment options for established PONV. However, a systematic review by Kazemi-Kjellberg and colleagues\textsuperscript{52} has evaluated several different antiemetic regimens and found that the NNT of 5-HT\textsubscript{3} RAs for established PONV is about 4 to 5. Treatment doses of 5-HT\textsubscript{3} RAs for established PONV are generally smaller than those needed for prophylaxis: ondansetron 1 mg, dolasetron 12.5 mg (similar to the recommended prophylactic dose), and granisetron 0.1 mg. Although ondansetron 1 mg has been shown to be as effective as ondansetron 4 mg for antiemetic rescue, most clinicians tend to use the 4-mg dose in practice. It should also be noted that in patients who received a 5-HT\textsubscript{3} RA for prophylaxis, no further benefit is achieved from repeat doses in the 6 hours after the initial dose.\textsuperscript{145} In such cases, alternatives to 5-HT\textsubscript{3} RAs are recommended and include dexamethasone 2 to 4 mg, droperidol 0.625 mg, or promethazine 6.25 to 12.5 mg, although dexamethasone and transdermal scopolamine are not recommended for emetic episodes that occur more than 6 hours postoperatively, because of their longer duration of action.\textsuperscript{24}

**SUMMARY**

Although awareness has greatly increased over the past several decades and the number of available treatment options has also increased, PONV and PDNV remain a common problem of ambulatory surgery. Appropriate management of PONV begins with an assessment of risk and baseline risk reduction, followed by consideration of antiemetic prophylaxis and, if necessary, rescue treatment. In patients who are at increased risk, combination therapy or multimodal approaches is recommended in preventing PONV and PDNV. Given the brief period of time that ambulatory surgery patients are under direct medical care, it is particularly important to recognize these problems and appropriately administer longer-acting antiemetics to prevent negative medical consequences, maximize patient satisfaction and return to normal activity, and minimize health care costs.
REFERENCES


Le & Gan


Predictive Factors of Postoperative Pain After Day-case Surgery

Hans-Fritz Gramke, MD,* Janneke M. de Rijke, PhD,† Maarten van Kleef, MD, PhD,* Alfons G. H. Kessels, MD, MSc,‡ Madelon L. Peters, PhD,§ Michael Sommer, MD,* and Marco A. E. Marcus, MD, PhD*

**OBJECTIVES**

Despite the growing number of ambulatory operations knowledge of predictive factors of postoperative pain after ambulatory surgery is limited. Therefore, the aim of this study was to identify predictive factors of postoperative pain after ambulatory surgery.

**METHODS**

In this cross-sectional study, 648 patients were included. Patient characteristics, type of surgery, and type of anesthesia were recorded. In addition, preoperative expectations of postoperative pain by the patient and preoperative high risk for postoperative pain by the clinician were assessed. Finally, several scores about psychologic parameters were measured: pain catastrophizing, surgical anxiety, and optimism. Stepwise logistic regression analysis was performed to identify factors that independently predict the risk of having postoperative pain (defined by a visual analog scale > 40 mm) on days 0 to 4.

**RESULTS**

The most important predictor of postoperative pain was the presence of preoperative pain. Other predictors were anticipated postoperative pain by the patient, younger age, and fear of short-term consequences of the operation. Regional anesthetic technique compared with general anesthesia decreased the risk of acute postoperative pain only on the day of the operation.

**DISCUSSION**

Several predictive factors of postoperative pain after ambulatory surgery were identified in this study. These factors should be taken into account when planning postoperative analgesia for ambulatory surgery.

**Key Words:** predictor, postoperative pain, acute pain, day-case surgery, ambulatory surgery


Sufficient control of postoperative pain remains a difficult problem. Despite extended research on this topic prevalence of postoperative pain has not changed very much over the last 20 years. About 30% to 60% of patients still have moderate-to-severe pain after surgery.1–3 It has been demonstrated that postoperative pain can affect patient recovery after surgery as well.4 In ambulatory surgery, it is very important that patients are ready to go home in predictable and short period. Delayed discharge or hospital admission must be avoided. Postoperative pain is an important factor that can delay or even impede discharge and therefore is interfering with the concept of ambulatory surgery.5 Furthermore, ongoing postoperative pain is an important factor for not resuming work after surgery.6

Another potential consequence of acute postoperative pain is the development of persistent postoperative pain.7–10 Prevalence rates of persistent postoperative pain after common operations as high as 10% to 50% have been reported.11 A correlation of the intensity of acute postoperative pain and the risk of developing persistent postoperative pain has been described.10,12,13

A growing number of operations are performed on an ambulatory basis. In many countries, ambulatory surgery accounts for more than 50% of all elective surgeries. In the ambulatory setting good postoperative analgesia is a challenge, because patients have to control their pain at home by themselves. That is, analgesia must be effective, easy to apply, and safe. However, the prevalence of acute postoperative pain after ambulatory surgery is very high.2,14 Therefore, preoperative detection of patients at high risk for postoperative pain would be very interesting for planning a tailor-made effective postoperative analgesic regimen for these patients. Knowledge of predictors of postoperative pain could help making decisions about optimal postoperative analgesia techniques.

Earlier reports evaluated several factors of somatic and psychologic nature in hospitalized patients.15–19 Whether these data can be transferred to ambulatory operations is not clear. Despite the growing interest in ambulatory surgery only few studies on predictive factors of postoperative pain specifically focused on this kind of surgery. In addition, the studies available are relatively small and do not include psychologic factors.14,20 Therefore, we designed this study to investigate predictive factors for postoperative pain after ambulatory surgery more extensively.

**PATIENTS AND METHODS**

**Patients**

A cross-sectional study was performed. The study protocol was approved by the institutional review board of the University Hospital Maastricht, the Netherlands. During a 16-week period, we enrolled patients undergoing elective ambulatory surgery at our institution. All adult
patients scheduled for elective ambulatory surgery were approached. Excluded were patients younger than 18 years, patients with limitations of self-expression, visual dysfunction, or Dutch language problems. Patients undergoing acute surgery were not included in this study. The prevalence data of postoperative pain of this cohort of patients have already been reported elsewhere.21

**Procedure**

On arrival at the ambulatory surgery unit patients were approached by a trained research assistant who explained purpose and methods of the study. During the whole study period pain intensity was measured by using a 100 mm visual analog scale (VAS), anchored “no pain” and “worst pain I can imagine.”

The type of anesthesia was not regulated by the study protocol. General and regional anesthesia techniques were used dependent on the choice of the individual anesthesiologist and patient.

Perioperative analgesia was applied according to the standard procedure at our ambulatory surgery unit. Preoperatively either acetaminophen 1000 mg/os (PO) or naproxen 500 mg PO were administered if not contraindicated. Immediately after surgery in the Post Anesthesia Care Unit (PACU), patients were treated with intravenous bolus administration of 1 to 5 mg piritramide if necessary until their pain scored less than 40 mm on the VAS. Analgesia was continued with acetaminophen 1000 mg PO 4 times daily or naproxen 500 mg PO twice daily. For use at home, the patients were provided with tablets of acetaminophen 500 mg (box of 20 tablets) or naproxen 500 mg (box of 10 tablets) together with written instruction concerning use and dosage. Additionally, a prescription for tramadol 50 mg PO up to a maximum of 3 times daily was provided, if the combination of acetaminophen and naproxen was not expected to be sufficient. The decision to provide acetaminophen or naproxen or both or to add a prescription for tramadol was left to the anesthesiologist.

The following criteria for discharge home were applied: ambulation sufficiently possible, alert and cooperative patient, no nausea and vomiting, oral intake of fluids, micturition, no severe postoperative pain, and person for escort available.

**Data Acquisition**

After obtaining written informed consent, sociodemographic variables were recorded (age, sex, level of education). The preoperative pain intensity was measured using the VAS before giving any analgesic. Only preoperative pain related to the planned surgery was registered. In addition we asked the patients about their expectations of the intensity of postoperative pain using the VAS. At last, we roughly divided the group in minor and intermediate surgery, based on the anticipated level of postoperative pain from the clinician’s point of view (Table 1). Major surgery with anticipated severe postoperative pain, which makes a more sophisticated postoperative pain therapy necessary, is not performed in the ambulatory setting at our institution. Psychologic characteristics were assessed using questionnaires: (1) Pain Catastrophizing Scale: 13 items measuring exaggerated negative interpretation of the meaning of pain;22 (2) surgical anxiety: the “Bypass Grafting Fear Scale” by Koivula and coworkers23 was modified to fit for ambulatory surgery (cardiac specific items and 1 item referring to death were left out), measuring 9 common fears in ambulatory surgery patients; (3) Life Orientation Test: 8 items measuring the personality trait optimism.24

Pain intensity was measured by the research assistants at 1 and 2 hours postoperatively and at discharge. At discharge home, a pain diary was provided to the patients for further evaluation of pain. Again a 100 mm VAS was used. The patients were briefed to fill out the diary in the evening of the day of the operation [postoperative day (POD) 0] and then 3 times daily (9.00 AM, 3.00 PM, and 9.00 PM) until the end of POD 4. On POD 3, patients were contacted by phone to encourage them to return the diary.

<table>
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<th>TABLE 1. Anticipated Level of Postoperative Pain for the Different Types of Surgery (Clinicians Point of View)</th>
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in a special prepaid envelope. When a diary was not returned within 14 days after surgery the patient was contacted by phone again.

**Statistical Analysis**

Mean pain scores on the day of the operation and on PODs 0 to 4 (POD 1 to 4) were calculated, using the average of the 3 scores obtained from each individual on each of the days. In this analysis, a mean pain score of higher than 40 mm on a VAS was considered to indicate relevant postoperative pain.28 29

The surgical anxiety questionnaire was subjected to principal component analysis with oblimin rotation to identify its factor structure. Two components were found that explained 60% of the total variance. The first component consisted of 6 items concerning the following fears: financial consequences, adverse health effects, non-successful operation, worries about family members, being dependent of care providers, and long duration of rehabilitation. Together these items constituted a subscale that was termed “fear of long-term consequences of the operation.” The second component contained 3 items with fears concerning: the operation itself, anesthesia, and pain. This subscale was termed “fear of short-term (immediate) consequences of the operation.”

Missing values in predictor variables were imputed according to the multiple imputation (MI) method described by van Buuren et al.28 In MI, each missing value is replaced by a set of M > 1 plausible values drawn from their predictive distribution. We performed MI with M = 3, obtaining 3 complete datasets, with imputed values for short-term fear (n missing = 33; 5%), long-term fear (n = 37; 5.7%), pain catastrophizing (n = 15; 2.3%), expected pain (n = 1; 0.2%), preoperative pain (n = 1; 0.2%), and optimism (n = 37; 5.7%). On each of the 3 complete datasets stepwise multiple logistic regression analysis was performed to identify the factors that independently predicted the risk of having postoperative pain (defined by a VAS > 40 mm) on days 0 to 4 after surgery. Easily obtainable predictors were included first. In the first block 3 variables were entered using a forced entrance procedure: anticipated pain level (minor, intermediate), age (3 groups: < 45 y, 45 to 59 y, and 60 y and older), and sex. In the second block education (low, middle, high), planned 24 hours admission (yes/no), type of anesthesia (general vs. regional), and preoperative pain (preoperative VAS > 10 mm yes/no) were entered using a forward procedure. Expected pain (VAS > 40 mm) and the psychologic parameters (pain catastrophizing, short-term and long-term fear, and optimism) were entered in the third block (forward procedure). Psychologic variables were dichotomized by median split. In all steps, a P value of 0.05 was used for keeping variables in the model. Next, the results (estimates of coefficients and standard errors) of the identical analyses on each of the 3 datasets were combined28 29 to calculate overall estimates, standard errors, and 95% confidence intervals (95%CI). Predictors from step 2 and 3 were included in the final model if they were significant predictors in more than 3 datasets. The models’ ability to discriminate between patients with and without unacceptable postoperative pain was estimated by the area under the receiver operating characteristics curve (AUC) for the successive blocks.

Missing values in outcome measures (pain scores) were not imputed. However, missing data could be subject to selection processes. Therefore, we investigated with logistic regression analyses whether these missing outcomes could be predicted with available covariates (age, type of operation, sex, etc.). The results revealed some significant relationships and were used to calculate a weight factor for each case. Analyses were performed with STATA version 8 (StataCorp LP, College Station, TX) and SPSS version 12 (SPSS Inc, Chicago, IL).

**RESULTS**

Seven hundred forty-four eligible patients were approached during the study period. Six hundred and sixty patients consented to participate. Twelve patients were excluded afterward because of logistic problems and 77 patients (12%) did not return the pain diary.

Patient characteristics are shown in Table 2. A wide variety of operations were performed (general surgery, orthopedics, ophthalmology, plastic surgery, gynecology, otorhinolaryngology, urology, and oral and maxillofacial surgery). General anesthesia was used in 62% of the patients. Regional techniques were used in 38% of the patients (spinal anesthesia, peripheral nerve blocks, retrobulbar and sub-Tenon’s anesthesia, intravenous regional anesthesia). Preoperatively, analgesic medication was used by 94 patients (15%) and preoperative pain was stated by 138 patients (21%) who reported pain intensity of more than 10 mm on the VAS.

Fifty-nine patients (9%) were treated in terms of a planned short-stay admission (< 24 h). Fifteen patients (2%) were admitted to the hospital on an unplanned basis, returned to the hospital or visited their general practitioner during the postoperative course.

Blockwise multiple logistic regression analysis was used to test for significant predictors of postoperative pain

| TABLE 2. Patient Characteristics |
|--------|--------|--------|
|        | n      | %      |
| Age    |        |        |
| < 45 y | 240    | 37     |
| 45-59 y| 232    | 36     |
| > 59 y | 176    | 27     |
| Sex    |        |        |
| Male   | 281    | 43     |
| Female | 367    | 57     |
| Education |     |        |
| Elementary school (“low”) | 221 | 34 |
| Intermediate (“middle”) | 247 | 38 |
| Higher degree/ university (“high”) | 170 | 26 |
| Missing data | 10 | 2 |
| Preoperative pain |        |        |
| VAS > 10 mm | 138 | 21 |
| VAS > 30 mm | 71 | 11 |
| Analgesic use before operation |        |        |
| Acetaminophen | 39 | 6 |
| Nonsteroidal anti-inflammatory drugs | 43 | 7 |
| Weak opioids | 12 | 2 |
| None | 554 | 85 |
| Anticipated postoperative pain level, based on the type of surgery |        |        |
| Minor | 452 | 70 |
| Intermediate | 196 | 30 |
| Type of anesthesia |        |        |
| General | 400 | 62 |
| Regional | 248 | 38 |

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(defined by a VAS >40 mm) on POD 0 to 4. Separate analysis was carried out for each POD. The step 1 variables (anticipated pain level, age, and sex) yielded an AUC ranging from 0.62 (95% CI: 0.59-0.64) on POD 0 to 0.72 (95% CI: 0.63-0.80) on POD 4. Inclusion of the step 2 variables (educational level, preoperative pain, and anesthetic technique) improved the model, with an AUC ranging from 0.70 (95% CI: 0.70-0.74) on POD 0 to 0.78 (95% CI: 0.72-0.84) on POD 4. In the final step, the psychologic variables were added to the model, increasing the discriminative ability of the model to an AUC ranging from 0.77 (95% CI: 0.75-0.80) on POD 0 to 0.81 (95% CI: 0.74-0.86) on POD 4.

The results for the variables of all steps are listed in Table 3. In the final model, preoperative pain (defined by a preoperative VAS >10 mm) was most strongly associated with acute postoperative pain (VAS >40 mm) during the whole study period (Table 3) followed by anticipated pain level (anticipated by the clinician based on the type of surgery) and expected pain (by the patient). This association was not found for expected pain (by patient) on POD 2. Younger age (<45 y vs. >60 y) also increased the risk of acute postoperative pain (VAS >40 mm) in the period from POD 1 to 3. The independent variable short-term fear was only associated with acute postoperative pain (VAS >40 mm) during POD 0 to 2, and dropped out of the model for POD 3 and 4.

For the independent variables sex, level of education, anesthetic technique, long-term fear, the trait optimism (Life Orientation Test), and pain catastrophizing no consistent association with acute postoperative pain (VAS >40 mm) was found. Patients with elementary school and intermediate educational level had an increased risk of postoperative pain compared with patients with higher degree level of education only on POD 1. Regional anesthetic technique decreased the risk of acute postoperative pain only on the day of the operation. A high Pain Catastrophizing Scale elevated the risk of postoperative pain only on POD 3 score.

**DISCUSSION**

In this study, the presence of preoperative pain was the best predictor of moderate-to-severe pain at home after day-case surgery. Central sensitization of nociceptive spinal dorsal horn neurons by chronic noxious stimulation from the affected part of the body could be a possible explanation. Differences in pain thresholds provide a genetic or social explanation for the predictive value of preoperative pain possible as well. It has been demonstrated

| TABLE 3. Results of the Logistic Regression Analyses for Postoperative Pain (Visual Analog Scale >40 mm) on the Day of Operation and on Postoperative Days 1 to 4 |
|-----------------------------------------------|---------------------|---------------------|---------------------|---------------------|---------------------|
| **Independent Variable**                     | **Day of Operation**| **POD 1**           | **POD 2**           | **POD 3**           | **POD 4**           |
|                                              | **n = 644**         | **n = 581**         | **n = 581**         | **n = 581**         | **n = 581**         |
|                                              | **OR (95% CI)**     | **AUC**             | **OR (95% CI)**     | **AUC**             | **OR (95% CI)**     | **AUC**             |
| **Step 1**                                    |                     |                     |                     |                     |                     |
| Anticipated pain level                        |                     |                     |                     |                     |                     |
| Intermediate vs. minor                        | 1.4 (0.9-2.2)       | 2.0 (1.2-3.3)       | 2.2 (1.3-3.9)       | 2.9 (1.5-5.5)       | 2.6 (1.4-5.5)       |
| Age (y)                                       |                     |                     |                     |                     |                     |
| <45 vs. 60+                                   | 1.4 (0.8-2.5)       | 2.8 (1.5-5.5)       | 2.4 (1.5-5.1)       | 2.2 (1.0-5.1)       | 1.7 (0.7-4.0)       |
| 45-59 vs. 60+                                 | 1.0 (0.6-1.8)       | 2.0 (1.0-3.9)       | 1.3 (0.6-2.9)       | 1.0 (0.4-2.5)       | 0.7 (0.2-1.9)       |
| Sex                                           |                     |                     |                     |                     |                     |
| Female vs. male                               | 0.9 (0.6-1.4)       | 1.2 (0.7-2.0)       | 0.8 (0.5-1.5)       | 1.3 (0.7-2.5)       | 1.4 (0.7-2.9)       |
| **Step 2**                                    |                     |                     |                     |                     |                     |
| Level of education                            | NE                  | 2.5 (1.3-4.8)       | NE                  | NE                  | NE                  |
| Low vs. high                                  |                     |                     |                     |                     |                     |
| Middle vs. high                               | 1.5 (1.3-2.9)       |                     |                     |                     |                     |
| Preoperative pain                             | NE                  | 3.6 (2.1-6.2)       | 3.7 (2.1-6.5)       | 3.7 (1.9-7.0)       | 3.1 (1.6-6.3)       |
| Yes vs. no                                    | 3.1 (2.0-4.9)       |                     |                     |                     |                     |
| Anesthetic technique                          | NE                  |                       |                     |                     |                     |
| Regional vs. general                          | 0.4 (0.2-0.6)       | NE                  | NE                  | NE                  | NE                  |
| **Step 3**                                    |                     |                     |                     |                     |                     |
| Expected pain (VAS >40 mm)                    |                     |                     |                     |                     |                     |
| Yes vs. no                                    | 2.1 (1.4-3.2)       | 2.4 (1.5-3.9)       | NE                  | 2.7 (1.4-5.2)       | 3.0 (1.5-6.2)       |
| Short-term fear                               | 1.7 (1.1-2.6)       | 1.9 (1.2-3.2)       | 2.2 (1.3-3.8)       | NE                  | NE                  |
| High (≥9) vs. low (≤9)                        |                     |                     |                     |                     |                     |
| Long-term fear                                | NE                  | NE                  | NE                  | NE                  | NE                  |
| Optimism (LOT)                                | NE                  | NE                  | NE                  | NE                  | NE                  |
| High (≥6) vs. low (≤6)                        |                     |                     |                     |                     |                     |
| Pain catastrophizing (PCS)                    | NE                  | NE                  | NE                  | NE                  | NE                  |
| High (≥28) vs. low (≤28)                      |                     |                     |                     |                     |                     |
| Pain catastrophizing (PCS)                    | NE                  | NE                  | NE                  | NE                  | NE                  |
| High (≥11) vs. low (≤11)                      | NE                  | NE                  | 2.2 (1.1-4.6)       | NE                  | NE                  |

Step 1 used a forced entry procedure, whereas in steps 2 and 3 only significant variables (P < 0.05) entered the model (forward procedure). The AUC for each step are presented and OR and 95% CI for all variables in the final models are tabulated.

AUC indicates area under the receiver operating characteristics curves; CI, confidence interval; LOT, Life Orientation Test; NE, variable not in the equation; OR, odds ratio; PCS, Pain Catastrophizing Scale; POD, postoperative day.
that patients with lower pain thresholds will have more intense postoperative pain.\textsuperscript{30} In addition, psychologic effects due to preoperative pain could play a role: for example, an effect on preoperative anxiety. In a report about predictors of postoperative pain in hospitalized patients, preoperative anxiety levels correlated highly with postoperative pain. In addition, the level of preoperative pain was found to be an independent predictor of severe postoperative pain in the immediate postoperative period in this investigation (within the first hour after arrival at the PACU).\textsuperscript{16}

Contradictory results are reported in the literature regarding preoperative expectations of postoperative pain (by the patient) contrary results are reported in the literature. In our study, the results of the logistic regression analysis showed a positive association between preoperative expectations of pain and the de facto occurrence of postoperative pain. A recent report of Mamie et al\textsuperscript{18} showed a predictive value of preoperative pain expectations as well. However, a validation procedure in a second patient group did not confirm these results. Preoperative expectation of pain is a parameter, which is influenced by many factors like previous experiences with surgery, memory, psychologic profile, and anxiety state of the patient. Besides, different definitions of “preoperative expectation of pain” are used in the different publications.\textsuperscript{18,31} For example, in our study we used, a quite distinct definition of “expectation of pain,” an expected VAS greater than 40 mm, others used less specific definitions like expectation of low or high postoperative pain.\textsuperscript{18}

Thus, contradictory results are not surprising and the clinical importance of this parameter is still difficult to evaluate.

The anticipated level of pain by the clinician also correlated well with postoperative pain in our study, indicating that clinicians are not completely ignorant about how much pain to expect after ambulatory surgery. Previous reports showed indeed that certain types of surgery are correlated with more postoperative pain than others.\textsuperscript{16,20} Example high levels of postoperative pain are commonly reported after orthopedic surgery, whereas levels of postoperative pain after cataract surgery are very low.\textsuperscript{20} A criticism may be that the anticipation of severe pain could have influenced the choice of anesthesia technique and postoperative analgesic treatment. This implicates a potential for confounding regarding postoperative pain and the interpretation of patient factors. We tried to minimize this by standardizing the postoperative pain treatment as much as possible.

Many investigations on postoperative pain after day-case surgery did not include the age of the patient into their analysis\textsuperscript{2,32,34} or did not find an association between age and postoperative pain.\textsuperscript{14} However, our results indicate that younger patients (< 45 y) are more likely to experience at least moderate pain (VAS > 40 mm) in the postoperative course. Age-related changes of pharmacokinetic and pharmacodynamic variables such as volume of distribution of opioids and sensitivity to antinociceptive effects of opioids could explain this phenomenon in part.\textsuperscript{35} Furthermore, experiences with postoperative pain from previous operations could influence expectations of the patients about postoperative pain. Finally, differences in activity level between age groups are another explanation for the higher risk of postoperative pain in the younger age group, as younger patients probably tend to resume activities like work or taking care of children sooner than the older age groups. These differences in activity level are not taken into account by the VAS.

Sex as a predictive factor for postoperative pain has been investigated in previous studies with conflicting results.\textsuperscript{14,18} In our study, sex was not an independent predictor for postoperative pain. Surprisingly, anesthetic technique is not considered in many reports on predictors of postoperative pain. In our study, regional techniques decreased the risk of acute postoperative pain on the day of the operation, which can be explained by residual blockade. However, this protecting effect of loco-regional techniques was not seen on the other days.

Previous reports showed a correlation of several psychologic parameters with postoperative pain. Preoperative anxiety, pain catastrophizing, and neuroticism were predictive factors for postoperative pain in previous investigations.\textsuperscript{19,36,37} Most of these studies investigated hospitalized patients and so not much data about psychologic parameters and postoperative pain after ambulatory surgery are available. Our study showed only limited associations of psychologic factors and postoperative pain in ambulatory patients. Fear of short-term consequences of the operation was associated with postoperative pain (POD 0 to 2). Pain catastrophizing increased the risk for postoperative pain only on POD 3. The other psychologic factors we tested showed no association with postoperative pain. Possibly, ambulatory surgery causes less emotional distress than “major” surgery in combination with hospitalization. This could be one contributing factor to the lesser impact of psychologic parameters on postoperative pain after ambulatory surgery.

The influence of the educational level on postoperative pain has received little investigation. Lower educational level was a significant predictor for postoperative pain after elective gallbladder surgery in a previous report.\textsuperscript{37} It has been suggested that differences in character trait and ability to cope with the pain could be the reason for this association. However, in the present investigation educational level was a significant predictor of postoperative pain only on POD 1. So, only a limited predictive value of this factor in ambulatory patients has been shown. The impact of postoperative pain on quality of life and functional status is an important aspect, which was not investigated in this study and should be considered in future research.

In conclusion, the present study shows the results of a large cohort of day-case surgery patients with a 4-day postoperative follow-up. The best predictor of postoperative pain in this population was the presence of preoperative pain. Other predictors were anticipated postoperative pain by the clinician, preoperative high expectations of postoperative pain by the patient, younger age, and fear of short-term consequences of the operation. Most of these factors are easily detectable and should be taken into account when planning postoperative analgesia for ambulatory surgery.

REFERENCES


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Preoperative screening, evaluation, and optimization of the patient's medical status before outpatient surgery

Bobbie Jean Sweitzer

Anesthesia and Critical Care, University of Chicago, Anesthesia Perioperative Medicine Clinic, Chicago, Illinois, USA

Correspondence to Bobbie Jean Sweitzer Director, Anesthesia Perioperative Medical Clinic, Associate Professor of Anesthesia and Critical Care, Associate Professor of Medicine University of Chicago, Chicago, IL 60637, USA


Purpose of the review
Preoperative evaluation and optimization of a patient’s medical condition are important components of anesthesia practice. With ever increasing numbers of patients with serious comorbidities having complex procedures as outpatients, the task of gathering information and properly preparing for their care is challenging. Improvements in assessment and management can potentially reduce adverse events, improve patient and caregiver satisfaction, and reduce costs.

Recent findings
A growing body of literature and evidence-based practices and guidelines can assist clinicians who work in the expanding field of preoperative medicine. Care providers from various specialties in medicine are developing innovative methods, tools, and knowledge to advance science and processes. Data-driven practices are beginning to close the information gap that has plagued this field of medical practice.

Summary
Preparation of patients before surgery is a necessary and vital component of perioperative medicine. Practices are developing to guide effective interventions that benefit patients and healthcare systems. Outpatients present special challenges to preoperative assessment.

Keywords
ambulatory surgery, anticoagulation, antiplatelets, bridging therapy, cardiac evaluation, consultation, coronary stents, outpatient surgery, preoperative evaluation, sleep apnea, testing

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Introduction
The Australian Incident Monitoring Study found that 11% of reports identified inadequate or incorrect preoperative assessment (478 of 6271) or preparation (248 of 6271) of patients that accounted for 3.1% (197) of adverse events [1]. More than half of the incidents were considered preventable, and an additional 21% were possibly preventable. There were 23 cases of major morbidity, and seven patients died. When the American Society of Anesthesiologists (ASA) published a practice advisory for preanesthesia evaluation in 2002, the task force concluded that adequately controlled studies for such evaluation were lacking [2]. This review of more recent publications demonstrates that the deficiency is gradually being corrected.

Cardiac evaluation
One of the most important documents for preoperative evaluation is an update of the guidelines for cardiac evaluation of patients before noncardiac surgery published by the American College of Cardiology and American Heart Association (ACC/AHA) [3**]. Recommendations for noninvasive stress testing, cardiac catheterization, and revascularization have been reduced. The revision was driven by the recognition that percutaneous coronary intervention (PCI), especially with vascular stents, is associated with greater perioperative risk if antiplatelet therapies are discontinued. Medical management alone may decrease adverse events, and frequently unpredictable rupture of coronary plaque, minor lesions, or thrombus is the culprit in 50% of fatal myocardial infarctions (MI) perioperatively [4**]. The ACC/AHA guidelines are organized according to steps. Strategies are suggested by the first step that applies to a patient without the need to progress through the entire algorithm (Fig. 1).

Step 1 considers emergency surgery only. Step 2 considers an active cardiac condition such as an acute MI, unstable or severe angina, decompensated heart failure, severe valvular disease (e.g. severe aortic stenosis), or significant arrhythmias (e.g. ventricular tachycardia or atrial fibrillation).
fibrillation with a rapid rate). These conditions warrant postponement for all except life-saving emergencies. Traditionally patients who have had an MI within the previous 3–6 months were not considered for elective surgery. More recent evidence suggests that an acute MI, occurring within the past 7 days, warrants postponing nonurgent surgeries. A recent MI, within the past 8–30 days with evidence of myocardium at risk (because of persistent symptoms or the results of stress testing) is a high-risk or active cardiac condition. However, a recent MI without evidence of myocardium at risk is considered equivalent to a history of coronary artery disease (CAD).

Step 3 considers the surgical severity. Patients without active cardiac conditions who need low-risk surgery, such as endoscopic or superficial procedures or outpatient surgery with a cardiac risk of generally less than 1%, do not need cardiac testing before surgery. Step 4 assesses the patient’s functional capacity. Asymptomatic patients with an average exercise capacity (can walk up two flights of stairs or four blocks) can proceed to surgery.

Step 5, the last and most complicated, considers patients with poor or indeterminate functional capacity scheduled for vascular, intermediate-risk procedures, or high-risk procedures. The number of clinical predictors alters the recommendations for, and likely the benefit of, cardiac testing. The clinical predictors were derived from the Revised Cardiac Risk Index (RCRI), which identifies ischemic heart disease, heart failure, cerebrovascular disease, diabetes, and renal insufficiency as serious comorbidities. A cohort study showed an incidence of major cardiac events of 0.4%, 0.9%, 7%, or 11% in patients with 0, 1, 2, or 3 risk predictors, respectively [5]. Patients with none of the clinical predictors proceed to surgery. Patients with three or more RCRI factors who need major vascular surgery are most likely to benefit from further testing. The guidelines recommend further testing only ‘if it will change management.’ Patients with one or two clinical predictors who need intermediate-risk surgery (1–5% risk of cardiac complications; orthopedic or intraabdominal procedures) or vascular surgery can proceed to surgery if heart rate is controlled or undergo
Noninvasive stress testing, catheterization, and coronary revascularization before noncardiac surgery lack definitive benefits for risk reduction. The ACC/AHA guidelines state, 'review of the literature suggests that PCI before noncardiac surgery is of no value in preventing perioperative cardiac events, unless indicated for an acute coronary syndrome.' The only randomized prospective study of revascularization [coronary artery bypass grafting (CABG) or PCI] vs. medical management before noncardiac procedures failed to show a difference in outcome [6]. Optimal medical management in stable, multivessel disease has been shown to be superior to revascularization in nonoperative studies [7,8].

The benefit of β-blockers, especially in patients at low-cardiac risk, is controversial [9*,10]. The only ACC/AHA class I recommendation for perioperative β-blocker therapy for patients having low-risk surgery or intermediate-risk surgery is to continue these drugs in patients who are already taking them. Starting β-blockers in patients scheduled for intermediate-risk surgery who have known ischemic heart disease or one or more RCRI predictors received a class II recommendation [3**]. The POISE (Percutaneous Ischemic Evaluation) trial showed both benefit and harm from β-blockers [11*]. Cardiac death, nonfatal MI, and cardiac arrest were reduced with metoprolol compared with placebo [5.8 vs. 6.9%; hazard ratio, 0.84; 95% confidence interval (CI), 0.70–0.99; P = 0.04]. Overall mortality and stroke, however, increased. Stroke was more common in patients with perioperative hypertension, bleeding, atrial fibrillation, or a history of cerebrovascular disease who received metoprolol. An editorial that accompanied the article highlights some of the study design issues that may have contributed to these findings [12**].

A prospective observational study of preoperative ECGs obtained in patients aged 50 years or older who had noncardiac surgery showed that abnormalities in the ECG did not improve prediction beyond risk factors identified by patient history [13*]. Abnormalities were found in 45% of the ECGs, and bundle branch blocks (right and left) were associated with postoperative MI and death but had no added predictive value over clinical risk factors. Many imaging tools are available to evaluate cardiac patients, including those that have been validated in patients who had noncardiac surgery, but others are just beginning to be implemented and await further studies. A comprehensive review of this subject includes a description of cardiac computed tomography, MRI of the heart, echocardiography, and stress testing [14*].

Recent percutaneous coronary intervention with or without stenting

Unplanned surgery in a patient with a recent PCI is a special challenge, especially in managing antplatelet therapies. Noncardiac surgery soon after revascularization (CABG or PCI with or without stents) is associated with high rates of perioperative morbidity and mortality [15*]. It may not be appropriate to care for some of these patients in facilities without immediate access to interventional cardiology. Patients who need noncardiac surgery within a year of revascularization are not good candidates for implantation of drug-eluting stents (DES). If preoperative revascularization is necessary, or in patients who need revascularization and are likely to require invasive procedures within the next 12 months, CABG or PCI without stenting or with a bare metal stent (BMS) should be considered [4**].

A joint advisory from the ACC, AHA, and the American College of Surgeons highlighted the importance of dual antiplatelet therapy and the risk of premature discontinuation with the following recommendations for prevention of premature discontinuation of dual antiplatelet therapy in patients with coronary artery stents [4**].

1. In patients who are undergoing preparation for percutaneous coronary intervention and are likely to require invasive or surgical procedures within the next 12 months, consideration should be given to implantation of a bare-metal stent or performance of balloon angioplasty with provisional stent implantation instead of the routine use of a DES.

2. Patients should be specifically instructed before hospital discharge to contact their treating cardiologist before stopping any antiplatelet therapy, even if instructed to stop such therapy by another healthcare provider.

3. Healthcare providers who perform invasive or surgical procedures and are concerned about periprocedural and postprocedural bleeding must be made aware of the potentially catastrophic risks of premature discontinuation of thienopyridine therapy. Such professionals who perform these procedures should contact the patient’s cardiologist if issues regarding the patient’s antiplatelet therapy are unclear, to discuss optimal patient management strategy.

4. Elective procedures for which there is significant risk of perioperative or postoperative bleeding should be
deferred until patients have completed an appropriate course of thienopyridine therapy (12 months after DES implantation if they are not at high risk of bleeding and a minimum of 1 month for bare-metal stent implantation).

(5) For patients treated with DES 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.

An excellent general review of coronary stents and the perioperative management of stents and antiplatelet therapy has been published [16**]. In another review, an algorithm for the management of antiplatelet therapies was proposed based on the risk of adverse cardiac events with that of bleeding in different types of surgery [17**]. This study highlighted evidence questioning the tradition of routinely discontinuing aspirin therapy for secondary prevention (after MI, stenting, stroke or cerebrovascular disease, or CAD) except for intracranial surgery.

Patients taking anticoagulants for the long term

The risk of bleeding in patients who continue to take anticoagulants must be balanced against the risk of thromboembolism if therapy is stopped and the costs and inconvenience of providing short-acting anticoagulants such as unfractionated or low molecular weight heparin (LMWH). The ACC/AHA guidelines recommend briefly reducing the international normalized ratio to the low or subtherapeutic range for minimally invasive procedures (dental work or superficial biopsies) and resuming the usual dose of oral anticoagulation immediately after the procedure [3**]. If the risk of bleeding with continued oral anticoagulation is high or the risk of thromboembolism without anticoagulation is high, the guidelines recommend heparin perioperatively. Others have found that oral surgeries can be performed safely in patients who continue taking oral anticoagulants [18] or that the risk of thromboembolism is low when warfarin therapy is interrupted for 5 days or less in patients who undergo minor, outpatient procedures [19*]. Prospective studies of the impact of periprocedural bridging therapy with LMWH have documented its safety in patients who required invasive procedures necessitating interruption of oral anticoagulants. Even in a large cohort of patients with mechanical heart valves, only one major bleeding and no thromboembolic complications occurred periprocedurally [20]. Bridging therapy in patients with atrial fibrillation or deep venous thrombosis resulted in a low incidence of bleeding after minor surgery or invasive procedures [21].

Patients with or at risk for sleep apnea

Obstructive sleep apnea (OSA), a common disorder (in 2–26% of the population) that is frequently undiagnosed or not treated, is associated with perioperative morbidity and mortality [22**]. Approximately 80% of men and 93% of women do not know they have OSA. The Berlin questionnaire, a widely used screening tool for OSA with 11 questions, was developed for a primary care population [23]. Another checklist of 12 items to elicit OSA was developed by ASA consensus [24]. Both of these tools were validated for the first time in a preoperative population by Chung et al. [22**,25*]. A simple questionnaire was developed and validated in a preoperative clinic by this same group [22**]. Four questions ask about snoring, tiredness during the day, observed apnea, and high blood pressure (STOP). The sensitivity of the STOP questionnaire (Fig. 2) was 65.6, 74.3, and 79.5% for mild, moderate, and severe OSA, respectively. Combined with body mass index (BMI), age, neck size, and gender the STOP-Bang scoring model (Fig. 3) had a sensitivity of 83.6%, 92.9%, and 100% for mild, moderate, and severe OSA, respectively, and a negative predictive value of more than 90% for patients with moderate-to-severe OSA. All three tools had a moderately high sensitivity for screening for OSA; the STOP questionnaire and the ASA checklist identified patients likely to develop postoperative complications [25*].

OSA is diagnosed with polysomnography, which is costly and time-consuming. When a screening protocol was used in a preoperative anesthesia clinic followed by home nocturnal oximetry in patients suspected to have OSA, patients who had oxygen desaturation five or more times per hour had significantly higher rates of postoperative complications than those with fewer desaturation episodes [26*]. In one review of preoperative management of patients with OSA, Mickelson [27] considered the appropriate surgical facility, preoperative use of continuous positive airway pressure, and preoperative medical consultation.

Evaluation of specific comorbid conditions

The worldwide epidemic of obesity continues to push the limits of anesthetic and surgical practices. More overweight patients are undergoing outpatient surgeries such as laparoscopic adjustable gastric banding even in the super-obese (BMI ≥ 50) [28]. Assessment before bariatric surgery includes laboratory tests, medical history, physical findings, and consideration of contraindications to surgery such as cognitive impairment, active cancer, advanced liver disease with portal hypertension, unstable CAD, and uncontrolled severe OSA with pulmonary hypertension [29,30].
Figure 2 STOP questionnaire

<table>
<thead>
<tr>
<th>Height ____ inches/cm</th>
<th>Weight ____ lb/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ____ Male/Female</td>
<td>BMI ____</td>
</tr>
<tr>
<td>Collar size of shirt: S, M, L, XL, or ____ inches/cm</td>
<td>Neck circumference* ____ cm</td>
</tr>
</tbody>
</table>

1. Snoring: Do you snore loudly (louder than talking or loud enough to be heard through closed doors)? Yes No
2. Tired: Do you often feel tired, fatigued, or sleepy during daytime? Yes No
3. Observed: Has anyone observed you stop breathing during your sleep? Yes No
4. Blood pressure: Do you have or are you being treated for high blood pressure? Yes No
5. BMI: BMI more than 35 kg/m²? Yes No
6. Age: Age over 50 years old? Yes No
7. Neck circumference: Neck circumference greater than 40 cm? Yes No
8. Gender: Gender male? Yes No

* Neck circumference is measured by staff.

High risk of OSA: answering yes to two or more questions
Low risk of OSA: answering yes to less than two questions

BMI, body mass index; cm, centimeter; kg, kilogram; L, large; lb, pounds; M, medium; OSA, obstructive sleep apnea; S, small; XL, extra.

Adapted with permission from [22**].

Few studies have defined perioperative outcomes for patients with pulmonary hypertension. In one cohort study, patients with pulmonary hypertension who had low-risk noncardiac procedures or intermediate-risk noncardiac procedures had significantly more postoperative heart failure (9.7 vs. 9%), delayed extubation (21 vs. 3%), in-hospital deaths (9.7 vs. 0%), and overall major adverse events (24 vs. 3.2%) than patients without pulmonary hypertension [31**].

Recent progress has been made in establishing evidence-based guidelines for the evaluation of patients with pulmonary disease to predict risk for postoperative pulmonary complications and to introduce risk-reduction strategies [32]. At-risk patients should be identified and modifiable risk factors need to be aggressively managed preoperatively [33*].

Airway evaluation

A study from France confirmed that difficult tracheal intubation was more frequent in obese (BMI ≥ 30) than in lean (BMI < 30) individuals [34**].

More importantly, the investigators found that thyromental distance, neck circumference and a Mallampati score of 3 or higher were additional predictors that improved upon BMI alone. A retrospective review compared difficulties with mask ventilation, laryngoscopy, and intubation in patients with a history of cervical spine limitation.

Figure 3 The STOP-Bang scoring model

| 1. Snoring: Do you snore loudly (louder than talking or loud enough to be heard through closed doors)? Yes No |
| 2. Tired: Do you often feel tired, fatigued, or sleepy during daytime? Yes No |
| 3. Observed: Has anyone observed you stop breathing during your sleep? Yes No |
| 4. Blood pressure: Do you have or are you being treated for high blood pressure? Yes No |
| 5. BMI: BMI more than 35 kg/m²? Yes No |
| 6. Age: Age over 50 years old? Yes No |
| 7. Neck circumference: Neck circumference greater than 40 cm? Yes No |
| 8. Gender: Gender male? Yes No |
| High risk of OSA: answering yes to three or more items |
| Low risk of OSA: answering yes to less than three items |
| cm, centimeter; lb, pounds; kg, kilogram; BMI, body mass index; OSA, obstructive sleep apnea; m, meters |

Adapted with permission from [22**].
The authors found a higher incidence across the entire spectrum of airway management in patients with limited cervical spine mobility, although the effect on mask ventilation was found only in patients at least 60 years old.

**Pregnancy testing**

Elective surgery is almost universally postponed for pregnant women, but controversy remains regarding the impact of anesthesia and surgery on pregnancy. After implementing a policy of routinely administering a pregnancy test to all women of child-bearing age, who were given the option of refusing the test after being advised of the risks, the incidence of newly diagnosed pregnancies on the day of surgery was 0.15% (95% CI 0.003–0.31), the incidence of false positives was 0.30% (95% CI 0.10–0.552), and the positive predictive value of a urine human chorionic gonadotrophin (hCG) was 50% [36]. The negative predictive value was not calculated, and the cost was $5.03 per urine test. In all but one woman with a positive test, the history stating time since last menses was either unavailable (did anyone ask?) or compatible with the test results, including false-positive results in periomenopausal women. The one case in which the history alone was not compatible with pregnancy was in a woman who had a spontaneous abortion. The design of this study did not allow comparison of an accurate patient history vs. routine pregnancy testing.

**Perioperative risk**

Using data from the Agency for Healthcare Research and Quality, Fleisher et al. [37**] developed an outpatient surgery admission index to identify patients at higher risk than normal of immediate, unplanned admission to the hospital. One point was assigned to the following identified risk predictors: age at least 65 years, duration of operating time at least 120 min, cardiac diagnoses, peripheral or cerebrovascular diseases, malignancy, human immunodeficiency virus positivity, or regional anesthesia. Two points were assigned to the use of general anesthesia because of the high odds ratio (11.94; 95% CI 10.41–13.70). For patients with scores of four or higher, the odds ratio was 31.96 (95% CI 26.29–38.86) and 2.8% of these patients required admission. A study from the United Kingdom identified age as a predictor of postoperative admission for pain control after day-case arthroscopic shoulder surgery [38]. Age at least 50 years adversely affected the same-day discharge of patients having laparoscopic cholecystectomies [39].

Most anesthesiologists are familiar with a visual analogue scale (VAS) for assessment of pain and nausea or for quantification and comparison. In a prospective study, surgeons’ predictions of major perioperative complications via a VAS were as useful as other well known indicators of risk such as age and duration of surgery [40].

**Logistics of preoperative evaluation**

The percentage of Dutch hospitals with an outpatient preoperative clinic increased from 50% in 2000 to 74% in 2004, and a survey found that a lack of financing and shortage of anesthetists to staff them were the most limiting factors [41]. Satisfaction with preoperative evaluation was highest among respondents in facilities in which all adult patients who had elective procedures were evaluated under supervision of an anesthetist, and satisfaction was lowest without a preoperative clinic. Improved logistics in the preoperative pathway was mentioned as the best benefit, and anesthetists attributed more benefits to the clinics than did internists or surgeons. A shortage of anesthetists was the most common reason for limiting preoperative clinic time to certain subgroups of patients. In the 33 hospitals without a clinic, implementation had been discussed and one-third had already made a decision to start a clinic.

Little research has been done on the design of appointment systems for preoperative clinics [42]. Time to appointment and patient waiting times in a preoperative assessment clinic can be reduced by grouping appointments according to patients’ ASA physical status or by using simulation models to test different methods [43].

In a multicenter prospective study from Italy, patient satisfaction was improved by providing patients with an anesthesia information leaflet preoperatively [44]. To objectively measure patients’ experiences with a preoperative clinic, Edward et al. [45] developed and validated a questionnaire, Patient Experiences with the Preoperative Assessment Clinic. When they used the questionnaire to solicit patients’ opinions after a clinic visit, they found wait time was the most problematic and the experience with the nurse the most favorable [46].

**Consultations**

In some practices and locales, medical consultation before surgery is almost routine. Yet few data support the necessity or the purpose of this exercise. In an observational cohort study, patients who had surgery and a medical consultation by a generalist did not have better quality of care (no improvement in glucose control, use of perioperative β-blockers, or prophylaxis for venous thromboembolism), and costs or length of stay did not differ compared with a matched group of patients without medical consultation [47]. A survey of surgeons in Canada regarding the perioperative role of internists revealed discrepant opinions about the need for a consultant to discuss risk with the patient [48]. The most common reasons prompting a medicine consult was the presence of, or risk factors for, cardiovascular disease or a
Conclusion
Preoperative evaluation and optimization of a patient’s medical condition before surgery can be challenging. An increasing body of evidence in the literature shows that best practices are improving care and processes to deliver this care. Preoperative medicine is an evolving subspecialty with an exciting future.

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. 811).


Guidelines for cardiac evaluation including recommendations for patients with hypertension, heart failure, valvular disease, cardiomyopathies, arrhythmias, conduction abnormalities, pacemakers and implantable cardioverter-defibrillators.


12 Fleisher LA, Poldermans D. Perioperative beta-blockade: where do we go from here? Lancet 2008; 371:1813–1814. Editorial according to publication of the POISE trial outlining the study’s design flaws and reviewing the risks and benefits of perioperative β-blockers.

13 van Kée WA, Broyson GL, Yang H, et al. The value of routine preoperative electrocardiography in predicting myocardial infarction after noncardiac surgery. Ann Surg 2007; 246:165–170. Showed that even though bundle branch blocks on preoperative electrocardiograms were associated with postoperative morbidity and mortality there was no added value beyond clinical predictors from the patient history.


Early surgery and antiplatelet discontinuation in patients with bare metal stents having noncardiac surgery was associated with an increase in perioperative cardiac events.


22 Chung F, Yegneswaran B, Liao P, et al. STOP questionnaire. A tool to screen patients for obstructive sleep apnea. Anesthesiology 2008; 108:812–821. This study developed and validated a simple questionnaire consisting of four questions related to snoring, tiredness during the day, observed apnea and high blood pressure (STOP) for screening for sleep apnea in surgical patients.


26 Hvarg D, Shaker N, Linnam B, et al. Association of sleep-disordered breathing with postoperative complications. Chest 2008; 133:1128–1134. This study showed that home nocturnal oximetry in patients with clinical features of obstructive sleep apnea is associated with an increased rate of postoperative complications.


Ambulatory anaesthesia


One of the few studies in the literature to examine the risk of surgery (including minor procedures) in patients with pulmonary hypertension.


Review of predictors to identify patients at risk for postoperative pulmonary complications and proven risk-reduction strategies.


Study identifying increased neck circumference (more than 43 cm) along with BMI, thyromental distance and Mallampati score 3 as predictors of difficult intubation.


Report of results of pregnancy testing on the day of surgery in a cohort of patients presenting for orthopedic procedures.


Using an administrative database this study identified predictors of which individuals were at highest risk for hospital admission immediately following ambulatory surgery.


A survey of anesthetists, surgeons, internists and administrators in Dutch hospitals regarding availability and benefits of preoperative anesthesiology clinics.


This study failed to show a benefit of medical consultation in surgical patients having major procedures, so it is unlikely such consultation would benefit patients undergoing outpatient surgery.

Recovery after ambulatory anesthesia
Janet D. Pavlin and Christopher D. Kent

Purpose of review
The purview of ambulatory anesthesia continues to broaden in response to national interest in controlling healthcare costs and eliminating unnecessarily expensive hospital stays. Recent advances in anesthesia allow us to minimize side effects and complications of anesthesia and surgery that might otherwise delay recovery and discharge. The purpose of this review is to highlight some of these latest advances in clinical care that may soon change how we practice.

Recent findings
In many instances, hospitalization has been necessary to permit adequate control of pain and opioid-related side effects after surgery. A variety of multimodal analgesic techniques are described in this review (including alpha-2 agonists, beta-blockers, corticosteroids, cyclo-oxygenase 2 inhibitors, and regional anesthetic blocks) that reduce requirements for opioids, thereby eliminating some of the undesirable opioid-related side effects. New antiemetic recommendations are included for management and prevention of postoperative nausea and vomiting. In addition, novel ways of reversing the effects of some anesthetic drugs (inhalational anesthetics and muscle relaxants) are described.

Summary
The research and advances in clinical care described will likely influence how we manage our patients in the future, eliminating the need for prolonged hospital stay after surgery.

Keywords
ambulatory anesthetic recovery, postoperative analgesia, postoperative nausea and vomiting

Introduction
The article reviews recent literature pertaining to developments that may improve the process of recovery from ambulatory anesthesia. Included are reports about new drugs or techniques for maintaining anesthesia and for eliminating or reversing anesthetic effects. Additional attention is devoted to the perioperative management of pain and emetic symptoms that commonly delay recovery after ambulatory surgery.

Anesthetic drugs
Research on new medications and creative approaches to the utilization of familiar anesthetic agents hold promise for improvements to ambulatory anesthetic recovery.

Dexmedetomidine
Dexmedetomidine produces sedation, anxiolysis, and analgesia with limited respiratory depression [1*]. Alhashemi [2] reported improved patient satisfaction but prolonged recovery after dexmedetomidine compared with midazolam sedation during cataract surgery (45 vs. 21 min). Ayoglu et al. [3] using a loading dose of dexmedetomidine 1µg/kg followed by patient-controlled dexmedetomidine sedation found no increase in recovery times when compared with no sedation but noted that intraocular pressure was favorably reduced with dexmedetomidine. Other studies examining its use for sedation during shockwave lithotripsy [4], third molar extraction [5], endoscopic sinus surgery [6], or electroconvulsive therapy [7] were underpowered for the evaluation of major safety outcomes but reported no differences in recovery profile, beyond a tendency toward lower blood pressure and heart rate in the patients treated with dexmedetomidine. The most significant role for dexmedetomidine may be for sedation in patients at high risk for complications from respiratory depression.

Remifentanil
The conclusions of a systematic review of 85 trials ($n = 13057$ patients) comparing remifentanil with other short-acting opioids (fentanyl, alfentanil, or sufentanil) for balanced anesthesia were that bradycardia and...
hypotension were more common intraoperatively, respiratory events requiring naloxone were less common during recovery, and remifentanil is not generally advantageous in most patients but may be useful in selected patients at risk for respiratory complications [8*].

Inhalational anesthetics
Rates of emergence delirium and agitation in children and rates of recovery in the elderly were reported to be similar with sevoflurane and isoflurane [9,10]. The Evaluation of NitrOxide in the Gas Mixture for Anaesthesia (ENIGMA) trial reported lower rates of major complications and severe postoperative nausea and vomiting (PONV) [odds ratio (OR) 0.5; 95% confidence interval (CI) 0.31–0.51] after inpatient surgery in 2050 patients randomly assigned to 80% of O₂; 20% nitrogen when compared with 70% nitrous oxide (N₂O); 30% oxygen. The complications endpoints included pneumonia, pneumothorax, pulmonary embolism, wound infection, myocardial infarction, venous thromboembolism, stroke, awareness, and death within 30 days.) An additional concern regarding N₂O has been raised by Culley et al. [11*], who reported that 70% N₂O profoundly, but transiently, reduced the activity of cortical methionine synthase and produced lasting impairment in spatial working memory in aging rats. It is unclear whether either of these studies is relevant to nitrous oxide use for short outpatient surgery.

Drugs/techniques for accelerated elimination or reversal of anesthetic effects
Two of the most recent advances in anesthetic recovery represent attempts to rapidly reverse anesthetic effects.

Sugammadex
Sugammadex is a synthetic γ cyclodextrin that combines with rocuronium to permit rapid reversal of neuromuscular blockade. De Boer et al. [12*] demonstrated reversal of profound rocuronium-induced muscle paralysis within 0.7–6.9 min after patients received sugammadex, 12–16 mg/kg administered 5 min after rocuronium 1.2 mg/kg. Pending approval by the US Food and Drug Administration (FDA), the expectation is that it may permit use of rocuronium for cases requiring rapid induction or complete paralysis throughout surgery or both, without concern for being able to reverse neuromuscular blockade at the end of surgery.

Isoflurane hyperpnoea
Previous studies by Vesely et al. [13] demonstrated the utility of hyperventilating patients at the end of an isoflurane anesthetic (up to two to three times the intraoperative level of ventilation) to speed up elimination of the inhalational anesthetic while maintaining PaCO₂ at 45–50 mmHg (isoflurane hyperpnoea). Katznelson et al. [14] have extended these observations to patients undergoing sevoflurane anesthesia. Time to extubation was shortened from 12.3 to 6.2 min (P = 0.047), and eligibility for discharge from 90.6 to 67.2 min (P < 0.01).

Analgesic techniques
Uncontrolled pain and opioid-related side effects are major contributors to delayed recovery after ambulatory surgery [15]. Gramke et al. [16*] recently reported that 26% of outpatients had moderate-to-severe pain [mean visual analogue scale (VAS) scores > 40 out of 100 mm] on the day of surgery, declining to 21, 13, and 10% on days 1–3, respectively. Numerous studies suggest that multimodal analgesia using nonsteroidal anti-inflammatory drugs (NSAIDs), beta-blockers, N-methyl D-aspartate (NMDA) inhibitors, steroids, and alpha-2 agonists is potentially the best way to address the problem of moderate-to-severe postoperative pain.

NSAIDS
NSAIDS and cyclo-oxygenase 2 (Cox-2) inhibitors in particular are known to reduce opioid requirements and improve pain control after surgery without compromising hemostasis. Most Cox-2 inhibitors have been removed from the market in the United States because of an increased risk of cardiovascular thrombotic complications with their long-term use. However, as suggested by Joshi et al. [17], the benefits of short-term perioperative use in patients without cardiovascular risks probably outweigh any potential adverse effects.

Recently, White et al. [18**], reported that celecoxib 400 mg orally (p.o.) initiated in the recovery room and 200 mg twice daily (b.i.d.) for 3 additional days after outpatient laparoscopy was associated with improved pain scores, higher patient satisfaction, earlier return of bowel activity, and earlier resumption of activities of daily living when compared with placebo. Similarly, celecoxib 400 mg initially followed by 200 mg b.i.d. for 14 days decreased pain, opioid use, PONV, and recovery room length of stay after anterior cruciate ligation repair [19**] and longer term decreased flexion contractures, and scar tissue requiring rearthroscopy [20**].

Beta-Blockers
Collard et al. [21] reported decreased postoperative fentanyl requirements, PONV, and time to discharge after an intraoperative infusion of esmolol (5–15 µg/kg/min) compared with a standardized anesthetic for laparoscopic cholecystectomy. In an earlier study, Coloma et al. [22] similarly found lower rates of PONV (4 vs. 35%) using esmolol vs. remifentanil infusions titrated to heart rate during gynecologic laparoscopy. In mice, intrathecal landiolol (a short-acting beta-blocker) inhibited pain

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responses to noxious stimuli and reduced generation of c-Fos in the spinal dorsal horn demonstrating a direct antinociceptive effect of beta-blockers at the spinal level [23]**. These studies build on previous work that had demonstrated that intraoperative esmolol reduced patient-controlled analgesia (PCA) morphine consumption postoperatively [24].

**Gabapentinoids**

Gabapentin is a gamma-aminobutyric acid (GABA) analogue anticonvulsant known to be effective in treatment of pain and anxiety. Hayashida et al. [25] found that gabapentin administered p.o. or intracerebroventricularly to rats decreased pain behavior in response to noxious stimuli; this analgesic effect was blocked by a specific alpha-2-adrenergic receptor antagonist (idazoxan). The same authors demonstrated decreased morphine use and increased norepinephrine concentrations in cerebrospinal fluid in patients who received preoperative gabapentin, 1200 mg, suggesting that gabapentin moderates pain by activation of centrally mediated descending noradrenergic pain modulation systems [26].

In clinical studies, gabapentin 1200 mg administered 1 h before surgery was associated with decreased tourniquet pain during hand surgery, lower VAS scores, and less analgesic use postoperatively [27]. The general conclusions of three reviews of safety and efficacy of peroperative gabapentin/pregabalin published in 2007 were that gabapentinoids reduce postoperative pain, opioid consumption, and opioid-related adverse effects [28**, 29,30].

Durmus et al. [24] reported that hysterectomy patients receiving preoperative gabapentin alone (1200 mg) or combined with acetaminophen 20 mg/kg had decreased pain and a 30–50% reduction of opioid requirements postoperatively. Gabapentin and dexamethasone an hour before varicocele surgery improved postoperative pain relief and diminished PONV [31]. Interestingly, Adam et al. [32] observed no difference in pain scores or analgesic consumption in patients who received gabapentin 800 mg with an interscalene brachial plexus block before shoulder surgery suggesting that local anesthetic blocks may interfere with the mechanism by which gabapentin modulates postoperative pain.

The role of intravenous (i.v) corticosteroids in multimodal analgesia was explored by Thagaard et al. [33], who found that dexamethasone 4 mg or betamethasone 12 mg did not provide any prolonged postoperative analgesic or antiemetic effects compared with ketorolac 30 mg.

**Controlled release opioids**

Jokela et al. [34] from Finland were unable to demonstrate any analgesic benefit of preoperative oxycotin 15 mg administered with 800 mg of ibuprofen before gynecologic surgery in contrast to a previous report of improved postoperative analgesia by Reuben et al. [35] in a similar surgical population.

**Peripheral nerve blocks**

Williams et al. [36] did not demonstrate any less nausea or improved sleep in patients receiving a single-shot femoral nerve block or femoral nerve catheter in conjunction with an ipsilateral hyperbaric bupivacaine spinal and a multimodal analgesia regimen (ketamine 0.2 mg/kg i.v., meperidine 100 mg with neostigmine 0.5 mg, and ketorolac 15 mg intrathecically with oxycodeone and rofecoxib, p.o.). Conceivably, an effective multiple drug regimen might make it difficult for any single modality such as a femoral nerve block to show further benefit.

The use of paravertebral blocks at both the thoracic and lumbar level has enjoyed a renaissance in recent years. Exadaktylos et al. [37] presented the results of a retrospective review indicating that patients receiving thoracic paravertebral block and general anesthesia for mastectomy and axillary node dissection had a decreased rate of cancer recurrence when compared with patients who had received general anesthesia and morphine analgesia. This observation would have to be duplicated in a randomized prospective trial before drawing any conclusions about paravertebral blocks and breast cancer surgery. Less dramatically, a randomized controlled trial (RCT) by Moller et al. [38] and a case series by Cooter et al. [39] demonstrated improved analgesia and decreased fentanyl use in the postanesthesia care unit (PACU) for patients receiving paravertebral blocks for breast surgery. Hadzic et al.’s [40] randomized trial of paravertebral block vs. general anesthesia for inguinal hernia repair suggested decreased bladder dysfunction, PONV, and pain in the block patients.

A case series by Bryan et al. [41]** primarily addressed the feasibility and safety of postdischarge perineural interscalene catheter analgesia for ambulatory shoulder surgery. The notable features of the series were the high success rate (98% for the catheters placed solely by ultrasound guidance) and the infrequency of even minor adverse events (9.7%).

**Recovery from spinal anesthesia for ambulatory procedures**

Chloroprocaine has been revived as an ambulatory spinal anesthetic and has replaced intrathecal lidocaine in some centers. A dose-finding study of intrathecal 2-chloroprocaine demonstrated no difference in home discharge times among 30, 40, or 50 mg chloroprocaine doses but a more frequent occurrence of inadequate duration of surgical anesthesia with the 30 mg dose for lower extremity procedures of 45–60 min duration [42].
Bay-Nielsen and Kehlet [43] raised a warning flag on the use of spinal anesthesia for inguinal hernia repair when their retrospective review of the Danish National Hernia Database suggested an increased incidence of cardiac arrest with spinal anesthesia. This is obviously an association, not causation, and it is possible that neuraxial anesthesia had been chosen for these patients because of their perceived higher risk status. There was also an association between a higher postoperative incidence of transurethral prostatectomies and neuraxial anesthesia; this is compatible with other data identifying inguinal surgery and neuraxial anesthesia as risk factors for postoperative bladder dysfunction. The neuraxial anesthetic agents used would need to be evaluated to better understand any potential relationship between urological complications and anesthesia.

Complications and challenges of ambulatory anesthesia recovery
Inadequate analgesia and PONV have historically been the most common complications of ambulatory surgery; in spite of recent advances, these problems continue to challenge anesthesiologists.

Postoperative and postdischarge nausea and vomiting
The Society of Ambulatory Anesthesia (SAMBA) summarized the state-of-the-art and science in the treatment and prevention of PONV in its updated guidelines in 2007 [44**]. These guidelines also addressed the related but somewhat distinct entity of postdischarge nausea and vomiting (PDNV) (Fig. 1). Two factors affecting decision making in this area of clinical practice are the ongoing

Figure 1 Prophylaxis and treatment considerations for postoperative nausea and vomiting

<table>
<thead>
<tr>
<th>Patient related</th>
<th>Environmental</th>
<th>Children risk factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of PONV</td>
<td>Postop opioids</td>
<td>Surgery &gt; 30 min</td>
</tr>
<tr>
<td>Motion sickness</td>
<td>Emetic surgery (type and duration)</td>
<td>Age &gt; 3 years</td>
</tr>
<tr>
<td>Female gender</td>
<td></td>
<td>Strabismus surgery</td>
</tr>
<tr>
<td>Non-smoker</td>
<td></td>
<td>History of PONV/relative with PONV</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient preferences</th>
<th>Consider</th>
<th>Level of risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fear of PONV</td>
<td>Cost-effectiveness</td>
<td>0 RF = 10%</td>
</tr>
<tr>
<td>Frequency of PONV causing headaches/migraine</td>
<td>Avoidance/minimization of Nitrous oxide Volatile anesthetics High-dose neostigmine Post-op opioids</td>
<td>1 RF = 10% – 20%</td>
</tr>
<tr>
<td></td>
<td>Patient risk</td>
<td>2 RF = 20% – 40%</td>
</tr>
</tbody>
</table>

Low<br>Wait and see<br>

Medium<br>Low risk<br>Pick 1 or 2 interventions for adults<br>Pick ≥ 2 interventions for children<br>

High<br> ≥ 2 interventions/multimodal approach<br>

Propofol anesthesia<br>

Regional anesthesia<br>

Dopamine<br>

Droperidol or haloperidol<br>

Prenethazine prochlorperazine promazine<br>

Dexamethasone<br>

Scopolamine<br>

Ephedrine<br>

Dimenhydrinate<br>

1 Use droperidol in children only if other therapy has failed and patient is being admitted to hospital<br>• Some of the drugs may not have been studied or approved by the FDA for use in children

FDA, US Food and Drug Administration; PACU, postanesthesia care unit; PONV, postoperative nausea and vomiting; POV, postoperative vomiting; RF, risk factor. Reproduced from [44**].

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Table 1 Results of several recent studies on postoperative nausea and vomiting

<table>
<thead>
<tr>
<th>Study</th>
<th>Medication/regimens evaluated</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>White et al. [45*]</td>
<td>Transdermal scopolamine, Ondansetron 4 mg, Droperidol 0.625 mg</td>
<td>No difference in emetic outcomes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>More dry mouth in TDS group</td>
</tr>
<tr>
<td>White et al. [46]</td>
<td>TIVA (no dolasetron), Sevoflurane + dolasetron 12.5 mg</td>
<td>No difference in PONV prior to discharge</td>
</tr>
<tr>
<td></td>
<td></td>
<td>More PONV in TIVA group</td>
</tr>
<tr>
<td>Wang et al. [47]</td>
<td>Placebo, Haloperidol 1 mg, Ondansetron 4 mg</td>
<td>No difference in PONV between haloperidol and droperidol to 24 h</td>
</tr>
<tr>
<td>Lee et al. [48]</td>
<td>Haloperidol 2 mg, Ondansetron 4 mg</td>
<td>No difference in sedation, recovery time, or QT interval</td>
</tr>
<tr>
<td>Rosow et al. [49]</td>
<td>Haloperidol 1 mg, Ondansetron 4 mg</td>
<td>No difference in PONV</td>
</tr>
<tr>
<td>Aouad et al. [50]</td>
<td>Placebo, Haloperidol 1 mg, Ondansetron 4 mg</td>
<td>Early prophylactic efficacy with haloperidol</td>
</tr>
<tr>
<td>Grecu et al. [51]</td>
<td>Haloperidol 1 mg, Ondansetron 4 mg</td>
<td>Combination therapy more effective</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No difference in any group after 2 h</td>
</tr>
<tr>
<td>Chu et al. [52]</td>
<td>Placebo, Dexamethasone 4 mg, Haloperidol 2 mg, Ondansetron 4 mg</td>
<td>Haloperidol = dexamethasone most effective</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No differences in single agents</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No difference in side effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>No QT prolongation</td>
</tr>
<tr>
<td>Paech et al. [53]</td>
<td>Dose combinations of ondansetron 2 or 4 mg and Dexamethasone 2 or 4 mg</td>
<td>Dexamethasone 2 mg combinations were less effective</td>
</tr>
<tr>
<td>Candioti et al. [54]</td>
<td>Granisetron 0.1 mg rescue after ondansetron 4 mg</td>
<td>No difference in efficacy</td>
</tr>
<tr>
<td></td>
<td>Ondansetron 4 mg rescue after ondansetron 4 mg</td>
<td>Complete response in 60%</td>
</tr>
</tbody>
</table>

PONV, postdischarge nausea and vomiting; PONV, postoperative nausea and vomiting; TDS, transdermal scopolamine; TIVA, total intravenous anesthesia.

The effect of the controversial 2001 FDA black box warning on the use of droperidol (which applies to doses of more than 2.5 mg, typically in excess of antiemetic dosing) and the expiration of the US patent for ondansetron in 2006.

The results of several recent studies are summarized in Table 1 [45*,46–54]. Overall, the studies support the general conclusions that comparable antiemetic effects were obtained with a variety of agents, combination therapy was more effective than single agents, and no significant effects on QT interval were observed.

One of the newest agents in the PONV prophylaxis arena is aprepitant, an oral NK1 receptor antagonist. In two separate randomized trials, apreptitant 40 mg p.o. was found to be similarly effective to ondansetron 4 mg i.v. for prevention of nausea and more effective for the prevention of vomiting [55*,56].

In a nonpharmacological approach to PONV prophylaxis, Arnberger et al. [57] compared the efficacy of the simple intervention of monitoring neuromuscular blockade at the median nerve over the P6 acupressure point. In a blinded assessment, nausea was statistically significantly decreased in the P6 stimulation group with no difference in vomiting.

Another nonpharmacological study evaluating PONV symptoms compared the ProSeal (The Laryngeal Mask Company Ltd, Henley-on-Thames, UK) laryngeal mask airway (LMA) with endotracheal intubation in women undergoing breast and gynecological surgery. In the LMA group, nausea was less frequent at all times (13 vs. 53%), and vomiting was less frequent out to 24 h [58]. The authors hypothesized that this effect was independent of the finding that the ProSeal patients received less morphine and suggested that this was due to the difference between subglottic endotracheal tube (ETT) and supraglottic stimulation. The evidence regarding the effect of the LMA on PONV is mixed as two previous studies suggested that there was an increase in PONV with use of the LMA [59,60] and another noted a decrease [61].

Major complications following outpatient surgery

Fleisher et al. [62*] studied inpatient hospital admissions immediately following outpatient surgery and generated an outpatient surgery admission index from independent predictors. The index is based on the following point values: 65 years or older (1), operating time longer than 120 min (1), cardiac diagnoses (1), peripheral vascular disease (1), cerebrovascular disease (1), malignancy (1), seropositive findings for human immunodeficiency virus (1), and regional (1) or general (2) anesthesia. Patients with scores of 4 or higher were admitted to hospital 2.8% of the time, with an OR for admission of 32 relative to patients with scores of 0–1.

Coldiron et al.’s [63] review of office surgery incidents over a 7-year period in Florida confirms the adage that...
there are no minor procedures, as there were 31 deaths reported. This database included both medically necessary and cosmetic procedures with and without anesthesiologist or certified registered nurse anesthetist (CRNA) involvement. Notably, 86% of the cosmetic surgery incidents and 78% of the deaths occurred with the use of general anesthesia, with liposuction being the single most common procedure associated with death under general anesthesia.

**Lack of a discharge escort**
Chung et al. [64] found that 0.2% of patients in their institution presented without a postoperative escort, some of these situations developed due to an escort no show, and in some instances the lack of an escort was known preoperatively. Chung and Asman [65] published two tragic and worrisome case reports of patients who were seriously injured in motor vehicle accidents while driving home after having ambulatory surgery under local anesthesia with minimal sedation. This stands cogently in contradistinction to a study of volunteers that suggested general anesthesia did not impair postanesthetic performance in simulated driving tests and reinforces the importance of not making exceptions to policies requiring escorts for ambulatory patients [66].

**References and recommended reading**

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- with outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 812–813).


This is a comprehensive review of a newer agent with multiple potential roles as a sedative or as an adjunct to general anesthesia.


The strengths and weaknesses of remifentanil as a component of anaesthesia are presented in this review.


This study in rats raises questions about the effects of nitrous oxide on neurologic function and recovery.


In this study, an agent with a novel mechanism for reversing amino-steroid neuromuscular blockade has advanced to the final stage of clinical trials.


This study provides greater awareness of and unresolved analgesic challenges raised in the movement to outpatient treatment of postoperative pain.


The randomized trial evaluates the role of celecoxib in multimodal analgesia for gynecologic surgery.


This study evaluates the role of celecoxib in enhancing recovery from a common painful ambulatory procedure.


This study examines long-term outcomes associated with the use of multimodal analgesia.


In this study, beta-blockers appear to have a mechanism of action that does more than provide intraoperative hemodynamic control, extending to modification pain mediators.


This literature review explores the role of the gabapentinoids in the postoperative recovery process.

Recovery after ambulatory anesthesia Pavlin and Kent 735


56 An oral agent used in the chemotherapy-induced nausea and vomiting is evaluated for PONV prophylaxis in this trial.


64 These study attempts to make the infrequent but significant problem of inpatient admission after ambulatory surgery more intelligible.


Effect of single-dose dexmedetomidine on emergence agitation and recovery profiles after sevoflurane anesthesia in pediatric ambulatory surgery

Masami Sato · Gotaro Shirakami · Misako Tazuke-Nishimura · Shogo Matsuura · Keiji Tanimoto · Kazuhiko Fukuda

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Abstract

Purpose To study the effects of dexmedetomidine (DEX), a selective $\alpha_2$-adrenoreceptor agonist, on emergence agitation (EA), recovery profiles, and parents’ satisfaction after sevoflurane anesthesia in pediatric ambulatory surgery.

Methods In a double-blind trial, 81 children (ASA PS 1 or 2, 1–9 years) undergoing same-day or overnight-stay surgery were randomly assigned to receive intravenous DEX 0.3 μg kg$^{-1}$ (n = 39) or saline (n = 42) over 10 min after induction of anesthesia. Anesthesia was induced and maintained with sevoflurane using a facemask or laryngeal mask airway with spontaneous respiration. Agitation was assessed with a 1–4 point scale and pain with a 0–10 point scale. The patients’ parents were interviewed 24 h after surgery, and adverse events and the parents’ level of satisfaction with perioperative care were recorded.

Results The incidence of EA (agitation scale score 3 or 4) was significantly lower in the DEX group (28%) than in the saline group (64%) ($P = 0.0011$). The mean pain scales in the DEX group were significantly lower than in the saline group during the stay in the post-anesthesia care unit (PACU) ($P < 0.01$). The incidence of adverse events, times to the first drinking and voiding in the PACU, time spent in the PACU, and parents’ satisfaction level were not different between the two groups.

Conclusion Intravenous DEX at a dose of 0.3 μg kg$^{-1}$ after induction of anesthesia reduced sevoflurane-associated EA and postoperative pain in pediatric ambulatory surgery, with no increase in the incidence of adverse events and with no change in parents’ satisfaction level.

Keywords Dexmedetomidine · Emergence agitation · Sevoflurane · Children · Ambulatory surgery

Introduction

Sevoflurane is a popular anesthetic for children used worldwide because of its low pungency, rapid onset, and fast recovery properties. However, it is associated with higher incidence of emergence agitation (EA) (up to 80% [1–3]) than halothane. EA in children is generally short-lived with no after-effect. However, it is a troublesome phenomenon, because it can result in injury to the patient or damage to the surgical site, leads to dissatisfaction and anxiety for the parents, and requires extra nursing care with associated costs. In pediatric ambulatory surgery, EA is a particularly difficult problem, because EA itself and its treatment using sedatives or analgesics may delay discharge and the patient’s return home. Extended hospital stays discourage both patients and their caregivers from undergoing ambulatory surgery [4]. Therefore, ambulatory pediatric anesthesiologists should try to prevent EA in order to provide efficient and high-quality care that is a positive experience for patients and their parents.

To reduce the incidence of EA, prophylactic use of benzodiazepines, opioid analgesics, and $\alpha_2$-adrenoreceptor...
agonists have been tried, but the results have been variable
[1, 5–14]. Dexmedetomidine (DEX), a highly specific 
$\alpha_2$-adrenoreceptor agonist (receptor selectivity, $\alpha_2/\alpha_1 = 1620/1$), has sedative and analgesic properties without significant respiratory depression at clinical dosages [15, 16]. DEX is reported to significantly reduce EA frequency after sevo-
flurane anesthesia in pediatric surgery and non-surgical procedures in inpatient [5, 6] and outpatient [7, 8] settings. However, these reports did not include follow-up data and measures of parents’ satisfaction levels. Follow-up is an important part of perioperative management of ambulatory surgery in order to find adverse events, give advice to patients and caregivers, increase their satisfaction, and improve practice. In this study, in addition to corroborating the effects of DEX on post-sevoflurane EA in children undergoing same-day or overnight stay surgery, we investigated the recovery profiles during the stay in the post-anesthesia care unit (PACU) and 24 h after PACU discharge, and also recorded parents’ satisfaction levels.

Materials and methods

We investigated 81 pediatric patients (ASA physical status
1 or 2, 1–9 years old, body weight >10 kg) who were scheduled to receive same-day surgery ($n = 50$) or over-
night stay surgery ($n = 31$) under general anesthesia between October 2004 and April 2007 in the Day Surgery
Unit (DSU), Kyoto University Hospital. The study was approved by the institutional ethics committee and informed consent was obtained from the parents. Patients who did not consent, or with mental retardation, neuro-
logical or heart disease, uncontrollable asthma, or any type of acute illness were excluded from this study.

All patients and their parents were admitted to the DSU in the morning on the day of surgery. They waited in the pediatric pre-anesthesia holding area in the DSU. The children received no premedication and moved to an operating room in the DSU accompanied by their mother or father. The parent was permitted to be present during induction of anesthesia. Children were randomly assigned to receive either saline (group S, $n = 42$) or DEX (group
D, $n = 39$) using a randomization list. General anesthesia was induced with 8% sevoflurane in 6 l min$^{-1}$ oxygen using a facemask, and they breathed spontaneously. An intravenous (i.v.) catheter was inserted after induction of anesthesia and the airway was secured with facemask or laryngeal mask airway (LMA). Patients in group D received DEX 0.3 $\mu$g kg$^{-1}$ diluted in 5 ml saline over 10 min via the i.v. catheter whereas patients in group S received 5 ml saline. The attending anesthesiologists, sur-
geons, and nurses were blinded to the treatment assignment of a patient. Anesthesia was maintained and adjusted by an attending anesthesiologist with 2–5% sevoflurane in 2 l min$^{-1}$ oxygen and 4 l min$^{-1}$ air to provide a stable heart rate (HR), blood pressure (BP), and pulse oximetric arterial oxygen saturation ($\text{SpO}_2$) with spontaneous respi-
ation. All patients received an acetaminophen (total 40 mg kg$^{-1}$) or diclofenac (total 1 mg kg$^{-1}$) suppository after induction of anesthesia and at the end of surgery. Ropivacaine infiltration into the surgical field was done except for laser irradiation or myringotomy with tube insertion. No urinary catheters were inserted. The HR, BP, $\text{SpO}_2$, endtidal concentrations of carbon dioxide and sevoflurane (ET$_{CO_2}$ and ET$_{sev}$), and respiratory rate (RR) were monitored throughout the procedure. At the end of surgery, sevoflurane was discontinued, and LMA was removed before the patients fully woke up in the operating room. The children were transferred to the PACU in the DSU after their eyes opened spontaneously.

In the PACU, parents were allowed to stay beside their child and $\text{SpO}_2$ and HR were monitored. A PACU nurse blinded to the patient assignment recorded adverse events, for example postoperative vomiting (POV) and urinary retention, and the drugs administered. In addition, they recorded a modified Aldrete score for children (0–10 point scale) [17], the times when they drank fluids and voided, and the time of discharge from the PACU. Postoperative nausea (PON) was not assessed because it is difficult to evaluate in children. Pain was treated with fentanyl 0.5 $\mu$g kg$^{-1}$ intravenously or an acetaminophen supposi-
tory 20 mg kg$^{-1}$, and POV was medicated with a dom-
deridone suppository 1 mg kg$^{-1}$. If $\text{SpO}_2$ fell to <92%, oxygen was given by use of a facemask.

Behavior during both the pre and post-operative periods was rated on a four-point agitation scale (1, calm; 2, not calm but could be easily calmed; 3, not easily calmed, moderately agitated, or restless; and 4, combative, excited, or disoriented) [2] by an observer blinded to the patient assignment. Agitation scores of 3 or 4 were defined as an agitation episode. Patients’ pain while in the PACU was assessed with the children and infants postoperative pain scale (CHIPPS, 0–10 point scale) [18] by the same obser-
ver. Children were discharged from the PACU when they were calm with minimum pain, no vomiting, stable vital signs, and could drink fluids and void. Patients who were scheduled for same-day discharge returned home directly. If the discharge criteria were not satisfied, they were transferred to the ward (unplanned hospital admission). Patients who were scheduled for an overnight-stay were transferred to the ward. If a problem prevented discharge and return home, the patient’s hospital stay was extended (unplanned extended hospital stay).

In the morning on the day after surgery, a PACU nurse or anesthesiologist blinded to the patient assignment fol-
lowed up each child with a telephone call or by direct
meeting with his/her parent; using a standardized questionnaire with some modifications as previously described [4]. Parents were asked about post-discharge symptoms including pain and POV, using a verbal rating score (0–10; 0, no symptom; 10, the severest symptom imaginable). Scores were also obtained for resumption of normal activity (RNA) (0–10; 0, no activity; 10, back to normal activity) and satisfaction with the global surgical and anesthesia care (0–10; 0, very dissatisfied; 10, very satisfied). The preference for an outpatient-based procedure was also evaluated (Question: If your child should undergo the same operation in the future, would you choose the outpatient setting again? Answer: Yes or no).

Statistical analysis was performed using SAS software (SAS Institute, Cary, NC, USA). Demographic data, for example age, body weight, duration of anesthesia and surgery, and the fluid volume infused, were compared using unpaired Student’s t tests. Categorical data expressed as a number or percentage were compared by chi-squared analysis and Fisher’s exact test. The Mann–Whitney U test was used to compare recovery times and modified Aldrete, agitation, pain, and post-operative interview scores. Intra and post-operative hemodynamic and respiratory variables in the same subjects were compared by use of the Bonferroni test after repeated-measures analysis of variance. Trends over time in the two groups were compared using repeated-measures analysis of variance and time-matched data were compared by use of the Bonferroni test. Differences at \( P < 0.05 \) were considered to be statistically significant.

**Results**

The two patient groups did not differ significantly with regard to preoperative characteristics, types of surgery, duration of surgery and anesthesia, and intraoperative i.v. fluid volume (Table 1). Agitation scale scores in group D were lower than in group S on discharge from the operating room (2(1–3), median (25th–75th percentile) vs. 3(2–3); \( P = 0.0049 \)) and on PACU admission (2(1–3) vs. 3(2–3); \( P = 0.012 \)). The incidence of EA (agitation score 3 or 4) was significantly lower in group D than in group S at discharge from the operating room (28 vs. 64%);
score was ≥9, and until taking a drink, voiding, and discharge from the PACU were no different between the two groups (Table 3). Incidences of POV, anti-emetic and analgesic medications, and oxygen supplementation were very low in both groups (Table 3). No patients required unplanned hospital admission/extended hospital stays. No parent whose child underwent same-day surgery made an emergency telephone call to the hospital, or returned to the hospital with his/her child after discharge and return home. Parents’ responses to the 24-h postoperative interview were no different between the two groups with regard to postoperative symptoms, RNA scores, preference for outpatient-based procedures, and global satisfaction scores (Table 4).

Discussion

This study indicates that DEX administration reduces the incidence of EA after sevoflurane anesthesia in children, confirming previous results [5–8]. Furthermore, this study demonstrates that DEX at a dose of 0.3 μg kg⁻¹ after induction of anesthesia does not affect recovery profiles and parents’ satisfaction levels.

The etiology of EA in children is not fully understood but possible risk factors are rapid emergence from anesthesia, intrinsic characteristics of an anesthetic, postoperative pain, preschool age, otolaryngologic surgical procedures, preoperative anxiety, and child temperament [1]. Meta-analysis of 23 randomized controlled trials revealed that EA occurred more frequently with sevoflurane than halothane [3]. Rapid awakening after sevoflurane anesthesia has been assumed to be a cause for the phenomenon. However, it is currently thought that rapid emergence is not the only cause of EA, because recovery from propofol anesthesia, which also has rapid emergence properties, is associated with low incidence of EA [19]. The genesis of EA after sevoflurane anesthesia has been uncertain up to now.

The presence of pain is thought to be one of the major causes of EA, but painless treatment does not guarantee calm emergence from sevoflurane anesthesia [1]. Isik et al. [7] reported that EA was seen in 48% of pediatric patients after sevoflurane anesthesia while undergoing magnetic resonance imaging. Since it is often difficult to distinguish EA in children from screaming because of pain, adequate postoperative pain treatment should be administered. The use of fentanyl as a preemptive analgesic reduces the incidence of EA [11, 12]. However, potent opioid analgesics are associated with various adverse postoperative symptoms, especially PON/POV, which delay post-anesthesia recovery and cause unplanned hospital admissions; thus, non-opioid analgesic techniques and minimization of opioid use are
Fig. 2  Time courses of heart rate (a) and systolic blood pressure (b). Values are mean ± SD. PACU post-anesthesia care unit, OR operating room, group S saline control group, group D DEX-treated group. P value compares trends over time with treatments (repeated-measures analysis of variance). †P < 0.05 versus just before anesthesia induction, ‡P < 0.05 versus just before DEX/saline i.v. (Bonferroni test after repeated-measures analysis of variance)

Table 2  Changes in respiratory variables during anesthesia

<table>
<thead>
<tr>
<th>Group</th>
<th>SpO2 (%)</th>
<th>RR (min⁻¹)</th>
<th>ET\textsubscript{CO}_2 (mmHg)</th>
<th>ET\textsubscript{sev} (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Just before anesthesia induction</td>
<td>99 ± 1.0</td>
<td>99 ± 1.3</td>
<td>31 ± 6.7</td>
<td>32 ± 6.1</td>
</tr>
<tr>
<td>Just before DEX/saline i.v.</td>
<td>99 ± 1.3</td>
<td>99 ± 0.7</td>
<td>32 ± 6.7</td>
<td>34 ± 6.7</td>
</tr>
<tr>
<td>Just after the end of DEX/saline i.v.</td>
<td>99 ± 1.2</td>
<td>99 ± 0.9</td>
<td>32 ± 4.7</td>
<td>41 ± 7.3</td>
</tr>
<tr>
<td>Operation start</td>
<td>99 ± 1.0</td>
<td>99 ± 1.0</td>
<td>34 ± 6.2</td>
<td>43 ± 7.7</td>
</tr>
<tr>
<td>Operation end</td>
<td>99 ± 1.1</td>
<td>99 ± 1.7</td>
<td>32 ± 7.3</td>
<td>43 ± 9.3</td>
</tr>
<tr>
<td>Emergence</td>
<td>99 ± 1.9</td>
<td>99 ± 1.7</td>
<td>30 ± 7.0</td>
<td>44 ± 7.0</td>
</tr>
</tbody>
</table>

Values are mean ± SD

P value compares trends over time with treatments (repeated-measures analysis of variance). *P < 0.05 versus Just before DEX/saline i.v., †P < 0.05 versus group S (Bonferroni test after repeated-measures analysis of variance)

S saline control group, D DEX-treated group, SpO2 pulse oximetric arterial oxygen saturation, RR respiratory rate, ET\textsubscript{CO}_2 endtidal concentration of carbon dioxide, ET\textsubscript{sev} endtidal concentration of sevoflurane
preferable in ambulatory surgery [20]. In our study, acetaminophen/diclofenac and ropivacaine infiltration were used for analgesia and the POV ratio was low (7%).

The effects of midazolam premedication on the incidence of EA remain controversial [9, 10] and midazolam has been reported to increase the incidence of prolonged recovery [10]. a2-Adrenoreceptor agonists, for example clonidine and DEX, have also been used for management of EA, because of their sedative and analgesic effects [1, 5–8, 14]. DEX is a more highly specific a2-adrenoreceptor agonist (a2/a1, 1620/1) than clonidine (a2/a1, 220/1). In our study, DEX at a dose of 0.3 μg kg\(^{-1}\) reduced the incidence of post-sevoflurane EA (from 64 to 28%), which is similar to previously reported reductions [5–8], and also reduced postoperative pain intensity. The previous reports on the beneficial effect of DEX on EA did not describe the postoperative recovery profiles up to 24 h after surgery or parents’ satisfaction. We studied children undergoing same-day or overnight stay surgery and followed up the recovery profiles not only in the PACU but also on the day after surgery. Our study suggests that DEX reduces EA and also reduces pain, without increasing the frequency of POV and other adverse symptoms up to 24 h after surgery with no change in parents’ satisfaction level.

In our study, DEX administration reduced the dose of sevoflurane required during surgery, confirming the anesthesia-sparing effect of DEX [15, 16]. It is possible that the reduced incidence of EA was because of the reduced sevoflurane dose. However, there is evidence that suggests the incidence of sevoflurane-associated EA

<table>
<thead>
<tr>
<th>Table 3 Recovery profiles in the PACU</th>
<th>Group S (n = 42), saline controls</th>
<th>Group D (n = 39), DEX-treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modified Aldrete score on PACU admission</td>
<td>10 (10–10)</td>
<td>10 (9–10)</td>
</tr>
<tr>
<td>Use of analgesic drug</td>
<td>1 (2%)</td>
<td>1 (3%)</td>
</tr>
<tr>
<td>Use of antiemetic drug</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Use of oxygen</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>3 (8%)</td>
<td>3 (7%)</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Time from PACU admission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>To modified Aldrete score ≥9 (min)</td>
<td>0 (0–1.5)</td>
<td>0 (0–5)</td>
</tr>
<tr>
<td>To drink fluids (min)</td>
<td>65 (50–108)</td>
<td>90 (63–131)</td>
</tr>
<tr>
<td>To void (min)</td>
<td>115 (90–130)</td>
<td>124 (76–160)</td>
</tr>
<tr>
<td>To actual discharge from PACU (min)</td>
<td>133 (104–165)</td>
<td>160 (128–205)</td>
</tr>
<tr>
<td>Unplanned admission/extended hospital stay</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 4 Data from interviews 24 h after operation</th>
<th>Group S (n = 42), saline controls</th>
<th>Group D (n = 39), DEX-treated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms after discharge*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleepiness</td>
<td>0 (0–0)</td>
<td>0 (0–1.5)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
</tr>
<tr>
<td>General malaise</td>
<td>0 (0–0)</td>
<td>0 (0–2)</td>
</tr>
<tr>
<td>Fever</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
</tr>
<tr>
<td>Sleeplessness</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
</tr>
<tr>
<td>Bleeding</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
</tr>
<tr>
<td>Pain</td>
<td>0 (0–0)</td>
<td>0 (0–1.5)</td>
</tr>
<tr>
<td>Hoarseness</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
</tr>
<tr>
<td>Appetite loss</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
</tr>
<tr>
<td>Thirst</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
</tr>
<tr>
<td>Urinary disturbance</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
</tr>
<tr>
<td>RNAa score</td>
<td>10 (9.25–10)</td>
<td>10 (9–10)</td>
</tr>
<tr>
<td>Preferencec</td>
<td>42 (100%)</td>
<td>38 (97%)</td>
</tr>
<tr>
<td>Satisfaction scored</td>
<td>10 (10–10)</td>
<td>10 (10–10)</td>
</tr>
</tbody>
</table>

Values are expressed as median (25th–75th percentile) or number (%)

PACU post-anesthesia care unit

* Verbal rating score; 0, no symptom; 10, the severest symptom imaginable

b RNA, resumption of normal activity; score 0, no activity; score 10, back to normal activity
c Preference for outpatient-based procedure; the ratio of positive answers to all answers
d Global satisfaction with the surgical procedure and anesthesia care; score 0, very dissatisfied; score 10, very satisfied
is not dose-dependent or exposure time-dependent [1]. In previous studies, DEX decreased EA frequency when the sevoflurane concentration was fixed [5, 7] and when \( \text{ET}_{\text{sev}} \) was similar in both DEX and placebo-treated groups [8].

DEX has possible hemodynamic side effects [15, 16]. Rapid bolus i.v. administration of DEX causes an immediate increase in BP and decrease in HR, and subsequent decrease in BP and HR [21]. Because rapid injection may result in excessive hemodynamic alterations, it is recommended that DEX be administered slowly. Administration of 0.5 \( \mu \text{g kg}^{-1} \) DEX intravenously over 5 min caused approximately 10 and 25% reductions in BP and HR, respectively, within 15 min after infusion in children anesthetized with 1 MAC of sevoflurane [22]. In our study, i.v. administration of 0.3 \( \mu \text{g kg}^{-1} \) DEX over 10 min decreased systolic BP by about 10%, and HR in group D was also approximately 10% lower than in group S from the end of DEX infusion until 30 min after PACU admission. No treatments for these reductions in BP and HR were required. The more stable HR and BP in our study compared with the previous report [22] are probably because of the lower dose and slower administration of DEX, and adjustment of the sevoflurane dose by the attending anesthesiologists. DEX has minor effects on the respiratory system [15, 16, 22]. In our study, RR, \( \text{ET}_{\text{CO}_2} \), and \( \text{SpO}_2 \) were similar in the two groups and no clinically meaningful respiratory adverse effects, for example laryngospasm, bronchospasm, or ventilatory depression, were noted during the perioperative period. Our method of DEX administration is safe in children with regard to hemodynamic and respiratory effects. Continuous administration of 0.2 \( \mu \text{g kg}^{-1} \text{h}^{-1} \) DEX did not change BP and HR significantly [8], and thus continuous infusion may be preferable from the perspective of hemodynamic stability; although it is somewhat inconvenient and there is a possibility that an effective dose may not be attained in a short-duration surgery/procedure.

A higher dose of DEX would further reduce the incidence of EA. However, this might cause excessive hemodynamic changes and sedation, thereby delaying post-anesthesia recovery and precipitating parents’ dissatisfaction. DEX at a dose of 0.5 or 1.0 \( \mu \text{g kg}^{-1} \) reduces post-sevoflurane EA significantly, but also prolongs the early phase of post-anesthesia recovery [6, 7]. In our study, 0.3 \( \mu \text{g kg}^{-1} \) DEX tended to slow post-anesthesia recovery, probably because of the residual sedative effect of DEX, but not to a statistically significant extent. In a study of patients undergoing inpatient surgery, caudally administered DEX (1.0 \( \mu \text{g kg}^{-1} \)) reduced the incidence of post-sevoflurane EA (from 27 to 7%), reduced the analgesic requirement, and improved the quality of sleep without hemodynamic instability; but also prolonged the duration of sedation [23]. The optimum dose and technique for administering DEX to reduce EA without adverse events in ambulatory pediatric surgery are not yet known. Further studies are needed to assess the effects of different doses and administration techniques of DEX.

In conclusion, this study demonstrates that a 0.3 \( \mu \text{g kg}^{-1} \) dose of i.v. DEX administered over 10 min after induction of anesthesia reduces post-sevoflurane EA and postoperative pain in pediatric ambulatory surgery. This method of DEX administration was safe and did not affect recovery profiles or parents’ satisfaction.

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References

Management of outcomes in the ambulatory surgery center: the role of standard work and evidence-based medicine
Douglas Merrill
The University of Iowa Hospitals and Clinics, The Carver College of Medicine, The University of Iowa, Iowa City, Iowa, USA
Correspondence to Douglas Merrill, MD, Medical Director, Ambulatory Surgery, Patient Safety Officer, The University of Iowa Hospitals and Clinics, Professor of Anesthesia, The Carver College of Medicine, The University of Iowa, Iowa City, Iowa, USA
E-mail: douglas-merrill@uiowa.edu

Purpose of review
Quality and safety in the manufacturing and airline industries have benefited from evidenced-based process-improvement strategies. This review investigates the rationale for application of these same processes in the ambulatory anesthesia setting.

Recent findings
Application of quality methodologies in healthcare and other service industries has yielded similar quality and safety improvements as in the manufacturing and airline industries. Anesthesiologists have embraced the use of some mandated care plans, but many such opportunities have been rejected by the specialty, to the detriment of the safety and quality of patient care. Implementation of such mandates and teamwork training in healthcare would improve the safety and quality of medical practice as they have so dramatically in the airline and manufacturing industries over the preceding 30 years.

Summary
Ambulatory surgery and anesthesia care is uniquely oriented to the application of repetitive processes in the provision of highly predictable and reproducible surgical services. Ambulatory anesthesiologists should lead the healthcare industry in the much wider adoption of standard practice protocols and team training to maximally improve the safety and quality of patients’ experiences.

Keywords
ambulatory anesthesia, aviation, best practice, evidence-based medicine, guidelines, outcomes, quality improvement, safety, standard practice protocols, teamwork

Introduction
Deliberate quality improvement programmes that include assessment, planned intervention and alteration in existing processes, as well as constant monitoring of outcomes, have been in use in manufacturing since the mid-20th century. More recently, those quality programmes that have been valuable in the manufacturing sector have been applied in the service industries, and have led to improved client satisfaction and other positive quality outcomes in a variety of nonmanufacturing settings [1]. Healthcare has benefited from the use of quality improvement techniques at the institutional level [2]. One example is the successful implementation of the Toyota Lean approach at the Virginia Mason Clinic, which resulted in marked improvements in the quality, safety and efficiency of patient care and in cost savings [3**].

At the core of these approaches are four basic tenets:

1. that systems and processes of manufacturing or service provision can be analyzed, and all relevant factors that contribute to their outcomes can be identified;
2. that such an analysis can discover any and all unnecessary variation in the provision of processes;
3. that such variation is likely the cause of any error or negative outcome of the process;
4. finally that systematic elimination of unnecessary variation in favor of consistent application of proven methodology will lead to quality improvement in the goods or services produced by the process.

Healthcare and manufacturing: similarities in quality improvement opportunities
The value of these systematic disciplines when applied to healthcare quality improvement derives from the similarities found among quality defects in both these manufacturing procedures and healthcare delivery. Although patients suffer heterogeneity in their responses to therapeutic interventions, most often these responses lie within a predictable range and are therefore akin to the impact of variables found in other industries, such

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as that which weather has on airline operations. This is particularly true in an ambulatory surgery center (ASC), where the nature of both surgical procedures and patients’ health delimit variation more so than may be true in a hospital ‘main’ operating room arena.

Indeed, most defects in healthcare quality are not due to patient variability, but are rather due to inherent flaws in the delivery systems themselves, just as is true in manufacturing. In both settings, the most common reasons for poor outcomes from application of a healthcare process are system problems, rather than individual errors [4]. Therefore, the most effective manner in which to increase the quality of healthcare is to identify and correct those system processes that allow (or may be predicted to allow) human error or other events to result in negative outcomes [5].

‘Standard work’ is the result of evidence-based medicine

The discussion of the use of regimens to manage therapeutic decisions simply represents the use of guidelines and protocols based upon collective expertise and evidence. These tenets of evidence-based medicine include the same concepts as ‘standard work’ used in manufacturing. As recently re-defined by David Eddy, evidence-based medicine has five fundamental aspects [6**]:

1. Principles (desired outcomes, for instance) are relatively immutable, whereas the methods decided upon as the best means to achieve those may change as evidence changes.
2. Evidence available will not always be definitive.
3. Evidence-based medicine has two distinct aspects: it will generate guidelines to cover large populations (e.g. outpatients at risk for nausea after surgery) and also will provide evidence of the best way for individual physicians to apply those guidelines.
4. Evidence will consist of literature-based findings, experience, and expert opinion. It will usually be a brew of these three, rather than a restrictive dependence upon peer-reviewed, randomized, controlled trials alone.
5. All clinical decisions should be based upon both the best available evidence supporting a given therapy and the measured outcome of the therapeutic decision. Thus, the routine use of a particular anesthetic technique without measuring outcome is not compatible with the practice of evidence-based medicine (or standard practice).

Nonroutine events

Attention paid exclusively to negative outcomes, with assignment of ‘blame’ for a single error (rather than targeting the responsible flawed processes that led to the error and allowed it to have consequences for the patient) has stymied quality improvement in healthcare over the last decades [7]. A better focus has been suggested, which is to consider the target of improvement to be the environmental susceptibility to ‘nonroutine events (NREs)’, defined as ‘any event that is perceived by care providers or skilled observers to be unusual, out of the ordinary, or atypical’ [8]. This approach allows preemptive assessment as well as root-cause analysis in the wake of actual NREs. ‘Root-cause analysis’ is the process by which multidisciplinary teams assess the causative factors that led or could lead to a negative event and rapidly intervene to change the nature of processes to abate the chance that such factors could again juxtapose in the future. The focus on NREs – rather than upon ‘error’ – allows recognition of proclivities (e.g. the anesthesiologist’s higher density of workload during induction and emergence) for their occurrence and consequent anticipation and avoidance [8].

In the specific area of anesthesia care, which constitutes a highly technical although repetitive set of procedures, the model of aviation safety has been invoked to portray the ideal means of improving patient safety and efficient practice. Checklists, monitoring, alarms, and simulation have all gained favor over the preceding decades as valuable emulations of the airline industry’s quality and safety improvement practices.

Guidelines regarding monitoring in anesthesia are generally well received and followed [9,10]. Practitioners are also able to rely upon professional society guidelines covering preoperative fasting, airway assessment and management, the use of regional anesthesia in the presence of anticoagulant therapy, preoperative evaluation, and conduct of cardiopulmonary resuscitation that are all borne of careful evaluation of evidence by experts.

However, it has been difficult for anesthesiologists – indeed all physicians – to emulate modern airline pilots in their willingness to surrender autonomy and create care pathways to reduce unnecessary individual variability. Crew Resource Management is the technique embraced by the airline industry to ‘flatten the hierarchy’ and de-emphasize autonomy in the cockpit. It is based upon the tenet that no one individual is remarkably more capable than average. Therefore, the attitude of ‘this is the way I do it and it works for me’ is now untenable in the cockpit. This de-emphasis of the individual and emphasis on use of proven techniques and teamwork is credited with the marked increase in safety over the past two decades in the airline industry.

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1 In this process, causative factors are distilled to the root factors, which must be identified and – ideally – excoriated, if future negative events are to be avoided. This root-cause analysis approach has been familiar in healthcare settings for some time, but often there has been insufficient inclusion of all stakeholders in the process. As a result, it is not possible to make the changes that will cause real improvement. Also, follow-up assessments of the efficacy of the process in preventing repetitive error are often omitted.
Guidelines and protocols: proven quality improvement but mixed acceptance

Irrational variation in healthcare delivery is inversely related to its quality, and so its reduction is a worthy target of quality improvement programs [11,12]. Guideline development and adherence will diminish variation [13]. The use of guidelines and protocols can eradicate complications, such as central line infections [14].

Protocols are effective for three reasons:

1. The evidence used in their creation must have suggested that such protocols were the ‘best’ approaches to the clinical problem at hand.
2. They diminish variation, which in turn decreases the opportunity for error and misunderstanding, increasing the chance of valid care [15].
3. They lead to cost reduction due to decreased use of expensive but unproven therapeutic approaches [16].

Unfortunately in anesthesia practice — and among all physicians — the translation of guidelines into protocols and adoption of nonemergency guidelines as required modes of ‘standard work’ are much less common, particularly in comparison with the number of guidelines available. At its base, this reluctance is born of the belief that we are each improved by our unique experiences, and that we each believe ourselves to be better than average [17]. This is in contrast to the areas of airline safety and manufacturing quality improvement, in which standard work is widely accepted as an ideal method to prescribe actions both in routine and in emergent situations.

Despite these facts, many guidelines regarding routine care are not well accepted or simply not used in current anesthesia practice. One example is the variability in drug costs engendered by anesthesia providers at the same location, working with the same surgeons, doing the same procedures [18]. Standard protocols regarding medication choices diminish such unnecessary variation, improve the quality of care and decrease cost [19].

Further, despite evidence in the literature of resulting superior patient experience or cost savings [20], the adoption and use of recommended restrictions on preoperative testing [21], standard protocols for prophylaxis/treatment of postoperative nausea and vomiting (PONV), or man-

dated use of particular regional techniques (driven by the surgical procedure rather than the anesthesia provider’s tendency) [22] are not found in most anesthesia departments and are frequently vehemently rejected [23].

Emergency response guidelines vs. preemptive guidelines

By contrast, use of guidelines is fairly common in the management of emergency procedures such as difficult intubation or the management of malignant hyperthermia crises. Yet, those situations arise much less frequently than the decisions regarding prevention of nausea, vomiting, or pain or regarding medication choice. Although the airline industry also employs training in standard responses to emergency situations, it has been most successful in the use of routine protocols whenever possible as part of a preemptive strategy to avoid error and safety impairment events, the ‘system safety’ concept [24].

Thus, though a good deal of medical research has targeted nonemergency preemptive strategies (e.g. PONV), this evidence has not led to guidelines used by all practitioners in a standard manner. This resistance is made all the more notable because several of industry’s lessons in quality improvement have proven applicable to healthcare and anesthesia. For example, the use of visual controls, a principle of the Toyota Lean Production system and others, has improved compliance with guidelines for timely antibiotic administration [25**].

Hierarchical institutional models

As noted above, another innovation in airline cockpit operations was due to the recognition that safety is enhanced by a flattening of the hierarchy, decreasing the inhibition of presenting bad news to pilots by copilots [26]. This ability for any part of the team to ‘stop the line’ to prevent the promulgation of quality defects is the cornerstone of aviation’s ‘crew resource management’ and is also a significant part of the Toyota Lean Production system. Likewise, this model has been an important factor in the improved safety record at the Virginia Mason Hospital system, which has adapted this process as its patient safety alert (PSA) system [27].

Creating a culture of safety, rather than one of blame and recrimination, can be accomplished only if the hierarchical system is ‘flattened’. However, many medical institutions

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2 Whenever I speak on this topic I begin by asking the audience, ‘How many of you provide above-average quality of anesthesia care?’ The audience response has been rapid and overwhelmingly affirmative on all occasions, followed most often by laughter as members realize the statistical improbability of their collective answer. This ‘better than average’ heuristic is not unique to physicians. In fact, the psychology literature shows that lower skilled people overestimate their abilities, whereas higher skilled performers underestim ate their own. Krueger J, Mueller RA. Unskilled, unaware, or both? The better-than-average heuristic and statistical regression predict errors in estimates of own performance. J Pers Soc Psychol 2002; 82:180–188.

3 An interesting disconnection between our acceptance of the importance of visual controls and our practice is the use of medication labels in the operating room. Almost 30% of providers do not use labels, and over half of those who do, do not read them! This latter fact probably reflects an over reliance on the use of colored labels, an approach currently endorsed by the American Society of Anesthesiologists, but one which may be less safe than use of black lettering on white labels. Orser BA, Chen RUB, Yee DA. Medication errors in anaesthetic practice: a survey of 687 practitioners. Can J Anaesth 2001; 48:139–146.
still grapple with unassailable hierarchy, which leads to insufficient communication of bad news, and consequent impairment of patient safety [28]. This set of attitudes is also obstructive to the establishment of a system of ‘near miss’ reporting, a system that does well in the aviation industry in which negative consequences are severe for not reporting and nonexistent for reporting [29]. In healthcare, ‘no harm, no report, no foul’ is the approach most often used, and we therefore miss the opportunities to alter error-inducing systems before catastrophes occur [30]. Challenges remain, including creation of a universally accepted nomenclature to determine which events are ‘near misses’ and which are of no significance.

The arguments for standard work are the same as those for evidence-based practice. If data exist, either in the literature or in individual practice, to show that specific techniques are associated with better outcomes or improve the safety profile of a surgical experience, then those data should be translated into guidelines and algorithms that will lead all practitioners to provide this optimal care. Of course, in the occasional situation in which such data do not exist or do not apply, then individual medical judgment of a careful practitioner is the best safeguard for a patient.

Routine events occur routinely, and nowhere is that more true than in ambulatory surgery. A surgery center typically restricts its practice to healthy individuals undergoing a relatively small list of procedures, thus yielding the perfect system for use of proven practice guidelines. Thus, patient safety, experiential quality, and cost could be improved by the increased application of required standard work in the ASC. For instance, this author used mandatory guidelines prohibiting the use of opioids in the preoperative and intraoperative period to diminish PONV significantly without increasing pain in the post anesthesia care unit (PACU) or diminishing patient satisfaction. The value of such guidelines can be evaluated only by close monitoring of outcomes. Indeed, such monitoring is absolutely necessary to create guidelines, because the tenets of evidence-based medicine practice require identification of best practices at the local level, an exercise achieved only by monitoring outcomes of each practitioner and the ASC.

We all follow some guidelines: how many hours to fast before anesthesia, whether or not to use a rapid sequence induction on C-section patients, airway management, using succinylcholine in patients with malignant hyperthermia, advanced cardiac life support (ACLS), cardiopulmonary resuscitation (CPR), using regional anesthesia in the presence of blood thinners, anesthesia machine checklists, monitoring the electrocardiogram during surgery and anesthesia, and using oximetry as a routine intraoperative monitor. Yet, it is clear that we have not taken advantage of the many other opportunities to improve patient outcomes that are afforded us by evidence-based medicine.

Conclusion
Duly noted is Thoreau’s [31] statement, ‘Any fool can make a rule and every fool will mind it.’ However, rules that result in improved care quality are worth following. Our true collective foolishness is our belief that we each are individually better than average, and that bending our own methods to rule-based practice would therefore deprive a patient of a uniquely higher quality experience. Practice groups should proactively review literature and decide ‘best practice’, create written guidelines, and then monitor for adherence and outcomes. Protocols that enhance patient outcomes and safety should be maintained, whereas those that do not should be altered until they do. Anesthesia practice in the ambulatory setting is repetitive and predictable and is therefore uniquely fitted to protocol-driven practice improvement. Ambulatory anesthesiologists should lead the way in this improvement in anesthesia safety and quality.

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. 813).

2 Parker BM. Six sigma methodology can be used to improve adherence for antibiotic prophylaxis in patients undergoing noncardiac surgery. Anesth Analg 2007; 101:140–146.
4 A superb review of how this system created safer medical care and the story of how it was implemented at one of the world’s leading medical centers.

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4 At the Virginia Mason Ambulatory Surgery Center, the preoperative and intraoperative use of opioid was restricted to only those patients for whom there was an indication (e.g., established preoperative opioid use), with the result that PONV decreased from over 6% to less than 3% and average time in PACU fell from almost 2h to less than 1 (results presented at the SAMBA Annual Meeting, May 2004, Seattle, Washington).


26 A good paper on implementation of an AIM system juxtaposed with the PQRI imperative of timely antibiotic administration as an example of the value of visual control systems to enhance safety and quality of care.


Ambulatory Surgery: How Much Testing Do We Need?

Deborah C. Richman, MBChB, FFA(SA), a, b, *

Preoperative testing is done to predict risk, alter management, and improve outcomes. If this is the premise, then each test needs to be considered with one or all of these three aims in mind.

Currently more than two thirds of surgeries in the United States are done on an ambulatory basis. Apfelbaum predicts the growth of ambulatory surgeries to be close to 80% of all surgeries in the United States within the next couple of years.

Patient selection is a major factor in running a successful ambulatory surgery unit with good patient outcomes. Different models of ambulatory surgery centers have different selection criteria. Some may offer full-service anesthesia and physically be part of the main hospital making admission a possibility, as part of the process. Others may not want the inefficiency of fiber-optic intubation for the difficult intubation and screen these patients out. Still others are free standing and admission is not an acceptable option, rather a complication and continuous quality improvement factor; consequently they have stricter selection criteria for appropriate patients.

Traditionally, preoperative testing has been part of the screening process for appropriate preoperative care and selection. Preoperative testing costs this country an estimated $18 billion annually. Ambulatory surgery is by definition low-risk surgery and patients, who are usually American Society of Anesthesiologists (ASA) physical status 1 or 2, expect to be discharged home safely. Mortality risk in ASA 1 and 2 patients is 0.06% to 0.08% and 0.27% to 0.4% in all surgeries, much lower in this low-risk category.

a Department of Anesthesiology, Stony Brook University Medical Center, Stony Brook, NY 11794-8480, USA
b Preoperative Services, c/o Department of Anesthesiology, Stony Brook University Medical Center, Stony Brook, NY 11794-8480, USA
* Department of Anesthesiology, Stony Brook University Medical Center, Stony Brook, NY 11794-8480.
E-mail address: drichman@notes.cc.sunysb.edu

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1932-2275/10/$ – see front matter © 2010 Elsevier Inc. All rights reserved.
Measuring differences in outcomes, when poor outcomes are so rare, needs appropriately powered, randomized controlled studies. Many studies have been published since the late 1970s supporting selective testing. Although various organizations, including the ASA and the Society for Perioperative Assessment and Quality Improvement, and agencies, such as Centers for Medicare and Medicaid Services, have supported appropriate and minimal testing there is still confusion about what is appropriate and resultantly minimal buy in into these cost-saving and evidence-backed initiatives.

EVIDENCE

It has long been accepted that no routine testing is indicated. Preoperative tests without specific indications lack utility. Few abnormalities detected by nonspecific testing result in changes in management, even in the elderly, and rarely have such changes benefited patients or lack of testing affected safe anesthesia.\(^6\) It has also been demonstrated that eliminating routine testing does not increase risk.\(^7\)–\(^9\) Although Schein’s work is procedure specific (cataract), these findings can potentially be extrapolated to other low-risk surgeries.

Statistically normal results are defined as within two standard deviations of the mean, which means that 5% of normal people will have an abnormal result when just one test is performed. The more tests, the more abnormal results, but not necessarily the more abnormalities. The major impacts of unnecessary testing are patient anxiety, increased costs, delays while waiting for further tests and consults, and possible injury from unnecessary workups. The economic impact is a combination of added testing costs and impact on operating room schedule. There are also medico-legal implications of not following up on abnormal test results.\(^10\)–\(^12\) Abnormal test results can lead to injury\(^10\) (1 in 2000) associated with further workup.

Routine testing has a frequency of abnormal results in 0.0% to 2.6% in multiple studies reviewed.\(^13\) When selective testing is done, abnormal results are more frequent: 30% in a study by Charpak and colleagues.\(^14\) These abnormal results are not unexpected and were more likely to change management.

Attempts have been made to introduce testing guidelines following evidence from the literature. These guidelines are not yet uniformly followed, despite more than 30 years of evidence and education. A recent retrospective chart review from Canada\(^15\) found a big variance in compliance with ordering guidelines (5%–98%). Only 61.6% of all the tests performed were normal, but management was affected by only 2.6% of the tests. Katz and colleagues\(^16\) found a similar magnitude of over ordering compared with local guidelines.

Kaplan and colleagues\(^11\) in his study of 2000 subjects found that 60% of tests were not indicated, and only 0.22% of these abnormal results prompted some management change. Another study of 991 subjects older than 40 years of age, by Ajimura and colleagues\(^17\) found 52.5% had some laboratory abnormality, but none lead to a change in management.

A recent pilot study from Canada advocates no preoperative testing in ambulatory patients. Chung and colleagues\(^8\) showed no difference between the routine testing and no testing groups in ambulatory surgery patients with regard to adverse events at 7 and at 30 days. There were several limitations to the study. Exclusion criteria selected out subjects with significant medical issues, especially cardiac and respiratory. Because bad outcomes are rare, the sample size was not large enough. Noncompliance was allowed; subjects wishing to be tested crossed over in the study. Further studies need to be done before no testing becomes the new routine. But the
importance of this study is again raising the lack of benefit in testing, and in the current health economic climate this fact cannot be ignored.

As the majority of ambulatory patients are ASA 1 and 2, the goal of assessing these healthier patients is to detect any previously unrecognized disease that may increase perioperative risk above baseline. Mortality is low.\(^{18}\) Warner and colleagues\(^{19}\) found a 1- to 30-day postoperative major morbidity and mortality of 0.08% (n = 33) in a group of 38,598 ambulatory surgery subjects. Four subjects died: two of myocardial infarcts and two of unrelated motor vehicle accidents.

Do patients who are not ASA class 1 or 2 need to be treated differently? Natof,\(^{20}\) in a study of more than 13,000 subjects, found that well-controlled subjects who were ASA class 3 were at no higher risk for postoperative complications than those in ASA class 1 or 2.

**SPECIFIC POPULATIONS**

**Age**

Older age is another concern as a risk factor. Previously published work by Chung and Mezei\(^{21,22}\) showed no increase in major cardiovascular complications in the elderly compared with younger subjects, and to their advantage, the older group had a lower incidence of postoperative nausea and vomiting.

Extremes of age may confer higher risk for postoperative admission especially in infants less than 55 to 60 weeks post-conceptual age and also in elderly patients older than 85 years of age.\(^{18}\) Preoperative testing does not appear to play a role in decreasing this risk.

Generally, age is not considered a risk factor for adverse outcomes in ambulatory surgery,\(^ {23}\) but a systematic review by Smetana and colleagues\(^{24}\) found that age greater than 60 (odds ratio [OR] 2.09) and greater than 70 (OR 3.04) to be an independent risk factor for the development of postoperative pulmonary complications in all surgeries. Again testing does not play a role in decreasing these complications, only identifying those at risk.

**Obesity**

Obesity is not a risk factor for major adverse outcomes.\(^{25}\) The review by Smetana and colleagues\(^{24}\) found one study where morbid obesity is a predictor of postoperative pulmonary complications, but this remains controversial. Obesity is however, an independent risk factor for deep vein thrombosis.\(^ {26}\)

**So What Do We Do?**

The preoperative history and physical (H&P) are the key elements in patient assessment, which is backed by legislation and professional society standards. Basic Joint Commission regulatory requirements for all patients include a history and physical performed within 30 days of the procedure.\(^ {27}\) In addition, ASA has standards and guidelines for preanesthesia care\(^ {28}\) that specifically state that no routine testing is indicated.

In the Australian Incident Monitoring Study,\(^ {29,30}\) inadequate preoperative evaluation and communication problems were shown to be sentinel contributing factors to preventable major adverse events (incidence 3.1%) including death and major morbidity. Laboratory testing or lack thereof was not implicated in these complications.

How preoperative assessment is achieved varies by institution. Some assess patients only on the day of surgery, others have all patients come through a preoperative evaluation clinic approximately 2 weeks before surgery. Some authors\(^ {31,32}\) have
found the latter method to be cost effective in reducing day of surgery cancellations, even in the healthier ambulatory population.

No testing substitutes for a history and physical examination. An important component of the history is assessing self-reported exercise tolerance. Reilly and colleagues\textsuperscript{33} showed that postoperative complications were inversely related to exercise ability. Although the study group was major surgeries, this can be extrapolated to ambulatory surgery.

Tests should only be ordered if the result will change the anesthetic or surgical plan or decrease the risk of the procedure. If medical condition is stable, then laboratory tests performed in the preceding 4 months\textsuperscript{34} to 1 year\textsuperscript{35} can be used.

The following tests are the minimum to be considered:

<table>
<thead>
<tr>
<th>Tests</th>
<th>Type and screen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Surgeries with anticipated blood loss</td>
</tr>
<tr>
<td></td>
<td>• Rhesus antibody result needed for possible Rhogam therapy.</td>
</tr>
</tbody>
</table>

**Pregnancy**

Beta human chorionic gonadotrophin (bHCG) assay is recommended but not mandated by the ASA, and policy is institution specific. Mandated testing will identify some previously undiagnosed pregnancies, and elective surgery is then postponed, but this testing comes with a cost. A study by Kahn and colleagues quantified this cost as $3273/true positive pregnancy test.\textsuperscript{36} Consider testing in all women of reproductive age, except after hysterectomy or oophorectomy. This testing can be done on the day of surgery but is recommended earlier if history suggests pregnancy is a possibility, as cancellations on the day of surgery have a bigger economic impact.

It is not clear what the extent of the risk of anesthesia is to the fetus, but current practice is not to do elective surgery in patients who are pregnant when it can be delayed, because there is risk to the fetus, especially in the first trimester, and increased risk for miscarriage.\textsuperscript{37}

**Hemoglobin**

Anemia is a marker of perioperative mortality.\textsuperscript{19,38} It is unclear if the increased risk is from the underlying causative disease or the anemia itself.

Hemoglobin preoperatively may be indicated in patients with symptoms of anemia, history of bleed, chemotherapy, radiotherapy, chronic renal failure, and clinical findings compatible with anemia. It is indicated as a baseline in surgery where significant blood loss (>500cc)\textsuperscript{39} is expected.

**Platelet count**

Platelet count is indicated if patients have personal or family history of bleeding or bruising.

**Coagulation studies**

Coagulation studies are only done when patients have a personal or family history of bleeding or bruising, in the presence of liver disease or metastases, severe malnutrition, Vitamin K deficiency, and patients on anticoagulant therapy. Abnormal results by routine screening have not shown clear positive predictive value for operative bleeding.\textsuperscript{40–43}
**Electrocardiogram**

Twenty million preoperative electrocardiograms (ECGs) are performed each year, but there is no consensus by practitioners about whom, if anyone, should get these tests. Recent publications have questioned the value of the routine preoperative ECG and prior publications that included the ECG as part of the perioperative risk assessment, may no longer be valid in this respect.

The utility of the screening 12 lead ECG for assessing for perioperative risk has been questioned. It is also unclear when an abnormal ECG should alter management. A meta-analysis found the resting ECG to be a poor screening tool for coronary artery disease. One study by Tervahauta and colleagues found that if evidence of CAD was present on screening ECG, there was higher mortality in this group, but the perioperative implications of this non-surgery–related work are not known. Van Klei and colleagues found, in a prospective observational study in subjects older than 50 years of age having non-cardiac surgery, that 45% of subjects had an abnormality on preoperative ECG, and bundle branch blocks were associated with postoperative myocardial infarction and death, but had no added predictive value over recognized risk factors such as gender, age, and the components of the revised cardiac risk index (high-risk surgery, history of one or more of the following: ischemic heart disease, congestive heart failure, chronic renal failure, cerebrovascular accident, insulin dependent diabetes).

Correll and colleagues found that age greater than 65 years was an independent predictor of preoperative electrocardiogram abnormalities but any management change was already indicated by the H&P. Rabkin and Horne showed new ECG changes caused no cancellations, only minor change in anesthesia technique in 1% of subjects, and no difference in outcome.

The specificity of an ECG abnormality in predicting postoperative cardiac adverse events is only 26% and a normal ECG does not exclude cardiac disease.

An ECG should not be done simply because of age. Previous recommendations for age-based testing were derived from the high number of ECG abnormalities found on patients who were elderly. The Centers for Medicare and Medicaid Services do not reimburse for preoperative or age-based ECGs.

The ASA Preoperative Evaluation Practice Advisory recognized that ECGs did not improve prediction beyond risk factors identified by patient history.

The AHA makes the following recommendations for preoperative ECG.

- **Class 1:** Recommendations for resting ECG are in patients undergoing vascular surgery or in those undergoing intermediate risk procedures who have known coronary artery, cerebrovascular, or peripheral vascular disease. If we accept ambulatory surgery as low risk, then this does not apply to the ambulatory subset of patients. But what about the 3-hour shoulder repair? Orthopedic surgery is considered intermediate risk, or does the arthroscopic component of this procedure make it an endoscopic procedure and thus a low-risk procedure? This question causes controversy.

- **Class 2a:** Patients for vascular surgery with no risk factors

- **Class 2b:** Patients with one risk factor for intermediate risk surgery

- **Class 3:** Patients for low risk surgery who are asymptomatic (ECG should not be performed because it is not helpful and may even be harmful).

These recommendations suggest that patients undergoing ambulatory surgery (low risk) should not get ECGs if they are asymptomatic. Patients with class 2 angina pectoris undergoing a knee arthroscopy are low risk and asymptomatic; which class does
this fall into? There is no doubt that there are still a lot of unknowns out there. Ideally, perhaps the annual ECG from the primary care physician (PCP) would be adequate if symptoms were stable over the interceding interval. Reading further into the text of the AHA guidelines and the primary article,\textsuperscript{18} it is suggested that stable (not asymptomatic) ambulatory patients need not have ECGs because morbidity and mortality associated with these procedures is so low and risk is negligible.

**Chemistry**
A review by Smetana and Macpherson\textsuperscript{13} found that only 1.8% of electrolyte tests affected management and most of these were predictable from patients' history of renal disease or diuretic use.

Electrolytes: Consider testing if there have been recent changes in medication known to affect electrolytes (eg, diuretics, steroids) or in patients on digoxin. Also consider checking potassium in end-stage renal disease.

Chronic renal failure with a creatinine greater than 2mg/dl is an independent risk factor for perioperative morbidity and mortality.\textsuperscript{2,24} Creatinine is indicated if patients are to receive contrast media. If the test is abnormal renal protective strategies can be used or an alternative study can be performed. Consider for risk assessment if it will affect informed consent, and no recent testing results are available.

Glucose should be checked on admission in patients who are diabetic and hourly in procedures lasting longer than 1 hour. Presuming that patients who are diabetic have good routine care, including regular glucose checks; a HBA1C less than seven; and assessment for end organ damage,\textsuperscript{57} specifically workup of cardiac symptoms or abnormal ECG and a serum creatinine, then it is not necessary to test further for minor surgery.

**Urinalysis**
Urinalysis (UA) is never indicated for anesthesia. For orthopedic surgery with hardware implants, a urinalysis is frequently ordered to decrease the risk for subsequent infection. It is rare that the organisms associated with asymptomatic bacteruria cause orthopedic infection, and the administration of preoperative prophylactic antibiotics, which is standard of care, is usually enough to prevent this anyway. However, the catastrophic outcome of an infected joint is cited by the surgeons as a reason to maintain the practice of ordering UAs. No difference was found in wound infections in knee surgery whether UA was normal or abnormal. It was estimated by Lawrence\textsuperscript{58,59} that the cost of treating wound infections (non-implant) was 500 times less than the cost of screening urinalyses and so these tests are not recommended.

**Liver function tests**
Albumin is a marker of chronic disease and markedly low levels may affect wound healing. It was the only laboratory predictor of postoperative pulmonary complications in the review by Smetana.\textsuperscript{24}

Patients with acute hepatitis should not undergo elective surgery. Child-Pugh\textsuperscript{60} grade C should also not undergo elective surgery. Those assessed as grade B are at increased risk and may benefit from therapy to improve their score before surgery. Decisions to perform these tests are guided by significant findings on history and physical examination.
**Chest X ray**

Chest X-Ray (CXR) abnormalities increase with age. A review of studies of routine preoperative CXRs by Joo and colleagues found that most abnormalities are predicted on history and physical examination. Only 10% of those investigated for an abnormal CXR had a change in management. CXR usually only confirms clinical findings and is not useful at reducing risk.

CXRs should be considered in patients with new signs or symptoms, history of end-stage renal disease, or decompensated heart failure, if it will change management. Patients with the latter are rarely candidates for the ambulatory setting except for minor procedures like ophthalmologic surgeries.

**Cardiac evaluation**

Cardiac evaluation is indicated based on the presence of active cardiac conditions and patients with these are not current candidates for elective ambulatory surgery. Patients with unexplained dyspnea on exertion may warrant an echocardiogram – Class 2a.

Heart failure, compensated and decompensated, carries increased risk for cardiac complications, approximately 5% to 7% and 20% to 30% respectively, and an echocardiogram may be considered for quantifying degree and type if it will change management.

**Pulmonary function testing**

Postoperative pulmonary complications (PPC) are a common event (incidence ranges from 0%–75%). They are more frequently associated with the presence of pulmonary risk factors and certain surgical factors: surgical site and length of procedure. Thoracic and upper abdominal surgeries are the highest risk procedures. Laparoscopic procedures significantly decrease the risk, so surgical site is not usually a predisposing factor in ambulatory surgery. Duration of surgery greater than 2.5 to 4 hours confers increased risk.

Independent patient risk factors for PPCs include smoking; pulmonary hypertension; obstructive sleep apnea (see later discussion); morbid obesity; moderate to severe chronic obstructive pulmonary disease; congestive heart failure; poor general health, including baseline functional status (physical and mental); and age.

Well-controlled asthma and upper respiratory tract infections (URIs) are not risk factors for PPCs in adults. Patients with an intercurrent bronchitis of bacterial etiology are at a higher risk for postoperative pneumonia, and antibiotic therapy administered preoperatively can decrease this risk. History, and not testing, affects outcome here.

A detailed history of pulmonary symptoms, medication compliance, presence of productive cough, and physical examination is adequate in patients undergoing ambulatory surgery. Pulmonary function testing (PFTs) is usually reserved for patients undergoing major non-ambulatory surgeries. A possible exception is the assessment of poorly controlled asthma to differentiate between severe asthma (not usually a candidate for ambulatory surgery) and inadequately treated bronchospasm. No studies have shown PFTs to improve outcomes.

**Arterial blood gases**

Arterial blood gases are not indicated in the ambulatory settings are they are markers of severe disease and these patients are not ambulatory candidates.
Sleep consult/polysomnography
Obstructive sleep apnea (OSA) is common with 4% of women and 25% of men having some degree of the disease. It is more common in the obese population. The majority are undiagnosed.

Patients should be screened for OSA. The STOP/BANG screen is a useful validated tool that can easily identify those who may have OSA. These patients can then be assessed for the need for further preoperative testing. The ASA has published Practice Guidelines for the Perioperative Management of Patients with OSA. It applies an OSA scoring system (Table 1). The score takes into account the severity of the OSA, the invasiveness of the surgery, and the need for postoperative opiates. To accurately ascertain this score, polysomnography (PSG) is necessary. It should be ordered when the result would change the decision about venue, type of anesthesia, or proceeding with surgery.

In surgeries performed under local with or without sedation, PSG is advised for patients concurrently for health maintenance and risk reduction, but the results are not superior to clinical assessment in changing perioperative management and this workup can be done after surgery by the PCP.

Those patients with an OSA score of 5 or 6 are not appropriate for free-standing ambulatory centers. Patients with a score of 4 should be assessed on a case by case basis, especially if surgery interferes with use of continuous positive airway pressure (CPAP) or other OSA treatment devices.

Patients also need to be monitored in recovery longer than their non-OSA counterparts. Patients with OSA should be first case or early enough in the day, especially in facilities that are not open overnight.

Pediatrics
Routine diagnostic testing in children is traumatic and this stress often leads to an uncooperative child on the day of surgery. Preoperative hemoglobin is not indicated in healthy children unless there is anticipated blood loss. It can be considered in ex-premature infants if clinically indicated or not recently tested. Coagulation tests do not predict surgical bleeding in healthy children with no history of bleeding tendency or family history of bleeding disorders. Many pediatricians and pediatric surgeons still insist on coagulation studies in surgeries where hemostasis is vital, specifically tonsillectomies and neurosurgical procedures.

| Table 1 |
| Scoring of Obstructive Sleep Apnea patient for management decisions |
| (maximum possible score = 6) |
| Choose the higher of the following 2 scores and add to OSA severity score below: |
| Opiate Need | or | Surgical Invasiveness |
| 0 = None | 0 = none |
| 1 = Low dose oral | 1 = Superficial/local anesthesia |
| 2 = High dose oral | 2 = Peripheral/general anesthesia |
| 3 = Parenteral/neuroaxial | 3 = Airway/major/abdominal |
| OSA Severity by PSG Result: |
| 1 = Mild |
| 2 = Moderate |
| 3 = Severe |
SUMMARY

Routine testing is not the standard of care. Table 2 provides a summary of indicated testing for Ambulatory Surgical procedures.

There is no doubt that we are still over-testing preoperatively. We know that testing rarely changes management, and rarely affects outcome. We need to base our testing decisions on a good history and physical and evaluation of effort tolerance, and then order only those tests which offer information about risk—needed for informed consent; and those where expected results would alter management or outcome. Testing may need to be individualized to level of patient medical care and patient compliance.

It is recommended that anesthesiologists should be doing the ordering as they do it more appropriately and with effective cost reduction.74

Pasternak,75 in an editorial advocates judicious testing and a formal structure for preoperative assessment for better implementation of evidence based management of patients.

There is already three decades of evidence in the literature supporting less testing, but as adverse outcomes are rare, we need better powered more inclusive prospective studies to back our current expert opinion based decisions.

<table>
<thead>
<tr>
<th>Test</th>
<th>Indicated</th>
<th>Guidelines</th>
<th>Exceptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>ECG</td>
<td>No</td>
<td>Class 3 AHA</td>
<td>—</td>
</tr>
<tr>
<td>Complete blood count</td>
<td>No</td>
<td>—</td>
<td>Anemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Anticipated blood loss</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Premature infants</td>
</tr>
<tr>
<td>bHCG</td>
<td>Yes by history</td>
<td>Institution specific</td>
<td>—</td>
</tr>
<tr>
<td>Coagulation studies/platelets</td>
<td>No</td>
<td>—</td>
<td>Personal/family history of bleeding diathesis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Anticoagulants</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Liver disease</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>? Tonsillectomy and neurosurgery - controversial</td>
</tr>
<tr>
<td>Liver function tests</td>
<td>No</td>
<td>—</td>
<td>Risk assessment –cirrhosis</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Acute history</td>
</tr>
<tr>
<td>Pulmonary Functions</td>
<td>No</td>
<td>—</td>
<td>Only as part of routine management of asthma</td>
</tr>
<tr>
<td>Arterial blood gases</td>
<td>No</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>UA</td>
<td>No</td>
<td>—</td>
<td>Insertion of hardware</td>
</tr>
<tr>
<td>PSG</td>
<td>No</td>
<td>ASA practice advisory</td>
<td>Diagnosis of severe OSA will change venue</td>
</tr>
<tr>
<td>CXR</td>
<td>No</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Type and screen</td>
<td>—</td>
<td>—</td>
<td>Anticipated blood loss &gt;500cc</td>
</tr>
<tr>
<td>Electrytes</td>
<td>No</td>
<td>—</td>
<td>Recent change in medications affecting potassium/electrolytes</td>
</tr>
<tr>
<td>Creatinine</td>
<td>No</td>
<td>—</td>
<td>Contrast dye study</td>
</tr>
<tr>
<td>Glucose</td>
<td>No</td>
<td>—</td>
<td>Morning of surgery</td>
</tr>
</tbody>
</table>
We must also remember that even with best evidence studies, circumstances vary at different institutions and testing needs to be locally customized to the individual variations and restrictions of the practice.

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27. Commission TJ. Joint Commission Standard: RC.02.01.03, PC.01.02.03, EP 5.


The Use of the Flexible LMA in Outpatient Nasal Surgery

UCSD Anesthesia Update 2008

Michael L. Bishop, M.D.
Clinical Professor of Anesthesiology
University of California, San Diego
Department of Anesthesia
Suitability for Outpatient Surgical Management

- Procedures that are “associated with postoperative care that is easily managed at home and with low rates of postoperative complications that [would] require intensive physician or nursing management.”

Lichtor 2006
The ideal anaesthetic technique for nasal surgery will provide a secure airway with protection of the tracheo-bronchial tree from blood and debris. In order to optimize the surgical field and minimize blood loss, a haemodynamically stable anesthetic is required, and often controlled hypotension is used.”

Moloney 2007
Additional Criteria

- Efficient induction with rapid securing of the airway
- Unfettered access to the surgical field
- No unexpected patient movement during surgery
- Rapid, smooth wakeup
- Stable and short PACU stay with minimal nausea and vomiting
- Rapid discharge from the facility
Standard Technique at UCSD

- General anesthesia
- Insertion of an endotracheal tube (ETT).
- Patient is turned 180 degrees so that the patient’s head and airway are relatively inaccessible to the anesthesia provider
- In order to decrease surgical bleeding the surgeons request:
  - mild head up position to decrease venous pressure
  - mild intraoperative hypotension
Flexible LMA
Arguments Against the Use of the Flexible LMA

- Difficulty in placement of an LMA and concern over security of the airway with an LMA, especially when the patient’s airway is inaccessible.
- Concern over soiling of the oropharynx by secretions and blood during the surgical procedure with resultant aspiration of these fluids past the cuff of the LMA into the tracheobronchial tree.
- Difficulty with induction and maintenance of mild hypotension in a patient who is spontaneously breathing with an LMA in place.
Difficulty with LMA Placement

- Prospective, randomized study
- 381 patients for elective outpatient surgery
- Compared LMA as an alternative to ETT
- NS for time to place LMA vs. ETT
- First attempt success: 91% LMA, 88% ETT
- Failure rate for placement 1% for either device

Joshi 1997
Adjunct to Placement of LMA

- Randomized, double blind, placebo-controlled
- 80 patients
- 1.5 mg/kg vs 0.9 % NS
- Significant decrease in incidence of coughing and airway obstruction with lidocaine
- Significant decrease in failure rate for insertion requiring deepening of anesthesia

Stoneham 1995
Security of the Airway with the LMA in Place

- Retrospective chart review
- Otologic surgery under general anesthesia
- 100 adult and pediatric patients
- Table turned 180 degrees
- Spontaneous ventilation for avg. 83 min
- No patient had displacement of LMA
- No patient required endotracheal intubation

Duff 1999
Security of the Airway with the LMA in Place

- Prospective randomized study
- 44 patients
- LMA vs ETT
- Peripheral orthopedic surgery under general anesthesia
- Fiberoptic evaluation of placement pre and post surgery in 22 patients with LMA
- No change in position of LMA

Cork 1994
Clinical Tests for Correct LMA Placement

- Prospective double-blinded observational study
- 150 adult ambulatory surgery patients receiving LMA placement
- Males received #4 LMA with 30 ml air
- Females received #3 LMA with 20 ml air
- Fiberoptic evaluation of adequacy of LMA placement

Joshi 1998
Clinical Tests for Correct LMA Placement

- Resistance to advancement of the LMA after insertion
- Anterior movement of the larynx with cuff inflation
- Movement of the LMA out of the oropharynx with cuff inflation
- Inability to advance the LMA after inflation
- Black line on LMA in midline
Clinical Tests for Correct LMA Placement

- Ability to ventilate the patient manually as evidenced by chest movement, condensation of expired gases, adequacy of expired gas volume and feel of the bag during manual ventilation
- Satisfactory capnographic curve
- Movements of the reservoir bag during spontaneous ventilation
Clinical Tests for Correct LMA Placement

- Ability to achieve airway pressure of 20 cm H$_2$O during manual inspiration with a fresh gas flow of 6 liters/min
# Clinical Tests for Correct LMA Placement

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>Overall Accuracy %</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistance to advance after insertion</td>
<td>100</td>
<td>0</td>
<td>91</td>
<td>NA</td>
</tr>
<tr>
<td>Anterior movement of Larynx</td>
<td>91</td>
<td>36</td>
<td>86</td>
<td>0.01</td>
</tr>
<tr>
<td>LMA moves out with cuff inflation</td>
<td>93</td>
<td>36</td>
<td>87</td>
<td>0.004</td>
</tr>
<tr>
<td>Inability to advance after inflation</td>
<td>100</td>
<td>0</td>
<td>91</td>
<td>NA</td>
</tr>
<tr>
<td>Black line in midline</td>
<td>96</td>
<td>57</td>
<td>92</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ability to ventilate manually</td>
<td>99</td>
<td>43</td>
<td>94</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Satisfactory capnographic trace</td>
<td>100</td>
<td>7</td>
<td>91</td>
<td>0.16</td>
</tr>
<tr>
<td>Movements of reservoir bag</td>
<td>100</td>
<td>14</td>
<td>92</td>
<td>0.001</td>
</tr>
<tr>
<td>Airway pressure of 20 cm H2O</td>
<td>95</td>
<td>71</td>
<td>92</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

- **Sensitivity**: percent of properly placed LMAs correctly identified by the test.
- **Specificity**: percent of improperly placed LMAs correctly identified by the test.
- **Overall accuracy**: probability of proper LMA placement given a positive test.
Concern Over Aspiration of Regurgitated Gastric and Oropharyngeal Fluids

- Aspiration of fluids has significant morbidity and mortality
- LMA does not provide as “secure” a seal as the ETT
Completeness of the Endotracheal Tube Seal

- Low pressure high volume cuffed ETT
- 30 patients
- Incidence of dye tracking past the cuff was 100%  
  
Seegobin 1986
Overall Risk of Regurgitation and Aspiration With Use of an LMA in Clinical Practice

- Incidence of perioperative regurgitation with LMA is approximately 0.1%
- Incidence of aspiration with use of an LMA is approximately 0.02%
- Similar to risks in tracheal intubation in elective surgery patients
- Described regurgitation and aspiration as “rare events”  

Keller 1999, 2004
Risk of Regurgitation With LMA Use

- Prospective randomized study
- 60 healthy patients
- Elective peripheral surgery under general anesthesia
- Hypopharyngeal probe for pH measurement
- No episodes of pH < 4 in either group
- No change in pH of > 1 unit in any patient

Joshi 1996
Effect of LMA Cuff Pressure on Regurgitation

- Cadaver study
- Flexible, standard or no LMA
- Proper placement of LMA confirmed with fiberoptic exam
- Significant increase in sealing pressure up to 20 ml air cuff volume, no further increase up to 40 ml

Keller 1999
Effect of LMA Cuff Pressure on Regurgitation

- Regurgitation pressure in control group was 7 cm H$_2$O
- Regurgitation pressure with LMA volume 0 ml was approx 19 cm H$_2$O
- Regurgitation pressure with LMA volume 10-40 ml was approx 50 cm H$_2$O
Contraindications to LMA Placement

- Obesity
- GERD
- Hiatal hernia
- Full stomach
- Diabetes
- Prior gastric surgery
- Drug use (narcotics)
- Pain
- Laparoscopic surgery
- Position during surgery
- Duration of surgery
- Pregnancy
- Depth of anesthesia
Australian Survey Results

- Survey of Australian anesthesiologists
- 57-73% would use LMA in patients with history of GERD or hiatal hernia if the patient was currently asymptomatic

Keller 2004
Risk of Aspiration of Oropharyngeal Fluids

- 64 patients spontaneously ventilating while receiving general anesthesia
- LMA placed and inflated to achieve a clinically acceptable seal
  - Defined as seal necessary to allow assisted ventilation
- 10 ml methylene blue injected into pharynx
- Fiberoptic exam via LMA at end of surgery

John 1991
Risk of Aspiration of Oropharyngeal Fluids

- Minimal dye leak in 5 of 64 patients (8%)
- Small amount of pooling inside bowl of mask in one patient whose LMA had become partially displaced during draping
- No dye seen in trachea of any patient
- “Leakage of blood past cuff less likely than dye because of greater viscosity of blood”
Risk of Aspiration of Oropharyngeal Fluids

- LMA placed with cuff seal average of 25 cm $H_2O$
- 15 ml barium injected into pharynx of patients with LMA in place
- Fiberoptic exam via LMA after placement and at end of procedure
- Postoperative xray of chest and neck
- No barium seen inside LMA cuff or on xray

Cork 1994
Risk of Aspiration of Oropharyngeal Fluids

- Randomized design
- 41 patients received LMA or ETT for nasal septorhinoplasty
- Positive pressure ventilation in both groups
- Fiberoptic exam pre and post procedure
- Blood inside LMA cuff in 1/19 patients and in the trachea in 7/23 pts (p< 0.01)

Rheineck Leyssius 1994
Risk of Aspiration of Oropharyngeal Fluids

- Prospective nonrandomized design LMA vs ETT
- 76 patients undergoing endoscopic sinus surgery or nasoseptoplasty
- Fiberoptic exam pre and post surgery
- Blood staining in any portion of glottis or trachea
  - LMA 19.5%   ETT  84.8%  (p<.001)
- Commented that ETT acted as conduit

Kaplan 2004
Risk of Aspiration of Oropharyngeal Fluids

- Randomized design LMA vs ETT
- 114 patients for endoscopic nasal surgery or nasoseptoplasty
- Moistened throat pack in LMA group
- Fiberoptic exam at end of surgery
- Amount of blood in airway
  - low in both groups
  - not significantly different

Webster 1999
Risk of Aspiration of Oropharyngeal Fluids

- Randomized design LMA vs ETT
- 109 children for T&A or adenoidectomy
- 19 patients with LMA had fiberoptic exam at end of surgery
- No patient with blood in larynx

Webster 1993
Risk of Aspiration of Oropharyngeal Fluids With Positive Pressure Ventilation Using an LMA

- Review Article
- Use of LMA with positive pressure ventilation
- Stated “several large scale studies have failed to show any link between positive pressure ventilation and pulmonary aspiration or gastric insufflation”
- Suggested airway pressure of 20 cm H$_2$O and tidal volume 6-8 ml/kg  
  Keller 2001
Summary of Aspiration Studies

- Use of LMA in nasal surgery does not increase the risk of aspiration
- Sealing pressure should be kept in the range of 15-20 cm H$_2$O
Hemodynamic Stability and the LMA

- **Cork (1994)**
  - With respect to HR and BP insertion and removal of ETT more hemodynamically stimulating than LMA ($p<.05$)
  - Intraoperative fentanyl requirement significantly higher in ETT group

- **Webster (1993)**
  - HR, BP and blood loss significantly less in LMA vs ETT group
Hemodynamic Stability and the LMA

- Prospective, randomized Design LMA vs ETT
- 20 patients for orthopedic, general or plastic surgery cases
- Isoflurane requirement significantly less in LMA group (p< .05)

Wilkins 1992
Summary of Hemodynamic Stability Studies

- LMA use vs ETT associated with
  - Decreased anesthetic requirements
  - Less hemodynamic stimulation
- Reasonable to expect facilitation of mild hypotension
- Respiratory depression with spontaneous ventilation
  - High narcotic dose
  - High inhalation or intravenous drug use
- Careful titration of vasoactive drugs may be preferable
  - Labetalol
  - Nicardipine
- Not associated with hypotension/bradycardia in PACU
Removal of LMA

- Randomized Design
- 63 adult patients for elective orthopedic surgery
- General anesthesia with LMA
- Significantly increased esophageal reflux if LMA removal delayed until patient able to open mouth on command vs removed at first sign of rejection
- Clinical aspiration or desaturation did not occur in either group

Cheong 1999
Additional Benefits of LMA

- Prospective randomized design
- 20 patients for peripheral surgery
- General anesthesia, spontaneously breathing with LMA
- Comparing the work of breathing in anesthetized patient using an LMA versus an ETT
- Significant decrease in the work of breathing in the LMA group as compared to the ETT group  
  Joshi 1998
Additional Benefits of LMA

- Cork (1994) also found a significant decrease in the work of breathing in patients with an LMA vs ETT
Additional Benefits of LMA

- Prospective randomized design
- 114 patients for intranasal surgery of nasoseptoplasty
- General anesthesia with LMA vs ETT
- Significantly decreased coughing and desaturation at the end of surgery with LMA vs ETT

Webster 1999
Additional Benefits of LMA

- Webster (1999)
  - Found significantly lowered incidence of desaturation on arrival in PACU in
    - Patients extubated awake with LMA vs patients extubated awake with ETT

- Cork (1994)
  - Found significantly decreased incidence of coughing and narcotic use in PACU in
    - Patients with LMA vs ETT
Additional Benefits of LMA

- Joshi (1997)
- 381 patients for outpatient surgery
- LMA vs ETT
- Incidence of nausea and vomiting significantly less at 24 hours in LMA group
- Duration of PACU stay significantly less in LMA group
Conclusions

- Literature suggests:
  - LMA for nasal surgery poses no increased risks vs ETT
  - May have significant advantages over ETT
    - lower anesthetic requirements
    - Smoother wake up
    - Smoother Lower anesthetic requirement and shorter PACU stay
Caveat

“The safe, efficient use of the fLMA in nasal surgery requires specific skills of the anaesthetist. The correct insertion technique needs to be mastered, and the optimum depth of anaesthesia for insertion needs to be reached. The anaesthetist must be able to identify malposition of the cuff and leaks in the seal, and must have practise in spontaneous, assisted and positive pressure ventilation”

Moloney 2007
Total intravenous anaesthesia techniques for ambulatory surgery
Henrik Eikaas and Johan Raeder

Department of Anaesthesia, Oslo University Hospital, Ullevaal, Oslo, Norway

Correspondence to Johan Raeder, MD, PhD, Department of Anaesthesia, Oslo University Hospital, Ullevaal, Kirkeveien, N-0407 Oslo, Norway
Tel: +47 22119690; fax: +47 22119857; e-mail: johan.raeder@medisin.uio.no

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Purpose of review
The purpose of the present review is to provide an updated discussion on the use of total intravenous anaesthesia (TIVA) for ambulatory surgery, based on results from recent studies put into the context of issues already known.

Recent findings
The current use of TIVA for ambulatory surgery seems to be abundant. It is encouraged by the simplicity of the method, increased experience and declining costs with the propofol and remifentanil combination. The TIVA methods are well tolerated and perceived to give good quality patient care; with rapid, clear-headed emergence and low incidence of postoperative nausea and vomiting. Cost-efficacy and other benefits of recovery from TIVA versus alternative techniques of anaesthesia seem to depend more on the patient and the individual perioperative setting than on the TIVA concept per se. Further development of TIVA will include the refinement of target control systems, the introduction of new drugs and adjuvants and advanced equipment for automatic drug delivery, as well as improved effect monitoring.

Summary
TIVA is well tolerated and simple. It is associated with less postoperative nausea and vomiting than inhalational anaesthesia and has no residual paralyses as are possible with locoregional techniques. Propofol with remifentanil seems to be the dominating TIVA technique, delivered either by conventional pumps or by target control systems.

Keywords
ambulatory anaesthesia, ambulatory surgery, postoperative nausea and vomiting, propofol, recovery, remifentanil, target control infusion

Introduction
When general anaesthesia is provided only with intravenous (i.v.) agents, this is called total i.v. anaesthesia (TIVA). The characteristics of TIVA compared with alternative techniques (i.e. locoregional anaesthesia, inhalational anaesthesia) have to do both with the concept per se, but also with the characteristics of the drugs which are used.

The TIVA concept is simple. An i.v. line is the only prerequisite, and everything you need for general anaesthesia will be supplied through this line. This means that there is no need for sophisticated gas delivery systems or scavenger equipment. There is no need for time consuming procedures such as establishing regional blocks or neuraxial blocks, and no risk of block failure and unpredictable duration of residual paralyses.

The TIVA drugs are generally less toxic than inhalational agents, with less risk of malignant hyperthermia and no pollution of environmental air or the atmosphere. TIVA usually implies giving dedicated component therapy with different drugs for different effects, typically one drug for the hypnotic effect (propofol, ketamine, methohexitol, midazolam) and another drug for analgesia and antiemetic action (remifentanil, other opioids, ketamine).

The development of ambulatory surgery brings with it increasing demands for a smooth anaesthetic service. In recent years more extensive procedures have been introduced into the ambulatory setting and more frail patients, such as stable American Society of Anaesthesiologists (ASA) III and even ASA IV patients, are accepted for ambulatory care. Also, ambulatory surgery is expanding from the fully equipped operating rooms into diagnostic suites and office-based settings, with less proximity to adequate backup and rescue facilities. Still, the basic requirement for anaesthetic care is to provide optimal safety, quality and cost-efficacy.

This review will focus on the recent international literature on TIVA in the ambulatory setting, addressing TIVA compared with alternative techniques of anaesthesia. The clinical issues in focus will be rapid induction, smooth maintenance, rapid emergence and adequate
pain control, with the patients being fully awake without side effects such as nausea, vomiting and shivering.

We also looked at recent developments in TIVA techniques and potential future aspects, such as automatic systems and upcoming drugs.

**Total intravenous anaesthesia versus alternatives**

The success of any TIVA technique will be based on its clinical characteristics evaluated against any potential alternative technique in the individual setting of one specific patient for one specific procedure. Whereas a lot of the characteristics of different techniques are well known from older literature, there are still aspects which may be important to document further.

**Total intravenous anaesthesia versus locoregional anaesthesia**

In a study of open haemorrhoidectomy, local anaesthesia was associated with less overall costs and less pain at days 1–10, whereas general anaesthesia had less pain at 90 min after surgery [1]. In a study of knee arthroscopy, the use of TIVA with propofol resulted in a shorter time to micturition, but otherwise had quite similar results to a regional anaesthetic technique of femoral nerve and sciatic nerve block [2]. In a more extensive study of ambulatory brachytherapy of the prostate, Flaishon et al. [3] found less urinary retention and faster discharge with TIVA than with inhalational anaesthesia and two different techniques of spinal anaesthesia.

**Total intravenous anaesthesia versus nitrous oxide supplementation**

In most reviews nitrous oxide is associated with increased risk of postoperative nausea and vomiting (PONV; [4]). This was recently confirmed in a large study of more than 2000 in-patients reported by Leslie et al. [5]. However, in a study of ambulatory orthopaedic patients, Mathews et al. [6] found no significant side effects of nitrous oxide when compared with remifentanil as an adjunct to general anaesthesia. The time to emergence was also similar in the two groups. Nitrous oxide is associated with rapid emergence and minor influence on respiratory function, and may be used as an adjunct to reduce the required dose of propofol. In a study of oocyte retrieval, Handa-Tsutsui et al. [7] found a 20% reduction in the required dose of propofol when nitrous oxide was used, without any obvious clinical benefits or drawbacks.

**Total intravenous anaesthesia versus inhalational anaesthesia**

This is an area in which numerous studies are currently being performed, and have also been performed during the past 1–2 years. Inhalational anaesthesia usually implies inhalational maintenance, with or without opioid supplement, after an i.v. induction. In a study of septo-rhinoplasty, Gokce et al. [8] did not find any significant differences between desflurane and remifentanil maintenance versus propofol and remifentanil. In a more detailed study of microsurgical vertebral disc resection, Gozdemir et al. [9] found shorter emergence and less nausea, but more shivering and postoperative pain in the propofol and remifentanil group than in the desflurane and nitrous oxide group. Increased incidence of postoperative shivering was also found after remifentanil and propofol in Röhm et al.’s [10] comparison with desflurane and fentanyl. Moore et al. [11] confirmed the well known benefit of reduced PONV after TIVA with propofol in mixed-case day surgery. Similarly, reduced PONV was found by Hong et al. [12] after breast biopsy with propofol and remifentanil anaesthesia. However, their result may be biased by the use of a longer acting opioid, fentanyl, in the control group. Inhalational induction with sevoflurane and nitrous oxide was slower, but smoother (i.e. less bradycardia and apnoea) and associated with slower emergence and less postoperative pain than the TIVA technique in this study [12]. In their large study of 1158 adults in ambulatory mixed surgery, Moore et al. [11] compared different methods of sevoflurane with/without nitrous oxide induction and/or maintenance versus propofol TIVA. They found more injection pain and hicups with propofol and more breathing and recalled discomfort with sevoflurane induction. Sevoflurane was associated with more PONV, but the major outcome results, such as time to discharge and unplanned hospital admissions, were similar in both groups [11].

The problem of coughing during emergence and extubation was addressed specifically in a study of lumbar disc surgery by Hohlfrieder et al. [13]. They found significantly less coughing with propofol and remifentanil than with sevoflurane, nitrous oxide and fentanyl. Aspects of early and late PONV were addressed by White et al. [14] in a study of day-case gynaecological surgery. They reported similar predischARGE PONV incidence when dolasetron was added to sevoflurane maintenance and compared with propofol and remifentanil. However, as discussed by the authors, the dolasetron effect is prolonged compared with propofol, explaining why the dolasetron and sevoflurane patients had less PONV after discharge [14].

Gas gastric emptying may also have an impact on PONV incidence. This was looked upon by Wallow et al. [15] in a study of ambulatory laparoscopic cholecystectomies. They found generally delayed and variable gastric emptying rate in their patients, but no difference between the propofol plus remifentanil group and the sevoflurane group [15].
As inhalational agents may be used in low-flow re-breathing systems, they may be more cost-effective than propofol. This was demonstrated in a study of sevoflurane and sufentanil versus propofol and sufentanil for laparoscopic cholecystectomy [16*].

There have been some reports on sevoflurane-induced convulsions [17] and potential negative effects in brain trauma patients [18], but these concerns do not seem to be very relevant in ambulatory procedures. Similarly, the benefits of preconditioning and protection against cardiac ischaemia with inhalational agents have not been demonstrated to be of clinical importance in ambulatory surgery so far, and may be disputed even for major surgery [19*]. More clinically important are the reports of emergence agitation in children, which are more frequent after sevoflurane than propofol anaesthesia [20].

**Developments, adjuncts and trends in total intravenous anaesthesia**

In recent years the combination of propofol as a hypnotic agent with remifentanil as an analgesic and antinociceptive agent seems to have emerged as the most popular TIVA technique. In many places this combination is synonymous with TIVA. Both drugs are supplied as a continuous infusion. Propofol may be titrated against an electroencephalogram (EEG)-based hypnotic monitor [e.g. bispectral index (BIS) or other] or kept at a fairly constant level to ensure sleep, whereas remifentanil delivery may be adjusted more frequently and vigorously according to surgical stimulation and nociceptive input.

Methohexital is a cheaper alternative to propofol. It was recently compared with propofol and midazolam for oral and maxillofacial surgery [21]. The methohexital patients had more adverse events, especially nausea. Propofol was better in this aspect, also when compared with midazolam.

As pump technology is expensive, there may still be an option for ketamine as a single all-purpose drug in settings of limited resources [22]. Ketamine is traditionally associated with slower emergence and some incidence of unpleasant hallucinations even when given in moderate doses for sedation [23*]. However, Friedberg et al. [24,25] have repeatedly reported a high success rate for ketamine sedation during plastic surgery under local anaesthesia. Propofol with an increasing supplement of ketamine for light or profound sedation during spontaneous ventilation gave no hallucinations and virtually no PONV. Recent publications in the ambulatory setting partly support this conclusion [26,27]. However, Aouad et al. [28] reported more agitation, Goel et al. [29] reported delayed recovery and a review from Slavik and Zed [30] concluded that there are no specific benefits with this technique. A recent interest has also been in low-dose ketamine infusion for the reduction of postoperative pain and hyperalgesia [31]. Still, the clinical relevance of this, if any, needs to be further tested in ambulatory anaesthesia.

The use of neuromuscular blocking agents (NMBAs) seems to be declining in ambulatory care, also when endotracheal intubation is used. Gravningbraten et al. [32] did not use NMBAs for ear, nose and throat (ENT) surgery and Paek et al. [33*] did without them for intubation in laparoscopic surgery without any problems. However, intubation without muscle relaxants requires a high dose of opioid to be successful. Thus, some cases of severe hypotension may be seen, especially in old and frail patients. Injury of the vocal cords has been described after intubation without NMBAs, but clinical studies have not been able to show fewer symptoms of airway trauma with curare than without [34,35].

Beta-blockers are adjuncts that are strongly recommended for surgery in patients with coronary disease, although their perioperative benefits in beta-blocker naïve patients are disputed and controversial [36]. Beta-blockers will stabilize the haemodynamics during surgery [37], but may also have other interesting effects in ambulatory surgery. In a study of cholecystectomies, Collard et al. [38**] used esmolol infusion instead of opioids, that is, remifentanil or fentanyl, during laparoscopic surgery. The results are remarkable as the beneficial effects of beta-blockers were evident throughout early recovery: less nausea, less pain and more rapid discharge [38**].

**Future development of total intravenous anaesthesia**

The future of TIVA may change, as a result of both upcoming new drugs and more sophisticated delivery and monitoring equipment.

Already, in most countries, the target control systems for TIVA have been launched. Initially, only the Diprifusor (AstraZeneca Pharmaceuticals, London, United Kingdom) with the Marsh pharmacokinetic model for plasma propofol was available. Now, the open target control infusion (TCI) systems are provided by many manufacturers, and there is a choice of different dosing models for propofol, remifentanil and other opioids. The idea of TCI is to deliver drug intravenously to maintain a precise drug level, either in the plasma (plasma TCI) or at the brain effect site (effect site TCI). The drug is infused automatically from a pump programmed with the patient’s demographic data (e.g. weight, height and age). The anaesthesiologist may adjust target levels according to variable clinical need during the procedure [39*]. Also, new monitoring devices are being introduced, in which...
the combined anesthetic effect of different TIVA drugs is simulated, added and displayed on the monitor [40]. A further development of TCI is the automatic, closed loop system which applies registration of effect by EEG or auditory evoked potential (AEP) and haemodynamics to adjust the TCI pumps automatically. Successful reports of such systems are emerging [41,42,43]. Such systems may simplify dosing further, but they all have a delay from clinical response to dose adjustment, and will certainly never be able to predict increased dose need ahead of especially painful surgical procedures.

Dexmedetomidine has already been launched in many countries as a promising analgesic and anxiolytic drug for sedation, both for minor procedures in children and for intensive care settings [44]. The potential of dexmedetomidine in ambulatory general anaesthesia is also being explored, but so far the prolonged recovery after high doses needed for anaesthesia compared with propofol may be a clinical limitation [45,46]. However, as the need for opioid may be reduced or even eliminated with dexmedetomidine, the incidence of PONV is also reduced. This point was shown in a study of laparoscopy with dexmedetomidine and desflurane by Salman et al. [46].

Propofol 5 mg/ml has recently been introduced and has shown less aching during induction in children compared with the present 10 mg/ml propofol, both solved in mixed long and medium chain triglyceride [47]. A produg of propofol, fospropofol, has been launched as a water-soluble alternative for sedation, but the prolonged induction time and increased rate of vein pain may limit the potential for replacing the original propofol [48]. The ongoing attempts to make an esterase-degraded, ultrashort-acting propofol analogue may be more interesting, but so far this drug (THRX-918661) has not come into published trials. Results from animal studies of the new, short-acting esterase-degraded benzodiazepine (CNS-7056) seem very promising [49]. The first human clinical study is in progress and seems to confirm an ultra-short duration combined with otherwise traditional benzodiazepine characteristics (G. Kilpatrick, personal communication).

Conclusion

The current use of TIVA for ambulatory surgery seems to be abundant. It is encouraged by the simplicity of the method, increased experience and declining costs with the propofol and remifentanil combination. The TIVA methods are well tolerated and perceived to give good quality patient care; with rapid, clear-headed emergence and low incidence of PONV. Cost-efficacy and other benefits of recovery from TIVA versus alternative techniques of anaesthesia seem to depend more on the patient and the individual perioperative setting than on the TIVA concept per se. Further development of TIVA will include the refinement of target control systems, the introduction of new drugs and adjuvants and advanced equipment for automatic drug delivery, as well as improved effect monitoring.

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. 824).


6. Large prospective study on the use of nitrous oxide and PONV. Only in patients with more than 2 h anticipated surgery were included; thus, the results may not be included in the ambulatory setting without reservation.


12. Moore JK, Elliott RA, Payne K, et al. The effect of anaesthetic agents on induction, recovery and patient preferences in adult day case surgery; a 7-day follow-up randomized controlled trial. Eur J Anaesthesiol 2008; 25:876–883. Recent publication on 8–10 year old data from 733 randomized patients. The patients were followed for 1 week. As the patient populations were mixed as to the kind of surgery and anaesthetic adjuvants, the results may be influenced by confounding aspects.


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19 Landoni G, Bignami E, Oliviero F, Zangrillo A. Halogenated anaesthetics and cardiac protection in cardiac and noncardiac anesthesia. Ann Card Anaesth 2009; 12:4–9. Updated review on the aspects of cardiac protection from halogenated inhalational agents; also addressing the fact that the impact and relevance of this topic for ambulatory anaesthesia have yet to be better studied.


23 Strayer RJ, Nelson LS. Adverse events associated with ketamine for procedural sedation in adults. Am J Emerg Med 2008; 26:985–1028. Recent review on studies which include ketamine as an adjuvant to TIVA for sedation. Unfortunately, this study does not address the claimed benefits of the propofol and ketamine method advocated for plastic surgery. There are no good, recent randomized studies to be found in the literature on this aspect.


Very interesting and well designed study of a innovative new technique for TIVA with esmolol as a major player. The results are very promising and should encourage the testing of esmolol by other groups and in other settings.

39 Leslie K, Clavisi O, Hargrove J. Target-controlled infusion versus manually controlled infusion of propofol for general anaesthesia or sedation in adults. Cochrane Database Syst Rev 2008:CD006059. Review on the potential benefits of the TCI concept, illustrating that this is a difficult area to study for evidence, as blinding is hard to achieve and study design bias is difficult to eliminate.


41 De Smet T, Bruyns MM, Neckebroek MM, et al. The accuracy and clinical feasibility of a new bayesian-based closed-loop control system for propofol administration using the bispectral index as a controllable variable. Anesth Analg 2008; 107:1200–1210. Shows a thorough presentation and discussion of the fairly complex algorithms and concerns which are necessary when designing a closed loop system, and then testing it in a limited patient population.


44 Carillo DS, Nossaman BD, Ramadhani Y. Desmedetomidine: a review of clinical applications. Curr Opin Anaesthesiol 2008; 21:457–461. Carillo et al. describe a fairly recent review on the potentials of desmedetomidine in different settings, addressing the need for more extensive exploration of the drug as it gets universally approved and more ready for tests in ambulatory settings.


