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Rapid Recovery From Ambulatory Surgery: 
The New Paradigm In Ambulatory Anesthesia

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INTRODUCTION

Ambulatory surgery continues to expand with complex patients having several comorbid conditions undergoing complex and invasive surgical procedures. Simultaneously, there is emphasis on enhanced postoperative recovery that has been shown to facilitate early discharge home and early resumption of normal daily activities. The process of enhanced recovery starts preoperatively and continues until the patient returns to activities of daily living. It involves preoperative optimization of patients' health, utilization of anesthetic techniques that optimize surgical conditions while ensuring rapid recovery with minimal side-effects, prevention of common postoperative complications, and aggressive rehabilitation with the aim of restoring the patient to the best health possible. This requires a multidisciplinary approach to perioperative care in which the anesthesiologist can play a lead role. The aim of this presentation is to discuss the current evidence for optimal perioperative care that would allow rapid recovery after ambulatory surgery in adults.

PREOPERATIVE ASSESSMENT AND OPTIMIZATION

Preoperative assessment and optimization of comorbid conditions is associated with improved perioperative outcome. Also, this avoids delays and cancellations on the day of surgery. Similarly, appropriate patient selection is critical in reducing perioperative complications and improving outcome. Patient selection for ambulatory surgery depends upon several factors including patient-related factors (i.e., presence and severity of coexisting comorbidities), surgery-related factors (i.e., invasiveness of surgery and surgeon's experience), anesthesia-related factors (i.e., type of anesthesia), and venue-related factors (i.e., hospital-based ambulatory surgery, free-standing ambulatory surgery center with or without overnight stay, and office settings).

ANESTHETIC TECHNIQUES FOR RAPID RECOVERY

An ideal anesthetic technique should provide smooth and rapid onset, optimal operating conditions, and rapid recovery, with minimal (if any) side-effects. The choice of anesthetic technique (i.e., general versus regional anesthesia) is an important determinant of recovery after ambulatory surgery. Use of local anesthetic techniques including peripheral nerve blocks with or without sedation/analgesia allows rapid recovery, reduces time to home readiness, provides postoperative analgesia, and reduces opioid requirements. However, use of spinal anesthesia may prolong the post anesthesia care unit (PACU) stay as well as delay ambulation and time to home-readiness. Therefore, while the role of local/peripheral nerve blocks is increasing, the role of spinal anesthesia in ambulatory surgery is diminishing.

There is lack of evidence regarding superiority of a specific general anesthetic technique (e.g., inhalation versus total intravenous anesthesia [TIVA]) with respect to discharge home after ambulatory surgery. The benefits of TIVA include the ability to provide general anesthesia without the need for an anesthesia machine. On the other hand, inhaled anesthetics exert some neuromuscular blocking effect, which may reduce the need for muscle relaxants and the potential for residual muscle paralysis.

It is necessary to avoid deep anesthesia, as it may delay emergence from anesthesia. Because different types of surgical stimuli (e.g., skin versus intra-cavity incisions) result in different degrees of hemodynamic response, the anesthetic and analgesic requirements may vary at different stages of the surgical procedure. However, determining the optimal anesthetic concentrations that would parallel the varying surgical stimuli, while preventing intraoperative awareness, remains challenging. Recent evidence suggests that titration of inhaled anesthetic using end-tidal concentrations (0.7-1.3 MAC values) and propofol TIVA using bispectral index (BIS) monitoring should prevent intraoperative awareness with recall.

AIRWAY MANAGEMENT

Supralaryngeal devices (e.g., laryngeal mask airway) have gained widespread popularity as general-purpose airway devices and are increasingly used for routine elective surgical procedures. Compared with the tracheal tube, these devices do not require muscle relaxation and laryngoscopy, and thus may prevent complications associated with tracheal intubation. These devices are tolerated at lower anesthetic concentrations than the tracheal tube and therefore allow titration of anesthetic concentrations to the surgical stimulus. With the patient breathing spontaneously, opioid requirements can be based on the respiratory rate while dosing requirements of sedative-hypnotic anesthetics can be titrated to end-tidal concentrations of inhaled anesthetics or brain function monitor. This may allow for an earlier emergence from anesthesia and improve perioperative efficiency. Although the safety of supralaryngeal devices in healthy patients has been established, their use in patients at high risk of regurgitation of gastric contents (e.g., gastroesophageal reflux disease, morbid obesity, laparoscopy, and lithotomy/prone position) remains controversial.

INHALED ANESTHETICS

The choice of inhaled anesthetics (i.e., desflurane versus sevoflurane) remains controversial. Although clinical differences between desflurane and sevoflurane, with respect time to home readiness, appear to be small, several studies have reported more rapid emergence from anesthesia with desflurane. A study analyzing data from published randomized trials as well as data from an electronic database found that desflurane reduced the

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average extubation time and the variability of extubation time compared with sevoflurane.8

NITROUS OXIDE

Because of its amnestic and analgesic properties, nitrous oxide (N₂O) can reduce the requirements of anesthetic and analgesic drugs.9 However, the routine use of N₂O is questioned due to concerns of increased incidence of postoperative nausea and vomiting (PONV) and pressure effects through expansion of closed spaces.10 However, the clinical significance of these side effects in modern anesthetic practice has been questioned.11 A systematic review assessing the emetic effects of N₂O found that the overall impact of avoiding N₂O on the incidence of PONV was modest (absolute 33% vs. 27%).12 In addition, propofol induction and use of prophylactic antiemetics, which is the current standard of care for ambulatory surgery, may further negate the emetic effects of N₂O.12

Another benefit of N₂O is that it facilitates the removal of other inhaled anesthetics (i.e., second gas effect), and allows rapid emergence from anesthesia.13 Furthermore, the analgesic effects of N₂O should reduce the need for intraoperative opioids and reduce opioid-related adverse effects. Of note, N₂O has been shown to reduce opioid-induced hyperalgesia14 as well as reduce the incidence and severity of persistent postoperative pain.15 Interestingly, a recent propensity-matched observational trial reported that N₂O reduced perioperative morbidity and mortality.9 A systematic review found that omission of N₂O significantly increased the risk of awareness.16

Overall, N₂O can improve the quality and safety of induction and maintenance of general anesthesia as well as facilitate recovery with clinically insignificant adverse effects. Thus, there is no convincing reason to avoid N₂O.

MUSCLE RELAXANTS AND REVERSAL OF RESIDUAL NEUROMUSCULAR BLOCKADE

Several studies have demonstrated that many patients return to the PACU with residual paralysis, defined as a train-of-four (TOF) ratio of <0.9, despite the signs of clinical recovery from neuromuscular blockade.17-19 Residual paralysis can increase the incidence of critical respiratory events in the PACU and prolong recovery time as well as increase postoperative morbidity and mortality.20,21 Residual paralysis may be particularly detrimental in patients with morbid obesity, sleep apnea and significant pulmonary disease.

The first step in reducing the incidence of residual paralysis is to use the smallest possible dose of muscle relaxant that will provide optimal surgical conditions, rather than to maintain a certain TOF count (e.g., one twitch of the TOF response). Because the clinical indicators currently used to detect return of neuromuscular function are not sensitive or specific and the TOF response has limited value at deeper levels of neuromuscular blockade, it is difficult to recognize residual paralysis in clinical practice.17-19 Nevertheless, anesthesia practitioners judge themselves as better skilled at avoiding residual paralysis than they do their colleagues, making them overconfident in their capacity to estimate recovery of neuromuscular function.22 Therefore, general opinion favors administration of an anticholinesterase inhibitor at the end of anesthesia unless quantitative methods of evaluation of neuromuscular function (e.g., acceleromyography) suggest adequate recovery (i.e., TOF ratio >0.9).

The questions commonly faced at the time of reversal include – should all patients receive a reversal? If so, should we always use a “full” dose of reversal? If not, what is the optimal dose of neostigmine? What is the optimal dose of glycopyrrolate?

It is well recognized that unwarranted administration of neostigmine (i.e., administration after recovery of the TOF ratio >0.9) can result in paralysis suggesting that neostigmine itself may have muscle relaxant properties.23 Therefore, routine administration of a “full” dose of neostigmine may not be appropriate. Current evidence suggests that the dose of anticholinesterase inhibitor should be titrated to the intensity of neuromuscular blockade at the time of reversal.24 Importantly, TOF monitoring of the ulnar nerve at the wrist, rather than the eye muscles, should be used to determine the dose of neostigmine. A recent study has shown that patients having TOF monitoring of the eye muscles had a greater than 5-fold higher risk of postoperative residual paralysis than those who had monitoring of the adductor pollicis.25 Of note, the ratio of neostigmine and glycopyrrolate should be 1:1 (by volume), in most cases.

Adherence to evidence-based practices related to NMB dosing, monitoring, and reversal has been shown to improve patient outcomes during the early recovery period.

Peripheral nerve stimulator assessment at the ulnar nerve

1. TOF count 4, with no fade - administer neostigmine 20 mcg/kg, ideal body weight
2. TOF count 4, with fade - administer neostigmine 30 mcg/kg, ideal body weight
3. TOF count 3 - administer neostigmine 40 mcg/kg, ideal body weight
4. TOF count 2 - administer neostigmine 50 mcg/kg, ideal body weight
5. TOF count 1 - administer neostigmine 60 mcg/kg, ideal body weight
6. No TOF response - delay reversal.

INTRAOPERATIVE ANTINOCEPTION

The sympathetic stimulation and hemodynamic responses from noxious surgical stimuli may be reduced by using N₂O, opioids, and non-opioid analgesics (i.e., the analgesic component). Opioids provide intraoperative analgesia, hemodynamic stability, and reduce requirements for hypnotic/sedatives. During induction of general anesthesia, laryngoscopy and tracheal intubation constitute profound noxious stimuli. Therefore, an opioid analgesic is commonly administered concurrently with an intravenous hypnotic/sedative (e.g., propofol) to provide clinically acceptable hemodynamic control. Also, opioids reduce anesthetic requirements.26,27 However, quantification of the drug interaction (i.e., additive or synergistic) is difficult. There appears to be a “ceiling effect” of opioids in anesthetic interactions, as opioids do not reduce the MAC values of inhaled anesthetics by more than two-thirds.26,27

The questions commonly faced with respect to intraoperative opioid use include – what is the optimal opioid choice and dose at the time of induction of anesthesia. Also, what is the optimal opioid choice and dose in the intraoperative period? What is the optimal opioid choice and dose at the end
of surgery that would provide optimal analgesia at the time of emergence without causing respiratory depression and delaying tracheal extubation?

The choice of intraoperative opioid is often based on empirical judgment. A rational opioid selection and dosing should contribute to rapid recovery after anesthesia. Fentanyl is the most commonly used opioid for intraoperative analgesia. Sufentanil, a fentanyl analog, is approximately 10 times more potent than fentanyl with a similar onset of action. In contrast to fentanyl, the context-sensitive half-time of sufentanil is significantly shorter. Remifentanil has unique pharmacokinetics and ultra-short duration that allows optimal matching of the dose with the varying degree of surgical stimuli at different stages of surgery. In addition, the short and predictable duration of remifentanil make it suitable in the high-risk population such as the elderly, morbidly obese, and those with obstructive sleep apnea. However, there appears to be a learning curve with the use of remifentanil.24 Optimal dosing of remifentanil would include avoidance of bolus dosing and an initial infusion rate of 0.25 μg/kg/min.25 A recent study found that remifentanil 0.5 mcg/kg caused similar ventilatory depression as fentanyl 1 mcg/kg.26 Because of its rapid offset of analgesic effect, it is necessary that a longer-acting opioid or non-opioid analgesic be used to provide postoperative analgesia. The benefits of remifentanil may be realized if a non-opioid analgesic technique can be utilized.

Optimal opioid dosing at the time of induction and during maintenance of anesthesia remains controversial. It is common practice to use relatively larger opioid doses at induction of anesthesia (“front loading”), particularly in longer surgical procedures. However, the validity of this approach is questionable. Larger opioid doses may result in significant post-induction hypotension and need for pharmacological support. Also, this may increase the potential for acute tolerance as well as delayed hyperalgesia, which may increase the degree of postoperative pain.33 Higher intraoperative opioid doses may increase opioid-related side-effects including nausea, vomiting, sedation, bladder dysfunction, and respiratory depression.

The need for intraoperative opioids is commonly based on hemodynamics (heart rate and arterial blood pressure). However, attempts to achieve “tight” hemodynamic control may result in use of larger opioid doses. Because intraoperative opioid overdose can only be recognized at emergence of anesthesia when the patient’s spontaneous ventilation is delayed, it is imperative that opioids are administered judiciously. In addition, the use of non-opioid analgesics to reduce the opioid-related side-effects may minimize postoperative complications and expedite recovery.

As a plan for postoperative analgesia, it is common practice to administer a long-acting opioid towards the end of surgery. The choice of long-acting opioid includes morphine and hydromorphone of which hydromorphone is preferable due to its superior pharmacokinetics.33 Compared with morphine, hydromorphone has a shorter plasmacentral nervous effectsite equilibration half-life. Hydromorphone has a quicker onset time and the concentrations at effect-site do not increase after titration has stopped.33 Therefore, hydromorphone may be better suited than morphine for titration of acute pain. Morphine is poorly suited by titration for immediate analgesia, as delayed respiratory depression may result due to the slow transfer of morphine to the effect site.

The dosing for hydromorphone could be based on the studies of morphine. Morphine (2-3 mg every 5-10 min) titrated to achieve a respiratory rate of 12-15 breaths per minute during emergence from anesthesia can enhance postoperative analgesia and reduce PACU stay without increasing the incidence of respiratory depression.33 The total dose of morphine usually required is 0.15 mg/kg. This dose usually does not delay awakening or delay tracheal extubation.33

INTRAOPERATIVE MECHANICAL VENTILATION

Optimal intraoperative ventilatory strategy would include use of lower tidal volume (6-8 ml/kg, ideal body weight) with positive end-expiratory pressure (PEEP).34 It is important to avoid hyperventilation as it may result in metabolic alkalosis and lead to postoperative hypoventilation. Most importantly, it is recommended that the end-tidal carbon dioxide (CO₂) levels be maintained around 40 mmHg rather than the traditional values of 30-35 mmHg. Higher CO₂ levels improve hemodynamics and improve tissue perfusion.

EMERGENCE FROM GENERAL ANESTHESIA

Towards the end of surgery, it is common practice to reduce the respiratory rate in an effort to build up end-tidal CO₂ levels and facilitate respiration. However, the reduced minute ventilation resulting from this practice may delay removal of inhaled anesthetic, and thus delay emergence from anesthesia. Therefore, the primary aim at the end of the surgery should be to maintain the minute ventilation in an effort to washout the inhaled anesthetic and facilitate emergence.35 One of the major concerns during emergence from anesthesia, particularly in obese and sleep apnea patients, is the risk of airway obstruction after tracheal extubation. Rapid emergence from anesthesia should prevent this complication.

PREVENTION OF POSTOPERATIVE COMPLICATIONS

One of the major goals of an ideal anesthetic technique is prevention of postoperative complications particularly pain, nausea, and vomiting. The other postoperative complications that can impede recovery include cardiovascular alteration (i.e., hypotension, hypertension, and rhythm disturbances), respiratory complications (i.e., airway obstruction, hypoventilation, bronchospasm, and pulmonary aspiration), temperature abnormalities, and surgical complications.

POSTOPERATIVE PAIN MANAGEMENT

The goal of pain management should be to minimize pain not only at rest, but also during mobilization and physical therapy. An ideal approach to optimal pain management starts with patient education, as it reduces anxiety, allows realistic expectation, and improves patient satisfaction. Procedure-specific, evidence-based analgesic techniques that are incorporated in a clinical pathway have the highest chances of being implemented consistently.36,37

Since the introduction of the intravenous formulation of acetaminophen, it has been increasingly used as a part of multimodal analgesia.38 An optimal multimodal analgesia technique would include acetaminophen combined with

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The analgesic efficacy of COX-2 specific inhibitors has been shown to provide superior analgesia compared with either drug alone. The analgesic efficacy of COX-2 specific inhibitors is similar to that of the traditional NSAIDs. Because the COX-2 specific inhibitors spare the COX-1 enzyme, they do not have any antiplatelet effects. Thus, they can be administered preoperatively, as there is no concern of increased perioperative bleeding. However, in the perioperative period, the cardiovascular and renal adverse effect profile of COX-2 specific inhibitors seems to be equivalent to that of traditional NSAIDs. Of note, acetaminophen exhibits an analgesic “ceiling” effect similar to NSAIDs and COX-2 specific inhibitors.

Infiltration of the surgical wound with local anesthetic can provide excellent analgesia that outlasts the duration of action of the drug and is recommended for routine use. Local anesthetic techniques provide pain relief until the onset of oral analgesics. The duration of analgesia can be increased by infusion of local anesthetics through a catheter placed in the layers of the skin. A new formulation of bupivacaine using liposomal technology which is reported to have a duration of up to 72 h has been recently been introduced into clinical practice. This may obviate the need for using continuous wound local anesthetic infusion. In addition, peripheral nerve blocks are increasingly being used to provide intra- and postoperative analgesia. The use of continuous perineural local anesthetic infusions after ambulatory surgery has been shown to extend the duration of analgesia and allow more extensive and painful surgical procedures to be performed on an outpatient basis. However, placement of these blocks may require preoperative and postoperative logistic planning.

Several systematic reviews have reported that dexamethasone 4–8 mg, IV administered either pre- or intraoperatively provides significant pain relief and reduces opioid requirements. A single dose of dexamethasone has not been shown to increase the incidence of surgical site infections, but it may increase blood glucose levels lasting for up to 24 hours postoperatively. However, the clinical significance of this increase in blood glucose levels is not known. Low-dose ketamine has been reported to reduce postoperative pain scores and opioid consumption as well as delay time to first opioid administration. A recent systematic review revealed that ketamine provided significant analgesic benefits in painful procedures including thoracic, upper abdominal, and major orthopedic surgeries. Interestingly, the analgesic effects of ketamine were independent of the type of intraoperative opioid administered, timing of ketamine administration, and the ketamine dose. The authors also concluded that the opioid-sparing effect of ketamine reduced the incidence of nausea and vomiting, but was associated with an increase in the incidence of neuropsychiatric disturbances. However, the role of low-dose ketamine as an adjunct to other non-opioid analgesics, in ambulatory surgery remains controversial, as the optimal dose and duration of administration is unknown. The role of anticonvulsants (e.g., gabapentin and pregabalin) in the outpatient setting needs to be clarified by further investigation. These analgesics should be administered on a regular “round-the-clock” basis with opioids used as “rescue” analgesics. Opioids should be used sparingly as opioid-related adverse effects delay recovery and return to activities of daily living. Tramadol, a weak opioid agonist and a weak norepinephrine and serotonin reuptake inhibitor, is commonly used in the perioperative period. Although it is generally well tolerated, side-effects include nausea, vomiting, dizziness, and drowsiness. Also, tramadol has a potential to cause seizures, and therefore should be used with caution in patients with increased intracranial pressures, epilepsy, and in patients receiving neuroleptic drugs. It is contraindicated in patients receiving monoamine oxidase inhibitors.

**POSTOPERATIVE NAUSEA AND VOMITING**

Postoperative nausea and vomiting (PONV) is one of the factors that can delay recovery. Although risk-based approaches for antiemetic therapy have been proposed, the compliance with these strategies has been shown to be poor. Therefore, prophylactic multimodal antiemetic therapy should be utilized in all ambulatory surgical patients. The number of antiemetic combinations could be based on the patient’s level of risk and surgical procedure. A combination of dexamethasone 4–8 mg, IV (after induction of anesthesia) and ondansetron 4 mg, IV (at the end of surgical procedure) could be used for most patients. Patients at very high risk of PONV (e.g., history of motion sickness, history of previous PONV, high opioid requirements for pain relief) may receive additional antiemetic therapy such as preoperative transdermal scopolamine or oral aprepitant. In addition, TIVA may be considered in these high-risk patients. Interestingly, a recent systematic review reported that metoclopramide 10 mg was effective in preventing PONV, and that it should be an alternative agent to prevent PONV. Patients requiring rescue antiemetic therapy in the immediate postoperative period could receive low-dose promethazine (6.25 mg, slow IV) or dimenhydrinate (1 mg/kg).

Post-discharge nausea and vomiting (PDNV) is a common and sometimes severe adverse outcome for ambulatory patients. The independent predictors of PDNV include female gender, age less than 50 years, history of PONV, opioids administered in the PACU, and nausea in the PACU. The overall incidence of PDNV can be determined by the presence of the total number of predictors.

**POSTOPERATIVE COURSE AFTER AMBULATORY SURGERY**

In addition to achieving rapid emergence from anesthesia, it is necessary that the recovery process be modified to improve patient throughput. The first step is to change from traditional time-based to clinical-based discharge criteria from the PACU and the phase II unit. Utilization of appropriate scoring systems allows patients to be safely discharged from the PACU and to be discharged home. If the criteria used to discharge patients from the PACU were met in the operating room, it would be appropriate to consider bypassing the PACU and transferring the patient directly to the phase II unit.

A clearly defined process should be established to ensure safe and timely discharge home. Appropriate modifications of current discharge criteria based upon recent literature should allow us to discharge patients expeditiously without compromising safety. The ASA practice guidelines recommend that the ability to tolerate oral fluids should not be part of a routine discharge protocol but may be appropriate for selected...
patients (e.g., likelihood of complications if fluids are not taken). Similarly, a routine requirement for voiding before discharge should not be a part of a discharge protocol and may only be necessary in selected patients (e.g., the type of surgery performed, prior history of urinary retention and anesthetic technique used).

A clear and coordinated post-discharge plan is necessary. Patients should be encouraged to ambulate and resume activities of daily living as early as possible. It is important to recognize that home-readiness is not synonymous with street-fitness. Therefore, patients should be given clear instructions and cautioned against performing functions that require complete recovery of cognitive ability. Although a majority of surgical care is being performed on an ambulatory basis, there is limited information regarding outcome after discharge home.52

**SUMMARY**

It is necessary to develop comprehensive, multidisciplinary, procedure-specific clinical pathways that involve the entire perioperative team (e.g., anesthesiologists, surgeons, pharmacists, and nurses). Preoperative patient education with clear instructions sets expectations, reduces patient anxiety and increases their satisfaction. The most important aspect of a general anesthetic technique is its ability to consistently achieve rapid recovery to patients’ normal functioning after termination of surgery. Thus, it is necessary to use anesthetic, analgesic, and muscle relaxant agents judiciously. Avoidance of residual muscle paralysis is critical. Opioid-related adverse effects may be associated with delayed recovery and thus opioids should be used judiciously, and non-opioid analgesics should be utilized whenever possible. Prophylactic multimodal analgesia and antiemetic therapy are critical in achieving rapid recovery. Post-discharge planning should include prevention and treatment of postoperative complications particularly pain and antiemetic therapy. Perioperative outcomes (e.g., time to home readiness, time to actual discharge, unanticipated hospital admission, hospital readmission, patient satisfaction, morbidity and mortality) should be recorded.

**REFERENCES**

30. Gelberg J, Jonmarker G, Stensvoist O, Werner O. Intravenous boluses of fentanyl, 1 µg kg⁻¹, and remifentanil, 0.5 µg kg⁻¹, give similar maximum ventilatory depression in awake volunteers. Br J Anaesth 2012; 108: 1028-34.


Size Matters: Perioperative Management of the Morbidly Obese

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INTRODUCTION

Obesity is defined as a Body Mass Index (BMI) > 30 kg/m², morbid obesity defined as > 35 kg/m², super morbid obesity >50 kg/m², and ultra-obesity >70 kg/m². As per WHO statistics, overweight and obesity are the fifth leading risk for global deaths with one in ten of the world’s adult population being obese. Morbidly obese patients have significant comorbid condition and cardiopulmonary changes that affect the pulmonary and cardiovascular system. Excess accumulation of fat in various locations in the body causes mechanical and metabolic problems. The mechanical problems like alteration in pulmonary function, obstructive sleep apnea and difficult airway challenges the anesthesiologist more than the metabolic problems like hypertension, dyslipidemia and insulin resistance. Both these factors increase the morbidity during the intra-operative and post-operative setting.

PHYSIOLOGICAL CHANGES

Obesity has a significant effect on the physiology of breathing. There is significant reduction in lung compliance as the result of increased pulmonary blood volume, closure of dependent airways and increased alveolar surface tension due to the reduction in functional residual capacity (FRC). But, the chest wall compliance is reduced in spontaneous breathing and normal in anaesthetised, paralyzed subjects. Regarding lung volumes, there is a reduction in FRC due to the mass load of adipose tissue around the rib cage, abdomen and the visceral cavity. Residual volume is relatively well preserved with minimal reduction in total lung capacity. Tidal volumes are often reduced in severe obesity, and breathing follows a rapid, shallow pattern. As the FRC is low, closing capacity exceeds the FRC, and airway closure can occur within the tidal breaths. As BMI increases, there is a reduction in expiratory flow and a decrease in FEV1 and FVC. But the ratio of FEV1 to FVC is preserved. CO diffusion capacity is normal or increased due to increase in pulmonary blood flow. The airway resistance is also significantly higher in the obese and it is related to the reduction in lung volume rather than airway obstruction. There is an increase in ventilation-perfusion mismatch in the dependent lower lung zone, since it is under ventilated and over perfused. Subjects with simple obesity have an enhanced respiratory drive, while the respiratory drive of subjects with obesity hypoventilation syndrome is either depressed or inappropriately suppressed.

CARDIOVASCULAR CHANGES:

Obesity is independently associated with left ventricular hypertrophy, characterized by increase in both left ventricular cavity size and wall thickness. An increase in left ventricular size also leads to atrial fibrillation. Anorexigenic drugs used to facilitate weight loss are associated with mitral and aortic valve regurgitation. In addition, myocardial contractility is reduced with diastolic dysfunction. Abdominal obesity is a well-defined risk factor for the development of atherosclerotic coronary artery disease. In obese patients, stroke volume and cardiac output are both increased, due to metabolic demand. Sympathetic activation likely results from sleep apnea and it prevents the normal nocturnal decline in blood pressure. In general obesity leads to hypertension, the probable mechanism is activation of the renin-angiotensin system may occur directly via signals from adipose tissue.

Sleep apnea associated with obesity could lead to left ventricular hypertrophy, hypertension, increased sympathetic tone, chronic hypoxemia, and exaggerated swings in intrathoracic pressure during obstructive episodes. The increase in right ventricular cavity size and wall thickness is related to obstructive sleep apnea (OSA).

Table 1: Obstructive Sleep Apnea Screening Tools

<table>
<thead>
<tr>
<th>STOP-Bang Questionnaire</th>
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<tbody>
<tr>
<td><strong>S</strong> Snoring: Do you more loudly/breath louder than talking or loud enough to be heard through closed doors?</td>
</tr>
<tr>
<td><strong>T</strong> Tired: Do you often feel tired, fatigued, or sleepy during daytime?</td>
</tr>
<tr>
<td><strong>O</strong> Observed: Has anyone observed you stop breathing during your sleep?</td>
</tr>
<tr>
<td><strong>P</strong> Blood Pressure: Do you have or are you being treated for high blood pressure?</td>
</tr>
<tr>
<td><strong>B</strong> BMI: BMI more than 35 kg/m²?</td>
</tr>
<tr>
<td><strong>A</strong> Age: Age over 50 years old?</td>
</tr>
<tr>
<td><strong>N</strong> Neck circumference: Neck circumference greater than 40 cm?</td>
</tr>
<tr>
<td><strong>G</strong> Gender: Male?</td>
</tr>
</tbody>
</table>

At risk of OSA: Yes to 3 or more questions for STOP-Bang.
Adapted from F Chung et al. Anesthesiology 2008;108:812-21

PREOPERATIVE ASSESSMENT

Morbidly obese patients are considered at high risk for perioperative complications and often undergo extensive testing for preoperative clearance, including chest X-ray, pulmonary function tests, non-invasive cardiac testing, and blood work. Although recent data indicate that extensive preoperative testing may not be necessary for every severely obese patient undergoing gastric bypass surgery, basic screening tests are imperative to identify the additional risk factors. Further preoperative testing should be individualized based on co-morbid conditions. Since nearly 70% of morbidly obese patients are prone to have OSA, screening test to diagnose and quantify OSA has been suggested to be mandatory. The gold standard for diagnosing OSA is overnight polysomnography. Since it is a time consuming and expensive test, the STOP-Bang questionnaire (Table 1) can be used as a screening tool. The STOP-Bang questionnaire has the highest methodological validity and reasonable accuracy in predicting a diagnosis of OSA11 and a STOP-Bang score of 5–8 identified patients with high probability of moderate/severe OSA12 (Figure 1). The addition of serum HCO3- level ≥ 28 mmol/L to a STOP-Bang score ≥ 3 improves the specificity for preoperative obstructive sleep apnea recognition. We propose a two step screening process. The first step uses a STOP-Bang
score to screen patients and the second step uses serum HCO3- in those with a STOP-Bang score ≥ 3 for increased specificity.\(^\text{13}\) (Figure 2)

Patients with positive STOP-Bang questionnaire are more likely to have increased postoperative complications.\(^\text{14}\) Also the Oxygen Desaturation Index from a high resolution nocturnal oximeter is a sensitive and specific tool to detect undiagnosed sleep disordered breathing in surgical patients.\(^\text{15}\) Co-morbidities associated with OSA are arterial hypertension, coronary artery disease, cerebrovascular disease, congestive heart failure, cardiac dysrhythmias and diabetes mellitus.\(^\text{16}\) Studies suggest that patients with OSA, who have been treated with CPAP preoperatively, have fewer perioperative complications than those untreated.\(^\text{17}\) A functional algorithm could help to guide possible screening and the management of the obese patients with OSA.\(^\text{18}\) Morbidly obese patients with OSA are prone for difficult intubation. But, a recent study on bariatric surgical patients has shown that there was no relationship between the severity of OSA, BMI, or neck circumference and difficulty of intubation. Only a Mallampati score of 3 or 4 and male gender predicted difficult intubation.\(^\text{19}\)

Obesity hypoventilation syndrome (OHS) is defined by the triad of obesity, daytime hypoventilation and sleep disordered breathing without an alternative neuromuscular, mechanical or metabolic cause of hypoventilation. It is a disease entity distinct from simple obesity and obstructive sleep apnea. OHS is often undiagnosed but its prevalence is estimated to be 10-20% in obese patients with obstructive sleep apnea and 0.15-0.3% in the general adult population. Compared to eucapnic obese patients, OHS patients present with severe upper airway obstruction, restrictive chest physiology, blunted central respiratory drive, pulmonary hypertension and increased mortality. The mainstay of therapy is non-invasive positive airway pressure.\(^\text{20}\) (Figure 3)

PREOPERATIVE PREPARATION

Preoperative sedative premedication should be avoided in morbidly obese patients with OSA. Obese patients have faster gastric emptying time, a large gastric volume and a high incidence of gastro esophageal reflux disease making them prone to aspiration. This risk increases further after post bariatric surgery.\(^\text{21}\) If concerned about the risk of acid aspiration, H2-receptor antagonists or a proton pump inhibitor can be given. Also, obese patients are at significant risk of venous and pulmonary thromboembolism and therefore mechanical and pharmacological method of perioperative thromboembolic prophylaxis must be considered.

The health care team should have special training in the issues relating to the care of morbidly obese patients. Patients should be encouraged to move themselves whenever possible. Operating table, trolley, bed and specific equipments like spine frame for spine surgery should be checked and labeled for its maximum weight bearing capacity. An “obesity pack” (including specific equipment, protocol guidelines and contact numbers) should be available for the emergency surgeries.

INTRAOPERATIVE MANAGEMENT

Airway management – Weight or BMI is just one of several factors to consider during an airway evaluation. A neck circumference greater than 43 cm is associated with an increased risk of difficult intubation.\(^\text{22}\) It is imperative to know the severity of OSA to predict the difficulty in mask ventilation & intubation. According to Brodsky et al.\(^\text{23}\) patients with a BMI > 35 kg/m\(^2\) have a six-fold higher risk for difficult laryngoscopy. However, Mashour et al.\(^\text{24}\) showed that there was no difference in difficult laryngoscopy in patients with BMI < 40 kg/m\(^2\) versus > 40 kg/m\(^2\).

Positioning with the head, neck and shoulders elevated in the head elevated laryngoscopy position (“HELP”) facilitates direct laryngoscopy. In morbidly obese patients, oxygen
saturation following preoxygenation falls more rapidly during apnea than in those with normal BMI. This effect can be limited by a 25 degree head-up position during preoxygenation, the combination of preoxygenation with reverse Trendelenberg position and nasopharyngeal oxygen insufflation, positive end-expiratory pressure (PEEP) of 10 cm H₂O and noninvasive bi-level positive airway pressure. Rapid sequence induction remains essential in the morbidly obese patients with gastro-esophageal reflux. In a series of 150 consecutive morbidly and super obese patients, awake fiberoptic intubation was used in only 6-7% of patients at high risk of difficult intubation. Videolaryngoscopic guided intubation with the Glidescope, Storz V-Mac or McGrath systems has a high success rate in the morbidly obese patients with a difficult airway.

PHARMACODYNAMIC & PHARMACOKINETICS OF ANESTHETICS

Physiologic changes in obesity affect distribution, protein binding and elimination of the various anesthetic agents. Obese patients have a smaller than normal fraction of total body water, increased blood volume, cardiac output and greater than normal fat content. In addition, glomerular filtration rate is increased and hepatic clearance is usually normal or increased. In general, lipophilic drugs have a large volume of distribution (Vd) based on the total body weight and hydrophilic drugs (muscle relaxant) dosing is based on the lean body weight. A recent study on rocuronium confirmed that the dose should be calculated based on the ideal body weight. Similarly cistatracurium and vecuronium dosing are based on the ideal body weight. Since the levels of pseudocholinesterase and extracellular fluid space are increased in obesity, succinylcholine dose is calculated based on the total body weight.

The volume of distribution (Vd) of remifentanyl in obese patients is less than expected, probably because of hydrolysis by blood and tissue esterases and dosing is based on the ideal body weight. A recent pharmacokinetic model of propofol in morbidly obese patients showed that the total body weight was the major determinant of clearance. Benzodiazepines are highly lipophilic drug. The single intravenous dose is based on the total body weight, but if a continuous infusion is used, the dose should be adjusted based on the ideal body weight rather than total body weight because the total clearance is not substantially changed as compared with non-obese subjects. Sevoflurane and desflurane have lower lipid solubility than isoflurane and similar emergence and recovery profiles in morbidly obese patients.

VENTILATION STRATEGIES

Following induction of anesthesia, atelectasis increases from 1 to 11% of total lung volume in the morbidly obese patients. Recruitment maneuvers (PEEP & Valsalva) can counteract these effects. The decrease in the compliance of the respiratory system and PaO₂ was significantly reverted by the application of sustained inspiratory pressure combined with PEEP, but not by either intervention alone. During bariatric surgery, pressure-controlled ventilation improves oxygenation compared with volume-control.

POSITIONING

The prone position is usually well tolerated by obese patients, since it helps in unloading of abdominal viscera and reduces pressure on the diaphragm, which improves the FRC. Lateral position is also relatively well tolerated. Trendelenburg position decreases total compliance and FRC, which leads to increased atelectasis and hypoxemia. Obese patients that are breathing spontaneously do not tolerate the Trendelenburg position. Their airway should be intubated and ventilation controlled or assisted. In supine position an increase in BMI proportionally decreases the FRC, pulmonary compliance and increases the ventilation/perfusion (V/Q) mismatch. These effects are significantly reverted by reverse Trendelenburg position. The lithotomy position increases intra-abdominal pressure and compression of the lungs, which can further reduce chest wall compliance.

FLUID BALANCE

Perioperative fluid administration in morbidly obese patients has double-edged implications. On one side, fluid restriction may result in acute tubular necrosis and organ dysfunction, while on the other, excessive fluid may lead to post-operative pulmonary complications. But the evidences are limited in this issue. In the presence of pneumoperitonium, urine output is not a useful guide and in general central venous pressure and pulmonary capillary wedge pressure are not sensitive to fluid challenge. Stroke volume variation guided optimization may have critical significance in limiting excessive fluid administration in morbidly obese patients undergoing bariatric surgery. A recent study compared high-volume (10 ml/kg/hr) fluid therapy versus low volume (4 ml/kg/hr) therapy in laparoscopic bariatric surgery patients and it did not find any significant difference between these two groups in post-operative renal function. Both groups had intra-operative oliguria, which was unresponsive to fluid administration.

LAPAROSCOPIC SURGERY

Morbidly obese patients have markedly reduced supine functional residual capacity, with further decrease in the Trendelenburg position and insufflation of the abdomen with CO₂. Morbid obesity and pneumoperitoneum have significant effects on respiratory mechanics, whereas PaO₂ was adversely affected only by increased body weight. Repositioning the patient from the supine position into the Trendelenburg or reverse Trendelenburg position had no effect on PaO₂, either before or after abdominal insufflation. In non obese patients the difference in PaCO₂/ETCO₂ was high with large tidal volumes (800ml), but in morbidly obese patients this difference was high with small tidal volumes. The endotracheal tube moves down more in morbidly obese patients during laparoscopic surgery and this is aggravated by the Trendelenberg position.

THORACIC SURGERY

Since morbidly obese patients already have a restrictive spirometry pattern, one lung ventilation could further affect the pulmonary function. Since predictive spirometric values are not indexed to weight, they may be inappropriate in obese patients. A large double lumen tube should be chosen to minimize airflow resistance during one lung ventilation and it is better to choose the tube size based on radiological imaging rather than gender or height based. One lung ventilation is technically possible in the lateral position, since abdominal content falls away from the body and unloads the dependent diaphragm.
tidal volume ventilation, intermittent alveolar recruitment, continuous positive airway pressure to the collapsed lung and positive end-expiratory pressure (PEEP) to the ventilated lung could help to avoid the hypoxia during one lung ventilation. In general morbidly obese patients are prone for post-operative pulmonary complication and it could be more with thoracic surgery.46,47

REGIONAL ANESTHESIA

Regional anesthesia offers distinct advantages, which allows minimal airway manipulation, avoidance of anesthetic drugs with cardiopulmonary depression, reduced post-operative nausea and vomiting and reduced perioperative opioid requirements. However, the rate of block failure increased incrementally with a higher BMI.48 Using ultrasound-guided regional anesthesia for peripheral nerve blocks in the obese population led to improved success rates.49 Epidural analgesia should be considered in obese patients undergoing laparotomy to improve postoperative spirometry.50 Since 50-68% of post bariatric surgery patients are prone to have Vitamin K deficiency due to malabsorption,51 documentation of normal coagulation function is necessary for neuraxial blocks. In previous studies, obese patients require less local anesthetic in their epidural and subarachnoid spaces in order to achieve the same level of block when compared with non-obese controls.52 In a study of impact of morbid obesity on epidural complication in labor, there was a higher incidence of systolic and diastolic hypotension and prolonged fetal heart decelerations.53 However, a recent study showed no difference in spinal bupivacaine requirement between obese and non-obese parturient.54

AMBULATORY ANESTHESIA

At one time, patients with BMI > 30 kg/m² or more was considered unsuitable for ambulatory anesthesia. Currently more importance is given to the comorbid conditions than the BMI alone. The ASA guideline has given risk assessment for patients with OSA to undergo ambulatory anesthesia.55 Points are given based on the severity of the OSA, the degree of invasiveness of the planned operation, and whether or not the patient will need a general anesthetic and postoperative opioid analgesia. ASA recommended that patients with a score above five should not be considered candidates for ambulatory surgery. It may not be safe to undergo patients with severe OSA requiring postoperative narcotic as ambulatory surgical patients.56 A recent review recommends that the majority of OSA patients may be done as ambulatory surgical patients with few adverse events.57 Society for Ambulatory anesthesia also published a consensus statement on preoperative selection of patients with obstructive sleep apnea scheduled for ambulatory surgery.58

POST-ANESTHESIA CARE

Whenever possible, patients should be extubated wide-awake in the sitting position and transferred to an appropriate postoperative environment. Morbidly obese patients are prone to have postoperative hypoxemia due to atelectasis.59 Though intraoperative lung recruitment maneuver are important to avoid hypoxemia, CPAP in the PACU helps to improve the oxygenation. Patients with OSA should be instructed to bring their CPAP or non-invasive positive pressure ventilation equipment to the hospital. It has been shown that the postoperative lung functions of bariatric surgery patients are better with Boussignac CPAP application on extubation rather than in the postanesthetic care unit.60 Compared with the venturi mask, the Boussignac CPAP mask improves the postoperative PaO2/FIO2 ratio in morbidly obese patients.61

POST-OPERATIVE PAIN MANAGEMENT

Pain control is important in obese patients, since it allows early mobilization and reduces the risk of deep vein thrombosis and pressure ulcers.62 The use of IV PCA is often inevitable in particular, if regional anesthetic techniques are not possible or difficult. Opioid administration is associated with increased perioperative airway obstruction and desaturations even without OSA.63,64 Epidural analgesia improves the spirometry in obese patients undergoing midline laparotomy.50 Similarly in cardiac surgery, patients with a BMI> 30 kg/m² had better analgesia and improved respiratory parameters with use of thoracic epidural analgesia than with conventional opioid-based analgesia.65

A multimodal pain management approach is particularly favored in obese patients, non-opioid analgesics should be considered wherever possible. The combinations of acetaminophen and NSAIDs are superior to the respective single therapy.56 However, the use of non-selective NSAID in bariatric surgeries should possibly be avoided because of a higher risk for gastric perforation.67 Though the evidences are limited in the usage of adjuvants like ketamine, lidocaine, clonidine, dexmedetomidine and gabapentin in obese population,68 it could be a viable option to reduce the perioperative opioid consumption. As per ASA guideline neuraxial opioids and the continuous setting during patient-controlled opioid analgesia is best avoided in obese patients with OSA.

CONCLUSION

Morbidly obese are a special group of patients, they need an extra care during the perioperative period. Understanding the anatomical, physiological, metabolic and pharmacological changes are imperative for the anesthesiologist to modulate the anesthetic technique for better outcomes. Advancement in anesthesia technology like video laryngoscopes, ultrasound and ventilatory modes in anesthesia workstations has made dramatic improvement in the peri-operative care of obese patients. At the same time advancement in minimally invasive surgery challenges the anesthesiologist, since most of the surgeries are being done as ambulatory procedures. A protocol practice and guidelines to manage these morbidly obese patients could optimise the peri-operative management. Further evidences are required in fluid administration, one lung ventilation and post-operative pain management in morbidly obese patients.

ENDNOTES


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Controversies in Pediatric Anesthesia: Myth Busters to the Rescue

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INTRODUCTION

Upper respiratory tract infections (URI) are common in toddlers and infants and are the main reason for visits to the emergency room or pediatricians offices. This is a large population that presents for routine surgery in the pediatric population. In recent years, with the advent of more potent influenza viral seasons we have seen a spate of children affected with viral infections especially during the winter months. There is an association with the presence of reactive airway disease in children who are recovering form a recent cold or upper respiratory infection.

PREOPERATIVE EVALUATION

The preoperative evaluation should consist of listening to the child’s lungs for rhonchi or wheezing. The potential for a lower respiratory tract infection following an upper respiratory infection is relatively common in children. It is also important to ask for a history of asthma or wheezing. Children who are exposed to common colds are at greater risk for reactive airway disease and can hence have a greater propensity for wheezing or bronchospasm during anesthesia. (Table 1-Risk factors)

Many attempts at preventing associated side effects with the presence of URI have been attempted. This includes the use bronchodilators as well as anti-sialogogues such as glycopyrolate or atropine. The advantage int eh group that received glycopyrolate demonstrated earlier dischage from the PACU as opposed to those who did not receive the drug. There were no significant differences in adverse events in children in the study group as opposed ot the placebo group (45.2% vs 37.5%)The data is sparse and current randomized trials have demonstrated no differences in outcomes after pre-treatment with any of the measures.

INDUCTION OF ANESTHESIA

A mask induction is preferred. This allows for a smooth induction. Using induction agents like ketamine can lead to more secretions and potential airway obstruction. As mentioned earlier, the use of glycopyrolate or atropine has not demonstrated better outcomes. Many of these children may be presenting for minor procedures like a myringotomy with PE tube placement that may not require the need for intravenous access. It is imperative that the anesthesiologist is prepared with the potential for rapid intervention in the event the patient develops laryngospasm.

AIRWAY INTERVENTION

URI is frequent in children who are presenting for adenotonsillectomy. The potential for laryngospasm after extubation as well as the potential for desaturation has prompted research into looking for alternatives other than endotracheal tubes for the procedure. The flexible laryngeal mask airway has been successfully used in our institution for adenotonsillectomy as an airway device. The research does not demonstrate any added benefits in the use supraglottic devices when compared to those that had an endotracheal tube in a large retrospective study when compared to a previous study that has demonstrated superiority of the LMA over an ETT. There has been ongoing debate as to whether extubating a patient with URI deep may be more beneficial to extubating them wide awake. In an interesting study, the investigators, in a randomized controlled trial, found no difference in the incidence of complications in either groups. There was an increased incidence of coughing in children who were extubated awake vs. those extubated deep (60% in Wake vs. 35% in deep extubation) However, the incidence of airway obstruction in deeply anesthetized patients was greater than wake extubation (26% vs. 8%).

POSTOPERATIVE MANAGEMENT

It is important to recognize that these children may be prone for desaturation in the postoperative period. In addition, they may be prone for bronchospasm, stridor or persistent coughing. It is important to keep this in mind while dealing with these children in the PACU. In addition, they may require additional observation in the PACU postoperatively.

REFERENCES

OBSTRUCTIVE SLEEP APNEA

Obstructive sleep apnea involving airway obstruction during sleep, hypoxemia and sleep disruption occurs in 1-3% of children, whereas in adults, it is diagnosed in 38% of men and 28% of women.

In adults, the prevalence of OSA is increased in patients with diabetes, patients over 60 years of age, patients who are overweight, have hypothyroidism, alcoholism and head and neck cancer.

Table 1. Childhood versus adult obstructive sleep apnea syndrome features

<table>
<thead>
<tr>
<th>Event</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central apnea</td>
<td>Pause in airway with absent respiratory effort, scored with &gt;20/1 or 2 missed breaths and a &gt;3% drop in oxygen saturation</td>
</tr>
<tr>
<td>Obstructive apnea</td>
<td>&gt;90% reduction of airflow despite continuing respiratory effort, scored when event lasts at least 2 missed breaths in children</td>
</tr>
<tr>
<td>Obstructive hypopnea</td>
<td>&gt;50% reduction of airflow with associated respiratory effort, scored when at least 2 missed breaths and &gt;3% drop in oxygen saturation or arousal</td>
</tr>
<tr>
<td>Mixed apnea</td>
<td>&gt;25% reduction in airflow, lasting at least 2 missed breaths, and containing absent respiratory effort initially (a central apneic pause), followed by resumption of respiratory effort without a resolution of airflow (an obstructive apnea)</td>
</tr>
<tr>
<td>Obstructive hypoventilation</td>
<td>End-tidal CO₂ &gt;50 mmHg for &gt;25% of the total sleep time with paradoxical respirations, snoring, and no baseline lung disease</td>
</tr>
</tbody>
</table>

Table 2. Respiratory events that can be seen during polysomnography

<table>
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</tr>
</tbody>
</table>

Table 3. Some congenital and medical conditions associated with obstructive sleep apnea syndrome

<table>
<thead>
<tr>
<th>Condition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achondroplasia</td>
<td>May not be seen</td>
</tr>
<tr>
<td>Apert syndrome</td>
<td>At end of each apnea</td>
</tr>
<tr>
<td>Beckwith-Wiedemann syndrome</td>
<td>Definitive therapy in most patients</td>
</tr>
<tr>
<td>Cerebral palsy</td>
<td>Most common therapy</td>
</tr>
<tr>
<td>Choanal stenosis</td>
<td>Common</td>
</tr>
<tr>
<td>Cleft palate patients after repair</td>
<td>Reduced delta and REM at end of each apnea</td>
</tr>
<tr>
<td>Crouzon syndrome</td>
<td>nOSA patients</td>
</tr>
<tr>
<td>Cystic Hygroma</td>
<td>Decreased delta and REM at end of each apnea</td>
</tr>
<tr>
<td>Down Syndrome</td>
<td>May not be seen</td>
</tr>
<tr>
<td>Hallermann-Streiff syndrome</td>
<td>Usually normal</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Less common than in adults but can be seen</td>
</tr>
<tr>
<td>Klippel-Feil syndrome</td>
<td>Often enlarged</td>
</tr>
<tr>
<td>Mucopolysaccharidosis</td>
<td>Male &gt; females</td>
</tr>
<tr>
<td>Obesity</td>
<td>Male &gt; females</td>
</tr>
<tr>
<td>Osteopetrosis</td>
<td>Race or gender may not be consistent</td>
</tr>
<tr>
<td>Papillomatosis (oropharyngeal)</td>
<td>Persistent daytime somnolence and obesity</td>
</tr>
<tr>
<td>Pierre Robin syndrome</td>
<td>Selected patients</td>
</tr>
<tr>
<td>Pfeiffer syndrome</td>
<td>Inconsistent results</td>
</tr>
<tr>
<td>Pharyngeal flap syndrome</td>
<td>Mucopolysaccharidosis</td>
</tr>
<tr>
<td>Prader-Willi syndrome</td>
<td>Common</td>
</tr>
<tr>
<td>Sickle cell disease</td>
<td>Most common therapy</td>
</tr>
<tr>
<td>Treacher-Colins syndrome</td>
<td>Most common therapy</td>
</tr>
</tbody>
</table>

Chronic OSA generally results in pharyngeal collapsibility with obstruction of the airway and subsequent hypoxemia and/or hypercarbia with chronic hypoxemia and hypercarbia pulmonary artery pressure increases, which can result in right ventricular hypertrophy and heart failure. Patients with OSA can also develop biventricular dysfunction. Increased sympathetic nervous system along with autonomic and endothelial dysfunction can result in systemic hypertension. With right ventricular dysfunction, the ventricular system can bulge into the LV thereby decreasing LV volume and cardiac output and increasing LV end diastolic pressure and left atrial pressure. In addition, OSA can result in large negative intrapleural pressure changes, increases in left ventricular afterload and the development of pulmonary edema.

Anesthetic concerns for children with OSA secondary to adeno-tonsillar hypertrophy must focus in on (1) age appropriate cardiovascular issues and (2) postoperative respiratory issues. Most anesthetic agents have been successfully used in children. However, Brown and colleagues have noted that recurrent hypoxemia in young children is associated with decreased opioid requirements. This finding has also been observed in rodents as well. Of note is the association of the nadir O₂ nighttime saturation with the dose of postoperative morphine (MS). Brown and associates has calculated a formula for the postoperative dose of morphine based on the patient's age and nadir nighttime pulse oximetry saturation.

MS (mg/kg) = 0.0007 • age (months) + 0.0021 • SaO₂ nadir % - 0.1138
In addition to the intraoperative challenges, some of the more difficult issues involve the management of the pediatric OSA patient in the postoperative period. Issues of pain relief, NSAID use, and opioid sensitivity are significant. Pediatric patients with OSA have an increased risk for postoperative respiratory complications.\cite{13,14,15} Children less than 3 years of age have twice the risk of postoperative respiratory complications as children 3-6 years of age.

In addition to the perioperative administration of opioids, pain control and maintaining hydration have become significant issues in the postoperative period after discharge from the hospital. Pain controls with acetaminophen, opioids and nonsteroidal agents have become the main components of at home pain therapy. However, all of the drug types have significant side effects.\cite{16,17,18}

The use of codeine both with and without acetaminophen has come under more intense scrutiny. Codeine is nonanalgesic and it needs to be metabolized to morphine in order for it to be effective. Codeine is metabolized through the CYP2D6 pathway. A number of polymorphic forms exist. Thus, there can be patients who are ultra-rapid and extensive metabolizers (thus prone to high levels of morphine) as well as poor metabolizers (patients who derive no analgesic benefit from the drug).

At home, death from respiratory arrest has been reported in a number of patients who turn out to be ultra-rapid or extensive metabolizers. Although evidenced based reviews of the Cochrane collaboration suggested that there is no risk of bleeding in the post-tonsillectomy adenoidectomy patient with NSAIDS, it is unclear if this applies to the use of ibuprofen.

How effective is adenotonsillectomy in children? Published studies have reached slightly different conclusions. In a study of 207 children (of which only one was obese) Guilleminault et al.\cite{19} noted that patients postoperative polysomnograms indices improved compared to their preoperative values, but still 46% of patients had AHI that was greater than 1. Of note was that risk factors associated with elevated AHI post surgery included preoperative deviated septums, mallampati scores of 3 and 4, retroposition of the mandible and enlargement of the inferior nasal turbinates.

Other studies have noted similar findings in that the adenotonsillectomy is not universally curative. The percentage of patients with normal AHI postoperatively varies from 27 to 90%. This variance is in part related to the definition used for OSA, i.e., AHI/RDI and the patient population being investigated.\cite{10,20}

In patients with obesity (BMI > 95%) the incidence of OSA can be as high as 40%. Mitchell and Kelly noted in a group of 30 obese children with pre- and posturgical polysomnograms the polysomnogram indices improved, but the vast majority of patients still had by definition OSA.\cite{21}

These findings have been substantiated in single center studies as well as literature reviews/metaanalysis. That is, adenotonsillectomy reduces the severity of OSA in children but is rarely curative.\cite{22,23,24}

In summary, obstructive sleep apnea in children is different from adults. Though the most common cause in pediatric patients is adenotonsillar hypertrophy, adenotonsillectomy is not always curative but greatly improves the patient’s symptoms. Whether it can influence the effects of obesity remains to be determined.

REFERENCES

18. Disia R, Coté CJ. Nonsteroidal anti-inflammatory drugs and hemorrhage following tonsillectomy: Do we have the data? Anesthesiology 2004;100:749-51.
It is hypothesized that incorporating a brain monitor, like the bispectral index (BIS), into routine anesthetic practice can improve anesthetic management and patient outcomes by eschewing both too light and unnecessarily deep anesthesia. By avoiding light anesthesia, intraoperative awareness and its attendant complications, like posttraumatic stress disorder, can be prevented. Evidence from several large trials suggests that a BIS-based protocol decreases intraoperative awareness with postoperative recall when total intravenous anesthesia with pharmacological paralysis is administered. However, when anesthesia is based on a potent volatile agent, a BIS-based protocol is not superior to a protocol based on exhaled anesthetic concentration in preventing awareness with recall (Figure 1). Unnecessarily deep anesthesia is almost certainly associated with prolonged recovery and poorer quality of recovery. More controversially, deep anesthesia has been postulated to increase directly a variety of postoperative complications, including mortality, delirium, cognitive decline, dementia, myocardial infarction, stroke, renal failure and cancer.

Some trials have indicated that a BIS-based protocol may decrease anesthetic administration and improve early recovery (discharge from post-anesthesia care unit, nausea, vomiting) compared with routine care or an alternative protocol but other trials have not replicated these findings. An association has been noted between the cumulative duration of low BIS and intermediate-term mortality (1-4 years); this association was independent of anesthesia duration or volatile anesthetic concentration. Other studies have not found that cumulative duration of BIS<45 in isolation was connected with increased mortality. A concurrence of low BIS, low anesthetic concentration and low blood pressure, the “triple low” phenomenon, has been linked to increased all-cause postoperative mortality. The clinical relevance of this finding is currently uncertain, and might simply reflect patient vulnerability. If the link between “triple low” and death is causal, the pathophysiologic mechanisms by which “triple low” could indiscriminately increase mortality, especially cancer deaths, are unclear. Thus, relations between intraoperative BIS values (or other surrogate measures of anesthetic depth) and adverse postoperative outcomes (e.g., death, myocardial infarction, stroke, renal failure, cognitive decline, dementia, cancer recurrence) require scrupulous investigation.

There is mounting evidence from several randomized, controlled trials that a BIS-based protocol can decrease postoperative delirium, possibly by decreasing anesthetic administration or by minimizing epochs of electroencephalographic burst suppression. The results of an unpublished meta-analysis of four randomized studies comparing BIS-guided anesthesia with a control group (routine care or an alternative protocol) suggest that BIS-guided anesthesia lessens postoperative delirium, with a summary odds ratio of 0.56 (95% confidence interval, 0.42 to 0.73) (Figure 2). Although the finding is compelling, the mechanism for decreased delirium is unclear because most large studies have not demonstrated that BIS-guidance alters average anesthetic administration. Furthermore, logic would suggest that if a slight reduction in general anesthetic administration is associated with improved clinical outcomes, the use of no general anesthesia (e.g., medical management or regional anesthesia) should result in substantially better outcomes. On the contrary, meta-analyses of trials that have randomized patients to general or regional anesthesia for surgical procedures and large effectiveness trials that have randomized patients to major surgery with deep general anesthesia versus non-surgical management (e.g., coronary artery bypass grafting versus percutaneous stenting) have failed to demonstrate an improvement in outcomes (e.g., mortality, cognitive decline, delirium, quality of life) up to five years later with regional anesthesia or non-surgical, non-anesthetic management. Before we can conclude that a minor decrement in anesthetic concentration (or anesthetic depth) improves outcomes, we must demonstrate that general anesthesia at any concentration is injurious to patients.

Although skepticism is important and we should not reach overly hasty inferences, there is accumulating evidence that brain monitoring helps practitioners to administer anesthesia more appropriately for some individual patients, and is therefore likely to be associated with some improvements in patient outcomes. Hence brain monitoring during general anesthesia could enjoy more widespread adoption. In the United Kingdom, for example, guidelines from the National Institute for Health and Care Excellence (NICE) recommend the use of electroencephalography-based brain monitoring, especially in vulnerable patients. Implementation of these guidelines has been controversial due to the lack of definitive evidence for the benefit of such monitors and insufficient information on what constitutes “vulnerability”. Thus, most anesthesiologists in the UK currently do not follow the NICE guidelines, and either through choice or unavailability of the devices, do not use electroencephalography-based brain monitors. Nonetheless, brain monitoring is heuristically appealing as the brain is the target organ of general anesthesia. The BIS is only one of many available brain monitors; while it has been an important advance and has helped focus the...
attention of the anesthesiology community on the brain, BIS has important limitations that must be addressed in future devices. New brain monitoring approaches rooted in principles of neurobiology are being explored and could make the administration of general anesthesia less based on gestalt and median population parameters, and more driven by measured effects on its target organ.

Figure 1. Evidence-based decision tree for protocol to prevent awareness with recall (AWR). B-Aware = B-Aware clinical trial; B-Unaware = B-Unaware clinical trial; BAG-RECALL = BIS or Anesthesia Gas to Reduce Explicit Recall clinical trial; BIS = bispectral index; ETAC = end tidal anesthetic concentration; MACS = Michigan Awareness Control Study; TIVA = total intravenous anesthesia.

Figure 2. Meta-analysis of randomized controlled trials assessing postoperative delirium with intraoperative bispectral index (BIS) guidance of anesthesia compared with an alternative approach (i.e., usual care or an alternative protocol). Odds Ratios less than one favor BIS guidance.

REFERENCES


29. Dahaba AA. Different conditions that could result in the bispectral index indicating an incorrect hypnotic state. Anesthesia and analgesia 2005;101:765-73.


The New Organizational Vital Sign: Quality and Patient Safety

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OBJECTIVES
- To define quality and describe why it is important in the current health care environment.
- To briefly illustrate Cleveland Clinic Quality and Patient Safety Institute infrastructure.
- To describe why using thresholds alone for quality metrics is not always optimal.
- To demonstrate practical applications of current process improvement metrics and quality initiatives from our Quality and Patient Safety Institute.

REFRESHER COURSE LECTURE
Batalden and Davidoff emphasized the inextricable link between the domains of professional development, health care delivery and patient outcomes to contribute to better outcomes for all three domains. They defined quality improvement as: “the combined and unceasing efforts of everyone—healthcare professionals, patients and their families, researchers, payers, planners and educators to make changes that will lead to better patient outcomes (health), better system performance (care) and better professional development (learning).” Implicit in their definition is their conviction that better outcomes necessitate quality improvement be integrated into all parts of a health care system.

Traditional approaches to quality assurance focused on the ‘tail’ where thresholds were used to establish a statistical tail; the subsequent goal was to concentrate quality improvement activities on the tail region to avoid being an outlier. Brent James has described this as ‘threshold-based quality assurance’. The pitfall of threshold-based quality assurance is that there is a risk for thresholds to become an end-in-themselves; i.e., these artificial boundaries may limit institutions from further quality improvements since they are within the boundary of what is deemed ‘good enough’.

Case Example
Health care systems, governmental and accrediting agencies and payers primarily collect outcomes data from sources used for administrative purposes. In contrast, clinical data sources, which are often prospectively collected are considered superior to administrative data in the assessment of patient outcomes. This on-going tension between administrative and clinical registries and the need for healthcare organizations to demonstrate accountability for the quality of care delivered necessitates a better understanding of the data sources used for public reporting. On a local level we found inconsistencies in quality events between administrative and clinical data sources. This prompted us to explore data used in the context of public reporting of quality outcomes and data used for quality improvement initiatives. Our study demonstrated considerable lack of concordance between administrative data sources and two separate sources of clinically collected data (NSQIP and CVIR). The inconsistencies were related to a number of factors: differences in definitions among the three sources of data, sequences of outcomes documentation, coding, abstraction and data management and presentation. Our work emphasized the need for a national consensus on data definitions and for physicians to become more actively involved in understanding and using quality data.

Case Example
High performing institutions have continuous quality improvement integrated at multiple levels in their health care system. Patient safety initiatives to reduce complications and improve outcome is the goal of quality and patient safety. We reported on the morbidity complications associated with reoperation for bleeding, a complication following cardiac surgical interventions. We developed and instituted a process improvement initiative to reduce the occurrence of this complication in our operative setting with the use of a formalized hemostasis checklist. A number of studies have reported on reductions in error with the use of formalized checklists. While common in other industries, checklists have only more recently been integrated into a number of workflow processes in healthcare and operative environments. Following our 12 – month staged checklist implementation we reported significant reductions in reoperation for bleeding events in our surgical setting.

Case Example
In multiple settings the presence of anemia is associated with increased morbidity and poor quality of life. In a large population of non-transfused cardiac surgical patients we previously reported on the prevalence of perioperative anemia and its morbidity complications. There were several predictors for low nadir hematocrit, some were potentially modifiable others were not. Within hospitalized patients the development of anemia occurring during the course of hospitalization is associated with an increased risk for both morbidity and mortality. Development of hospital-acquired anemia is multifactorial and related to factors such as procedural blood loss, phlebotomy, in addition to blunted erythropoiesis of chronic disease. We examined the prevalence of hospital-acquired anemia, and mortality and resource utilization in over 400,000 hospitalizations within our health care system. We reported that anemia acquired during the course of hospitalization was common and associated with increased in-hospital mortality, length of stay and total charges. It appears to be a ‘hazard of hospitalization’ that is potentially modifiable.

CONCLUSION
W. Edwards Deming noted “Improve constantly and forever the system of production and service, to improve quality...
and productivity, and thus constantly decrease costs.” A well-designed quality and patient safety infrastructure provides the tools to measure, document and continually evaluate processes-of-care within a health system. Key to this infrastructure is the development of a culture of safety. The operative setting is particularly complex microsystem however well designed work processes and attention to continuous improvement and safe delivery of care ultimately benefit patient outcome. The value for patients and a health system is a high level of quality of care delivered in a safe and efficient manner.

REFERENCES
Anesthesia for Common Pediatric Surgical Emergencies: Are you Well Equipped?

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INTRODUCTION

The operating room is an environment where all cases are entertained. Perhaps the most difficult ones are the pediatric emergencies. Most children and infants differ from adults in several aspects. (i) they do not, at most times, have a past history of anesthetic exposure; (ii) they are generally healthy and do not have cardio-pulmonary problems. This leads to a scenario where they are healthy yet have underlying pathology that leads to a potential for rapid deterioration in the patient’s condition. This lecture will deal with 4 major clinical pediatric emergency scenarios that are seen in most hospitals and may lead to rapid alteration in a child’s condition. (Table-1).

<table>
<thead>
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<th>Preoperative preparation:</th>
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<td>It is important to understand a few common themes with all of these patients. This includes any family history of complications associated with anesthesia including but not limited to a history of malignant hyperthermia. In addition, a thorough history of previous experience with anesthesia as well as any associated abnormalities including congenital heart disease as well as other congenital anomalies are important to obtain prior to providing anesthesia. Preoperative fasting guidelines are important, however, except for the pyloromyotomy, most of these patients will have some degree of urgency and will require rapid anesthetic care. It is important to also keep in mind that the presence of trauma can decrease gastric emptying time. The main caveat in urgent vs. emergent surgery is to recognize the nature of intervention needed and the condition of the patient.</td>
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Pyloric Stenosis:

This is a fairly common emergency that can present to most institutions. There is an incidence of 1:500 in all live births with a propensity to occur in first born males in the family. They are often healthy infants who otherwise have recurrent history of vomiting and often present to the ED with significant dehydration. They often present with a hypochloremic, hypokalemic metabolic alkalosis. However, there are studies that also demonstrate a hyperkalemic state in some infants.1

Preoperative preparation:

It is crucial that the infant is well hydrated. These infants are generally significantly dehydrated with absent skin turgor and with a sunken fontanelle. In addition, it is important to ensure that the child is also not hypoglycemic at the time of presentation due to significant vomiting. It is important to hydrate the child prior to induction of anesthesia. The surgery is urgent but never emergent.

Induction and maintenance of anesthesia: A rapid sequence induction is generally planned. It is important to ensure that the stomach is adequately suctioned prior to induction of anesthesia. Preoxygenation is important since these infants have a tendency to desaturate rapidly. The use of a small dose of hypnotic followed by a muscle relaxant will allow for adequate placement of the endotracheal tube. The debate of whether to use succinylcholine vs. a non depolarizing agent like rocuronium has been studied.7 The time to recovery may be slightly prolonged with the non-depolarizing agent. It is also important to recognize the surgical technique for the procedure. In the event it is a laparoscopic procedure, careful attention has to be paid to the insufflation pressures for the abdomen. Higher pressures may lead to compression of the inferior vena cava leading to further drop in blood pressures. A subumbilical approach has been compared to the laparoscopic technique, the LAP technique may lead to a faster recovery and a shorter operating time.3 Total intravenous Anesthetic (TIVA) vs. inhaled anesthetics have been studied in this population demonstrating a rapid return to baseline with ultra-short acting opioids like remifentanil.4 We have utilized transversus abdominal plane blocks (TAP) for managing pain in the postoperative period thereby avoiding opioids for the surgery.

Emergence and postoperative care: Emergence from surgery and a fully awake. Maintaining an intravenous access is important for the infant to ensure absence of hypoglycemia in the immediate postoperative period. These children do very well and often have a rapid recovery to their normal state within hours of surgery.

Airway foreign body:

Airway foreign body is perhaps the most common emergent procedure in children besides trauma. Most presentation of airway foreign bodies occurs later than the actual ingestion of the foreign body. There is usually a history of cough or persistent wheezing, an occasional history of ingestion may be present. Very rarely there is stridor or significant desaturation.5 It is important to recognize the ‘when, what and where’ the aspiration happened.6 The common rule of thumb is (i) the FB is often organic; (ii) lodged in the bronchial tree; (iii) right side having a higher propensity than the left side; few are radio-opaque (11%); and have a mortality of about 0.42%.6

Preoperative evaluation:

A plain film of the chest may be obtained by the ED doctor prior to consultation of the ENT service.7 This could reveal a foreign body (if radio-opaque) or may demonstrate collapse of the lung or hyperinflation. Generally organic material like peanuts may not be seen in a plain film. Historic information including the ingestion of organic material can usually be

Table 1: Common pediatric emergencies

<table>
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<th>Airway foreign body</th>
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<tr>
<td>Pyloric stenosis</td>
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<td>Supracondylar fracture for closed reduction</td>
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<td>Tonsillectomy with bleeding</td>
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Ventilatory modes, especially jet ventilation, may be associated with infection. 66% of bleeding occurs in the tonsillar bed, 27% in the nasopharynx and 7% where it is combined. The incidence is about 2.15% in a large retrospective analysis. In addition, there is a Cochrane analysis that has demonstrated that there is barely 10

**Induction and Maintenance of Anesthesia:**

There are multiple methods reported in literature regarding the anesthetic management of foreign body retrieval in children. The three techniques include inhalation induction with spontaneous ventilation; TIVA using propofol and remifentanil; and using manual jet ventilation. Usually if possible, an intravenous access is obtained usually in the ED. A smooth mask induction with spontaneous ventilation with sevoflurane and nitrous/oxygen is carried out. After securing the airway, it is crucial to allow for spontaneous ventilation since there is a potential for dislodging the foreign body during retrieval. Factors leading to hypoxemia include younger patient, plant seed as foreign body, long surgical duration, pneumonia during the procedure and in some instances spontaneous ventilation. Ventilatory modes, especially jet ventilation, may potentially benefit in children. TIVA has been associated with breath holding, longer duration of emergence and potential for laryngospasm. Maintenance can be achieved using inhaled anesthetics or intravenous infusions.

**Foreign Body Removal:**

The foreign body can be removed using several techniques. The common technique is to use a rigid ventilating bronchoscope with a forceps to retrieve the foreign body. More recently, fiberoptic bronchoscopes have been used to retrieve the foreign body. The main problem is when the foreign body is lost while in the process of retrieval especially if lodged in the main trachea. The most important and potentially life saving technique would be to advance the foreign body to one of the bronchi and ventilate the child through the other lung. Children tend to desaturate rather rapidly and the situation could become dangerous. It is important to prevent coughing and bucking, some anesthesiologists use 1% lidocaine spray for the cords prior to airway instrumentation.

**POSTOPERATIVE COMPLICATIONS:**

These include laryngeal edema, bronchospasm, hypoxic cardiac arrest, pneumothorax, pseudo-mediastinum, tracheal and bronchial laceration. It is imperative that there is a fair amount of communication with the surgeon before and during the procedure. The outcome of the child is based on proper communication as well as the superb skills of the surgeon and the anesthesiologist.

**Bleeding Tonsils:**

This is one of those unfortunate events after a routine tonsillectomy in children. There are many factors that may lead to bleeding including poor hemostasis, bleeding diathesis including von Willebrand disease that is not diagnosed, infection, and foreign body irritation. Tonsillar bleeding occurs in 2 phases, and early phase that is associated with poor hemostasis or bleeding issues, and a secondary bleed that occurs in the first week, which is associated with secondary infection. 66% of bleeding occurs in the tonsillar bed, 27% in the nasopharynx and 7% where it is combined. The incidence is about 2.15% in a large retrospective analysis. In addition, there is a Cochrane analysis that has demonstrated that there is barely and association with the use of NSAIDs.

**PREOPERATIVE PREPARATION:**

Although this seems like an emergency, it is imperative to stabilize the patient prior to induction of anesthesia. They are often dehydrated and may have a low hemoglobin count. It is imperative that the fluid status is first assessed. In addition, it is important to remember that the child is anxious and is nervous. An intravenous catheter placement is important prior to the induction of anesthesia. As mentioned earlier, it is important to make sure that the patient is well hydrated. Checking blood pressures and pulse pressures may be useful to determine of they are compromised. In addition, looking for skin turgor as well as checking for orthostatic hypotension especially in the older child may point to an acute hypovolemic state. Blood should be sent for type and cross match and if it is an emergency, and if the child looks quite hypovolemic, it may be necessary to have blood available in the OR prior to induction of anesthesia.

**Induction of anesthesia:**

The child is likely to be anxious. It is important to hydrate the patient prior to induction of anesthesia. The child is like to also be a full stomach as they potentially could have swallowed a lot of the blood from the oropharynx. Attempts to keep the child with the face turned onto a side may be helpful in keeping the blood from being aspirated. An IV rapid sequence induction is usually planned with either propofol or ketamine (if the child is unstable) and succinylcholine or high dose rocuronium. A stylet is used for the endotracheal tube. After securing the airway, the surgeon should be ready to look for active bleeders. In the event there is no active bleeder that is visualized, there should be further investigations including a bleeding profile as well as an INR. This may shed light to a potential for a bleeding diathesis. We prefer giving some antiemetic prior to extubation since these patient have a propensity to vomit after surgery.

**POSTOPERATIVE PERIOD:**

This is one of those instances where a routine outpatient procedure can change to an inpatient admission. It is important to observe these patients for at least 6 hours after surgery.

**Supracondylar fracture reduction:**

This is a common presentation to an ED in the summer months. Most of these children are healthy and have sustained an injury while in a playground or in school. They present with significant pain and may require to go to the operating room sooner.

**PREOPERATIVE PREPARATION:**

NPO time is important. The presence of the traumatic event can lead to decrease in gastric emptying thereby leading to a potential full stomach setting. In addition, it is important for the surgeon to determine if there is a need for checking the vascular supply or the potential for nerve damage. A simple test for checking the integrity of the radial nerve (thumbs up sign), ulnar nerve (crossing the fingers); and median nerve (completing a circle with the index finger and thumb).
Anesthesia induction:

Since most of these patient are not emergent but urgent, they are generally scheduled during working hours except if there is any significant loss or absent pulses or if there is a propensity for compartment syndrome. A LMA is generally acceptable. After reduction of the fracture, we place an indwelling intravenous catheter in the supraclavicular area using saline to recognize the area of needle placement. Once the child is awake and alert, we do the neurocheck on the patient prior to injection of local anesthetic solution.

CONCLUSIONS

Pediatric emergencies are generally more difficult than in adult situations due to need to calm the child as well as provide an optimal scenario for providing the care. As more non-invasive techniques are being designed, surgery may become more relevant in certain cases than others.

REFERENCES

Use of ultrasound guidance has become a very popular technique for performing regional anesthesia. The rapid growth in popularity of this technique can be attributed to real time visualization of the nerves that are to be anesthetized as well as the ability to identify surrounding vital structures. Following an introductory discussion this refresher course will provide descriptions of three ultrasound guided regional blocks—interscalene, infraclavicular, and femoral nerve blocks. The lecture will include cases associated with their use.

With the use of ultrasound, anatomy including nerves, muscle, veins, arteries, and bones can be observed in real time. As the anatomy is defined, one can advance a needle to the desired location, administer local anesthetic, observe anesthetic spread, make adjustments as necessary and attain the desired regional anesthetic block. This is in contrast to the nerve stimulator technique during which the needle should not be moved once optimal position is obtained by a twitch response and local anesthetic has been injected. However, based on the ASRA Evidence-Based Medicine Assessment of Ultrasound Guided Regional Anesthesia and Pain Medicine: Executive Summary, despite its growth in popularity data does not support ultrasound as a better method to decrease complication rates than traditional methods. Possible reasons include inexperience of those performing the procedure, misinterpretation of images, or inability to visualize or identify needle location.

Ultrasound machines are both transmitters and receivers of sound waves. As these sound waves cross various tissue planes and anatomic structures there is reflection of some percent of the emitted sound waves back to the probe. The sound waves that are reflected back from various structures are then depicted on the ultrasound screen as a function the structure's density, the contrast between that object and surrounding structures, and other influences. Fluid filled vessels do not reflect sound waves well and are noted on the screen as a dark or black image. This is referred to as anechoic in character. When some sound waves are reflected back, the image on the screen is grey appearing and this is referred to as hypoechoic. Strong reflections of sound waves back to the transducer are noted on the screen as hyperechoic or white images. Bone is typically noted as a hyperechoic structure, as is the needle used to perform the block. The more parallel the needle is to the long axis of the probe, the more hyperechoic the needle appears. As the needle is angled, the reflection becomes less intense. This results from the fact that fewer sound waves are reflected directly back to the probe.

The two general approaches or techniques for performing ultrasound guided nerve blocks are the in plane and out of plane techniques. When performing the in plane technique the needle is advanced along the long axis of the ultrasound probe, while in the out of plane technique, the needle is advanced perpendicular to the long axis of the probe. With the in plane technique the entire needle especially the tip needs to be visualized. As the needle is advanced, it is easy to “lose” visualization of the needle tip. If this occurs, minor side-to-side “rocking” of the probe may bring the tip back into visualization. Needle tip visualization is important so that medication is injected in the desired location and the person injecting the medication knows where the medication is being injected. To aid needle visualization, some needles are manufactured with a hyperechoic needle tip.

In the out of plane technique, as the needle is advanced, a hyperechoic “dot” or image will become visible as the needle crosses the probe. When the “dot” is initially noted, it indicates the needle tip. As the needle is advanced further the reflection that is noted is the reflection of the shaft of the needle and should not be mistaken for the needle tip. Advocates of this technique note that the needle has to travel less distance and is not as uncomfortable for the patient. They utilize the reflected image as well as movement of tissue to help determine needle tip location. Another technique for identifying the needle tip is by hydrolocation which is injection of a small amount of fluid and noting the site at which it is injected.

**INTERSCALENE GENERAL CONSIDERATIONS/LANDMARKS:**

We have had excellent success with interscalene blocks performed for shoulder surgery. This block can be performed under ultrasound guidance via one of three approaches, the anterior in plane, the posterior in plane, and the out of plane approach. Be careful of the phrenic nerve with the anterior approach if it is performed at the C6 level as it can possibly be in the needle path.

The anterior approach is performed at approximately the C6 level or lower. For landmark orientation purposes identify the cricoid cartilage. This is at the C6 level. By positioning the ultrasound probe perpendicular to the length of the neck, anatomic structures including the nerves are visualized in cross section. The round trunks of the brachial plexus at this level distinguish themselves by having a hyperechoic rim with a hypoechoic center. The major vessels, the carotid artery and the internal jugular vein are observed in cross section as well. The carotid artery can be visualized and identified by its pulsations. In close proximity to the carotid artery is the internal jugular vein, which is compressible. The internal jugular vein can be observed to increase in size if the patient is asked to Valsalva. As the probe is placed into a more lateral position on the neck, the anterior and middle scalene muscles are identified as relatively hypoechoic structures on either side of the brachial plexus. If the ultrasound probe is now swept from a cephalad to caudal position, the roots and trunks of the brachial plexus can be seen to traverse down the neck into the supraclavicular area where the subclavian artery is located. Some regional anesthesiologists prefer to perform the block at this level or start the visualization and identification of the brachial plexus at this level and then move cranially. Caution is advised when performing a
supraclavicular block however, as the lung is in this area and while ultrasound provides direct visualization, there is a risk of pneumothorax.\textsuperscript{13}

**TECHNIQUE: \textsuperscript{1,2,9,11,12}**

For the anterior approach, place the patient in the supine position. Turn the head slightly away from the side undergoing the block. Properly prepare the skin and probe. Utilize sterile gel. Place the ultrasound probe on the neck at approximately the C6 level or slightly lower with the probe positioned perpendicular to the long length of the neck so that a cross-sectional view of the nerves is noted. Visualize the carotid artery and the internal jugular vein. Move laterally to locate the anterior scalene muscle and the brachial plexus between the anterior and middle scalene muscles. Move the probe in a caudad direction until you obtain the best visualization of the brachial plexus trunks. Place the needle medial to the probe and angle the needle laterally for an anterior in plane approach. Avoid the carotid artery and internal jugular vein as well as the phrenic nerve. Advance the needle through the sternocleidomastoid muscle and the anterior scalene muscle until the fascial plane in the interscalene area of the brachial plexus is pierced. Aspirate to make sure you are not intravascular and then inject local anesthetic with intermittent aspiration. Accurate location of the injection is validated by observing spread of local anesthetic around the trunks of the brachial plexus.

Suggestions: If the brachial plexus is not readily visualized at this level place the probe more caudad, toward the supraclavicular area. At this level the brachial plexus is more superficial in location and more easily visible. Once identified, the brachial plexus can be traced back up the neck.

An ultrasound guided posterior approach for an interscalene block is a popular technique.\textsuperscript{12} When performing this approach, be cautious that you are always visualizing the needle as you move it anteriorly. There are many important structures anteriorly that should not be pierced.

The third technique, the out of plane technique is utilized by others and was popularized by the group in Vienna.\textsuperscript{3} In one sense it is similar to the nerve stimulator technique as it is performed with the needle positioned between the anterior and middle scalene muscles.

**INFRACLAVICULAR NERVE BLOCK: \textsuperscript{1,2,3,9,11,15}**

The real time visualization of this deeper block has resulted in its popularity as a block to be performed under ultrasound guidance. (1,3,9,11) The patient is placed supine. The ultrasound probe is placed on the lateral portion of the chest wall medial to the coracoid process (1-2 cm) and just inferior to the clavicle allowing for insertion of the needle, and the anatomy is visualized. (9) As an indication that the probe is too medial, the pleura will be visualized. The probe should be moved laterally. The long axis of the probe is positioned along the long axis of the patient in a cephalad to caudal direction. The ultrasound images that are obtained are short axis views of the brachial plexus, the axillary artery and the axillary vein in the infraclavicular area. There must be sufficient room between the clavicle and the probe to allow the needle to be advanced. (1) Some advocate abducting arm to help increase the space below the clavicle for the needle. (15)

Visualizing the anatomy, one notes the more superficial pectoralis muscles and deep to these the axillary artery and vein. The artery and vein are visualized as dark anechoic to hypoechoic structures indicating that they are fluid-filled vessels. The nerves are adjacent to the artery and have a hyperechoic consistency throughout. The brachial plexus cords are located at this level with the lateral cord, lateral to the artery and located at approximately the 3 to 5 o’clock position, the posterior cord at the 6 o’clock position relative to the artery, and the medial cord located at around 10 o’clock.\textsuperscript{1} Note that there is considerable variation in the location of these cords. However, the lateral cord is usually the most visible cord and therefore is the best target for the local anesthetic.

After proper preparation of the probe and skin, the needle is advanced in the in plane technique along the long axis of the probe toward approximately the 5 o’clock position of the artery. Based on the anatomic relationships, the lateral cord, named relative to its position to the axillary artery, is the cord that is located in this area. After proper needle placement and aspiration local anesthetic is injected with intermittent aspiration to ensure you are not intravascular. If spread is not adequate around the axillary artery, the needle can be moved and additional local anesthetic injected.

**FEMORAL NERVE BLOCK: \textsuperscript{1,2,14}**

The femoral nerve is located lateral to the femoral artery and vein. The nerve is deep to two fascial planes, the fascia lata and the fascia iliaca. In order to obtain an effective block, local anesthetic needs to be injected beneath the fascia iliaca. With the probe placed perpendicular to the long axis of the femur, the nerve, artery and vein are visualized in cross section from lateral to medial. The femoral artery is pulsatile, the femoral vein is medial to the artery and compressible and the femoral nerve is lateral to the artery and is an oval to triangular shaped structure.

**TECHNIQUE UTILIZING THE IN PLANE APPROACH\textsuperscript{1}**

The described technique will be an in-plane technique with the probe perpendicular to the long axis of the femur and the approach from lateral to medial. This probe position provides a cross sectional view of the nerve, artery and vein.

The patient is placed supine. After proper preparation of the probe and groin area, locate the femoral nerve, artery and vein in the groin with the ultrasound probe which is placed perpendicular to the long axis of the leg. The nerve is located lateral to the artery. The artery is notable by its pulsatile nature and the vein is medial to it and compressible. Advance a needle toward the femoral nerve in the in plane approach from the lateral to medial. Continue advancing the needle beneath the fascia iliaca while avoiding the nerve. After needle placement and proper aspiration, inject local anesthetic with intermittent aspiration and observe for proper spread of the anesthetic around the femoral nerve.

**REFERENCES**


Perioperative Antiplatelet Drugs with Coronary Stents and Dancing with Surgeons: Can We Ever Agree about Bleeding versus Ischemic Risk?

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PHARMACOLOGY OF ANTIPLATELET DRUGS

Aspirin, usually in combination with a thienopyridine (Table 1), is the present-day cornerstone of oral antiplatelet therapy for the prevention of (a) neointimal hyperplasia, with resulting in-stent restenosis and (b) acute stent thrombosis, after placement of a bare-metal stent (BMS) or a drug-eluting stent (DES). 1-4 This oral antiplatelet therapy is especially important during the initial critical but often delayed period of reendothelialization of the lumen of the BMS or DES. 5,6 Aspirin irreversibly inhibits platelet cyclooxygenase (COX-1) activity and in turn the synthesis of thromboxane A2. 6 The thienopyridines [e.g., clopidogrel (Plavix®)] irreversibly bind to the platelet P2Y12 receptor and inhibit adenosine diphosphate (ADP) receptor-mediated platelet activation and aggregation. 6 Both aspirin and clopidogrel are “selective platelet-receptor” inhibitors that are considered weaker and thus safe antiplatelet agents. The co-administration of aspirin and clopidogrel results in enhancement of beneficial platelet inhibition, since they act via the above different platelet receptors. 7

Clopidogrel is a pro-drug that must be transformed by the hepatic CYP2C19 isoenzyme into its active metabolite to become clinically effective. 9 A reported 1% to 6% of Caucasians, 1% to 8% of African Americans, and 12% to 23% of Asians are CYP2C19 deficient (poor metabolizers) and thus at risk of treatment failure. 10 A subset of patients also display diminished or absent response to aspirin (“aspirin resistance”), likely due to a combination of clinical, biological, and genetic properties affecting platelet function. 11 This has raised the concern of drug resistance, with both clopidogrel and aspirin, which has been associated with an increased risk of an acute thrombotic event. 12,13 This is problematic because while there is commercially available CYP2C19 clinical genotyping, 14,15 there is no readily available, reliable laboratory measure of platelet function. 13,16

The proton-pump inhibitors, omeprazole (Prilosec®) and esomeprazole (Nexium®) are also hepatically metabolized by CYP2C19. Omeprazole and esomeprazole compete with clopidogrel for the CYP2C19 isoenzyme, thus decreasing the conversion of clopidogrel into its clinically active metabolite and possibly reducing its cardioprotective effect. 17,18 This drug-drug interaction prompted the U.S. Food and Drug Administration (FDA) in November 2012 to issue a safety labeling change, warning against the concomitant use of esomeprazole or omeprazole with clopidogrel. 19

While clopidogrel and ticlopidine (Ticlid®) are metabolized solely by the hepatic cytochrome P450 system, prasugrel (Effient®) is also converted to its active thiolactone by carboxylesterase 2 hydrolysis during its intestinal absorption, resulting in a reportedly more predictable antiplatelet effect with prasugrel. 20-22 Ticagrelor (Brilinta®) is a distinct cyclopentyl-triazolo-pyrimidine, which binds reversibly, and directly without biotransformation, to the P2Y12 receptor on platelets. 8,21,22 Cangrelor is an intravenously administered cyclopentyl-triazolo-pyrimidine, with rapid onset and return of normal platelet function within 60 minutes of discontinuation, which is currently awaiting U.S. FDA approval. 22,23

Of note, given the rapid onset of action of prasugrel or ticagrelor and their potential to decrease the risk of acute stent thrombosis, current international guidelines recommend prasugrel and ticagrelor in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI). 24-26 However, in June 2009, the European Medicines Agency (EMA) authorized six generic versions of clopidogrel, and in May 2012, the U.S. FDA approved generic clopidogrel. The net effect of these available generics on the previous dominant worldwide market share of proprietary Plavix® remains to be determined. Ultimately, the clinical benefits associated with prasugrel and ticagrelor need to be offset against their increased cost, promoting the need for an algorithm for using these new drugs in the primary PCI setting. 27

PATHOPHYSIOLOGY AND EPIDEMIOLOGY OF A PERIOPERATIVE MAJOR CARDIAC ADVERSE EVENT WITH CORONARY ARTERY STENTS

With the advent of percutaneous coronary intervention (PCI), in particular, coronary artery stenting, interventional cardiology has made significant progress in the management of coronary artery disease. 3 The scope of interventional cardiology

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Table 1. Current U.S. Food and Drug Administration (FDA) approved antiplatelet drugs* 6

<table>
<thead>
<tr>
<th>Drug</th>
<th>Platelet effect reversible?</th>
<th>Discontinuation before a procedure for recovery of adequate platelet function*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspirin</td>
<td>No</td>
<td>7 to 10 days</td>
</tr>
<tr>
<td>Clopidogrel (Plavix®)</td>
<td>No</td>
<td>5 days</td>
</tr>
<tr>
<td>Prasugrel (Effient®)</td>
<td>No</td>
<td>7 days</td>
</tr>
<tr>
<td>Ticlopidine (Ticlid®)</td>
<td>No</td>
<td>14 days</td>
</tr>
<tr>
<td>Ticagrelor (Brilinta®)</td>
<td>Yes</td>
<td>5 days</td>
</tr>
</tbody>
</table>

*Per U.S. FDA approved package insert

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has also greatly increased with the development of the BMS and DES (Table 2), and the associated use of antiplatelet drugs.\textsuperscript{2}

While such strategies have reduced the need for more invasive coronary artery bypass grafting (CABG) surgery, a major adverse cardiac event (MACE) can occur after coronary artery stent placement. While the definition of a MACE has varied considerably and hence the validity of such a composite end point in cardiovascular studies has been questioned,\textsuperscript{5,30,33-35} in patients who have undergone a PCI, a MACE conventionally includes any of the following:

- Death from all causes
- Q-wave and non-Q-wave myocardial infarction (MI)
- Coronary artery stent thrombosis and occlusion
- Target vessel restenosis (TVR)
- Target lesion revascularization (TLR)
- Coronary artery bypass graft (CABG)
- Stroke

Specifically, acute coronary artery stent thrombosis and occlusion carries a very high morbidity and mortality.\textsuperscript{2,5} In the modern era of second-generation stents, high-pressure stent deployment, and current antithrombotic regimens, angiographic confirmed stent thrombosis has reported a high incidence of death or myocardial infarction at the time of acute stent thrombosis.\textsuperscript{31} Clinical and angiographic risk factors for early stent thrombosis (within 30 days of initial stent placement) and late stent thrombosis (LST) (> 30 days after initial stent placement) have been well-defined\textsuperscript{4,5,28,32} to include:

- Premature discontinuation of antplatelet therapy
- Advanced age (> 75 years)
- Acute coronary syndrome (at the time of initial stent placement)
- History of coronary artery stent thrombosis
- Diabetes (poorly controlled with a Hgb A1C > 9.0)
- Low ejection fraction (LVEF < 30%)
- Anemia (with Hgb < 10 g/dL)

- Chronic renal insufficiency (Cr > 2.0 mg/dL)
- Prior brachytherapy for prostate or cervical cancer
- Stent in left main artery, proximal LAD, proximal RCA, or proximal dominant circumflex artery
- Long stents, multiple, or overlapping stents in a single vessel
- Ostial or bifurcation lesions
- Post-CABG stent(s) in saphenous vein graft(s)

A 0-19 point scoring system for risk of LST (low, medium, high, very high) has been developed.\textsuperscript{28,32} However, several studies have identified the most important risk factor for LST is the complete and premature discontinuation of dual antplatelet therapy.\textsuperscript{28,32}

Perioperative coronary artery stent thrombosis is likewise a catastrophic, often life-threatening complication that can occur in patients with either a BMS or DES.\textsuperscript{5,30,33-35} Non-cardiac surgery appears to increase the risk of acute stent thrombosis, myocardial ischemia and infarction, and death, especially when patients undergo surgery soon after stent implantation.\textsuperscript{29,36} The incidence of these complications is further increased when dual-antiplatelet therapy is abruptly discontinued preoperatively.\textsuperscript{29,37,38} This is likely due to a rebound hypercoagulability that lasts upwards of 90 days after such abrupt cessation of antiplatelet therapy.\textsuperscript{39,40} This rebound is marked by an inflammatory prothrombotic state, increased platelet adhesion and aggregation, and excessive thromboxane A2 activity.\textsuperscript{37,41,42} Surgery itself further promotes an inflammatory response and prothrombotic state, which, in the presence of an incompletely reendothelialized DES, can lead to an acute stent thrombosis, with likely myocardial infarction and/or death.\textsuperscript{37,41,42}

In one Mayo Clinic study, the incidence of a MACE was reportedly lowest when non-cardiac surgery was performed at least 90 days after PCI with BMS placement—but remained at 2.8% thereafter.\textsuperscript{34} In a concomitant Mayo Clinic study, the risk of a MACE with non-cardiac surgery after DES placement was observed to not be significantly associated with time between stenting and surgery, but the observed MACE rates were lowest after 365 days— but remained at 3.3% thereafter.\textsuperscript{35}

### Table 2: Currently U.S. Food and Drug Administration (FDA) approved bare-metal stents (BMS) and drug-eluting stents (DES).\textsuperscript{28,29}

<table>
<thead>
<tr>
<th>Stent (manufacturer, FDA approval date)</th>
<th>Generation</th>
<th>Type of stent</th>
<th>Drug eluted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liberti* (Boston Scientific) First</td>
<td>BMS: 316L Stainless steel</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>VeriFLEX* (Boston Scientific) First</td>
<td>BMS: 316L Stainless steel</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Bx Velocity (Cordis/J&amp;J) First</td>
<td>BMS: 316L Stainless steel</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Vision (Abbott) Second</td>
<td>BMS: Cobalt chromium</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Driver/Integrity (Medtronic) Second</td>
<td>BMS: Cobalt chromium</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Omega (Boston Scientific, trials underway) Third</td>
<td>BMS: Platinum Chromium</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Cypher (Cordis, 4/2003) First</td>
<td>DES: 316L Stainless steel</td>
<td>Sirolimus</td>
<td></td>
</tr>
<tr>
<td>Endeavor (Medtronic, 2/2008) Second</td>
<td>DES: Cobalt chromium</td>
<td>Zotarolimus</td>
<td></td>
</tr>
<tr>
<td>Promus (Medtronic-marketed Xience) Second</td>
<td>DES: Cobalt chromium</td>
<td>Everolimus</td>
<td></td>
</tr>
<tr>
<td>Promus Element (Medtronic, 11/2011) Third</td>
<td>DES: Platinum chromium</td>
<td>Everolimus</td>
<td></td>
</tr>
<tr>
<td>Taxus Ion (Boston Scientific, 2/2012) Third</td>
<td>DES: Platinum chromium</td>
<td>Paclitaxel</td>
<td></td>
</tr>
<tr>
<td>Resolute (Medtronic, 2/2013) Third</td>
<td>DES: Cobalt chromium</td>
<td>Zotarolimus</td>
<td></td>
</tr>
</tbody>
</table>

*Liberti* BMS was renamed VeriFLEX BMS by Boston Scientific in late 2009, to prevent continued confusion and inadvertent implantation of Taxus Liberti DES and vice versa.
Subsequent analyses of large-scale Canadian patient registry data and population-based administrative health care databases have revealed the earliest optimal time for elective surgery is 180 days after BMS implantation and 180 days after DES implantation. However, in a cohort of Dutch non-cardiac surgery patients who experienced a MACE, 45% were receiving single and 55% dual antiplatelet therapy. So indeed it would appear that timing is everything, at least with elective non-cardiac surgery in patients with a coronary artery stent.

RISK OF INTRAOPERATIVE AND POSTOPERATIVE SURGICAL BLEEDING WITH ANTIPLATELET DRUGS

In the above two Mayo Clinic studies on the optimal timing of non-cardiac surgery after BMS and DES placement, the continuation of dual antiplatelet therapy at the time of surgery did not increase the risk of major surgical bleeding. However, in the above Dutch study of the optimal timing of non-cardiac surgery versus stent placement, the risk of severe, “life-threatening” bleeding (defined as fatal bleeding, intracranial bleeding, or bleeding requiring surgical intervention or transfusion of ≥ 4 units of blood or blood products) was reported to be 4% with single antiplatelet therapy and 21% with dual antiplatelet therapy.

Based upon an extensive review of the available literature, after excluding cardiac surgery (with full intraoperative heparinization for cardiopulmonary bypass), surgical blood loss is increased 2.5% to 20% by aspirin alone, and 30% to 50% by aspirin and clopidogrel—but with no increased risk of bleeding related mortality except during intracranial surgery. Of note, transfusion rates are reportedly increased by 30% with continuation of dual antiplatelet therapy at the time of surgery.

It is generally felt that antiplatelet therapy (aspirin and/or clopidogrel) should be continued throughout the perioperative period, except in cases where the risk of morbidity and mortality from bleeding during and after surgery significantly outweighs the risk of acute stent thrombosis, as with procedures likely to be associated with major (massive) blood loss or performed in a closed space (e.g. intracranial, intraspinal, posterior eye chamber, transurethral prostatectomy). While the latter circumstances are frequently quite evident, the former is often more subjective and hence ambiguous.

CURRENT EVIDENCE AND GUIDELINES FOR THE PERIOPERATIVE MANAGEMENT OF ANTIPLATELET DRUGS IN PATIENTS WITH A CORONARY ARTERY STENT

The optimal perioperative management of patients with a coronary artery stent remains a very significant yet challenging patient safety issue for clinicians. The U.S. FDA and the American Heart Association/American College of Cardiologists (AHA/ACC) have recommended continuing dual-antiplatelet therapy in patients with a DES for one year and in patients with a BMS for six weeks. Unless medically contraindicated, all patients with any type of coronary artery stent should remain on lifelong aspirin monotherapy. These therapies for the prevention of stent thrombosis have major implications for anesthesiologists and surgeons. Not surprisingly, these recommendations regarding the optimal duration of and perioperative continuation of antiplatelet therapy continue to be debated—both in the literature and in routine clinical practice. Hence the title of this paper, “Dancing with Surgeons: Can We Ever Agree about Bleeding versus Ischemic Risk?”

PRINCIPLES AND USE OF CONSENSUS DECISION-MAKING

Consensus decision-making is one form of group decision making. Consensus decision-making does not require unanimity but instead seeks the agreement of the majority of participants as well as the resolution of or mitigation of minority held objections. Consensus decision-making is applicable to the management of complex clinical conditions—in particular, the development of clinical practice guidelines and clinical care pathways, involving a variety of healthcare providers.

Specifically, the Consensus-Oriented Decision-Making (CODM) model has been successfully applied to arrive at a consensus among local clinical stakeholders about the management of patients with coronary artery stents. Offering a detailed, step-wise description of the consensus process, the CODM model can be applied in any type of decision-making process. It outlines a process in which proposals can be collaboratively built with full participation of all stakeholders. The CODM model allows groups to be flexible enough to make decisions when they need to, while still following a format that is based on the primary values and goals of consensus decision-making. The CODM model involves seven steps:

1. Framing the topic
2. Open Discussion
3. Identifying Underlying Concerns
4. Collaborative Proposal Building
5. Choosing a Direction
6. Synthesizing a Final Proposal
7. Closure

ACHIEVING INSTITUTIONAL STAKEHOLDER CONSENSUS ABOUT PERIOPERATIVE ANTIPLATELET DRUGS FOR CORONARY ARTERY STENTS

Coordinated care by all clinicians involved with a coronary artery stent patient is essential to avoid a high incidence of perioperative cardiac mortality and morbidity. Currently, though, as noted above, there are limited published data to guide surgeons, anesthesiologists, cardiologists, and primary care physicians, on the optimal care of patients with indwelling coronary artery stents presenting for non-cardiac surgery. Surgery on a patient on antiplatelet therapy thus creates a dilemma: Is it better to withdraw the drugs and reduce the hemorrhagic risk or to maintain them and reduce the risk of a myocardial ischemic event? In either case, optimal perioperative care includes prompt recognition of myocardial ischemia and/or infarction. If stent thrombosis occurs, rapid triage to an interventional catheterization laboratory is essential for restoration of coronary blood flow.

From July 2011 to November 2011, the above seven step CODM model was followed to arrive at a consensus, among the
institutional clinical stakeholders at the University of Alabama at Birmingham Health System (UABHS), and to develop a protocol for the perioperative management of patients with indwelling coronary artery stent(s) undergoing elective surgery at our satellite university hospital without an on-site cardiac catheterization laboratory. Subsequently, between January 2013 and March 2013, this CODM model was also reiteratively applied by a UABHS Anticoagulation Task Force to create two evidence-based and local expert opinion-supported protocols (Figure 1a and Figure 1b), which standardized the preoperative management of antiplatelet therapy in patients with an indwelling coronary bare metal stent or drug-eluting stent.

This small yet multidisciplinary clinical task force included representatives from anesthesiology, cardiology, critical care medicine, gynecology, hospitalist medicine, pulmonology, transfusion medicine, and surgery. The efforts of this task force were enhanced the well-established UAB Department of Anesthesiology Section on Quality and Patient Safety and the departmental electronic Anesthesiology Dashboard, which provided an online mechanism for efficient sharing of pertinent published articles and successive protocol drafts.

*Day of Surgery Proviso:* For patients scheduled for elective surgery who have independently stopped antiplatelet therapy prior to presentation to UAB on the day of surgery, the
Figure 1b. Protocol for preoperative antiplatelet therapy with an indwelling drug-eluting stent (DES) (*See “Day of Surgery Proviso” below)
following steps can be used to guide the joint decision making by the anesthesiologist and surgeon:
1. Determine whether it would have been indicated—based on the BMS protocol or DES protocol—for the patient to stop single or dual antiplatelet therapy.
2. If discontinuation of the antiplatelet drug and/or aspirin is indicated by the protocol, the surgery may proceed as planned.
3. If continuation of aspirin is indicated per the protocol, and the patient has been off aspirin for more than 5 days:
   (a) if there is a high risk of morbidity or mortality from bleeding during and after the planned procedure, obtain Cardiology consult for management recommendations;
   (b) if there is an intermediate risk from bleeding during and after the planned procedure, give 81 mg of aspirin prior to surgery; and
   (c) if there is low risk of morbidity or mortality from bleeding during and after the planned procedure, give 325 mg of aspirin prior to surgery.
4. If continuation of another antiplatelet drug (other than aspirin) is indicated by the protocol, and the patient has been off this drug for more than 5 days, options include:
   a) Give 600 mg of clopidogrel and proceed with surgery a minimum of 2 hours later.
   b) Give 300 mg of clopidogrel and proceed with surgery a minimum of 4 hours later.
   c) Reschedule surgery for a later date. In this case, give 300 mg of clopidogrel and start clopidogrel 75 mg daily.
   d) If there is a high risk of morbidity or mortality from bleeding during and after the planned procedure, obtain Cardiology consult for management recommendations.

REFERENCES


Servin FS. Is it time to re-evaluate the routines about stopping/keeping platelet inhibitors in conjunction to ambulatory surgery? Curr Opin Anaesthesiol 2010;23:691-6.


Is There a Link Between Acute Pain and Chronic Pain?

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OVERVIEW

Pain is a normal physiologic response to injury. The presence of pain signals impending tissue injury and signals the need to protect the injured area during healing. Under some circumstances, pain persists after all tissue has healed. We now have a detailed understanding of the physiologic mechanisms that are responsible for the initial perception of acute pain and the neuronal changes that rapidly lead to an increase in sensitivity of the injured region. At the same time, efforts to use combinations of analgesics and analgesic techniques including regional analgesia have been closely studied and shown to provide excellent pain relief. Despite our best efforts, some patients go on suffer from long-term chronic pain after the acute event. In this review, we will examine the basic physiologic mechanisms that lead to the perception of acute pain, our current understanding of the neuronal mechanisms that produce sensitization immediately after injury, and the risk factors that are associated with persistent pain after surgery. Our discussion will include an examination of the role for specific analgesic techniques in improving pain control in the immediate post-operative period and how we might identify those at greatest risk for persistent pain and develop analgesic regimens most likely to minimize the risk of persistent pain.

SENSITIZATION AND THE PROMISE OF PRE-EMPTIVE ANALGESIA

Pain is produced by physical, thermal, or chemical stimuli that can potentially induce tissue injury. Between the site of the stimulus and pain perception, a complex sequence of electrochemical events takes place, which are collectively called nociception (Figure 1). Different stimuli can lead to the perception of pain. These include mechanical, thermal, and chemical stimuli. Mechanical forces, heat, and chemical changes result in increased firing in nerve terminals within tissue – this process is referred to as transduction. Afferent axons carry signals from the site of peripheral stimulation toward the spinal cord where the signals are relayed to higher centers within the central nervous system. This process is called transmission. The magnitude of incoming nociceptive traffic reaching the central nervous system can be modified before reaching higher centers, a process termed modulation. Stimulation of the periaqueductal gray region within the midbrain and the periventricular gray matter lateral to the hypothalamus produces profound analgesia in humans. These regions have been found to contain high concentrations of endogenous opioid neurotransmitters. The periventricular gray matter and the periaqueductal gray matter are interconnected and also connect anatomically with the rostroventral medulla. The rostroventral medulla sends descending projections via the dorsolateral funiculus to the dorsal horn of the spinal cord. Norepinephrine, serotonin, and systemically administered opioids all likely produce their nociceptive effects through activation of these descending inhibitory pathways.

Pre-clinical studies have demonstrated that peripheral injuries can trigger long-lasting increases in the excitability of neurons, a process termed sensitization. This occurs both at the level of the primary afferent nociceptive peripheral neuron (peripheral sensitization) and the dorsal horn of the spinal cord (central sensitization). This is manifest as a reduction in the threshold for activation of nociceptive neurons; subsequently normally non-painful stimuli are perceived as painful (allodynia) and minor painful stimuli now produce severe and long-lasting pain (hyperalgesia). This increase in gain in the nervous system, the sensitization, serves as a normal and protective response to injury. The sensitization is a reminder that the injured area needs to be protected to allow the tissue injury to proceed without interruption from repeated injury. In the absence of pain, like that seen in diabetics with loss of normal peripheral sensation who suffer from poorly healing ulcers in the extremities, recurrent injury goes unnoticed, healing is poor, and amputation of affected digits is common.

Under most circumstances, as injured tissue heals, sensitization gradually diminishes toward normal sensation. Nonetheless, persistent pain after injury is common. When pain persists along with the characteristics of sensitization after all tissue injury has healed, we call it neuropathic pain. The notion that the sudden barrage of incoming nociceptive traffic reaching the spinal cord is what leads to sensitization and that by applying an analgesic intervention prior to the traumatic event (surgical incision) we might reduce or even eliminate nociceptive traffic is what led to the concept of preemptive analgesia. We know

Figure 1. Schematic representation of nociception: the normal physiologic processes that lead to pain perception. Sites where specific analgesics may modify normal pain perception and sensitized neuronal structures are shown.
examining much the same group of studies examined combined, they concluded that pre-emptive administration analgesia. When the data from all three outcome measures were point in time after surgery to represent significant preemptive reduction in a single pain scores at any time after surgery, Ong and colleagues accepted reduction in a single pain scores during the first 24 postoperative hours, Ong and colleagues used the more rigorous criteria of pain scores summed over the first 24 hours following surgery, perhaps a better measure of a truly meaningful clinical effect. While there may be statistically significant reductions in pain scores and supplemental analgesic use after surgery with use of a preemptive analgesic approach, these differences are small and are unlikely to impact on the patient’s overall pain experience. The largest differences appear early after emergence from anesthesia in the first few hours after surgery: if a pre-emptive approach was used, patients are more likely to emerge from anesthesia with good pain control. Perhaps the take home message from this enormous body of work is simply that anesthesiologists should not wait until after emergence to begin, by whatever route is chosen, to administer analgesics.

Why doesn’t preemptive analgesia work? In a recent review, Katz and colleagues5 take us through the history of pre-emptive analgesia and posit a number of reasons that the overly simplistic approach of administering a single analgesic just prior to surgical incision is so inadequate in improving postoperative analgesia and other outcomes. They tell us that the classic view of preemptive analgesia assumes that intraoperative painful stimuli contribute to postoperative pain more than postoperative stimuli. But, experimental studies demonstrate that sensitization is caused by factors other than the incision and subsequent intraoperative events alone. Our focus should shift to reducing the impact of noxious preoperative, intraoperative, and postoperative events.

**PERSISTENT POST-SURGICAL PAIN: RISK FACTORS AND PREVENTION**

When pain persists for more than 3 to 6 months after surgery, normal post-surgical healing is complete, and there is no alternate ongoing process (e.g. infection) to explain the ongoing pain, persistent postsurgical pain (PPP) is present. Persistent postsurgical pain is surprisingly common after many of the most frequently performed surgeries (Table 1).

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Estimated incidence of chronic pain</th>
<th>Estimated chronic severe (disabling) pain (&gt;5 out of score of 10)</th>
<th>US surgical volumes (1000s)†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amputation</td>
<td>30 – 50%</td>
<td>5 – 10%</td>
<td>159 (lower limit only)</td>
</tr>
<tr>
<td>Breast surgery (mastectomy and lumpectomy)</td>
<td>20 – 30%</td>
<td>5 – 10%</td>
<td>479</td>
</tr>
<tr>
<td>Thoracotomy</td>
<td>30 – 40%</td>
<td>10%</td>
<td>Unknown</td>
</tr>
<tr>
<td>Inguinal hernia repair</td>
<td>10%</td>
<td>2 – 4%</td>
<td>609</td>
</tr>
<tr>
<td>Coronary artery bypass surgery</td>
<td>30 – 50%</td>
<td>5 – 10%</td>
<td>598</td>
</tr>
<tr>
<td>Cesarean section</td>
<td>10%</td>
<td>4%</td>
<td>220</td>
</tr>
</tbody>
</table>

Table 1. Estimated incidence of chronic postoperative pain and disability after selected surgical procedures (adapted with permission from reference 5). †National Center for Health Statistics, Ambulatory and Inpatients Procedures, USA, 1996.
We know much about the preoperative risk factors that are predictive of the appearance of PPP. Risk factors include the magnitude and location of the surgical insult, genetic susceptibility, preceding pain, psychosocial factors, age and gender. Indeed, recent studies clearly demonstrate that patients with specific single nucleotide polymorphisms (SNPs) have a genetically conferred resistance to both acute and chronic pain. Despite advances in our understanding of what leads to persistent pain after surgery and the ease with which we can identify those at greatest risk, it is unclear how best to approach the management of pain during the perioperative period in a way that will minimize the risk of persistent pain.

**FROM PRE-EMPTIVE TO PREVENTATIVE ANALGESIA**

The limited approach provided by preemptive analgesia – simply providing the analgesic before the incision is made – may minimally improve pain relief, but is unlikely to reduce the incidence of persistent pain after surgery. The concept of preventative analgesia has emerged during the past few years. The idea is to combine a number of different analgesics with mechanisms that differ and that may well impact directly on the mechanisms behind development of persistent pain in efforts to improve postoperative pain control and prevent the development of persistent pain. A handful of trials suggesting that such a preventative approach may be effective have appeared. Lavand’homme and colleagues randomized patients undergoing colectomy to receive a combination of analgesics including local anesthetics, opioids, and clonidine intravenously or via neuraxial administration and examined the effect on postoperative hyperalgesia surrounding the surgical incision as well as persistent pain as far as 12 months after surgery. The use of epidural analgesia as part of a multimodal regimen dramatically reduced the incidence of persistent pain at 12 months after surgery, suggesting that this multi-pronged, preventative approach might well improve on the original concept of pre-emptive analgesia. Subsequent clinical trials using the same approach have yielded conflicting results. Buvanendran and colleagues demonstrated that the use of oral pregabalin during the immediate perioperative period in patients undergoing total joint replacement reduced the incidence of persistent pain several months after surgery, again emphasizing that specific analgesics continued through the perioperative period might well reduce the long term problem of PPP. These small, preliminary studies show promise, but need confirmation through large-scale, multi-center trials.

**FUTURE DIRECTIONS**

Major trials are now underway that incorporate prospective identification of risk factors into analgesic trials. If we identify high-risk patients through genetic screening or by specific characteristics known to correlate with the development of persistent pain after surgery, will we be able to modify the outcome? As an anesthesiologist in practice today, we can do nothing more than design the very best analgesic regimens with the tools we have at hand – regional anesthesia, systemic opioids and adjuvant analgesics – and trust that our efforts will succeed. When our initial approach proves inadequate, we should rapidly shift gears and provide analgesia through some alternate means; removing and replacing a non-functioning epidural promptly or switching to intravenous opioids as quickly as possible to avoid periods of prolonged inadequate analgesia. In the very near term, we are likely to gain a better understanding of how to take those identified as at high risk for a poor pain experience and combine our existing analgesic approaches in to a tailor-fit prescription for each patient that will minimize the chances of poor analgesia and persistent pain.

**REFERENCES**

Popular Misunderstandings in Neuroanesthesia

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PERSPECTIVE

I have committed considerable profession time to anesthesia for neurologic surgery. That commitment has caused me to hear a great deal related to neuroanesthesia. I have been asked by faculty colleagues in anesthesia, “What do you suppose might have gone wrong during that case yesterday?” I have listened to ABA oral exam candidates misapplying or frankly misunderstanding fundamental principles. I have been involved in third party scrutiny of procedures that were perceived to have gone astray. I acknowledge that those interactions inform the selection of topics that follows (rather than “evidence based” material from the peer reviewed literature). Not all of the topics will be addressed during the course of the presentation.

THE LOWER LIMIT OF CBF AUTOREGULATION

Diagrams that appear in standard texts have frequently depicted the lower limit of human cerebral blood flow autoregulation (LLA) as being a mean arterial pressure (MAP) of 50 mmHg. While this number may in fact be a reasonable representation of the LLA in several animal species, it is unlikely to be an accurate value in adult humans. The first rendering of a CBF autoregulation curve was probably that drawn by Lassen.3 His diagram depicted an LLA that might be easily interpreted to be 50 mmHg. On close inspection, however, the inflection point is probably at 60 mmHg. However, the inflection point on that hand-drawn curve (where ever it is) is anchored by only two CBF values, both of which were obtained in pregnant females at term in whom blood pressure was lowered using cerebral vasodilating drugs and in whom base line pressures were probably well below the population average for normal adult humans. Furthermore, numerous subsequent investigations2 (see Drummond4 for additional references) suggest that the LLA in non-anesthetized adult humans is nothing less than 70 mmHg. However, it should be acknowledged that the “rules” might be different during general anesthesia for at least two reasons. The first is the frequent inclusion of vasodilating substances in anesthetic recipes. Vasodilators might serve to shift the autoregulation curve in a leftward direction. The second resides in the observation that sympathectomy in both experimental animals and humans during hypotension increases CBF.4 This suggests that the normal autonomic response to hypotension includes some vasoconstriction of large extracranial and perhaps intracranial vessels thereby producing effective right shifting of the autoregulation curve. If a general anesthetic were to effectively prevent that autonomic response, it is possible that some resultant left shifting of the curve might occur. The reality, however, is that there has been exceptionally little systematic study of normal (non cerebrally injured) adult human cerebral autoregulation during anesthesia. The only context in which extensive study has occurred is during cardiopulmonary bypass (typically involving, hypothermia, non-pulsatile flow, relative anemia and high-dose narcotic anesthesia). In those circumstances, which is very poorly representative of the physiology that prevails during the majority of general anesthetic states, the LLA is in fact about 65 mmHg (with a very large confidence interval indicating considerable inter-individual heterogeneity.5 However, it seems inappropriate to extrapolate that average value (obtained in the context of non-pulsatile flow, low hematocrit and well maintained cardiac output) to all other anesthetic circumstances. In fact, it further seems likely that what pertains to any one anesthetic circumstance, e.g., spontaneous ventilation during anesthesia with a volatile agent, might not be relevant in another, e.g. a TIVA anesthetic with remifentanil and propofol. We know very little about the LLA during general anesthesia in humans and conservative assumptions should be made in the absence of more detailed knowledge.

THE PHYSIOLOGIC CENTRAL NERVOUS SYSTEM BLOOD FLOW RESERVE

Many clinicians may well respond to the preceding discussion of the LLA with their own observation that numerous patients in the span of their experience have tolerated MAPs in the 40s, 50s and 60s, i.e., well below the proposed LLA of 70 mmHg. That is inevitably true. Patients tolerate blood pressures below the LLA because there is a substantial CNS blood flow reserve. CNS flow can fall by approximately 40% of baseline values before symptoms of ischemia begin to occur.6,8 That reserve is, in essence, a physiologic buffer that protects patients in the event of hypotension. However, it is important that clinicians recognize the situations in which that buffer may not be present, often because it has been encroached upon by some preexisting pathologic process. The most common situations in which the buffer is likely to have been attenuated occur in circumstances in which CNS tissue is under increased pressure. This may occur in the circumstances of increased ICP, increased ocular pressure or when CNS tissue is under extrinsic pressure, e.g., compressed under retractors or by a bulging disc. The significance of these situations is that the principal determinant of flow to the tissue is “transmural pressure” rather than “blood pressure”. Transmural pressure (which is commonly but probably erroneously referred to as “perfusion pressure” equals MAP minus local tissue pressure. Among the most commonly overlooked situations in which tissue pressure is increased (and the effective perfusing pressure is therefore less for a given value of MAP) is in the circumstances of spinal stenosis, in particular cervical spinal stenosis. In that group of patients, the normally wide latitudes for intraoperative blood pressure that anesthesiologists commonly allow should be tightly restricted. It is our approach at UCSD to maintain MAPs during anesthesia in these patients (at least until the decompression is complete) very close to normal waking levels. The agent we use most commonly to achieve this is phenylephrine. This introduces
another common misconception, which is addressed in the second paragraph below.

THE EFFECT OF HYDROSTATIC GRADIENTS ON CPP

In patients who undergo anesthesia in horizontal positions (supine, prone, lateral), it is standard to measure blood pressure with cuffs or transducers at the level of the heart. When positions are used that result in a vertical height difference between the height of the heart and the head, a pressure differential between the two that is equivalent to the weight of a column of blood of that height can be expected to occur. That gradient will be equal to approximately 2 mmHg for each one inch of height difference. The standard teaching in neuroanesthesia has long been that blood pressure should be transduced at (or an arithmetic correction imposed to correct to) the level of the external auditory meatus (EAM). Clinicians who are unfamiliar with the use of the sitting position have occasionally failed to make this correction in transducer height, or have raised it only to the level of the heart with sometimes severe adverse consequences for the perfusion of the brain and/or the cervical spinal cord. This issue has been popularized recently in the context of injuries occurring in the so called “beach-chair position”. A minority have disputed this notion, arguing that siphon-like mechanism maintains CBF in spite of reductions in CPP calculated in the manner above.9 Unless and until there is wider proof of that concept, conventional hydrostatic gradient concepts should apply, and arterial transducers should be raised to the level of the EAM or arithmetic corrects should be applied to cuff pressures in order to “think” in terms of BP at the EAM.10

ALPHA 1 AGONISTS AND CEREBRAL VASOCONSTRICTION

It is often asserted that the various alpha1 agonists are significant CNS vasoconstrictors. While that may be so in canines, it is not true in humans. See “Miller's Anesthesia”, 6th Ed., Ch. 21, p 818 for references. (The references were regretfully omitted in the corresponding section in the 7th edition – Ch. 13, p 311.) In human investigations done many years ago, alpha one agonists were infused directly into the cerebral circulation in concentrations sufficient to produce substantial increases in systemic arterial pressures; and no changes in CBF were observed. The concern that phenylephrine is a CNS vasoconstrictor has too often restricted its use in situations where there was a pressing need to augment CCP. Clinicians should “get it out of their heads”. Phenylephrine is NOT a significant CNS vasoconstrictor in the doses that we commonly employ. When blood pressure support is warranted in patients who have sustained SAH or TBI or when CNS structures are under compression (spinal stenosis, retractor pressure), after assuring appropriate volume status and depth of anesthesia, phenylephrine is a reasonable choice!

THE EFFECT OF VOLATILE AGENTS ON CBF

Figures that appear widely in standard texts indicate that the common volatile agents (isoflurane, sevoflurane and desflurane) cause little or no increase in CBF at sub-MAC concentrations. In the majority of elective neurosurgical patients that is almost certainly true. In fact, in subjects with generally normal cerebral physiology, CBF actually decreases from the awake state to reach a nadir in the vicinity of 0.75-1.0 MAC. Thereafter, CBF increases in parallel with increasing end-tidal concentrations of volatile agents.11 This superficially unusual bi-phasic pattern is almost certainly the product of the very substantial suppression of cerebral metabolic rate that occurs with the initial exposure to volatile agents. The reduction in CBF is probably largely a “coupled” reduction in the CBF recurring as a consequence of the reduction of CMR. The important issue for clinicians is that in patients in whom CMR has already been depressed by either pathologic processes or CMR suppressing drugs (benzodiazepines, narcotics, propofol) or who have sufficiently disordered physiology that the coupling mechanism may not be functional, volatile agents may act as potent vasodilators even at the sub-MAC concentrations that are normally associated with a reduction in CBF. The consequence for the clinician is that in patients with badly impaired intracranial compliance (or, as some would say, “elastance”) especially in whom those in whom CMR is already depressed, volatile agents should be introduced very cautiously. In the ideal, in those extreme circumstances, they should probably not be introduced unless ICP is being monitored or until the cranium is open and the brain can be observed directly.

OBSTRUCTION OF VENOUS DRAINAGE

The venous side of the cerebral circulation is a passive, but relatively large intracerebral compartment. It is quite commonly the cause of raised intracranial pressure or “tightness” in the surgical field and is relatively under-recognized. The cerebral venous drainage is easily obstructed by anything that puts pressure on the underlying jugular veins including circumferential ties and cervical collars. Extremes of head position can also obstruct venous drainage. Any rotation of the head that is sufficient to put tension on the sterno-cleido-mastoid muscles is sufficient to compress the underlying jugular vein. In addition, the jugular veins drain downstream into the chest. Accordingly, anything that raises intrathoracic pressure can impair cerebral venous drainage. This includes a medley of common entities including coughing against an endotracheal tube, kinking of the endo-tracheal tube, bronchospasm, and pneumothorax. Confirmation of the patency of the jugular venous system and verification of normal airway pressures are accomplished easily and should be the first things that the clinician does when evaluating increased intracranial pressure or a tight surgical field.

HYPERVENTILATION

It has become a well-established concept that the vasoconstriction associated with hyperventilation has the potential to cause sufficient cerebral vasoconstriction to result in ischemia when imposed on the low flow circumstances that can prevail after acute cerebral injuries, in particular head injury12 and sub-arachnoid hemorrhage (SAH). Routine hyperventilation in neuroanesthesia and neurosurgical critical care has ceased. While prophylactic hyperventilation is never appropriate, hyperventilation is by no means totally “verboten”. Hyperventilation remains an adjunct in the management of patients with critically increased ICP at risk of herniation in whom other measures, short of barbiturate coma, have proven inadequate. Its use should be as brief as allowed for by patient circumstances.
TENSION PNEUMOCEPHALUS

Tension pneumocephalus is a phenomenon that can occur when gas is trapped within the intracranial space with no communication to the outside atmosphere. The phenomenon is widely associated with the sitting position and many clinicians associate its occurrence with the use of N\textsubscript{2}O. It most certainly is a phenomenon that can be both caused or exaggerated by N\textsubscript{2}O and many clinicians will have decided to omit N\textsubscript{2}O from the anesthetics used for posterior fossa procedures done in the sitting position as a result. However, the assumption that one no longer needs to be concerned about tension pneumocephalus if one has made the decision to omit N\textsubscript{2}O is an erroneous one. Clinically significant, and even life threatening, tension pneumocephalus can occur in the absence of the use of N\textsubscript{2}O. Imagine a situation in which a craniotomy has been performed in a head up posture with the craniotomy located such that a significant portion of the cranium is above the surgical site. With optimal venous drainage, mannitol administration, hyperventilation, the use of anesthetic agents that reduce brain bulk and opening of the arachnoid membrane resulting in drainage of CSF, a substantial potential space can occur between the surface of brain parenchyma and the highest point of the skull. That space will fill with air. When the procedure is concluded and the patient is restored to a near supine position, venous blood, arterial blood, CSF and extra cellular fluid all begin to return. Albeit that the oxygen is absorbed quickly from the air within the cranium, the remaining nitrogen can represent a substantial and unyielding “mass” that will diffuse away only very slowly (over a period of days).\textsuperscript{13} Frontal craniotomies performed in a brow up position in which the frontal bone is removed and replaced, are particularly prone to the development of tension pneumocephalus in the immediate postoperative period. Tension pneumocephalus is an underappreciated and under-recognized cause of postoperative delayed awakening, delirium and non-awakening. When it is suspected, the diagnosis can be made by a cross table lateral X-ray or, more commonly, in these days of readily available CT scans, by computed tomography. The treatment entails a twist drill hole and dural perforation, ideally performed by the surgeon.

THE BRAIN PARENCHYMA IS INSENSATE BUT THE CRANIAL NERVES ARE NOT

When Wilder Penfield performed the brain surface stimulation surveys that lead to the development of the now familiar homunculus diagrams, the craniotomies were performed under local anesthesia. While the meninges have some innervation and required gentle handling and some local anesthesia at the skull base, brain stimulation and/or resection of brain parenchyma required no anesthesia whatsoever. The brain parenchyma is insensate. Accordingly, when a general anesthetic is used for intracranial neurosurgery, the intracranial portion requires only “light” anesthesia. An error occasionally made by clinicians is the failure to anticipate stimulation of the extra-axial but intracranial portion of cranial nerves. The issue arises most often in the context of procedures formed in the vicinity of the fifth cranial nerve. The fifth cranial nerve subserves the sensation from the entire face and mouth. Stimulation of the extra axial portion of the fifth cranial nerve can result in very sudden arousal. In circumstances in which this has occurred in non-paralyzed patients, the arousal has resulted in sudden straining against the endotracheal tube with herniation of brain around retractor and around the edges of the bony craniotomy. Substantial injury to brain parenchyma and adverse neurologic events have occurred. Where feasible, patients should be maintained paralyzed during surgery in this vicinity of CN V. When patients are not paralyzed, clinicians should be very attentive to the possibility of arousal and should be ready to deepen anesthesia at a second’s notice, e.g., a syringe of induction agent should be maintained in line at all times.

STRIDOR/NARROW AIRWAY

Swelling and expanding hematomas occurring after carotid endarterectomy or anterior cerebral dissection/fusion procedures have the potential to encroach upon the extra-thoracic airway. The clinician should keep several principles in mind. 1) The airway will always look much worse on the inside than it does on the outside. Swelling of peri-glottic structures is a larger component of airway compromise than is mechanical encroachment. I suspect that the enlarging mass impairs lymphatic and venous drainage. When one visualizes in the airway, there is often remarkable swelling of peri-glottic structures. 2) Stridor is a late (and ominous sign). Delaying in the face of progressive enlargement of the neck until stridor occurs raises the likelihood of extreme difficulty in securing the airway. 3) Racemic epinephrine (or Heliox) may “buy you time” in the event of respiratory compromise, but they should not be viewed as cures. When an airway has become sufficiently narrow to produce stridor and labored respiration (and concomitant turbulent flow), very small increases in airway diameter will reduce airway resistance enough to mitigate symptoms. But the clinician should assume that progressive swelling will occur if the mass lesion is not relieved and distress will recur.

REFERENCES

6. Astrup J, Symon L, Branston NM, et al.: Cortical evoked potential and extracellular K\textsuperscript{+} and H\textsuperscript{+} at critical levels of brain ischemia. Stroke; 8: 52-57, 1977
INTRODUCTION

Physicians, scientists, journalists, and the lay public prefer a plausible explanation (particularly if accompanied by a molecular mechanism) to an admission of ignorance. As a result, unproven hypotheses, opinions and plausible guesses are repeated in lectures and textbooks and become embedded in the canon of our specialty.

We will consider a representative subset of unproven (and, in some cases, disproven) hypotheses and assertions during the course of this brief presentation. The reader should judge whether these old chestnuts arise from the scheming of “liars, damned liars, or scientific experts,” (using a description of unreliable witnesses attributed to Robert Giffen), and should decide whether they now deserve to be called out as anesthesia myths.

RESUSCITATION TOPICS

Is Normal Saline “Normal” or Beneficial?

Intravenous fluid therapy arose in the 1800s as a means of combating dehydration from cholera, then became part of routine care for surgical patients in the 1900s. At present, the IV fluids of choice for adults in most surgical suites are either 0.9% (normal) saline or a “balanced” salt solution (Normosol, Plasma-lyte, or lactated Ringer’s (Hartmann’s) solution). The sad truth is that multiple lines of evidence demonstrate that use of 0.9% saline leads predictably to an increased incidence of hyperchloremia, a condition associated with worse outcomes (including longer lengths of stay and a greater likelihood of death). In the absence of hypochloremic metabolic alkalosis there are sparse indications for large volumes of 0.9% saline, and no good reasons to use 0.9% saline as a routine maintenance solution.

Cricoid pressure improves patient safety during emergency intubations

Cricoid pressure was introduced to medicine by Brian Sellick in 1961. In 26 patients considered at risk for aspiration, no regurgitation occurred during or after application of cricoid pressure in 23. In 3 patients, regurgitation occurred only after cricoid pressure was relieved following tracheal intubation. Sellick surmised that cricoid pressure had prevented regurgitation from occurring before and during intubation in these 3 patients. Nevertheless, Sellick provided no details regarding induction drugs, ventilation, patient body habitus, or other relevant factors that might also explain his findings.

Sellick made several key assumptions.

1. That the cricoid cartilage, esophagus, and anterior surface of the vertebral body would be in constant alignment;
2. That his maneuver would fully occlude the esophagus and prevent gastric contents from refluxing past the cricoid;
3. That his maneuver would reduce the incidence of pulmonary aspiration associated with “full stomach” conditions;
4. That cricoid pressure had no adverse consequences.

Current data using computed tomography and magnetic resonance imaging techniques show that assumptions 1 and 2 are false. There are no outcome studies supporting assumption 3, but such studies likely would not be feasible given rates of medically consequential aspiration during emergency surgery of ≤1 per 1000. As for assumption 4, multiple studies have shown that cricoid pressure can worsen the clinician’s view of the airway during direct laryngoscopy. If one were to grade the quality of the evidence supporting the use of cricoid pressure using standards of the Oxford Centre for Evidence Based Medicine, a grade no better than D could be assigned! In a recent survey, only 30% of Swiss and 52% of Austrian anesthesiologists use cricoid pressure as part of rapid sequence induction. Nevertheless, some regard cricoid pressure both standard care and standard of care.

GENERAL ANESTHETIC TOPICS

Invasive monitoring increases hemodynamic stability during induction

Many books and oral examination candidates emphasize the value of invasive hemodynamic monitoring during induction of general anesthesia for “sick” patients. But is there any evidence that having information from a central line or a pulmonary artery catheter increases hemodynamic stability during induction? In a randomized comparison, inductions conducted without benefit of pulmonary artery catheter data required no more interventions to maintain stable hemodynamics than inductions “guided” by data from the pulmonary artery catheter. Moreover, placement of the pulmonary artery catheter after induction of general anesthesia took less time than when performed before induction. Finally, there are no convincing data showing that pulmonary artery catheterization reduces the likelihood of mortality in this or any other circumstance.

A slow induction increases hemodynamic stability

Many clinicians recommend a “slow, careful induction” in cardiac and other sick patients. But, is there evidence that a slow induction results in fewer hemodynamic perturbations than a well-conducted rapid sequence induction? In patients scheduled for coronary artery surgery, rapid sequence induction with sufentanil and succinylcholine produced similar hemodynamics and necessitated no more interventions with vasoactive drugs or IV fluid boluses than a slower (2 min) opioid-relaxant induction or a very slow, careful (5-10 min) opioid-relaxant induction.
REGIONAL ANESTHETIC TOPICS

pKa predicts speed of onset of regional anesthesia

All local anesthetic compounds (save for benzocaine) in widespread clinical use have a tertiary amine nitrogen, the protonation of which is influenced by the pH of its environment. The charged (protonated) form of the local anesthetic is less membrane permeable than the uncharged (neutral base) form of the compound.15 It has long been assumed that when two local anesthetic compounds are compared for speed of onset, the compound with the reduced pKa will have the faster onset of action, because after injection, a larger fraction of this compound will be in the neutral form as compared to the compound with the larger pKa. The only problem with this “truisim” is that it is incorrect. It is true that lidocaine has a smaller pKa and a faster onset than bupivacaine. But, chloroprocaine has the largest pKa of all and it has the fastest onset of all local anesthetics, even faster than lidocaine, disproving the “rule.”16 Moreover, the pKa rule fails even when used to compare structurally similar compounds given that tetracaine has a smaller pKa than procaine or chloroprocaine, but has by far the slowest onset of these three drugs.

Methemoglobinemia and prilocaine

Methemoglobinemia has long been associated with prilocaine, the only local anesthetic that is metabolized to o-toluidine. According to many textbooks, prilocaine will reliably produce medically important degrees of methemoglobinemia when doses >600 mg are administered. Vasters et al. found that serious degrees of methemoglobinemia can arise after prilocaine doses as small as 400 mg in fit adult patients.17 Interestingly, in a North American study, the local anesthetic most commonly associated with dangerous methemoglobinemia was benzocaine.18

Interscalene blocks and general anesthesia

In 2000 a report appeared in Anesthesiology describing 4 patients who experienced disastrous neurological complications after undergoing interscalene blocks while anesthetized.19 The author suggested (and the suggestion was repeated in an American Society of Regional Anesthesia guideline) that “Interscalene blocks should not be performed in anesthetized or heavily sedated adult or pediatric patients.”20,21 But, does the evidence show that anesthetized or heavily sedated patients are more likely to have neurologic damage?

There are case reports of nerve damage after interscalene blocks performed in awake patients. Children routinely undergo nerve blocks (including interscalene blocks) while anesthetized and infrequently experience nerve damage.22 Moreover, large series of interscalene blocks performed in patients receiving general anesthesia report an incidence of adverse neurologic events no more frequent than that reported after interscalene blocks performed without general anesthesia.23,24 Is it reasonable to issue a practice guideline based only case reports and opinions that, in effect, labels the use of deep sedation or general anesthesia before interscalene block as malpractice when there are large published series that provide contradictory evidence?

Intraneural injections and nerve damage

William S. Halsted, the first physician to perform brachial plexus blocks in North America, injected cocaine into nerves under direct vision. Yet most modern textbooks indicate that intraneural injections must be avoided because they will consistently result in persisting deficits. Recent articles tend to emphasize the differences between intraneural injections that disrupt nerve structure and those that do not.25 They also emphasize the fact that unintended intraneural injections commonly take place despite use of either ultrasound guidance, motor nerve stimulation, or both, and that awake patients most often will not report symptoms during these injections.26

CONCLUSIONS

There are many long-accepted practices and published guidelines in anesthesia that either are not supported or are contradicted by the available data. Myths and unproven hypotheses continue to masquerade as received knowledge in our specialty.

REFERENCES


ABSTRACT

Non-physiological ventilation in healthy lungs induces acute lung injury (ALI). Protective lung ventilation in patients with ALI improves outcomes. Protective lung ventilation in non-injured lungs and in the absence of a primary pulmonary insult may initiate ventilator-induced lung injury (VILI), as evidenced by inflammatory markers. VILI has important implications remote to the lungs and may be associated with significant morbidity and mortality. Volatile anesthetics may have a lung-protective effect. Excess fluids may contribute to perioperative lung injury.

Anesthesiologists manage a heterogeneous group of patients in the peri-operative period; from patients with healthy lungs, and patients with “at risk” lungs, through to patients with severe chronic obstructive pulmonary disease (COPD). More patients are at risk for ALI during surgery than previously thought. Appropriate peri-operative management may prevent or ameliorate this lung injury.

INTRODUCTION

Patients are at risk for several types of lung injury in the peri-operative period. These injuries include atelectasis, pneumonia, pneumothorax, broncho-pleural fistula, acute lung injury and acute respiratory distress syndrome (ALI/ARDS). Anesthetic management can cause, exacerbate or ameliorate most of these injuries. Lung-protective ventilation strategies using more physiologic tidal volumes and appropriate levels of PEEP can decrease the extent of this injury. This review will look at the effects of mechanical ventilation and its role in VILI with specific reference to patients with severe COPD requiring general anesthesia and surgery.

Chronic Obstructive Pulmonary Disease

The most common chronic respiratory illness in the surgical population is chronic obstructive pulmonary disease (COPD) which incorporates three disorders: emphysema, peripheral airways disease and chronic bronchitis. Any individual patient may have one or all of these conditions, but the dominant clinical feature is impairment of expiratory airflow. Assessment of the severity of COPD is on the basis of the FEV1% of predicted values. The American Thoracic Society categorizes Stage I >50% predicted Stage II: 35-50%, and Stage III <35 Stage I patients should not have significant dyspnea, hypoxemia or hypercarbia and other causes should be considered if these are present.

Respiratory Drive:

Many stage II or III COPD patients have an elevated PaCO2 at rest. It is not possible to differentiate these “CO2-retainers” from non-retainers on the basis of history, physical examination or spirometric pulmonary function testing. This CO2-retention seems to be more related to an inability to maintain the increased work of respiration (Wresp) required to keep the PaCO2 normal in patients with mechanically inefficient pulmonary function and not primarily due to an alteration of respiratory control mechanisms. It was previously thought that chronically hypoxemic/hypercapnic patients relied on a hypoxic stimulus for ventilatory drive and became insensitive to PaCO2. This explained the clinical observation that COPD patients in incipient respiratory failure could be put into a hypercapnic coma by the administration of a high concentration of oxygen (FiO2). Actually, only a minor fraction of the increase in PaCO2 in such patients is due to a diminished respiratory drive, as minute ventilation is basically unchanged. The PaCO2 rises because a high FiO2 causes a relative decrease in alveolar ventilation and an increase in alveolar dead space and shunt by the redistribution of perfusion away from lung areas of relatively normal V/Q matching to areas of very low V/Q ratio because regional hypoxic pulmonary vasoconstriction (HPV) is decreased and also due to the Haldane effect. However, supplemental oxygen must be administered to these patients postoperatively to prevent the hypoxemia associated with the unavoidable fall in functional residual capacity (FRC). The attendant rise in PaCO2 should be anticipated and monitored. To identify these patients preoperatively, all stage II or III COPD patients need an arterial blood gas.

Nocturnal Hypoxemia

COPD patients desaturate more frequently and severely than normal patients during sleep. This is due to the rapid/shallow breathing pattern that occurs in all patients during REM sleep. In COPD patients breathing air, this causes a significant increase in the respiratory dead space/tidal volume (VD/VT) ratio and a fall in alveolar oxygen tension (PAO2) and PaO2. This is not the sleep-apnea-hypoventilation syndrome (SAHS). There is no increased incidence of SAHS in COPD.

Right Ventricular (RV) Dysfunction

Right ventricular dysfunction occurs in up to 50% of COPD patients. The dysfunctional RV is poorly tolerant of sudden increases in afterload such as the change from spontaneous to controlled ventilation. Right ventricular function becomes critical in maintaining cardiac output as the pulmonary artery pressure rises. The RV ejection fraction does not increase with exercise in COPD patients as it does in normal patients. Chronic recurrent hypoxemia is the cause of the RV dysfunction and the subsequent progression to cor pulmonale. Patients who have episodic hypoxemia in spite of normal lungs (e.g., Central Alveolar Hypoventilation, SAHS, etc.) develop the same secondary cardiac problems as COPD patients. The only therapy, which has been shown to improve long-term survival and decrease right heart strain in COPD is oxygen. COPD patients who have resting PaO2 <55 mmHg...
should receive supplemental home oxygen and also those who desaturate to <44 mmHg with exercise. The goal of supplemental oxygen and is to maintain a PaO₂ of 60-65 mmHg. Compared to patients with chronic bronchitis, emphysematous COPD patients tend to have a decreased cardiac output and mixed venous oxygen tension while maintaining lower pulmonary artery pressures.

**Bullae**

Many patients with moderate or severe COPD with develop cystic air spaces in the lung parenchyma known as bullae. These bullae will often be asymptomatic unless they occupy more than 50% of the hemithorax, in which case the patient will present with findings of restrictive respiratory disease in addition to their obstructive disease. A bulla is a localized area of loss of structural support tissue in the lung with elastic recoil of surrounding parenchyma. The pressure in a bulla is actually the mean pressure in the surrounding alveoli averaged over the respiratory cycle. This means that during normal spontaneous ventilation the intra-bulla pressure is actually slightly negative in comparison to the surrounding parenchyma. However, whenever positive-pressure ventilation is used the pressure in a bulla will become positive in relation to the adjacent lung tissue and the bulla will expand with the attendant risk of rupture, tension pneumothorax and bronchopleural fistula. Positive-pressure ventilation can be used safely in patients with bullae provided the airway pressures are kept low and there is adequate expertise and equipment immediately available to insert a chest drain and obtain lung isolation if necessary.

**Flow Limitation**

Severe COPD patients are often "flow-limited" even during tidal volume expiration at rest. Flow-limitation is present in normal patients only during a forced expiratory maneuver. Flow-limitation occurs when an equal pressure point (EPP) develops in the intra-thoracic airways during expiration. During quiet expiration in the normal patient the pressure in the lumen of the airways always exceeds the intra-pleural pressure because of the upstream elastic recoil pressure which is transmitted from the alveoli. The effect of this elastic recoil pressure diminishes as air flows downstream in the airway. With a forced expiration the intra-pleural pressure may equal the intra-luminal pressure at a certain point, the EPP, which then limits the expiratory flow. Then, any increase in expiratory effort will not produce an increase in flow at that given lung volume.

Flow-limitation occurs particularly in emphysematous patients, who primarily have a problem with loss of lung elastic recoil and have marked dyspnea on exertion. Flow-limitation causes dyspnea because of stimulation of mechanoreceptors in the muscles of respiration, thoracic cage and in the airway distal to the EPP. Any increase in the work of respiration will lead to increased dyspnea. This variable mechanical compression of airways by over-inflated alveoli is the primary cause of the airflow obstruction in emphysema.

Severely flow-limited patients are at risk for hemodynamic collapse with the application of positive pressure ventilation due to dynamic hyperinflation of the lungs. Even the modest positive airway pressures associated with manual ventilation with a bag/mask at induction can lead to hypotension since these patients have no increased resistance to inspiration but a marked obstruction of expiration. In some of these patients this has contributed to the “Lazarus” syndrome in which patients have recovered from a cardiac arrest only after resuscitation and positive-pressure ventilation was discontinued.

**Auto-PEEP**

Patients with severe COPD often breathe in a pattern that interrupts expiration before the alveolar pressure has fallen to atmospheric pressure. This incomplete expiration is due to a combination of factors which include flow-limitation, increased work of respiration and increased airway resistance. This interruption leads to an elevation of the end-expiratory lung volume above the FRC. This positive end-expiratory pressure in the alveoli at rest has been termed auto-PEEP or intrinsic-PEEP. During spontaneous respiration the intra-pleural pressure will have to be decreased to a level which counteracts auto-PEEP before inspiratory flow can begin. Thus, COPD patients can have an increased inspiratory load added to their already increased expiratory load.

Auto-PEEP becomes even more important during mechanical ventilation. It is directly proportional to tidal volume and inversely proportional to expiratory time. The presence of auto-PEEP is not detected by the manometer of standard anesthesia ventilators. It can be measured by end-expiratory flow interruption, a feature available on the newer generation of intensive care ventilators. Auto-PEEP has been found to develop in most COPD patients during one-lung anesthesia. Paradoxically it has been found that a small amount of added PEEP (e.g. 5cmH2O) can decrease Auto-PEEP and hyperinflation in many ventilated COPD patients.

**Preoperative therapy of COPD**

There are four treatable complications of COPD that must be actively sought and therapy begun at the time of the preanesthetic assessment. These are: atelectasis, bronchospasm, respiratory tract infections and pulmonary edema. Atelectasis impairs local lung lymphocyte and macrophage function predisposing to infection. Pulmonary edema can be very difficult to diagnose by auscultation in the presence of COPD and may present very abnormal radiological distributions (unilateral, upper lobes, etc.). Bronchial hyper-reactivity may be a symptom of congestive failure or may represent an exacerbation of reversible airways obstruction. All COPD patients should receive maximal bronchodilator therapy as guided by their symptoms. Only 20-25% of COPD patients will respond to corticosteroids. In a patient who is poorly controlled on therapy, or who has marked obstruction of expiration, a trial of corticosteroids may be beneficial.

**Physiotherapy:** Patients with COPD have fewer postoperative pulmonary complications when a perioperative program of intensive chest physiotherapy is initiated preoperatively. Among the different modalities available (cough and deep breathing, incentive spirometry, PEEP, CPAP, etc.) there is no clearly proven superior method. Family members or non-physiotherapy hospital staff can easily be trained to perform effective preoperative chest physiotherapy and this should be arranged at the time of the initial preoperative assessment. Even in the most severe COPD patient, it is possible to improve exercise tolerance with a physiotherapy program. Little improvement is seen before one month. Among COPD...
patients, those with excessive sputum benefit the most from chest physiotherapy.

A comprehensive program of pulmonary rehabilitation involving physiotherapy, exercise, nutrition and education can improve functional capacity for patients with severe COPD. These programs are usually of several months duration and are generally not an option in resections for malignancy although for non-malignant resections in severe COPD patients, rehabilitation should be considered. The benefits of short duration rehabilitation programs prior to malignancy resection have not been fully assessed.

Smoking: Pulmonary complications are decreased in thoracic surgical patients who cease smoking for > 4 weeks before surgery. Carboxyhemoglobin concentrations decrease if smoking is stopped >12 hr. It is extremely important for patients to avoid smoking postoperatively. Smoking leads to a prolonged period of tissue hypoxemia. Wound tissue oxygen tension correlates with wound healing and resistance to infection. There is no rebound increase in pulmonary complications if patients stop for shorter (< 8 week) periods before surgery.

Post-operative Analgesia: It was initially theorized that thoracic epidural analgesia (TEA) could diminish the diaphragmatic inhibition, which is known to occur after thoracotomy. Such dis-inhibition was shown for TEA after upper abdominal surgery. Indeed a post-thoracotomy animal model demonstrated similar dis-inhibition. However, a post-thoracotomy human study of patients with moderate COPD failed to show any improvement of diaphragmatic contractility by TEA even though respiratory function (tidal volume) was improved. This is not easy to explain but it may be similar to the concept of increasing cardiac output without increasing myocardial contractility by changing loading conditions for the ventricle. The diaphragm inserts on the chest wall, and by decreasing chest splitting the diaphragm may be returned to a mechanically more efficient position on its force-length (Starling) contraction curve without affecting its actual contractility.

In patients with severe emphysema it has been shown that analgesic doses of TEA Bupivacaine do not cause any significant reduction in lung mechanics or increase in airway resistance. In volunteers a thoracic level of epidural blockade increases FRC. This increase is largely due to an increase in thoracic gas volume caused by a fall in the resting level of the diaphragm without a fall in tidal volume. This contradicts earlier studies, which found no change in FRC with TEA. The different results are probably related to the more advanced methodology of the more recent work. FRC is considered the most important determinant of oxygenation in the postoperative period. Although it is possible to deliver an opioid to the spinal cord receptors via a lumbar catheter in adequate amounts for analgesia, the beneficial effects of local anesthetics on respiratory mechanics require a thoracic catheter.

The only large randomized prospective study of epidural vs. systemic analgesia was the MASTER trial performed in Australia, mainly for upper abdominal surgery. Postoperative respiratory failure was significantly reduced in the epidural group (23% vs. 30%) with no differences in other types of complications or mortality. This beneficial effect of thoracic epidural analgesia seems to be most pronounced in patient with underlying lung disease such as COPD. In a retrospective propensity-based analysis of patients with COPD who had major abdominal surgery, the use of TEA was associated with a lower incidence of post-operative pneumonia (11% vs. 16%) and a lower 30-day mortality (5% vs. 9%). This trend also seems to apply to thoracic surgery where a retrospective analysis found TEA was associated with a three-fold decrease in respiratory complications in COPD patients after lung resection. A large retrospective review of over 80,000 surgical patients in the Ontario Health Insurance database found a small significant reduction in overall mortality related to the use of epidural anesthesia and analgesia (1.7% vs. 2%) and this difference was most notable in thoracic and orthopedic surgery.

MECHANICAL VENTILATION

Historically, Anesthesiologists have been taught to ventilate patients in the peri-operative period with relatively large tidal volumes. Volumes as high as 15ml.kg⁻¹ ideal body weight have been suggested to avoid intra-operative atelectasis. This far exceeds the normal spontaneous tidal volumes (6ml.kg⁻¹) common to most mammals. Recent studies have identified the use of large tidal volumes as a major risk factor for development of lung injury in mechanically ventilated patients without acute lung injury (ALI). Gajic reported that 25% of patients with normal lungs ventilated in an ICU setting for 2 days or longer developed ALI or ARDS. The main risk factors for ALI were use of large tidal volumes, restrictive lung disease and blood product transfusion. A prospective study from the same group have found that tidal volumes > 700mls and peak airway pressures > 30cm H2O were independently associated with the development of ARDS. An intra-operative study of patients having oesophageal surgery compared the use of tidal volumes of 9 ml.kg⁻¹ without positive end-expiratory pressure (PEEP) during two- and one-lung ventilation vs. 9 ml.kg⁻¹ during two-lung ventilation and 5 ml.kg⁻¹ during one-lung ventilation with PEEP 5 cmH₂O throughout. They found significantly lower serum makers of inflammation (cytokines IL-1β, IL-6 and IL-8) in the lower tidal volume plus PEEP group. The study did not find any major difference in post-operative outcome between the two groups; however it was not powered to do this. The study did demonstrate better oxygenation in the lower tidal volume group during and immediately after one-lung ventilation, but not after 18h. In a study looking at conventional vs. protective ventilation in critically ill patients without lung injury, de Oliveira and colleagues randomized patients to ventilation with either 10-12ml.kg⁻¹ or 6-8ml.kg⁻¹ predicted body weight. In both groups a PEEP of 5 was applied and the FiO₂ titrated to keep SpO₂ > 90%. At 12hours post-ventilation, inflammatory markers in broncho-alveolar lavage fluid (TNFα and IL-8) were significantly higher in the larger tidal volume group. Choi and colleagues compared 12ml.kg⁻¹ without PEEP vs. 6ml.kg⁻¹ with 10cm PEEP and showed pro-coagulant changes in lavage fluid of the larger tidal volume group after 5 hours of mechanical ventilation. A recent randomised-control trial in 150 critically ill patients without ALI compared tidal volumes of 10ml.kg⁻¹ vs. 6ml.kg⁻¹ predicted body weight. The conventional tidal volumes were associated with a sustained plasma increase in inflammatory cytokines.

Of importance is recent work suggesting that non-injurious or so-called protective ventilatory settings can induce lung
IN LUNG PROTECTION

VENTILATOR INDUCED LUNG INJURY (VILI)

The phenomenon of VILI is well recognized, and can be particularly significant in surgical specialties that require large transfusions, cardiopulmonary bypass and associated lung ischemia-reperfusion injury. The deleterious effects of mechanical ventilation may be mediated by localized inflammation and the systemic release of inflammatory cytokines (bio-trauma). Mechanical stretch from cyclical alveolar opening and closing sets up an inflammatory response in the alveolar epithelial cells and the vascular endothelial cells. Hyperinflation causes nuclear translocation of NF-kB (a key regulator of the expression of multiple genes involved in inflammatory response) and up-regulation of other pro-inflammatory cytokines. Polymorphonuclear leukocyte recruitment and activation appear to be key component of the mechanical stretch induced inflammatory response. The balance between apoptosis and necrosis is unfavourably altered by both ischemia-reperfusion and mechanical stretch.

Bio-trauma not only aggravates ongoing lung injury but also has important systemic consequences due to the spill over of these inflammatory mediators into the systemic circulation, inducing remote organ dysfunction. A study looking at novel mechanisms of remote organ injury resulting from VILI showed that mechanical ventilation can lead to epithelial cell apoptosis in the kidney and the small intestine with accompanying biochemical evidence of organ dysfunction. In mice undergoing injurious mechanical ventilation, alveolar stretch induced adhesion molecules not only in the lung but also in the liver and kidney. In addition, cytokine and chemokine expression in pulmonary, hepatic and renal tissue after mechanical ventilation was accompanied by enhanced recruitment of granulocytes to these organs. These studies go some way as to explain the remote organ dysfunction seen with ALI/ARDS, and the role optimising ventilatory strategies play in ameliorating this.

This leads to the question; are the lung protective strategies in ARDS applicable to the peri-operative environment, specifically in patients with healthy lungs? A paper looking at this question highlights the lack of randomised-controlled trials looking at best intra-operative tidal volume, PEEP, and use of intra-operative lung recruitment. While outcome studies are lacking, based on what we know about the effects of mechanical ventilation, it seems not unreasonable to aim towards protective ventilatory strategies in peri-operative practice.

PERI-OPERATIVE SURGICAL ENVIRONMENT FACTORS

There are multiple factors in the surgical environment that can contribute to lung injury. The most obvious being the surgical approach. Site of operation is an important predictor of pulmonary complications, with upper abdominal and thoracic incisions being the most important (any surgery approaching the diaphragm). A decrease in respiratory complications has been documented if major cavitary procedures can be done with minimally invasive vs. open techniques. Atelectasis occurs frequently following open surgical procedures and in up to 90% of patients undergoing general anaesthesia. It is a pathological state that can contribute to or attenuate lung injury. Thus anaesthesiologists must be aware of techniques to avoid or treat it. While open to debate, retrospective and prospective studies have shown that appropriate thoracic epidural analgesia reduces the incidence of respiratory complications (atelectasis, pneumonia and respiratory failure) after major abdominal and thoracic surgery. The benefits of epidural analgesia seem to be in direct proportion to the severity of the patients underlying lung disease. Patients with COPD seem to derive the most benefit from epidural analgesia. Reviews comparing Para-vertebral block (PVB) vs. epidural analgesia in patients undergoing thoracic surgery showed equivalent analgesia efficacy but a better side effect profile and lower complication rate with PVB. Aggressive physiotherapy with CPAP in the post-operative period in patients after major abdominal surgery who develop early desaturation leads to lower rates of major respiratory complications.

ROLE OF VOLATILE ANESTHETIC AGENTS IN LUNG PROTECTION

Volatile agents have immune-modulatory effects. Much work has been done, especially in the cardiac setting, on the role of volatiles in Ischemia-Reperfusion Injury (IRI) and in pre- and post-conditioning. Recent studies in models of ALI, during OLV and in cases of lung ischemia-reperfusion suggest that volatiles may act as pre- and post-conditioning agents inducing lung protection by inhibition of the expression of pro-inflammatory mediators. Isoflurane pre-treatment in an endotoxin mediated animal model of lung injury exerted protective effects, as evidenced by reduction of polymorphonuclear recruitment and microvascular protein leakage. Post-conditioning with sevoflurane attenuated lung damage and preserved lung function in an in vivo rat ALI model. In a prospective study, patients undergoing thoracic surgery with OLV were randomised to either...
Looking at inflammatory markers in the non-ventilated lung, they showed an attenuated inflammatory reaction. Significantly, the sevoflurane group had an improved outcome and significantly lower overall number of adverse events. A study comparing OLV (Vt 10ml.kg⁻¹) with desflurane vs. propofol anaesthesia looked at the inflammatory response in the ventilated lung. The inflammatory markers IL-8, IL-10, PMN elastase and TNFα were significantly lower in the desflurane group.

While much work remains to be done, this exciting work does point towards a role for volatiles in attenuating the pro-inflammatory response in the lungs to a host of insults, whether this is pre, during or post insult.

ULTRA-PROTECTIVE LUNG VENTILATION

Following along the continuum of lung protective ventilation in ALI/ARDS is the concept of ultra-protective ventilation. This concept utilizes pumpless extracorporeal lung assist, specifically the Novalung® ILA membrane ventilator, and near static ventilation. A brief description of the Novalung® is appropriate; it is a membrane ventilator that allows O₂ and CO₂ gas exchange via simple diffusion.⁶⁷ The membranes are biocompatible and provide a non-thrombogenic surface. It is designed to work without a mechanical pump in an Arterio-Venous configuration, thus requiring an adequate mean arterial pressure to drive flow. Flow rates are typically 1-2L.min⁻¹, or approximately 15% of cardiac output. CO₂ clearance is controlled by varying the oxygen flow rate. It must be noted that oxygenation may be variable and may not be sufficient in severe hypoxic disorders. As compared with conventional ECMO, the Novalung® is a simple, pumpless portable device. Anti-coagulation requirements are much reduced with an aPPT target of 55s. Bleeding complications and blood product requirements are significantly less.

ARDSnet and animal data demonstrates that lower tidal volumes (3ml.kg⁻¹) compared with 6-12ml.kg⁻¹ significantly reduces endothelial and epithelial injury.⁶⁶,⁶⁷ In other words “protective” tidal volumes can still induce VILI. However clearance of CO₂ and oxygenation become an issue at these lower minute volumes. The Novalung® allows for this marked reduction in MV and the simultaneous correction of PaCO₂ and pH. An animal model of post-pneumonecetomy ARDS using the Novalung® and tidal volumes of 2.2mls.kg⁻¹ and respiratory rate of 6 showed significantly better outcomes compared with conventional lung protective strategies.⁶⁸ Case reports in humans in a variety of clinical scenarios have been encouraging.⁷¹ Tidal volumes £ 3ml.kg⁻¹, low inspiratory plateau pressure, high PEEP and low respiratory rates are all possible with the Novalung® in situ, causing less VILI and subsequent remote secondary organ failure. The use of extracorporeal membrane oxygenation (ECMO) in combination with protective ventilation has been shown in a randomized trial to significantly increase the survival rate to 63% vs. 47% with conventional ventilation strategies, in patients with severe ARDS.⁷²

FLUIDS, INFLAMMATION AND THE GLYCOCALYX

A retrospective cohort study looking specifically at intra-operative risk factors for ARDS in critically ill patients found that for patients receiving fluid resuscitation > 20ml.kg⁻¹.hr⁻¹ the odds of developing ARDS were 3 times greater than if < 10ml.kg⁻¹.hr⁻¹ was given (odds ratio 3.1, 95% CI = 1.0-9.9 p = 0.05)⁷³. Vt:IBW⁻¹ (ml.kg⁻¹) and number of blood products were not associated with ARDS in this study. Of interest the majority of patients were ventilated with a Vt:IBW⁻¹ of 8-10ml.kg⁻¹ and an intra-operative PEEP of 0. It has long been a concern that excess amounts of intravenous fluids predispose patients to develop ALI.

However, it has been a conflicting concern for Anesthesiologists that fluid restriction in thoracic surgery may contribute to postoperative renal dysfunction which previously was reported to be associated with a very high (19%) mortality.⁷⁴ In a recent review of >100 pneumonecetomies at our institution, acute kidney injury (AKI) as defined by the RIFLE classification⁷⁵ occurred in 22% of patients.⁷⁶ However, there was no association of AKI with fluid balance and there was no increased 30-day mortality in the AKI patients. AKI was associated with preoperative hypertension and complex surgical procedures such as extra-pleural pneumonecetomy. A similar retrospective study looking at all pulmonary resection patients found that acute kidney injury (AKI), as defined by the Acute Kidney Injury Network criteria which occurred in 67/1129 (6%) patients was not associated with a statistically significant increase in mortality vs. non-AKI patients (3% vs. 1%).⁷⁷

Fluid requirements vary widely between patients and procedures and ultimately represent the sum of preoperative deficits, maintenance requirements, and ongoing losses. Fluid management for major esophageal surgery is particularly challenging. Preoperative fluid deficits in patients with severe esophageal disease may be substantial, though they have not been well defined.⁷⁸ Fluid requirements in patients undergoing esophageal procedures may be complicated by the fact that patients may be relatively hypovolemic after long preoperative fasts, particularly if esophageal obstruction or dysphagia limit fluid intake. Perioperative losses occur via a number of mechanisms including urinary, gastrointestinal, and evaporative losses, bleeding, and interstitial fluid shifting. This shift of fluid from the vascular compartment into the interstitial space accompanies surgical trauma and is likely to reflect vascular injury and loss of endothelial integrity. So called “third space” losses describe fluid loss into non-interstitial extra-cellular spaces which are not in equilibrium with the vascular compartment and thus considered to be a “non-functional” extra-cellular fluid compartment. However, it is very possible that the “third space” does not exist and was described as a result of measurement errors in early studies of the fluid compartments in the body.⁷⁹

One of the factors complicating fluid management for esophageal resection is that thoracic epidural analgesia has been shown to improve outcome for these patients⁸⁰ but it use tends to contribute to hypotension. Hypotension is well known to contribute to ischemia of the gut anastomosis⁸¹ and treatment with excessive fluids is likely to exacerbate the problem.⁸² Many surgeons are concerned about the effects of vaspressors on the anastomotic gut blood flow.⁸³ However, several animal studies suggest that treatment of intraoperative hypotension with nor-epinephrine does not cause any reduction of gut blood flow in the presence of normovolemia.⁸⁴,⁸⁵

An ideal fluid regimen for major surgeries, including esophageal surgery, is individualized and optimizes cardiac output and oxygen delivery while avoiding excessive fluid...
administration. There is some evidence that fluid therapies which are designed to achieve individualized and specific flow-related hemodynamic endpoints such as stroke volume, cardiac output, or measures of fluid responsiveness such as stroke volume variation (collectively referred to as goal directed fluid therapy) may provide a superior alternative to fixed regimens or those based on static measures of cardiac filling, such as central venous pressure which does not predict fluid responsiveness or correlate with circulating blood volume after transthoracic esophagectomy.86,87

In addition to the potential importance of the amount and timing of fluid administration, there is some clinical evidence that the choice of fluid type may be important in affecting clinical outcomes.88 Intravascular colloid retention during treatment of hypovolemia may approach 90% vs. 40% when administered during normovolemia.89

The relationship of hydrostatic and oncotic pressure to determine fluid flux across a semi-permeable membrane was described in a classic equation developed in 1896 by Starling.89 Several clinical observations such as the relative resistance of the intact organism to develop edema and the inability of therapy with hyperoncotic agents to draw fluid from the pulmonary interstitium into the vascular compartment are not explained by the Starling formula.90 This discrepancy is now attributed to the glycocalyx, a micro-cilial layer that lines the endothelium and acts as a molecular sieve. This layer tends to increase the oncotic pressure on the inner surface of the endothelium and decrease leukocyte and platelet adhesion to the endothelium. The glycocalyx deteriorates during ischemia-reperfusion injury and in the presence of a wide variety of inflammatory mediators such as cytokines and probably contributes to the increased vascular permeability seen in these situations. Also, the glycocalyx deteriorates in the presence of atrial natriuretic peptide and may explain the increase in plasma protein filtration that has been seen with colloid boluses. Protecting the glycocalyx may be among the Anesthesiologist’s most important duties perioperatively. Volatile anesthetics may have a protective effect on the glycocalyx.91

OTHER THERAPIES FOR LUNG PROTECTION

Beyond those already discussed, there are several therapies that may play a future role in lung protection. Permissive hypercapnia’s place in protective ventilation has been alluded to earlier, but as found in the original ARDSnet data, may be protective in the presence of higher tidal volumes.92 Hypercapnic Acidosis (HCA) is protective in a variety of models of ALI. Beneficial effects include attenuation of lung neutrophil recruitment, pulmonary and systemic cytokine concentrations, cell apoptosis and free radical injury.93 Inhaled Hydrogen sulfide shows beneficial effects in a model of VILI via the inhibition of inflammatory and apoptotic responses, independent of its effects on body temperature.94 Inhaled aerosolized activated protein C in a sheep model of ALI demonstrated improved oxygenation as well as lung aeration (as assessed by CT scan)95 β-adrenergic agonists have potential benefits by increasing the rate of alveolar fluid clearance by increasing cellular cAMP and have anti-inflammatory properties.96 A randomized-control trial in 40 patients with ALI showed a decrease in extra-vascular lung water and plateau airway pressure with intravenous salbutamol, although it showed no differences in outcome97 Randomized placebo-controlled trial of several different therapies including surfactant, prone positioning, inhaled nitric oxide and anti-inflammatories have not shown significant clinical benefits in patients with established ALI.98 While it is unreasonable to expect there to be a single therapy (or “magic bullet”) that will prevent ALI, the above exciting research does hold promise in both furthering our understanding and management of injured or at risk lungs.

SUMMARY

To summarize what we know:

1) Non-physiological ventilation in healthy lungs induces ALI.
2) Protective lung ventilation in patients with ALI/ARDS improves outcome.
3) Protective lung ventilation in non-injured lungs and in the absence of a primary pulmonary insult may initiate VILI (as evidenced by inflammatory markers)
4) VILI has important implications remote to the lungs and may be associated with significant morbidity and mortality.
5) Volatile anesthetics may have a lung-protective effect
6) Excess fluids may contribute to perioperative lung injury. Anesthesiologists manage a heterogeneous group of patients in the peri-operative period; from patients with healthy lungs, and patients with “at risk” lungs, through to patients with severe COPD. More patients are at risk for ALI during surgery than previously thought. Appropriate peri-operative management may prevent or ameliorate this lung injury. Applying protective ventilatory strategies seems reasonable based on our current understanding of mechanical ventilation and lung injury.

ENDNOTES


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et al. Sevoflurane ameliorates gas.
Low tidal
et al. Anesthetic-induced improvement
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PP . Intraoperative risk factors for acute respiratory distress syndrome in critically ill
Hughes C, Weavind L, Banerjee A, Mercaldo ND, Schildcrout JSS, Pandharipande
2009; 64: 121-127
Hughes C, Weavind L, Banerjee A, Mercaldo ND, Schildcrout JSS, Pandharipande
PI. Intraoperative risk factors for acute respiratory distress syndrome in critically ill patients. Anesthesia and Analgesia 2010; 111: 464-467


Beck-Schimmer B, Schimmer RC. Perioperative tidal volume and intraoperative lung strategy in healthy lungs: where are we going? Best Practice and Research Clinical Anesthesiology 2010; 24: 199-210


Tusman G, Bohm SH, Suarez-Shipman F. Alveolar recruitment improves ventilatory efficiency of the lungs during anestheisis. Canadian Journal of Anaesthesia 2004; 51: 723-727


Epidural anaesthesia and analgesia in thoracic surgery: a randomized trial. Anesthesiology 2005; 102: 834-854


Beck-Schimmer B, Schimmer RC. Perioperative tidal volume and intraoperative lung strategy in healthy lungs: where are we going? Best Practice and Research Clinical Anesthesiology 2010; 24: 199-210


89. Starling EH. On the absorption of fluids from the connective tissue spaces. J Physiol 1896, 19: 312-26
Tighten Your Belts! Reduce Your Transfusion Costs with Pre-Operative Management of Anemic Patients

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CURRENT BEST PRACTICES IN PERIOPERATIVE PATIENT-CENTERED BLOOD MANAGEMENT

Blood management has been defined by the Society for Advancement of Blood Management (SABM) as "the timely application of evidence-based medical and surgical concepts designed to maintain hemoglobin concentration, optimize hemostasis and minimize blood loss in an effort to improve patient outcome."1 Formalized blood management is being driven by and gaining momentum because of known and unknown blood risks; preservation of a local, regional and national blood supplies; and escalating blood product costs.2,3

Approximately 15 million packed red blood cell (PRBC) units are transfused annually in the United States and 85 million are transfused annually worldwide.4,5 However, blood transfusion practices vary widely and often do not follow current evidence-based best practices.7 Furthermore, while blood transfusion is a mainstay of treating surgical blood loss, it is not without risk, especially in developing countries with inadequate screening of donor blood.7,8 An increasing number of patients thus refuse blood products, seek autologous donation, or request so-called "bloodless surgery" due to the perceived risk of blood transfusion.9

Known risks of allogeneic transfusions include transmissible infectious agents, transfusion reactions, and effects on immunomodulation (e.g., postoperative infection and tumor progression).1 Not surprisingly, the risks associated with allogeneic PRBC transfusions differ significantly between countries with a low versus high human development index (HDI): an index based on life expectancy, literacy, enrollment in further education, and per capita income.4 In countries with a low HDI, the risk of infection (HIV, hepatitis B, hepatitis C, and malaria) is elevated, whereas in countries with a high HDI, immunological reactions (hemolytic transfusion reactions, alloimmunization and immunosuppression) are predominant.8

Published data also support a major association between intraoperative blood transfusion and morbidity and mortality in patients undergoing noncardiac surgery.10 A recent retrospective analysis examined the association between blood transfusion and 30-day morbidity and 30-day mortality, in patients undergoing noncardiac surgery.11 Of note, this significantly increased risk of morbidity and mortality was present with mild anemia (hematocrit > 29% and < 39% in men and > 29% and < 36% in women) and moderate-to-severe anemia (hematocrit ≤ 29% in men and women).12 An even stronger association between anemia (hemoglobin < 13.0 g/dL for men and < 12.0 g/dL for women) and increased 90-day mortality (aOR of 2.36) was observed in a retrospective Canadian health system cohort of non-cardiac surgery patients.13

Preoperative anemia is a common condition among surgical patients; however, its reported prevalence varies widely, ranging from 5% to 75% depending on the type of surgery, the patient’s age, gender, co-morbidities, as well as the criteria used for defining anemia.16,17 The most frequent causes for existing preoperative anemia are iron deficiency and anemia of chronic disease.18,19 In a national audit of patients undergoing elective orthopedic surgery in the United States, 35% were found to have hemoglobin of < 13 g/dL at the time of preadmission testing.20,21 A recent systematic review observed an average 24% prevalence of preoperative anemia in total joint replacement patients, resulting in a 45% perioperative transfusion rate.22

Lastly, with the ageing of the population in the United States, and other developed countries, voluntary blood donation pools and rates continue to decrease,24 which will likely increase the occurrence of acute blood shortages and elective surgery cancellations.18,25,26 This shrinking donor availability, combined with measures to reduce the risks of infection transmission (e.g., increasingly restrictive donor screening criteria) have increased the direct costs of blood products.26,27 It has been estimated that the total cost per unit of PRBC is in excess of $1000 ($250 acquisition cost X 4), resulting in annual hospital expenditures of $1.63 to $6.03 million.28

Given these various motivating factors, patient blood management (PBM) (i.e., “blood conservation”) is thus being widely advocated.26,29,30 PBM has been defined by SABM as “the appropriate provision and use of blood, its components and derivatives, and strategies to reduce or avoid the need for a blood transfusion.”1 This concerted effort is better termed, patient-centered blood management,31 to reflect the increasing
emphasis on patient-centeredness in other areas of medicine and the consumer-perspective of healthcare.32-34

PBM incorporates an evidence-based approach that is multidisciplinary (anesthesiology, critical care medicine, surgery, and transfusion medicine) and multi-professional (physicians, nurses, pump technologists, and pharmacists).3,29,35,36 PBM focuses on the treatment of the individual patient and comprises goal-directed transfusion therapy and appropriate pharmacotherapy.18,37 PBM is fundamentally based on three strategies or pillars: (1) optimizing of the patient's (preoperative) erythrocyte mass, (2) minimizing diagnostic, therapeutic, or intraoperative blood loss, and (3) increasing individual clinician's tolerance towards anemia and adherence to valid blood transfusion triggers by prudently capitalizing on physiologic tolerance of anemia.18,26

FUNDAMENTALS OF A PREOPERATIVE ANEMIA MANAGEMENT PROGRAM

A key to achieving such optimal surgery-related patient-centered blood management is a formal preoperative anemia management program (PAMP). Commensurate with the promulgated principles and the above first strategy or pillar of PBM, a formal PAMP primarily identifies surgical patients who are anemic and thus at risk for transfusion and implements a preoperative management plan aimed at reducing or eliminating the presence and/or risk of anemia and the need for allogeneic transfusion, hence reducing the inherent risks, inventory pressures, and the escalating costs associated with transfusion.3,18,26

To this end, a multidisciplinary panel of physicians was recently convened by the Network for Advancement of Transfusion Alternatives (NATA) with the aim of developing practice guidelines for the detection, evaluation, and management of preoperative anemia.18,26

Table 1. Network for Advancement of Transfusion Alternatives (NATA) recommendations for the detection, evaluation, and management of preoperative anemia.18,26

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>GRADE</th>
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<tr>
<td>Elective orthopedic surgical patients should have an Hgb level determination four weeks before surgery, if possible</td>
<td>Grade 1C</td>
</tr>
<tr>
<td>Further laboratory testing for differential diagnosis in those with anemia</td>
<td>Grade 1C</td>
</tr>
<tr>
<td>Nutritional deficiencies should be treated to rising Hgb before surgery to be within the normal range</td>
<td>Grade 1C</td>
</tr>
<tr>
<td>Erythropoiesis-stimulating agents be used for anemic patients in whom nutritional deficiencies have been ruled out, corrected, or both</td>
<td>Grade 2A</td>
</tr>
<tr>
<td>Intravenous iron administration during the preoperative period for patients undergoing orthopedic surgery who are expected to develop severe postoperative anemia</td>
<td>Grade 2B</td>
</tr>
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</table>

Strength of recommendation: Is risk/benefit clear?
Yes = strong recommendation = Grade 1: “We recommend”
No = weak recommendation = Grade 2: “We suggest”

Quality of Evidence
High-quality evidence ✪ A (meta-analyses, randomized controlled trials)
Moderate-quality evidence ✫ B (randomized controlled trials with limitations, observational studies with large effects)
Low- or very low-quality evidence = C (observational studies, randomized controlled tried with major limitations)

Transfusion Alternatives (NATA) with the aim of developing practice guidelines for the detection, evaluation, and management of preoperative anemia (primarily in elective orthopedic surgery) and formulating recommendations using the GRADE working group methodology.16,20 Based upon a systematic literature review and critical evaluation of the evidence, this NATA panel made a series of recommendations (Table 1).

DEVELOPMENT AND IMPLEMENTATION OF AN ANESTHESIOLOGY-BASED PREOPERATIVE ANEMIA MANAGEMENT PROGRAM

A patient-centered approach to blood management has been advocated by the American Society of Anesthesiologists.31 However, currently, the presence of preoperative anemia is commonly accepted de facto by anesthesiologists. The planned surgery is typically performed as scheduled, without any preemptive corrective action, but instead simply with a lower clinician threshold for intraoperative PRBC transfusion as the default therapy.18,26 *This phenomenon is especially noteworthy given the ethical and medico-legal requirement to inform such anemic patients preoperatively on their risks versus benefits with regard to anesthesia and surgery and to plan concomitant diagnostic and treatment measures.18 In order to meet with these requirements, it has been proposed that patients should be initially seen in an outpatient preoperative clinic as soon as possible, but at least three to four weeks prior to their planned surgery so that appropriate anemia management can be initiated.18 At many institutions (including mine), this hiatus is not feasible, primarily due to a wide patient catchment area and resulting patient inconvenience. This has prompted implementing at our institution a more compressed 12 to 16 day preoperative anemia treatment regimen (Figure 1), which is currently the subject of a prospective conjoint randomized controlled clinical trial and formal healthcare economic evaluation.

Figure 1. Protocol for Preoperative Anemia Management Program (PAMP).
A number of studies have demonstrated the safety and efficacy of the preoperative use of an erythropoietic stimulating agent (ESA) like recombinant human erythropoietin (Table 2), especially in the orthopedic population, in reducing the need for allogeneic red cell transfusion. Of note, the reported side-effect profile and adverse event rate (e.g., deep venous thrombosis) in the active treatment versus control groups has been comparable. There is less pain with the subcutaneous injection of epoetin alfa as compared to darbepoetin alfa. Moreover, epoetin alfa is less expensive and more effective than darbepoetin alfa for an equipotent longitudinal regimen.

The FDA currently requires all erythropoiesis-stimulating agents (ESAs) to be prescribed and used under a risk management program, known as a risk evaluation and mitigation strategy (REMS), to ensure the safe use of these drugs. The ESAs included in this REMS are marketed under the names Epogen, Procrit, and Aranesp. Per the FDA: “Healthcare professionals who prescribe ESAs for anemia not caused by cancer chemotherapy are required to provide a copy of Medication Guide to each patient or their representative when an ESA is dispensed.” Furthermore: “Healthcare professionals who use ESAs only for non-cancer uses are not required to enroll in the ESA APPRISE Oncology program.”

Patients should receive iron supplementation (Table 3), preferably intravenously, throughout the pre-surgical use of an ESA to optimize red blood cell production and to avoid iatrogenic functional iron deficiency. Large, single, total replacement doses of all parenteral iron preparations (including iron sucrose) are conventionally given by IV infusion over one hour. These high doses have greater incidence of side effects. However and alternatively, low doses (100 mg to 200 mg) of iron sucrose have been reportedly given safely as a two-minute slow IV push. Ferumoxytol can be given over 20-60 seconds. Iron sucrose was initially approved by the US Food and Drug Administration (FDA) in 2000 and for non-dialysis dependent iron deficiency in 2005. Of note, despite its apparent clinical advantages, ferumoxytol has yet to be FDA approved for treatment of non-dialysis dependent iron deficiency.

The conventional wisdom that surgical patients should be transfused to maintain a hemoglobin of 10 g/dL and a hematocrit of 30% is no longer valid for most patients. Present clinical practice guidelines now recommend restrictive red cell transfusion practices, with the goal of minimizing exposure to allogeneic blood (from an unrelated donor). Specifically, the American Association of Blood Banks (AABB) has recently recommended adhering to a more restrictive transfusion strategy (7 to 8 g/dL) in hospitalized, stable patients (Grade: strong recommendation; high-quality evidence).

Pertinent to an anesthesiology-based PAMP, a reasonable intraoperative blood conservation protocol applies same restrictive transfusion trigger (Hgb < 8 g/dL), but also takes into consideration the patient’s intraoperative estimated allowable blood loss and hemodynamic stability. Specifically, if the patient has lost > 30% of his/her estimated blood volume (based upon ideal body weight for height) and requires the administration of an intravenous medication (vasopressor) for hypotension, the patient will be transfused with 1 (one) unit of PBRCs. Repeat transfusion with PBRCs will occur based on these same criteria. Likewise pertinent to an anesthesiology-based PAMP, consistent with these AABB guidelines, in postoperative surgical patients, transfusion should be considered at a hemoglobin concentration of 8 g/dL or less for symptoms of chest pain, orthostatic hypotension or tachycardia unresponsive to fluid resuscitation, or congestive heart failure (Quality of evidence: high; strength of recommendation: strong). However, on-going appropriate training, education, and awareness are needed to avoid local guideline-based protocol violations and to limit unnecessary further exposure to allogeneic blood transfusion and its related risks.

### Table 2. Commercially available erythropoietic stimulating agents (ESA)

<table>
<thead>
<tr>
<th>ESA</th>
<th>Equipotent Dose</th>
<th>Equipotent Dose</th>
<th>Equipotent Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Darbepoetin alfa (AranespÆ)</td>
<td>200 mcg</td>
<td>100 mcg</td>
<td>60 mcg</td>
</tr>
<tr>
<td>Epoetin alfa (EpogenÆ)</td>
<td>40,000 units</td>
<td>20,000 units</td>
<td>10,000 units</td>
</tr>
<tr>
<td>Epoetin alfa (ProcritÆ)</td>
<td>40,000 units</td>
<td>20,000 units</td>
<td>10,000 units</td>
</tr>
</tbody>
</table>

**ROLE OF AN ANESTHESIOLOGY-BASED PREOPERATIVE ANEMIA MANAGEMENT PROGRAM IN A PERIOPERATIVE SURGICAL HOME MODEL**

Varied and fragmented care plans, undertaken by different practitioners, currently expose surgical patients to lapses in expected standard of care, increase the chance for operational mistakes and accidents, result in unnecessary and potentially detrimental care, and adversely affect the patient health care experience. Standardization of perioperative processes is increasingly recognized as needed to optimize not only resource utilization and quality but also patient safety, well-being, and satisfaction. Likewise, the medical community and the public are increasingly embracing shared decision-making, a process by which healthcare choices are made jointly by the practitioner and the patient. Like the Medical Home model that has been implemented in the primary care practice setting, the Perioperative Surgical Home has thus been proposed by the American Society of Anesthesiologists and other stakeholders as an innovative, patient-centered continuity of care model that emphasizes shared decision-making. In the Perioperative Surgical Home model, anesthesiologists serve as the surgical patient’s primary perioperativeivist, providing highly integrated, continuity of care throughout the preoperative, intraoperative, and postoperative periods. This broadening of anesthesiologists’ scope of practice should promote such standardization and shared decision-making, thus likely improving clinical outcomes and decreasing unnecessary resource utilization. A patient-centered, anesthesiology-based Preoperative Anemia Management Program is a logical component of such a multifaceted Perioperative Surgical Home.

While a pre-anesthetic patient assessment has been a longstanding required element of any anesthetic, it has been historically performed in close proximity to the scheduled surgery and has routinely only collected a limited set of clinical data, including laboratory testing. In patients with...
a greater chronic disease burden, such a perfunctory pre-anesthetic assessment does not permit the more comprehensive evaluation, or as indicated, a formal consultation, which a more comprehensive Preoperative Assessment, Consultation and Treatment (PACT) Clinic affords.71 The goals of such a PACT Clinic are to identify, to communicate, and whenever possible to minimize the patient-specific, attendant risks of surgery and anesthesia. Logistically, an anesthesiology-based Preoperative Anemia Management Program can be located in such a PACT Clinic, given that preoperative patient optimization readily includes assessment for anemia and the administration of subcutaneous recombinant erythropoietin and intravenous iron to reduce or eliminate surgical allogeneic blood transfusions.71

**BUSINESS MODEL THAT DEMONSTRATES THE COST SAVINGS AND “ADDED VALUE” OF A PREOPERATIVE ANEMIA MANAGEMENT PROGRAM**

Minimizing the need for surgical transfusions has not only physiologic but also economic benefits.20 Preoperative treatment of anemia with recombinant human erythropoietin (rHuEPO) [e.g., epoetin alfa (PROCRIT®), manufactured by Amgen Inc., Thousand Oaks, CA for Janssen Products, LP, Horsham, Pennsylvania] and intravenous iron (IV Fe) [e.g., iron sucrose (Venofer®), American Regent, Inc., Shirley, NY] has been advocated to reduce the need for allogeneic transfusion.73,74 Such treatment is covered by the Center for Medicare & Medicaid Services (CMS) and commercial payers (e.g., Blue Cross & Blue Shield).

A retrospective review of University of Alabama (UAB) Hospital administrative and clinical data from 2011 revealed a cross-sectional 39% prevalence of preoperative non-macrocystic anemia (Hgb < 12.5 g/dL and MCV < 100 fL in females and males) among 358 total hip arthroplasty (THA) patients, resulting in 352 PRBC units being transfused in the 128 preoperatively anemic patients (Vetter et al., 2012 American Society of Anesthesiologists Annual Meeting). Of note, despite receiving a PRBC transfusion, the preoperatively anemic patients had a mean Hgb of 8.8 gm/dL (SD 1.1) at time of hospital discharge. The local direct (wholesale) cost of epoetin alfa (PROCRIT®) is $381/dose (40,000 IU) and the direct (wholesale) cost of iron sucrose (Venofer®) is $63/dose (200 mg), the latter with an estimated administration cost of $50/dose. The estimated total cost of a PRBC unit at UAB Hospital is $1000 ($250 acquisition cost X 4).28 Treating these 128 anemic THA patients with preoperative ESA + IV Fe therapy (three weekly doses/patient) and postoperative IV Fe (single dose) (applying the protocol in Figure 1) would cost $178,560 versus $352,000 for the estimated total cost of the 352 transfused PRBC units—a net annual savings of $173,440. Further savings would be realized by inclusion of other elective major surgical procedures (e.g. total knee arthroplasty) or if the third dose of epoetin alfa is not needed on the day of surgery.

The Patient Protection and Affordable Care Act (PPACA) of 2010 seeks to reign in spiraling healthcare costs by fundamentally transforming healthcare delivery via (a) new care models that deliver more cost effective and coordinated care and (b) incentive-based reimbursement.75,76 In this new healthcare paradigm, providers—including anesthesiologists—will be paid not just for the quantity but the quality and value of the services they provide.71,77,78 Value-based purchasing of health care,79,81 pay for performance,82,83 and a changing payment paradigm that includes bundled payments and/or accountable care arrangements84 are all powerful motivators to improve health care delivery and outcomes—particularly in the perioperative setting.71 Hospital-physician collaborations will continue to evolve toward greater economic integration, including major financial gain and risk sharing.85,86 Greater level of payment will be based on the reduced resources used by those care delivery teams achieving superior outcomes, thereby fostering innovation and reducing waste.87 To be successful, the nascent Perioperative Surgical Home model—including for example, a comprehensive Preoperative Assessment, Consultation, and Treatment Clinic and a robust Preoperative Anemia Management Program—will need to create strategic added value for a hospital and health system as well as payers.71,88 This added value will strengthen the position of anesthesiologists as they navigate and negotiate in the face of finite and more likely decreasing fiscal resources (i.e., making do with less).71

**CONCLUSIONS**

Intraoperative blood transfusions have been associated with increased morbidity and mortality, raising uncertainty about the actual clinical benefits of banked allogeneic blood. Moreover, increasing costs, competing demands, and a shrinking pool of blood donors mandate better patient-centered blood management strategies. A Preoperative Anemia Management Program (PAMP) may be a viable, cost-effective opportunity to improve patient-centered outcomes and more efficient use of finite healthcare resources. Establishing a PAMP within an existing Preoperative Assessment, Consultation, and Treatment (PACT) Clinic appears viable. Both the PAMP and PACT Clinic can be components of an institutional Perioperative Surgical Home.

**REFERENCES**

11. Bernard AC, Davenport DL, Chang PK, Vaughan TB, Zwischenberger JB. Intraoperative transfusion of 1 U to 2 U packed red blood cells is associated with


70. Warner MA. The Surgical HomeTM. ASA Newsd 2012;76:30-2.


78. Kaplan RS, Porter ME. How to solve the cost crisis in health care. Harv Bus Rev 2011;89:46-64.


88. Owens DK, Quee A, Chou R, Shokekell P. High-value, cost-conscious health care: concepts for clinicians to evaluate the benefits, harms, and costs of medical interventions. Ann Intern Med 2011;154:174-80. in this REMS are marketed unand Aranesp®. Per the FDA:

ENDNOTES


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