REVIEW COURSE LECTURES

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Airway Management of the Obstetric Patient: What's New?

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Learner Objectives

After participating in this activity, the learner will be able to:

1. Describe the role of videolaryngoscopy in managing the obstetric airway
2. Describe the role of supraglottic airway devices in managing the obstetric airway
3. Indicate the roles of ultrasonography and the Vortex approach in managing a difficult airway
4. Review the effectiveness of high-flow humidified nasal oxygen delivery for the parturient
5. Appreciate the importance of extubation strategies for obstetric patients

Difficult and failed tracheal intubation in obstetric patients is a major problem with potentially devastating consequences. In a landmark study by Harkins, et al., maternal fatalities were attributed to airway-related problems in 52% of cases[1]. Fortunately, improved pre-operative airway assessment and preparedness, availability of advanced airway technologies, better clinical and simulation training, and the widespread use of guidelines and algorithms have significantly contributed to a safer environment for airway management for the parturient, resulting in decreased general anesthesia-related morbidity and mortality[2]. The reported incidence of difficult and failed intubation varies largely with the definitions used to describe the airway event.

Suresh, et al.[3] define difficult intubation for obstetric patients as: "the difficulty encountered during laryngoscopy and the inability of an experienced anesthesia practitioner to intubate within the time provided by one dose of succinylcholine", and failed intubation as: "the inability to secure the airway with two attempts, which includes the best attempt at intubation using the conventional laryngoscope or the use of an alternative airway device to assist with tracheal intubation". The Society for Obstetric Anesthesia and Perinatology Research Committee coordinated a review of 257,000 anesthetics performed in 30 institutions between October 2004 and June 2009 (SCORE Study), and reported a failed intubation incidence of 1:553 cases. In patients with a failed intubation, there were no hypoxemic arrests[4]. Using Mckeen's definition for failed intubation in obstetric patients[5] ("inability to secure the airway after a single dose of succinylcholine and no more than two attempts at intubation using a conventional laryngoscope or an alternative airway device"), Rajagopalan, et al.[6] retrospectively reviewed airway management for Cesarean deliveries (CD) between 2006–2013. The authors reported a 1:232 incidence of failed intubation. In all cases of failed intubation in that series, the airway was successfully managed with a laryngeal mask airway (LMA).

General anesthesia (GA) is the fastest approach to reliably anesthetize a patient for a category 1 CD. The longer time associated with establishing neuraxial anesthesia in cases of emergent CD for fetal compromise can result in both delay in delivery and neonatal morbidity. In a recent systematic review of meta-analyses, Krom, et al.[7] demonstrated that, in patients with an anticipated difficult airway undergoing category 1 CD for fetal distress, surgical anesthesia was established with a GA using a rapid sequence induction and videolaryngoscopy in a significantly shorter time (100 s) than spinal anesthesia (6.3 min). Reluctance to convert an inadequate neuraxial anesthetic to a GA frequently results in maternal pain/discomfort and emotional distress, and increased liability for the anesthesiologist[2,8].

With the declining rate of GA for CD, familiarity with the obstetric airway is decreasing. The choice of anesthetic for CD, as reported in the National Anesthesia Clinical Outcomes Registry (NACOR) between 2010 and 2015, demonstrated that only 5.8% of CDs in the United States are performed under G[9]. As a consequence, there are residents graduating without hands-on experience in managing the airway in the parturient[10]. Simulation-based teaching has been criticized for a lack of reproducibility of the stressful environment associated with the extreme urgency of a CD. However, as shown by Balki, et al., didactic teaching combined with repeated high-fidelity simulation sessions using a validated checklist, improved anesthesia residents' technical and non-technical skills in that setting[11].

Airway changes during pregnancy and labor are progressive and persist into the post-partum period. For that reason, the same planning and precautions taken for airway management in the pre-partum patient should be followed for at least 48 hours after delivery[12].

The Role of Video Laryngoscopy in Managing the Obstetric Airway

Videolaryngoscopy offers the advantage of improved glottic visualization and a higher first attempt endotracheal intubation success rate in both a predicted and unexpected difficult airway. Its use is also associated with a high success rate of rescue intubation. There are several reports of the successful use of videolaryngoscopes in obstetric patients, for initial intubation in patients with normal or predicted difficult airway, or as rescue devices after failed direct laryngoscopy[13–18]. A retrospective analysis by Aziz, et al.[13] reported the successful use of the GlideScope to intubate the trachea in all patients on the first attempt. Shonfeld, et al. described the successful use of the C-MAC in 27 patients, and the Airway Scope has been described for intubating two patients for unscheduled intraoperative awake endotracheal intubation during Cesarean Delivery[15,17].

In a recent prospective, randomized trial, Blajic, et al.[18] compared C-MAC and King Vision videolaryngoscopes and direct laryngoscopy, for tracheal intubation in patients undergoing category 2–4 CDs, as used by three experienced attending anesthesiologists. The time to intubate the trachea using a rapid sequence induction technique was similar for all devices. The authors concluded that the C-MAC was the easiest to use based on the subjective assessment of the anesthesiologists and the need for fewer airway optimization maneuvers. However, the highest rate of grade 1 laryngeal view was obtained with the King Vision videolaryngoscope.

A potential disadvantage of videolaryngoscopy is the increased incidence of pharyngeal trauma with devices requiring a stylet to facilitate intubation[19]. The increased upper airway tissue friability in obstetric patients might make them more prone to this complication.

The Role of Supraglottic Airway Devices in the Managing Obstetric Airway

In a difficult intubation situation, adequate oxygenation and ventilation takes priority over endotracheal intubation. Failed intubation must be declared after two unsuccessful attempts to intubate the trachea with direct or videolaryngoscopy. Supraglottic airway devices (SAD) (Laryngeal Mask Airways (LMAs) and Non-LMAs) have been continually evolving. These improvements have resulted in safer tools for airway management. SADs should be used early in the airway algorithm to minimize the risk of airway trauma and hypoxia. Among numerous available SADs, the choice should be made based on availability, user preference and expertize. Preference should be given to second generation SADs that separate the alimentary and respiratory tracts (such as the LMA Supreme), as they provide greater airway protection over first generation SADs. No more than two attempts at supraglottic ventilation are allowed.

If adequate oxygenation and ventilation are possible, a SAD may be left in situ until completion of the CD. The decision to leave a SAD in place, or proceed to an exchange with an endotracheal tube after delivery, should be based on adequacy of oxygenation and ventilation as well as the expected length of surgery. Several techniques to facilitate tracheal intubation through a SAD have been described, including blind intubation or facilitation by light wands, optical stylets, or a fiber-optic bronchoscope[20].

The Role of Ultrasonography in Managing the Obstetric Airway

Ultrasound imaging of the upper airway is emerging as a simple, non-invasive technique to help evaluate the airway. Ahuja, et al. described the use of airway sonography to assess dynamic airway dimensional changes in preeclamptic patients[12]. Ultrasonography can be used to reliably locate the cricothyroid membrane to facilitate front-of neck access should it be necessary[21,22]. Point-of care ultrasonography has shown that the cricothyroid membrane is located significantly deeper for obese parturients when compared with normal-weight parturients[22].

High-flow Humidified Nasal Oxygen

Effective preoxygenation in preparation for general anesthesia for Cesarean Delivery should be aimed to achieve an end-tidal oxygen concentration of > 90% within 3 min. Delivery of high-flow humidified nasal oxygen has been shown to significantly delay hypoxemia following induction of general anesthesia in the general population[23]. However, high-flow nasal oxygen pre-oxygenation was less effective when compared with standard flow-rate facemask in non-laboring pregnant patients[24].

Managing Extubation in the Parturient

Myhre, et al. reviewed anesthesia-related maternal deaths in Michigan between 1985 and 2003. Eight fatalities were anesthesia-related, with all cases of death due to airway problems (airway obstruction or hypoventilation) occurring during emergence and recovery from anesthesia. No airway-related death occurred during induction of anesthesia[25]. In 2012, the Difficult Airway Society (DAS) in the United Kingdom published guidelines for the management of tracheal extubation which highlighted the importance of a stepwise approach. This approach included planning, preparing, and executing tracheal extubation, as well as post-extubation follow up[26].

The successful use of an airway exchange catheter for staged extubation has been described in a pregnant patient with an unexpected difficult intubation[27]. Airway exchange catheters are well tolerated by awake and spontaneously breathing patients, and should be considered to increase extubation safety in pregnant patients with difficult intubation and/or suspected difficult extubation.

The Vortex Approach

The Vortex concept was developed by Chrimes as a visual cognitive aid to help implement difficult airway management algorithms[28]. Currently, there are no reports of implementing the Vortex approach in obstetric anesthesia.

Conclusion

The incidence of failed intubation in obstetric anesthesia is significantly higher than in the general population. Recently developed guidelines and algorithms offer a systematic approach for managing the difficult airway in obstetric anesthesia. With further technological advances and operator comfort, it seems that video laryngoscopes will likely become the first option for the initial approach to intubation for CD. With an emphasis on adequate oxygenation rather than endotracheal intubation, SADs should be used early in the airway algorithm. When considering a SAD, preference should be given to 2nd generation SADs. Point-of care ultrasonography is emerging as a simple, non-invasive technique to help evaluate the airway in obstetric patients.

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Ambulatory Surgery in Patients with Morbid Obesity: Quo Vadis?

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Background

Morbid Obesity is becoming increasingly prevalent worldwide with increasing numbers of these patients presenting for both elective and emergency surgery. Almost concurrently, and over the past few decades, ambulatory (out-patient) surgery has become popular and well-established for a wide variety of elective procedures. It is therefore not surprising that we find ourselves at the crossroads of ambulatory surgery in patients with morbid obesity and need to determine the way ahead.

Established guidelines and protocols have identified patients and surgical procedures suitable for ambulatory surgery. Healthy individuals are undergoing shorter duration procedures which are associated with rapid recovery, minimal pain and require limited postoperative monitoring[1-3]. It is also probably important that all patients in this setting achieve same-day discharge from the surgical facility. When suitability of other patient populations are being considered for ambulat ory surgery, invasiveness of the surgical procedures, anesthetic technique and postoperative pain management are also taken into consideration. The overall focus of ambulatory surgery is achieving early discharge without compromising patient safety and outcomes[1].

Perioperative morbid obesity presents with many well-described anesthetic challenges that include delayed emergence and perioperative cardio-respiratory adverse events[4-6]. These exact concerns may preclude the inclusion of some patients with morbid obesity for ambulatory surgery[7,8]. Indeed, both large database and other prospective studies mirror clinical experience- patients with morbid obesity are at increased risk of both immediate complications, unplanned admissions or delayed re-admissions after ambulatory surgery[9,10]. Wide variations exist in ambulatory surgery for patients with morbid obesity- not only between different geographical regions and healthcare systems, but inconsistencies often exist between anesthesia providers within the same institution. This variability in practice can lead to unpredictable rescheduling or cancellations on the day of surgery and/ or unanticipated delayed discharges, transfers and readmissions in the postoperative period. As expected, these reduce the overall credibility, efficiency, and economics of ambulatory surgery and contribute to highly unsatisfied patients.

This review will revisit the perioperative implications of morbid obesity, discuss their relevance in ambulatory setting and attempt to identify a pragmatic way forward with this conundrum.

Perioperative Implications of Obesity and Morbid Obesity

If all patients with obesity are deemed ineligible for ambulatory surgery, timely access to elective surgical care could be compromised with increases in both direct and indirect costs to patients and/or healthcare systems. It is therefore important to identify co-morbidities in this patient population that may preclude safe surgery in the ambulatory setting.

It is well appreciated that the perioperative implications of obesity are not an absolute, but rather a spectrum, depending on the degree of obesity and co-morbidity burden[2,6-8]. The degree of obesity is almost universally measured using the Body Mass Index (BMI), which has been widely reported in previous and ongoing research. As a simple ratio of the patient's weight (in Kg) to the square of their height (in m^2), it is evident that this metric can, over or under estimate the degree of obesity in patients with short or tall stature, respectively. Nevertheless, the standard classification of obesity continues to define obesity and morbid obesity as BMI>30 kg/m^2 and BMI> 40 kg/m^2 respectively[4].

More recently, extensive experience with elective weight loss (bariatric) surgical populations has established the adage '*Look beyond the BMI*'. This has led to interest in determining the content and distribution of the excessive weight as possible predictors of increasing perioperative risk[11]. Indeed, as proportion of fat increases and the distribution becomes more central, the perioperative risk increases. Experts from various Obesity Anesthesia Societies recommend the use of ratio of the waist circumference to the height (Figure 1). Using this, central obesity is more objectively defined when the waist circumference exceeds half the height, and this corresponds to increasing perioperative risk. In our opinion, this metric should be added to the standard preoperative ambulatory surgery assessment and the specific impact of distribution of obesity on perioperative risk need to be confirmed by future research.

Could perioperative risk estimations in similar patient cohorts be used to screen patients with morbid obesity being considered for ambulatory surgery? In this context, it may be useful to examine the Obesity Surgery Mortality Risk Score (OSMRS or deMaria's Score) that has been validated to predict perioperative morbidity and predicts mortality after elective weight loss surgery (Table 1)[12]. In addition to BMI, this score gives equal weightage to patient demographics (age and gender) and two other comorbidities (systemic hypertension and pulmonary embolism or hypertension). Estimates from large series and databases have validated the OSMRS. This score estimates that above BMI 50 kg/m^2, a man over 45 years with either systemic or pulmonary hypertension will have up to a 12-fold increase in 90-day mortality when compared to similar surgery in a younger woman without the same medical problems. Another emerging interest is the preoperative level of activity and mobility also is important in the assessment of patients with morbid obesity. Musculoskeletal pain (joint and spine related) and immobility may be relative contraindications for ambulatory surgery. Interestingly, the modified frailty index measuring these has been shown to identify increased risk of perioperative complications in patients with obesity undergoing ambulatory surgery[13]. Further research will be required to assess the use of OSMRS and frailty index to better guide the selection of patients with morbid obesity being considered for ambulatory surgery.

Obesity is otherwise associated with other comorbid conditions, including metabolic syndrome, diabetes, hypertension, cardiomyopathy, pulmonary hypertension, hypoventilation syndrome, and obstructive sleep apnea (OSA). These should be sought, diagnosed, treated and managed appropriately for all patients with BMI> 30 kg/m^2 scheduled for surgery in the ambulatory setting as described elsewhere[4].

Amongst these co-morbidities, Obstructive Sleep Apnea (OSA) is the most frequently occurring medical problem in patients with morbid obesity and probably one that impacts their suitability for ambulatory surgery the most. Excellent reviews elsewhere have discussed in detail the diagnoses, management and risk stratification of OSA in relation to ambulatory surgery[2,14,15]. Unfortunately, despite these, perioperative OSA continues to be a discussed, debated (and disagreed on) in academic circles and on the clinical frontlines. In our opinion, all patients with obesity (BMI>30 kg/m^2) must be objectively screened for OSA with the STOPBANG tool. For OSA diagnosis and treatment to occur effectively and without disruption of patient flow-through the ambulatory setting, this intervention should be incorporated early into the work-up at the family physician's (GP's) office or latest in surgeon's outpatient clinic. It is useful to add the serum bicarbonate measurement to the STOPBANG score, as this significantly improves the prediction of clinically relevant OSA16. All patients with positive screening tests should undergo formal testing for OSA, where those diagnosed should acquire and use their prescribed respiratory support therapy. The duration of preoperative therapy is still being determined, but emerging consensus suggests a minimum of 6 weeks of treatment before any elective ambulatory surgery[17]. This may be adequate time to for the patient with newly diagnosed OSA, to both adapt and clinically benefit to the device, well before the scheduled ambulatory surgery. This in turn will contribute to compliance in the most complication- vulnerable postoperative period and reduce overall morbidity and mortality[18,19].

The importance of OSA in ambulatory surgery cannot be overemphasized- undiagnosed and untreated OSA is the leading cause of postoperative re-intubation and/or prolonged ventilation[20,21]. Beyond the potential morbidity, increased costs and potential for serious complications, undiagnosed and/or untreated OSA can be disruptive to the flow of care for the other patients in the ambulatory setting. Beyond the clinical realm, untreated OSA can have a very significant societal, public safety and economic impact- in many jurisdictions; untreated OSA has overtaken alcohol as the leading cause of impaired driving in road traffic accidents[22,23].

Other experts have suggested an OSA scoring system specifically for use in ambulatory surgery[2]. This is based on the severity of OSA, the invasiveness of surgery and anesthesia, and need for postoperative opioids. This score needs to be reconsidered in the context of studies where despite predominant regional anesthesia use, OSA was independently associated with prolonged LOS and complications[24]. Therefore, we believe that irrespective OSA severity, proposed surgery, planned anesthetic technique or pain management strategy, patients with morbid obesity who have untreated OSA should not be scheduled to have any elective surgery, and definitely not in the ambulatory setting.

Lessons Learned from Enhanced Recovery and Bariatric Surgery

A major driver for improvements in the perioperative care of patients with morbid obesity has been the widespread acceptance, use and standardization of weight loss (bariatric) surgery over the past two or more decades. This has resulted in multiple benefits to the overall care of these patients. More recently some bariatric programs have also implemented enhanced recovery after surgery (ERAS)

principles to better define the standards of care, provide quality assurance benchmarks and allow for outcome comparisons between centers. This concept of 'enhanced recovery after bariatric surgery' (ERABS) has improved the overall perioperative safety and outcomes for patients with morbid obesity[25]. In our bariatric program, ERABS has revolutionized preoperative evaluation, education and optimization; standardized protocol-based anesthetic care with recommendations for postoperative monitoring and discharge criteria[26].

Extending beyond bariatric surgery, anesthesia for these patients may see an increasing level of comfort, confidence and familiarity with the perioperative challenges of morbid obesity. The extensive experience in bariatric anesthesia is also being converted into good quality evidence and finding application to ambulatory surgery. The influence of ERABS on ambulatory surgery is understandable, some bariatric centers are exploring offering elective weight loss surgery in the ambulatory setting[27-29].

While it may be a useful to explore and replicate the successes of bariatric surgery in the ambulatory setting, a word of caution is warranted. Bariatric surgical patients undergo extensive preoperative education and optimization. They are also generally well- informed, present for surgery with active engagement and have plans for extended postoperative care, if required. These may not be possible to achieve with the current resources available to the general ambulatory surgical patients- the very premise of ambulatory surgery is time and resource efficiency with minimal variation in perioperative time and predictable patient flow. Other less well studied predictors of successful transition of patient care from hospital to home- based care are their socio-economical, educational, cultural and financial factors. Again, time spent in preparing patients in ERABS programs provides the team with important information beyond clinical predictors and all these need to find objective ways of being applied to ambulatory surgery[30].

The location of the ambulatory surgery center and access to inpatient facilities including intensive care can also influence the patient selection and this remains highly variable. Often within the same system, ambulatory surgery may be offered in an independent stand-alone center or affiliated semi-detached center and fully integrated inpatient facility. In the latter, the ambulatory model is used within the traditional surgical setting and patients can be discharged home the same day. This may be the safest and most efficacious way to introduce or explore ambulatory bariatric surgery in patients with morbid obesity.

The Way Forward- Safety & Outcomes

Detailed description of the anesthetic management of the patient with morbid obesity undergoing ambulatory surgery has been described elsewhere[4,14,15]. To ensure improved patient safety and outcomes, special attention should be made to airway management and pain management[31,32]. Figure 1 summarizes many important considerations for the perioperative care of patients with morbid obesity and can be adapted for the ambulatory setting (SOBA Single Sheet, reproduced with permission).

But to ensure that ambulatory surgery works well for patients, providers and healthcare systems, we must start with careful patient selection. The ASA and SAMBA consensus guidelines remain rather unclear about ambulatory surgery in patients with BMI>50 kg/m^2.[1,2] Our suggestion is more definitive- patients with BMI>50 kg/m^2 are unsuitable for ambulatory surgery, irrespective of the co-morbidity burden, OSA, procedure, facility or provider expertise. Between BMI 30 and 50 kg/m^2, certain patients can undergo some ambulatory surgical procedures (Table 2). Irrespective of the facility and provider it is paramount that just like their inpatient counterparts, these patients are adequately prepared and their co-morbidities (including OSA) are optimized and treated. Other than airway surgery, with appropriate equipment, expertise and experience, it is likely that most procedures that are routinely carried out in the ambulatory setting for the non-obese patient population can be offered to patients with morbid obesity. If these criteria and recommendations are used, further research can then focus on determining the predictors of delayed discharges, complications and/or unplanned admissions.

As perioperative physicians faced with decisions regarding ambulatory surgery for patients with morbid obesity, this is a practical and pragmatic way forward.

Figure 1: Identifying Central Obesity (waist > half height) predicts increased perioperative risk. (From SOBA Single Sheet- Reproduced with Permission. Available online at www.sobauk.co.uk).

Preoperative Evaluation

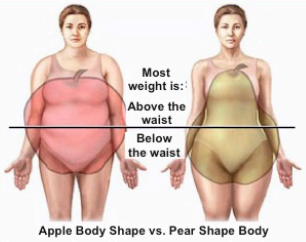
S	Snoring: Do you snore loudly (louder than talking or heard through a closed door?	
T	Tired: Do you often feel tired fatigued or sleepy during the daytime?	
O	Observed: Has anyone observed you stop breathing during your sleep?	
P	Blood Pressure: Do you have or are being treated for high blood pressure	
B	BMI: BMI > 35kg/m²	
A	Age: Age > 50	
N	Neck: Neck circumference > 40cm (16 inches)	
G	Gender: Male	

Any of:
Poor functional capacity
Abnormal ECG
Uncontrolled BP/IHD
SpO_2 <94% on air
If Bicarb > 28 OHS Likely
Previous DVT/PE
STOP-BANG>5

→ Yes → Consider:
Blood gases/Sleep Studies
Preoperative CPAP
Echocardiagram
Cardiorespiratory referral
Need experienced anaesthetic team
If major surgery consider HDU

→ No → Maybe suitable as Day case surgery
SEE BELOW

Central Obesity (waist > half height)
Difficult airway /Ventilation problems more likely
Greater risk of CVS disease, thrombosis
↑Risk of Metabolic syndrome:
Central Obesity plus Hypertension
Dyslipidaemia, Insulin resistance



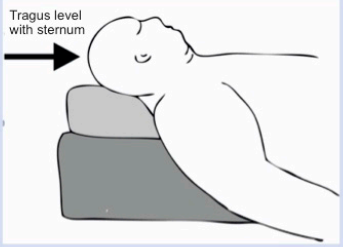
Apple Body Shape vs. Pear Shape Body

Peripheral Obesity
(Fat outside body cavity)
Less co-morbidity

Intra Operative Management

Suggested Equipment
Suitable bed/trolley & operating table
Gel padding, wide strapping, table extensions/arm boards
Forearm cuff or large BP cuff
Ramping device, step for anaesthetist, difficult airway equipment, ventilator capable of PEEP and pressure modes. Hover mattress or equivalent.
Long spinal, regional and vascular needles.
Ultrasound machine.
Depth of anaesthesia and neuromuscular monitoring.
Enough staff to move patient.

Ramping
Ear level with sternum. Reduces risk of difficult laryngoscopy, improves ventilation.



Anaesthetic Technique
Consider premed antacid & analgesia, careful glucose control & DVT prophylaxis.
Self-position on operating table.
Preoxygenate & intubate in ramped position +/- CPAP. Minimize induction to ventilation interval to avoid desaturation. Commence maintenance anaesthesia promptly.
Tracheal intubation is recommended.
Avoid spontaneous ventilation. Use PEEP.
Use short-acting agents e.g. desflurane or propofol infusion, short-acting opioids, multimodal analgesia. PONV prophylaxis.
Ensure full NMB reversal.
Extubate and recover in head up position.

Drug dosing- what weight to use?
Induction agents: titrate to cardiac output- this equates to lean body weight in a fit patient.
Competitive muscle relaxants: use lean body weight.
Suxamethonium use total body weight
Neostigmine: Increase dose. Measure response
Opioids: Use Lean body weight. Care with obstructive apnoea!
TCI propofol: IBW plus 40% excess weight
If in doubt, titrate and monitor effect!

Lean Body Weight this exceeds Ideal body weight in the obese and plateaus ≈100kg for a man, ≈70kg for a woman.
Ideal Body Weight in Kg - Broca formula
Men: height in cm minus 100 Women: height in cm minus 105

Suggested dosing regimes for anaesthetic drugs

Lean Body Weight Up to Max-Males 100kg Females 70kg	Adjusted Body Weight Ideal plus 40% excess
Propofol induction	Propofol Infusion
Thiopentone	Alfentanil
Fentanyl	Neostigmine (max 5mg)
Rocuronium	Sugammadex (see package insert)
Atracurium	Antibiotics
Vecuronium	Low Molecular weight Heparin
Morphine	
Paracetamol	
Bupivacaine	
Lidocaine	

Post Operative Management

PACU discharge: Usual discharge criteria should be met. In addition, SpO_2 should be maintained at pre-op levels with minimal O_2 therapy, without evidence of hypoventilation.
OSA or Obesity Hypoventilation Syndrome: Sit up. Avoid sedatives and post-op opioids. Reinstate CPAP if using it pre-op. Additional time in recovery is recommended, only discharge to the ward if free of apnoeas without stimulation. Patients untreated or intolerant of CPAP who require postoperative opioids are at risk of hypoventilation and require continuous oxygen saturation monitoring. Level 2 care is recommended. Effective CPAP reduces this risk to near normal.
Ward care: Escalation to Level 1, 2 or 3 care may be required based on patient co-morbidity, the type of surgery undertaken and issues with hypoventilation discussed above. General ward care includes: multimodal analgesia, caution with long-acting opioids and sedatives, early mobilisation and extended thromboprophylaxis.

Table 1:
Obesity surgery mortality risk score (OSMRS). Score designed to predict risk of mortality from bariatric surgery- assign 1 point each for risk factors. (deMaria et al 2007)

Risk Factors (Score 1 point each)	Total OSMRS Score: Risk Class and Mortality
Age >45 years	<2: Class A- Lowest risk (mortality 0.2%)
Body mass index > 50 kg/m2	2, 3: Class B- Intermediate risk (mortality 1.1%)
Gender- Male sex	>3: Class C- High risk (mortality 2.4%)
Risk for pulmonary embolism/ PHT	
Hypertension	

Table 2:
Patient selection criteria and summary of suggested anesthetic techniques for ambulatory surgery in patients with morbid obesity.

Inclusion Criteria	Anesthetic Technique
BMI 30 to 50 kg/m2	Avoid Sedative Premedication, bring CPAP machine.
OSMRS Class A	Prefer Regional Anesthesia GA: Prefer TIVA with monitored depth of anesthesia • Predict &Manage the Morbid Obesity Difficult Airway • Avoid/ Reduce opioids with Local /Wound Infiltration • Multimodal analgesia- ketamine, lidocaine and/or dexmedetomidine • Triple PONV Prophylaxis • Full neuromuscular blockade reversal Ensure awake, stable and comfortable with head elevated (Ramp) position
No OSA or treated and compliant	
Non-Central Obesity	
Non- Airway Surgery	
Others- Site Specific Inpatient Accessibility Social Factors	Postoperative Monitoring (ETCO2, RR, SpO2) Pain controlled with oral analgesics Discharge Criteria & Readmission information

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Cardiovascular Outcomes in Transcatheter Aortic Valve Replacement: Implications for Anesthesiology

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Transcatheter aortic valve replacement (TAVR) has revolutionized the management of aortic valve stenosis and redefined the paradigm of care in structural heart disease. This RCL will be presented in two portions. Part I outlines the recent advances in TAVR with a particular emphasis on neuroprotection (Dr John T Augoustides). Part 2 presents the data from two large meta-analyses published by our group. The first study focused on comparing the long term outcomes in TAVR versus surgical aortic valve replacement and the second meta-analysis compared outcomes following general anesthesia versus local anesthesia for TAVR (Dr Harish Ramakrishna).

Part 1: Neuroprotection after Transcatheter Aortic Valve Replacement

Since the first transcatheter aortic valve replacement (TAVR) was performed in 2002, this procedure has evolved into a mainstream therapeutic option to manage severe aortic stenosis. The indications for TAVR have gradually expanded from patients with excessive operative risk to low-risk patients with severe aortic stenosis. Despite the clinical progress, neurologic injury after TAVR remains a serious complication of TAVR. In prior landmark trials for balloon-expandable TAVR, the reported stroke incidences at 30-days in the inoperable, high-risk and intermediate-risk cohorts were 6.7%, 5.5%, and 6.4% respectively. The stroke risk, however, has steadily fallen to below 5% in the contemporary era. This steady reduction in stroke risk is likely attributable to multiple factors, including hardware refinements, and robust clinical experience of the heart team.

What causes Neurological Injury after TAVR?

In studying cerebrovascular events after TAVR, a temporal pattern has been established, with approximately one-half of events occurring within 48 hours of TAVR (early phase), an increased incidence within 30 days (delayed phase), and another increase at 1 year (late phase). This temporal distribution suggests varied causes of stroke, including procedural factors in the early phase and patient-related and postoperative treatment-related factors in the late phase. The etiologies of stroke after TAVR include procedural and non-procedural factors (refer to Table 1).

(i) Embolic Injury

Due to the calcific nature of the stenotic aortic valve and co-existing aortic atherosclerotic disease, the hardware manipulations during TAVR result in cerebral embolization as a routine with a risk of subsequent clinical stroke. The embolic material has been identified to consist of thrombus, calcium, tissue fragments and foreign material. The current evidence suggests that limiting embolization events may reduce the risk of stroke after TAVR.

Atrial fibrillation, especially new-onset atrial fibrillation, also increases the risk for stroke associated with TAVR. A meta-analysis (N = 14078: 26 clinical trials) reported from the TAVR population the incidences of chronic and new-onset atrial fibrillation to be 33.4% and 17.5% respectively. Furthermore, multiple trials have also demonstrated that atrial fibrillation significantly increased the risk of stroke after TAVR due to cerebral embolization.

(ii) Non-Embolic Etiologies

Non-embolic sources of cerebral injury during TAVR are primarily caused by hypotension with falls in cerebral perfusion. Severe hypotension can occur due to induction of general anesthesia, bleeding, valve positioning, and rapid ventricular pacing during valve intervention. Cardiovascular collapse may rarely occur as acute aortic regurgitation after valve deployment, coronary occlusion, aortic rupture, and acute aortic dissection. Fluctuations in cerebral perfusion pressure can lead to ischemic insult and also decrease washout of embolized material, exacerbating their effects. In contrast to cerebral hypoperfusion, acute hypertension following acute relief of aortic stenosis with valve deployment in TAVR can lead to cerebral hyperemia and hemorrhagic stroke.

Pre-existing factors such as chronic hypertension, history of stroke, carotid vascular disease, diabetes, chronic atrial fibrillation, and smoking may exacerbate the risk of stroke after TAVR. Furthermore, the current literature has also highlighted the following significant predictors for stroke after TAVR: female gender, chronic kidney disease, and new-onset atrial fibrillation. Significant procedural predictors for stroke after TAVR include total procedural time, total time the delivery catheter was in vivo, rapid ventricular pacing, valve repositioning, and level of heart

team experience (refer to Table 1). These collective risk factors for stroke after TAVR can be managed in a systematic perioperative fashion to minimize the stroke risk (refer to Table 2).

What are the Neuroprotective Strategies in TAVR?
(i) Possibilities in the Preoperative Phase
Baseline co-morbidities, including hypertension, hyperlipidemia, diabetes, smoking, and atrial fibrillation, should be optimized, given their roles in stroke risk. Furthermore, detailed high-quality imaging can facilitate the assessment of stroke risk factors such as aortic atheroma, aortic valve calcification severity, left atrial size (risk of atrial fibrillation), carotid vascular disease, and baseline cerebrovascular disease.

(ii) Possibilities in the Intraoperative Phase
(a) Heart Team Experience
A major factor in reducing intraoperative stroke risk during TAVR is the experience of the heart team performing the procedure. The stroke risk is reduced as centers gain experience due to factors such as reduced hardware manipulation within the aorta, and shorter procedural times. The maturation of alternative access routes for TAVR has offered the heart team viable options to avoid severely diseased aortic segments to minimize cerebral atheroembolism and subsequent stroke.

In the first decade of TAVR, general anesthesia was the anesthetic of choice. As the TAVR procedure has matured and heart teams have gained considerable experience, monitored anesthesia care has become a common anesthetic approach. The advantages of monitored anesthetic care include shorter procedural times, reduced intraoperative inotrope and vasopressor requirements, lower hospital costs, as well as shorter lengths of stay both in the intensive care unit and hospital. Furthermore, this technique allows for an earlier, more accurate neurological exam and perioperative surveillance.

(b) Embolic Protection
The convincing evidence for cerebral embolization during TAVR has prompted the development of devices to capture this debris before it reaches the cerebral circulation. The Embrella Embolic Deflector (Edwards Lifesciences, Irvine, California, USA) consists of two porous polyurethane petals within a nitinol frame that cover the right brachiocephalic trunk and left common carotid artery during TAVR deployment. The device is deployed through the right radial artery. The filters allow blood to flow through while particles larger than 100μm are deflected away from the protected vessels. Clinical trials have demonstrated reductions in both embolic events on transcranial Doppler and new embolic lesion volume on magnetic resonance imaging.

The Sentinel Cerebral Protection System (Claret Medical, Santa Rosa, California, USA) is the second generation of a device previously known as the Claret Montage Dual Filter System (Claret Medical, Santa Rosa, California, USA). The refined design included an improved delivery system and two independent filters that cover the right brachiocephalic trunk and left common carotid artery. Clinical trials demonstrated the safety and feasibility of this device, with reductions in both new cerebral lesions, clinical and neurocognitive deficits.

A recent prospective propensity-matched clinical trial (N = 802: 280 received the Sentinel device) demonstrated a significant reduction in clinical stroke associated with embolic protection from the Sentinel device (odds ratio 0.29; 95% confidence interval 0.1-0.93; P = 0.03). The composite endpoint of all-cause stroke and mortality was also significantly reduced in the embolic protection group (odds ratio 0.30; 95% confidence interval 0.12-0.77; P = 0.01).

The TriGuard Embolic Deflection System (Keystone Heart, Caesarea, Israel), deployed from the femoral artery, consists of a mesh filter that covers all three major arch vessels. Like the Embrella deflection system, this Triguard deflects debris into the descending aorta and away from the cerebral circulation. Unlike the previous two embolic protection devices, the Triguard protects all regions of the brain. A clinical trial demonstrated the safety of the device, and showed a non-significant decrease in new cerebral lesions and neurologic deficits compared to the control arm. Although non-significant, this is favorable trend has laid the groundwork for a larger clinical trial that is currently underway.

A recent meta-analysis (N = 1225) demonstrated a significant reduction in stroke risk in the first week after TAVR (relative risk ratio 0.56; 95% confidence interval 0.33-0.96; P < 0.05). A second meta-analysis demonstrated a significant reduction in new ischemic cerebral lesion burden. A third meta-analysis also demonstrated a significant reduction in clinical stroke at 30 days due to embolic protection during TAVR (odds ratio 0.55; 95% confidence interval 0.31-0.98; P = 0.04). Since these meta-analyses have combine data from smaller studies of different embolic protection devices, there is a considerable heterogeneity in the data.

Although embolic protection devices have yet to demonstrate a definite neuroprotective advantage, they have been adopted in clinical practice, given the favorable safety and efficacy. Thus, while the application of these devices is not yet a standard of care in TAVR, their deployment is safe and reasonable.

(iii) Possibilities in the Postoperative Phase
Since new-onset atrial fibrillation increases the risk for stroke after TAVR, its early detection and protocol-driven management are essential. Due to the thrombogenic nature of the TAVR procedure and prosthetic valve, optimal perioperative anticoagulation is necessary to prevent thromboembolism (refer to Table 2). While intravenous heparin is preferred for adequate intraoperative anticoagulation, such levels of anticoagulation may be unacceptable postoperatively due to the high risk of major bleeding. Dual antiplatelet therapy with aspirin and clopidogrel has been recommended to minimize the risks of valve thrombosis after TAVR. Recent meta-analysis has challenged this practice due to excessive bleeding risk (relative risk 2.52; 95% confidence interval 1.62-3.92; P < 0.0001) with no difference in stroke risk, suggesting that monotherapy may be adequate. In TAVR patients who take coumadin for atrial fibrillation, dual antiplatelet therapy has also not recommended due to the excessive risks of bleeding. Future trials will identify the nest antithrombotic strategy after TAVR, examining the options both for platelet blockade and the novel oral anticoagulants.

Part 2: Analysis of Meta-Analytic Data in TAVR
From humble beginnings in 2002 when Alain Cribier performed the first TAVR procedure under conscious sedation, TAVR has now established itself as the de-facto gold standard for the management of aortic stenosis, this has largely been aided by landmark trials such as the PARTNER trial (for the Edwards balloon expandable valve) which indicated superiority over conservative management and non-inferiority to AVR for 1-year mortality in high-risk patients with Society of Thoracic Surgeons (STS) 30 day mortality scores of 11.6% and 11.8%, respectively. Particularly when compared with medical management in the high risk cohort, the 1 year mortality was dramatically reduced from 50.7% to 30.7%- a significant 20% absolute risk reduction. Subsequently the PARTNER 2 trial indicated that in intermediate risk patients with an STS score of 5.8%, TAVR was non-inferior to surgery for death/disabling stroke at 2 years. The self-expanding Medtronic CoreValve was also tested against AVR in high surgical risk patients in the US Corevalve study with an STS score of 7.4% and a 1-year mortality benefit was seen for TAVI over AVR. It is within this milieu that our cardiovascular outcomes research group decided to comprehensively study TAVR vs SAVR outcomes and we have published 2 large meta-analyses to this effect For the first meta-analysis we sought to determine the long-term (≥1 year follow-up) safety and efficacy TAVR compared with SAVR in patients with severe AS. Fifty studies enrolling 44,247 patients met the inclusion criteria. The mean duration follow-up was 21.4 months. No difference was found in long-term all-cause mortality (risk ratios (RR), 1.06; 95% confidence interval (CI) 0.91–1.22). There was a significant difference favoring TAVR in the incidence of stroke (RR, 0.82; 95% CI 0.71– 0.94), atrial fibrillation (RR, 0.43; 95% CI 0.33–0.54), acute kidney injury (RR, 0.70; 95% CI 0.53–0.92), and major bleeding (RR, 0.57; 95% CI 0.40–0.81). TAVR had significant higher incidence of vascular complications (RR, 2.90; 95% CI 1.87–4.49), aortic regurgitation (RR, 7.00; 95% CI 5.27–9.30), and pacemaker implantation (PPM) (RR, 2.02; 95% CI 1.51–2.68). TAVR demonstrated significantly lower stroke risk compared to SAVR in high-risk patients (RR, 1.49; 95% CI 1.06–2.10); no differences in PPM implantation were observed in intermediate-risk patients (RR, 1.68; 95% CI 0.94–3.00). In a meta-regression analysis, the effect of TAVR baseline clinical features did not affect the long-term all-cause mortality outcome The second meta-analysis had the goal of studying the comparative outcomes of LA and GA for patients with severe aortic stenosis undergoing TAVR. Twenty-six studies and 10,572 patients were included in the meta-analysis. The use of LA for TAVR was associated with lower overall 30-day mortality (RR, 0.73; 95% CI, 0.57–0.93; P<0.01), use of inotropic/ vasopressor drugs (RR, 0.45; 95% CI, 0.28–0.72; P<0.001), hospital length of stay (LOS) (DM, 22.09; 95% CI, 23.02 to 21.16; P<0.001), intensive care unit LOS (DM, 20.18; 95% CI, 20.31 to 20.04; P<0.01), procedure time (DM, 225.02; 95% CI, 232.70 to 217.35; P<0.001); and fluoroscopy time (DM, 21.63; 95% CI, 23.02 to 20.24; P<0.02). No differences were observed between LA and GA for stroke, cardiovascular mortality, myocardial infarction, permanent pacemaker implantation, acute kidney injury, paravalvular leak, vascular complications, major bleeding, procedural success, conduction abnormalities, and annular rupture. We concluded that use of LA for TAVR is associated with a lower 30- day mortality, shorter procedure time, fluoroscopy time, ICU LOS, hospital length of stay, and reduced need for inotropic support. An updated meta-analysis on the same subject published in 2018 reinforced these findings.

The innovations in technology and science will ensure that transcatheter procedures are indeed the definitive component of the therapeutic armamentarium in structural heart disease. The key issues that will remain to be resolved include transcatheter valve thrombosis, paravalvular leak, biocompatibility, durability, rhythm disorders, prevention of stroke/transient ischemic attack and optimal antithrombotic management. In addition the ongoing low risk trials and emerging transcatheter solutions for bicuspid valve disease and aortic regurgitation will continue to create an increasing impact on our specialty and reinforce the increasing importance of the cardiovascular anesthesia specialist.

Table 1: Etiologies of Stroke after Transcatheter Aortic Valve Replacement

Procedural Factors: Atheromatous and Calcific Emboli	Catheter manipulation within an atheromatous thoracic aorta Hardware manipulation across a calcific aortic valve Balloon inflation events Valve deployment
Procedural Factors: Alternative Emboli	Air embolism Thromboembolism
Procdural Factors: Variations in Perfusion	Watershed ischemia due to hypoperfusion Acute hypertension after valve deployment
Non-Procedural Factors	Female Gender Atrial fibrillation Prior stroke Diabetes Chronic Kidney Disease Atheromatous arterial disease Chronic hypertension

Adapted from Reference 157: Patel PA, Patel S, Feinman JW, et al: Stroke After Transcatheter Aortic Valve Replacement: Incidence, Definitions, Etiologies and Management Options. Journal of Cardiothoracic and Vascular Anesthesia 32:968-81

Table 2: Strategies for Neuroprotection in Transcatheter Aortic Valve Replacement

Preoperative Strategies • Optimize modifiable risk factors – hypertension, hyperlipidemia, smoking, diabetes, and atrial fibrillation • Detailed imaging studies – atheroma severity, aortic valve calcium • Appropriate patient selection by the heart team
Intraoperative Strategies • Experienced heart team – procedural skill and efficiency • Optimal anesthetic management • Embolic protection devices • Adequate perioperative anticoagulations • Maintain cerebral perfusion
Postoperative Strategies • Aggressive management of atrial fibrillation • Optimize antithrombotic and/or anticoagulation • Rapid diagnosis of stroke • Prompt referral for medical and/or interventional stroke treatment

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Emergency General Surgery, the Elderly and Non-Beneficial Surgery: The Problems, Solutions and Outcomes

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Learner Objectives

After participating in this activity, the learner will be able to:

1. Assess how to improve care for elderly patients in their hospital;
2. Assess and measure outcomes for emergency general surgery;
3. Implement a care bundle that has been proven to reduce mortality for emergency general surgery.

INTRODUCTION

Aging

The world population is ageing. This will be one of the most significant transformations of the 21st century with impact in nearly all sectors of society. Globally, population aged 60 or over is growing faster than all younger age groups and is expected to more than double by 2050: from 962 million globally in 2017 to 2.1 billion in 2050 and 3.1 billion in 2100.[1]

In the U.S. the population age 65 years or older numbered 47.8 million in 2015 which accounts for approximately 15% of the U.S population or about one in every 7 Americans.2 This was an increase of 30% since 2005, compared with an increase of only 5.7% for the under-65 population.[2]

A child born in 2015 could expect to live 78.8 years, more than 30 years longer than a child born in 1900 (47.3 years). This is mainly due to reduced infant mortality rates. However, there has also been a reduced death rate for people aged 65-84.[2]

There is no "typical" older person. The resulting diversity in the capacities and health needs of older people is not random, but rooted in events through life, that can often be modified. Though most older people will eventually experience multiple health problems, older age does not imply dependence.[3]

In hospital, assessing each older person individually, and measuring elements such as frailty, mental test scores, co-morbidities and level of independence is key to assessing risk, stratifying services and enabling speedy discharge.

Emergency General Surgery

Emergency general surgery (non-traumatic) carries a significant mortality. In the UK this is approximately 11%[4] but is higher in the USA and the rest of Europe at approximately 15-20%.[5,6] In addition, patients over the age of 70 years confer an even higher mortality. In the UK this is estimated at 20%, but some UK centres are reporting mortality rates of up to 50% for this cohort of patients.[4,7]

In the UK, the current standard of care for an older patient being admitted for emergency general surgery is that their complete care is delivered by the admitting surgical team; from the emergent surgery to the post-operative care afterwards.

If the patient needs gerontology support; for example in the form of medication reviews or to plan discharge to rehabilitation hospitals, this is done in a reactive manner, i.e. when it becomes apparent that the patient requires the additional support rather than proactive care, when the patient is admitted.

There are certain areas of specialty where proactive care by gerontologists occur and care for the patient is shared by the surgical team as well as the gerontology team. This is mainly in emergency orthopaedic care; with patients suffering from fractured neck of femurs. This level of care has been extended to elective orthopaedic care at certain hospitals.[8]

Four hospitals in England were funded to proactively care for older patients over the age of 70 undergoing emergency general surgery.

Specific data was collected on these patients that is not collected by the National Audit. This included measuring preoperative frailty scores[9], where patients were admitted from/to, abbreviated mental test scoring, pain scores post surgery and Post Operative Morbidity Scoring data for complications.[10] Length of stay and 30-day mortality was also collected. The patients were also followed up with a phone call up to 6 months after hospital discharge. Prospective data was collected with standard care being delivered i.e. with no gerontology input, and afterwards, when gerontology review was taking place.

Non-beneficial surgery

The mortality rate from emergency laparotomy in the UK is approximately 11%. If those 11% of deaths are examined further, it becomes apparent that 40% of those patients die within the first three days of undergoing surgery.

Groups of patients at high risk of mortality after emergency surgery has been identified, and include elderly patients with multiple co-morbidities, existing cognitive impairment and frailty.[11]

Can we offer holistic care for older patients undergoing emergency general surgery, given that these patients are already deemed high risk and can we adequately identify those patients where the treatment burden is greater than the benefit?

RESULTS

The average 30-day mortality rate was 11% for patients undergoing emergency general surgery over the age of 70.

Preoperative average frailty scores in both groups using the 9-point Rockwood scale was 4; 'Vulnerable.'

Interestingly, in standard baseline care, approximately 25% of patients were reviewed on average, at least once by a gerontologist as reactive care.

The results show that the average length of stay decreased from 24 days with standard, baseline care to 20 days with implementation of a gerontologist.

The range also decreased from 1-130 days at baseline to 1-64 days with implementation. This has a direct effect on hospital costs.

CONSLUSION AND SUMMARY

Holistic care for patients with complex needs can be beneficial in reducing long stays in hospital and potentially complications. It has been shown that older patients undergoing a Comprehensive

Geriatric Assessment (CGA) in the Emergency Department can decrease readmissions into hospital.[12]

Is it time for gerontologists to take more of a central role in the perioperative care of older emergency surgical patients?

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Pain Outcomes, Patient Registries and Learning Health Systems: Delivery of Best Pain Care at Lower Cost

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INTRODUCTION

Pain is a subjective experience; therefore, unlike many other chronic diseases, there is no single objective measurement to best characterize the extent of the problem or to evaluate treatment outcomes. Measuring a patient's pain means putting together objective data with the patient's subjective reports to create a comprehensive view of the pain state. Complicating the measurement of pain is the fact that there is often a wide variability in how much pain a given stimulus or injury will cause. This variability is influenced by genetics, mood, beliefs, early life experiences with pain, gender, ethnicity, and other factors.[1]

Chronic pain is often associated with an overall reduction in the patient's quality of life and may cause depression, anxiety, impaired social and physical function, and sleep disturbance. Therefore, to best capture the pain experience and its impact, it is necessary to also define and characterize these related domains.

Why is it important to measure pain in a standardized and accurate way? Evidence-based medicine relies on testing treatments, and uses the outcomes of those tests to support clinical decision-making. The outcomes are also used to convince colleagues, patients, and payers of the most efficacious treatments. Standardization of outcome reporting will allow for comparison of treatments, and the systematic review of the studies that already exist to help answer the most pressing questions in the field of pain.

CONSIDERATIONS IN SELECTING AN OUTCOME MEASURE

Any tool used to measure pain should be appropriate for the clinician and patient needs. It is of little use, for example, to have a patient fill out multiple forms if the provider lacks the staff or infrastructure to utilize the data. In defining a standard set of outcome measures, the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) consortium granted most weight to the following criteria[2]:

a) Reliability—The instrument should demonstrate test-retest, inter-rater and internal reliability.
b) Validity—The scale should measure what it is intended to measure.
c) Responsiveness—The scale must display the ability to detect changes over time and to distinguish between treatments.
d) Appropriateness—The scale's content should be in keeping with the measured outcome and relevant to the patient population being studied.
e) Burden—The scale should be easy to administer, complete, and score.

UNIVARIABLE MEASURES

Unidimensional scales measure pain as a single quality varying only in intensity. These methods are most effectively used in clinics and acute settings. Examples include:

Verbal Rating Scale

The Verbal Rating Scale (VRS) consists of a series of categorical descriptors ordered in increasing intensity (i.e., none, mild, moderate, severe). The advantages of the VRS are that it is easy to administer and report, particularly for elderly patients.[3] Disadvantages are that it has fewer response choices and the categorical options limit statistical analysis. It has demonstrated ability to distinguish treatment effect, test-retest reliability, and convergent validity.[4]

Visual Analog Scale

The Visual Analog Scale (VAS) is typically a 10-cm line anchored with "no pain" at one end and "worst pain" at the other. The patient marks a point on the line, and the clinician measures the length of the line on a 101-point scale.[5] The advantages of the VAS are that there is good evidence for responsiveness, validity, and test-retest reliability, and scores can be treated as ratio data.[6] The limitations are that it can be time-consuming, and elderly people may have difficulty using the scale.[7]

Numerical Rating Scale

The Numerical Rating Scale (NRS) is the most frequently used univariable instrument. It consists of a rating scale from 0 to 10 (or 0 to 100 in some versions). Patients may respond verbally or by circling the appropriate number. It demonstrates sensitivity to change and test-retest reliability, and correlates well with other measures of pain intensity.[8] The NRS is recommended by IMMPACT as a core domain measure for future chronic pain clinical trials.[9]

Patient Global Impression of Change

The Patient Global Impression of Change (PGIC) represents an attempt to capture pain improvement more broadly using a single item measure. The patient is asked to rate their current status compared to a prior time point

(e.g. very much improved). This scale is applicable to many conditions and treatments but lacks sensitivity.[10] It is recommended by IMMPACT as a core domain measure and can be particularly helpful in gauging the clinical importance of changes.[11]

EMOTION MEASURES

Clearly, there is a relationship between pain and emotional distress; there is also evidence of relative independence. Measurements of depression include the Patient-Reported Outcomes Measurement Information System (PROMIS) Emotional Distress – Depression Item Bank.[12] Beck Depression Inventory (BDI),[13] Zung Self-Rating Depression Scale,[14] and Hamilton Rating Scale for Depression.[15] Anxiety and fear measures include the PROMIS Emotional Distress–Anxiety Item Bank,[16] Pain Anxiety Symptoms Scale,[17] State-Trait Anxiety Inventory,[18] and Fear-Avoidance Beliefs Questionnaire (FABQ).[19]

MULTIDIMENSIONAL MEASURES

Chronic pain requires a more comprehensive assessment than a univariable or single-domain measure can provide. Multidimensional measures often combine several dimensions of pain, disability, emotional affect, and effect on quality of life into a single instrument. Commonly used scales include:

Brief Pain Inventory

The Brief Pain Inventory (BPI) was developed to measure both the intensity of pain and the interference it has in the patient's life.[20] The BPI consists of a 17-item scale that typically takes under 15 minutes to complete. The BPI Interference Scale, in particular, has been validated as a measure of physical functioning in multiple domains and is recommended by IMMPACT as a core health related quality of life measure.[21]

McGill Pain Questionnaire

The McGill Pain Questionnaire (MPQ) was developed to specify the qualities of pain.[22] Pain is scaled in three dimensions (sensory, affective, and evaluative) with 20 sets of words for each dimension. A four-point scale accompanies each word, and for each term, users chose where on that scale they fall. Multiple studies have supported the reliability and validity of the MPQ for specific pain syndromes.[23] The Short-Form McGill Pain Questionnaire (SF-MPQ) was developed for research purposes and consists of 15 words from the sensory and affective categories, with a four-point rating scale for each. It results in a pain intensity VAS score and overall assessment of pain VRS score.[24]

West Haven-Yale Multidimensional Pain Inventory

The West Haven-Yale Multidimensional Pain Inventory (WHYMPI) best assesses adaptation to chronic pain.[25] It can yield clinically useful information regarding pain coping styles. It is composed of 52 items with 12 subscales. Patients respond to the questions on a seven-point scale. The WHYMPI interference scale correlates with physical functioning and is recommended by IMMPACT as an alternative to the BPI.[26]

Medical Outcome Study 36-Item Short-Form Health Survey and Treatment Outcomes of Pain Survey

The 36-Item Short-Form Health Survey (SF-36) is a frequently used measure of function and quality of life.[27] It consists of eight subscales, and while widely used, it features only two questions related to pain and there are concerns about insensitivity to change when measuring an individual patient.

The Treatment Outcomes of Pain Survey (TOPS) is an extension of the SF-36 specifically designed for patients with chronic pain.[28,29] It consists of 120 items with a 61-item follow-up. It has been found to be sensitive to change and have good validity.

OBJECTIVE MEASURES

Several physiologic variables have been suggested as surrogates for pain, including autonomic activity,[30,31] or biomarkers of pain intensity.[32] Caution with interpreting these peripheral measures is urged, as they can be influenced by arousal other than pain and can be modulated by medications. Physical function tests, such as range of motion and strength, have also been used as proxies for pain;[33,34,35] however, these only modestly predict self-reported pain scores. More recently, attempts to objectively measure pain have focused on using neuroimaging. Indeed, recent studies suggest that brain imaging can be used to objectively distinguish evoked painful stimuli[36] and the presence of chronic low back pain.[37] Despite these promising early reports, there is still much research to be done to validate its use. Furthermore, given the expense and time involved, it is more likely that neuroimaging will primarily be used to help guide further research and understanding of the brain mechanisms involved in pain. All of these data reinforce the complexity of pain and as such, it is unlikely that an objective measure for pain will soon emerge.

CLINICAL TRIALS AND OUTCOMES DATA

The need to document data that will guide and justify appropriate pain treatments has resulted in efforts to define and standardize outcome measures for pain and similar, related disease states. IMMPACT defined six core outcome domains that should be considered when designing clinical trials.[38] IMMPACT went on to define specific validated measures for each of the core outcome domains in IMMPACT-II.[39]

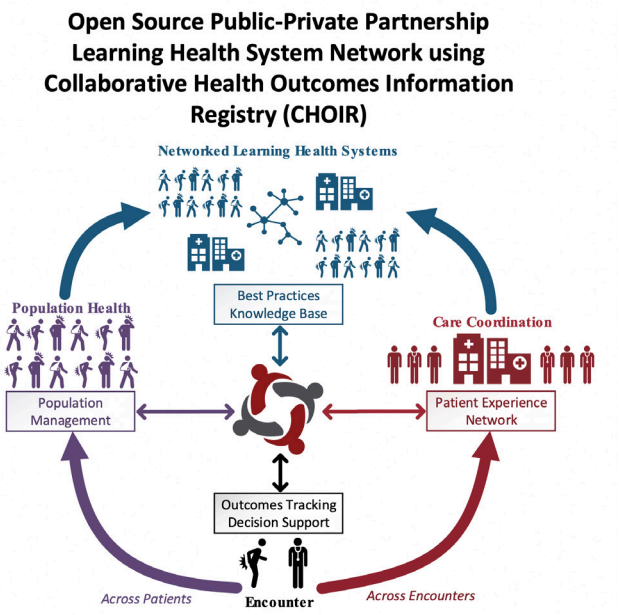
LEARNING HEALTH SYSTEMS AND PRECISION PAIN MEDICINE

Despite an increase in the number of available pain therapies, more than 100 million people in the U.S. still live with pain. Little is known about which treatments are best for which patient, or even about the efficacy and safety of various treatments over time. In recognizing this problem, the IOM Pain Report called for "greater development and use of patient outcome registries that can support point-of-care treatment decision making, as well as for aggregation of large numbers of patients to enable assessment of the safety and effectiveness of therapies." Coinciding with this call for patient registries is the recognition that Learning Health Systems (LHSs) are an important aspect of the future of medicine.[40] The core features of LHSs[41] combine science, informatics, incentives and culture that are then aligned for continuous improvement and innovation. The Institute of Medicine recently extolled the virtues of LHSs, and in 2013 the National Science Foundation convened a workshop where it was declared that LHSs can rapidly inform decisions that have transformative effects on improving health.[42]

The Collaborative Health Outcomes Information Registry (CHOIR; http://CHOIR.stanford.edu) is one LHS developed to collect information on pain patients and the effectiveness of therapies. The military has also developed a system to address this need, called Pain Assessment Screening Tool and Outcomes Registry (PASTOR).[43] The rest of this discussion will use CHOIR as a model platform. CHOIR is an open source, open standard, free, secure, electronic, LHS designed to capture detailed, longitudinal patient-reported outcomes data on physical, psychological, and social health. CHOIR was developed to: inform point-of-care decision making, provide software-based decision making, and act as a platform for (1) comparative effectiveness research, (2) longitudinal outcomes research, and (3) practice-based evidence trials.

CHOIR also integrates NIH Patient Reported Outcomes Measurement Information System (PROMIS) measures to efficiently and rapidly capture 15-20 domains of physical, psychological and social functioning. The role that psychological and social factors play in the incidence, magnitude, and persistence of pain, as well as the associated costs of care, have increasing come to light. At the same time, there has been a demand to measure and monitor psychological and social factors in order to better manage these complex diseases. An additional strength of PROMIS measures is that they allow comparisons of individual patients against national population norms.[44,45]

CHOIR was developed to allow for low-cost, large, prospective, observational studies on thousands of



patients in a "real-world" clinic setting. In addition to the broad research utility of CHOIR, the system provides computer-assisted documentation, which has proven indispensable and invaluable in delivering comprehensive, targeted interdisciplinary pain treatment. The platform is designed to be customizable to different settings (inpatient and ambulatory), providers, and disease conditions. CHOIR provides rapid real-time, longitudinal feedback to clinicians regarding standardized quantitative outcomes to guide decision-making regarding various treatments. Standardized data capture can be included as part of ongoing, routine management. CHOIR, and other LHSs, have the potential to address many fundamental questions regarding pain treatment and efficacy, and will allow for further characterization of optimal patients for specific therapies.[46,47] Testing of CHOIR has shown that it reduces patient response burden by as much as 75% as compared to using traditional measures. This reduced burden, in turn, has been shown to facilitate continued patient participation.

While evidence-based medicine is the standard for supporting clinical-decision making, the paucity of prospective, placebo-controlled randomized trials in pain medicine has generated an urgent need to accurately and consistently measure relevant patient outcomes with the goal of defining the most safe and effective treatments. There is also a need to standardize the assessment and reporting of outcomes to allow for comparison across studies and different patient populations. In addition to prospective, placebo-controlled randomized trials, which can be difficult to generalize due to participant homogeneity, and require a large amount of resources

(due to sample size), systematic practice-based evidence may provide more useful data in the form of prospective, observational, cohort studies.[48]

President Obama called for a Precision Medicine Initiative. Precision medicine is an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person. While the near-term focus of precision medicine has been on cancers, the long-term aim is to apply this knowledge to the whole range of health and disease – including pain management.[49] This effort will require a further advances in molecular biology, 'omics (e.g. genomics, metabolomics, proteomics), and bioinformatics. LHSs will play a significant role in integrating this systems-based information in order to derive accurate prevention and treatment recommendations. These LHSs and precision pain medicine are within our grasp. Successful implementation will ultimately realize the call by the IOM Relieving Pain in America Report to provide everyone with the best pain assessment, prevention and treatment.

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Patient Selection for Ambulatory Surgery: Can Any Patient Be an Outpatient?

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Learner Objectives

After participating in this activity, the learner will be able to:

1. Understand the importance of patient selection for ambulatory surgery
2. Describe the approach to determining patient selection for ambulatory surgery
3. Justify appropriate selection of challenging adult patients scheduled for day surgery
   a. High comorbidity burden, older age, morbid obesity, obstructive sleep apnea (OSA), cardiovascular disease (e.g., myocardial ischemia/infarction, cardiac implantable electronic devices [CIED], coronary stents), pulmonary disease, previous stroke/transient ischemic attack (TIA), diabetes mellitus (DM), malignant hyperthermia (MH) susceptibility
4. Emphasize the need for developing procedure specific inclusion/exclusion criteria for patient selection

Introduction

For day surgery to be safe and efficient, careful selection of procedures and patients is crucial. However, there is an uncertainty amongst anesthesiologists, who must determine patient suitability for ambulatory surgery. Identifying suitability for an ambulatory surgery is a dynamic process that depends on a complex interplay between the surgical procedure, patient characteristics, expected anesthetic technique (e.g., sedation/analgesia, local/regional anesthesia, and general anesthesia), and social factors. In addition, the ambulatory setting (i.e., short-stay [23-h stay], hospital-based ambulatory center [HOPD], free standing ambulatory center [ASC], and office-based surgery) may also influence the ability to manage complex patients based upon the availabilities of personnel and equipment. Also, admission from HOPD is easily facilitated, whereas transfer from an ASC or office-based facility requires transport in an ambulance and potential delay in early initiation of treatment.

Several studies have analyzed large administrative and/or clinical databases such as Medicare database, the American College of Surgeons' National Surgical Quality Improvement Program (ACS-NSQIP) database and the State Ambulatory Surgery and Services Databases (SASD) to determine the predictors of postoperative adverse outcomes (e.g., complications rates, unplanned hospital admission rates and 30-day readmission rates). These predictors (e.g., age, weight, burden of comorbidity) have been used to determine suitability of a surgical procedure in an ambulatory setting. Despite several limitations, these studies can be used to guide clinical decision-making regarding patient selection.

Surgical Procedure

Surgical procedure-related factors that may influence perioperative outcomes include invasiveness of the procedure, duration of surgery, potential blood loss and need for blood transfusion (intraoperative and/or postoperative), degree of postoperative pain, and need for specialized postoperative care including postoperative parenteral therapy. With improvements in surgical techniques such as minimally invasive approach, the use of tranexamic acid (TXA), and improved analgesics techniques, surgical procedures that were considered inappropriate (e.g., major joint replacement surgery) are increasingly being performed in an outpatient setting.

Patient Characteristics

Patient characteristics that can influence patient selection include comorbidity burden (ASA physical status), age, obesity, sleep-disordered breathing (e.g., OSA), cardiovascular disease (e.g., heart failure [HF], myocardial infarction [MI], severe valvular disease, atrial fibrillation [AF], significant coronary stents, and CIED), pulmonary disease (e.g., reactive airway disease-asthma and COPD exacerbation), pulmonary hypertension, kidney insufficiency/failure, cerebrovascular disease (TIA/CVA), bleeding disorders, poorly controlled diabetes mellitus (DM), significant hepatic disease (e. g., Childs C), sickle cell disease/trait, neuromuscular disease (e.g., quadriplegia, peripheral motor neuron disease, myasthenia gravis), known or suspected difficult airway, MH susceptibility, cognitive function (e.g., mentally challenged patients, inability to patients to care for themselves postoperatively), psychiatric illness, chemo-/radiation therapy, treatment for substance abuse (e.g., buprenorphine), acute drug/alcohol intoxication, and pregnancy.

Burden of Comorbid Conditions

There is a general agreement that patients with a high burden of comorbidities, particularly those with poorly stabilized medical conditions (i.e., American Society of Anesthesiologists [ASA] physical status >3) are not suitable for ambulatory surgery, particularly if the surgical procedure requires administration of general anesthesia.

Examples for patients considered as ASA physical status 4 (i.e., not suitable for ambulatory surgery) include recent (<3 months) MI, drug eluting coronary stents, cerebrovascular disease (TIA/CVA), new onset or unstable angina, new onset or decompensated heart failure, severe valve dysfunction, high grade AV block, acute respiratory disease, end stage renal disease not undergoing regular dialysis, sepsis, and disseminated intravascular coagulation[1].

Age

Although older patients may have higher burden of comorbidities, age alone should not be used to determine suitability for ambulatory surgery[2]. In recent years it is recognized that functional impairment, cognitive impairment, and frailty, were associated with increased postoperative complications[3]. In fact, frailty is associated with increased perioperative morbidity, independent of age, anesthesia type, and comorbidities. Therefore, it is recommended that frailty rather than age should be considered when selecting patients for ambulatory surgery[4].

Obesity

Several studies have identified an association between obesity and adverse postoperative outcomes[5]. Therefore, weight (or BMI) limit is commonly used as an exclusion criterion for patient selection. Several studies have reported that the super obese (i.e., BMI >50 kg/m2) have higher incidence of postoperative complications[6,7]. Therefore, this patient population should be chosen carefully, particularly if general anesthesia is necessary. In contrast, patients with BMI <40 kg/m2 may be suitable for ambulatory surgery assuming that their comorbid conditions, if any, are optimized[7]. For patients with BMI between 40 and 50 kg/m2, a thorough preoperative assessment is necessary to identify obesity-related comorbid conditions (e.g., OSA, obesity-related hypoventilation syndrome, and pulmonary hypertension, as well as resistant hypertension, coronary artery disease, and HF)[8,9].

Obstructive Sleep Apnea

Because OSA is a part of a spectrum of diseases such as COPD, DM, AF, and HF, it should be considered in isolation, but in relation with the severity of associated comorbidities[10]. Also, mild OSA with low risk for comorbidities is associated with low perioperative risk. Several studies in hospitalized patients have reported a higher risk of perioperative complications in OSA patients. However, studies in the ambulatory surgical population have not been able to show a increase in complications. The Society for Ambulatory Anesthesia (SAMBA) consensus statement recommends that patients with a known diagnosis of OSA, who are typically prescribed positive airway pressure [PAP] therapy, may be considered for ambulatory surgery if their comorbid medical conditions are optimized and they are able to use a PAP device in the postoperative period[9]. If the patients are unable or unwilling to use PAP device after discharge should be treated as those in presumed OSA diagnosis category (diagnosis based on screening tools such as the STOP-Bang). This category of patients can be considered for ambulatory surgery if their comorbid conditions are optimized and if postoperative pain relief can be provided predominantly with non-opioid analgesic techniques. The SAMBA consensus statement did not provide any guidance for OSA patients undergoing upper airway surgery due to limited evidence. However, recent studies suggests that airway surgery performed on outpatient basis is generally safe and routine hospital admission is not necessary, except for patients undergoing combined surgical procedures, tongue base surgery, those with a higher preoperative apnea/hypopnea index, or those with high postoperative opioid requirements[11].

Cardiovascular Disease

Ambulatory surgery carries a low (<1%) risk of perioperative cardiac complications (i.e., MI or cardiac arrest (MICA)])[12]. The risk of MICA can be calculated by using a cardiac risk calculator that incorporates patient variables (i.e., age, ASA physical status, functional status, and preoperative serum creatinine) and surgical procedure[13,14]. Several studies have reported that patients with HF and AF are at a higher risk of perioperative complications than those with coronary artery disease[15]. Patients with symptomatic (e.g., fatigue, dizziness, lightheadedness, syncope, palpitations, chest pain or tightness, and shortness of breath) new onset AF may not be suitable for ambulatory surgery. Patients with CIED may be at risk of perioperative arrhythmia and asystole. Also, in the case of implantable cardioverter defibrillators (ICD) there is a concern that electromagnetic interference may be misinterpreted as an arrhythmia leading to inappropriate shock[16]. It is recommended that patients with CIED may safely undergo ambulatory surgery assuming that appropriate equipment and support is readily available[16]. Another challenging group of patients include those with coronary artery stents. It is recommended that patients with acute percutaneous cardiac intervention (PCI) or bare metal coronary stents (BMS) should have their elective surgery delayed for 30 days, while those with newer (second and third generation) drug eluting stents (DES) should have their elective surgery delayed for 6 months[17]. Overall, elective surgery should be postponed until the patient is on dual antiplatelet therapy. If necessary, consultation with the patient's cardiologist and the surgeon is recommended to address issues such as timing of surgery, management of anticoagulation, and other potential risk reduction strategies. Because urgent

PCI is the best management for acute perioperative stent thrombosis, access to interventional cardiology should be considered in the selection criteria for higher risk patients seeking ambulatory surgery.

Pulmonary Disease
Patients with reactive airway diseases such as asthma and COPD can be challenging. However, well-controlled asthma or COPD does not seem to increase risk for perioperative complications.

Previous stroke/TIA
The timing of elective surgery in patients with history of stroke/TIA remains controversial. Elective surgery is generally avoided within 3 months of stroke/TIA. A large observational trial suggests that there is a higher risk of postoperative MACE if the surgical procedure is performed within 9 months of stroke/TIA. Interestingly, low- and intermediate-risk surgical procedures pose the same relative risk of MACE compared with high-risk surgical procedures. After 9 months, the associated risk stabilized, although it was higher in this patient population compared with patients with no stroke[18,19].

Diabetes Mellitus
For DM patients with high preoperative blood glucose level (BGL), anesthesiologists face a dilemma with regards to deciding the BGL above which elective surgery should be postponed. The recommendations from SAMBA state that it may be acceptable to proceed with surgery in patients with preoperative hyperglycemia but with adequate long-term glycemic control, barring any significant complications of hyperglycemia such as ketoacidosis and hyperosmotic states[20]. In patients with chronically poorly controlled diabetes mellitus, the decision to proceed with ambulatory surgery should be made in conjunction with the surgeon and take into account patient comorbidities and the risks of surgical complications.

Malignant Hyperthermia
A recent position statement from SAMBA and the ASA Ambulatory Surgical Care Committee states that MH susceptible patients can safely undergo a surgical procedure in an free-standing ambulatory surgery center as long as the patient is administered a trigger-free anesthetic. Preoperative dantrolene prophylaxis not indicated. Also, point-of-care blood gas analysis not needed. Also, there is no need for extended postoperative observation.

Summary
As older and sicker patients undergo more complex surgical procedures in an ambulatory setting, patient selection has become the cornerstone of safe and efficient perioperative care. Rather than considering the factors in isolation, the interaction of patient comorbid conditions, the planned surgical procedure and anesthetic technique, should be considered. Developing and implementing protocols (or clinical pathways) for patient selection is the best way to improve patient safety. Overall, it is better to develop procedure specific exclusion criteria, rather than inclusion criteria, for patients that are not candidates for ambulatory surgery.

The first step in determining appropriate patient selection includes preoperative assessment and identification of any comorbid conditions, which should be optimized to minimize risks. In addition, assessment of functional status and frailty would add to patient safety. The social situation should be evaluated to determine whether the patient has help at home for postoperative care. Education of the patients and their caregivers regarding the need for increased vigilance after discharge home is critical. Outpatients should be capable of understanding instructions for pre- and postoperative care, and should be accompanied home by a responsible escort. Someone should also be available to care for the patient during the first night after surgery and be able to assist them in obtaining emergency medical care if needed.

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Perioperative Medicine and Enhanced Recovery: Current State and Future Directions

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Learner Objectives

After participating in this activity, the learner will be able to:

1. Understand the changing healthcare landscape and the importance of embracing perioperative medicine.
2. Discuss key components in adult and pediatric ERAS protocols.
3. Demonstrate the outcomes and value of the enhanced recovery strategy
4. Discuss implementation strategies including resource allocation for the protocols.

Abstract

Enhanced recovery After Surgery (ERAS) are multimodal perioperative care pathways designed to attenuate the stress response during the patients' journey through a surgical procedure, facilitate the maintenance of preoperative bodily compositions and optimize organ function, and in doing so achieve early recovery. ERAS integrate a range of perioperative interventions to maintain physiologic function and facilitate postoperative recovery.[1] Pathways are not limited to adult patients, with emerging evidence in the adolescent, young child, infant, and neonatal populations. Concepts unique to pediatric ERAS protocols are described in separate, later sections.

Successful implementation of ERAS pathways requires collaboration between surgery, anesthesia, perioperative nursing to provide optimal perioperative care as well as having the support of hospital administration. Anesthesiologists play a vital role in facilitating recovery because they routinely manage some of the key elements of ERAS (i.e., preoperative assessment and patient education, perioperative fluid management, short acting anesthetic agents, optimal multimodal analgesia, prevention of postoperative nausea and vomiting (PONV) and other opioid related side effects as well as close monitoring during surgery.

Preoperative Nutrition

Sub-optimal nutritional status is a strong independent predictor of poor postoperative outcomes.[2] Malnourished surgical patients have significantly higher postoperative mortality, morbidity, length of stay (LOS), readmission rates, and increased hospital costs. As defined by the National Surgical Quality Improvement Program (NSQIP), malnutrition is among the few modifiable preoperative risk factors associated with poor surgical outcomes, including mortality, in surgical patients. Further, appropriate perioperative nutritional therapy has been shown to specifically improve perioperative outcomes in GI/oncologic surgery, where the greatest risk of baseline malnutrition risk (~65%) occurs. Postoperative nutritional support is vital in maintaining nutritional status during the catabolic postoperative period and underscored by evidence for early and sustained feeding following surgery as part of ERP protocols. In fact, the advancement of oral intake has been identified as an independent determinant of early recovery following colorectal surgery.[3]

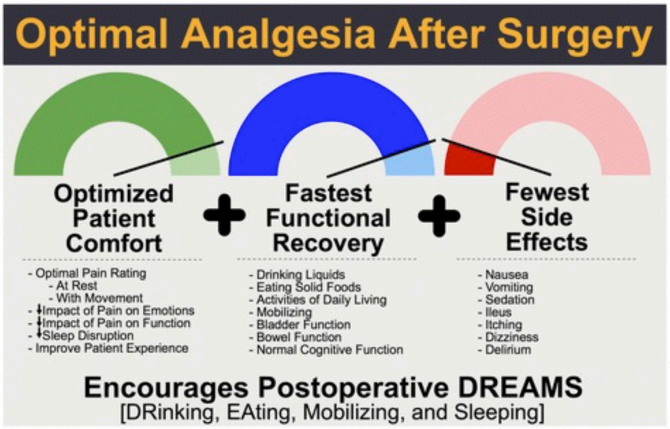
Management of Postoperative Pain

Rationale for Multimodal Analgesia

The ideal analgesic regimen would provide effective pain relief, reduce opioid related side effects and surgical stress response and improve clinical outcome e.g. morbidity, mortality and hospital stay. The concept of multimodal analgesia was introduced to achieve these goals by combining various analgesic techniques and different classes of drugs to improve postoperative outcome.[4] However, available data are conflicting and do not necessarily resulted in improved outcome and concomitant reduction in adverse effects of opioids. The failure to improve clinical outcome may be due to inappropriate combination and dosing of analgesics.

The effectiveness of individual analgesics is enhanced by the additive or synergistic effect of two or more drugs acting by different mechanisms. For example, the synergism between alpha-adrenergic and opioid systems has been demonstrated.[5] Similarly, combination of acetaminophen and non-steroidal anti-inflammatory drugs provides additive analgesic effect in mild to moderate acute pain. The addition of COX-2 inhibitors or NSAIDs reduces opioid requirements by 20-30% with the reduction of opioid related side effects and better analgesia. Similarly, ketamine has been shown to reduce the pain scores and lower analgesic requirement when added to a multimodal epidural analgesia.[6]

Figure 3.

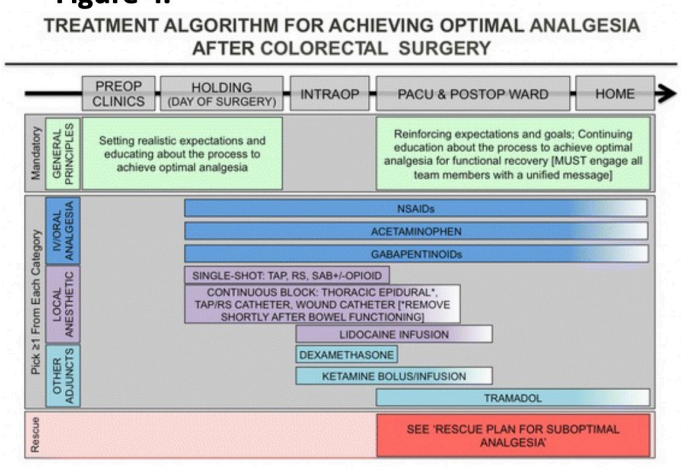


Peripheral Nerve Blocks (PNB)

Appropriate nerve blocks depending on the site of surgery are useful in providing short to intermediate-term pain relief after surgery. Direct visualization of neural tissue with ultrasound technology and the utility of stimulating catheters has made placement of indwelling catheters safer and more accurate. Continuous infusion of local anesthetics through a peripheral nerve catheter is becoming increasingly popular in both hospital and ambulatory setting to achieve prolonged analgesia.[7] For example, continuous femoral nerve block has been shown to reduce duration of hospital stay and the frequency of serious complications, reduced length of stay and costs, decreased incidence of PONV, and lower rates of unexpected admissions after ambulatory surgery. Systemic agents co-administered during PNB such as opioids and clonidine have been found to enhance intraoperative and postoperative analgesia.

A successful ERAS pain management strategy takes into considerations factors that include optimizing patient comfort, fastest functional recovery with fewest side effects. *(Figure 3)* A treatment algorithm is shown in Figure 4.

Figure 4.



Management of PONV

Identification of patients at high risk for PONV enables targeting prophylaxis to those who will benefit most from it. Patient, anesthesia, and surgery related risk factors have been identified. Anesthesia related risk factors include the use of volatile agents, nitrous oxide, opioids[8,9] and high doses of neostigmine (>2.5 mg) for the reversal of neuromuscular blockade.[10] Patient related factors include female gender, history of PONV or motion sickness, and non-smoking status. High levels of anxiety and postoperative pain, especially of pelvic or visceral origin, may also be associated with a higher incidence of PONV. There are at least four major receptor systems involved in the etiology of PONV. Its success prompted similar research in the field of PONV. Most of studies suggest better efficacies against PONV can be achieved by the use of two or more synergistic antiemetics acting at different receptors compared with monotherapy.[11-13]

Recommended Strategy for PONV Prophylaxis

The management strategy for PONV has been summarized by a recent SAMBA sponsored PONV consensus guidelines.[14] First, the risk of PONV should be estimated for each patient. For patients at moderate to high risk for PONV, regional anesthesia should be considered. If this is not possible or contraindicated and a general anesthetic is used, strategies to minimize the baseline risk of PONV should be adopted, e.g. minimize the use of opioids, avoid high dose neuromuscular reversal drugs and the use of propofol maintained anesthesia. Second, the use of combination antiemetic therapy and more appropriately a multimodal approach in high-risk patients is recommended. However, the best available combination and the optimum doses of antiemetic agents when used in combination are yet to be established. Ondansetron should be considered in any prophylactic regimen as it is now generic and hence has a low acquisition cost.

Perioperative Fluid Management

The underlying principles guiding fluid management in any setting are to maintain central euvolemia, i.e., avoid excess and deficiency. In other words, maintain a full circulation to allow normal optimal cellular perfusion whilst avoiding any peripheral or interstitial edema, and associated increase in body weight. Episodes of hypovolemia, if undetected can lead to hypoperfusion and organ dysfunction, with associated adverse outcomes. Importantly, and perhaps not as readily acknowledged, excess fluid administration can result in tissue edema and adverse outcomes. Whilst both these processes can be extreme, more commonly they are subtle with the splanchnic circulation particularly at risk.

Pediatric ERAS Protocols
The tenants of pediatric ERAS protocols are similar to adult ERAS protocols, as they seek to maintain and return to homeostasis as quickly as possible after surgery. Several core principles include preoperative counseling, minimizing fasting, avoiding bowel preparation preoperatively and liquid carbohydrate loading, utility of multimodal opioid-sparing analgesia, and avoidance of nasogastric tubes, early feeding, and euvolemic maintenance postoperatively[15]. Of relevance, adequate pain management and utility of multi-modal analgesia strategies are integral to pediatric ERAS protocols.

Differences Between Adult and Pediatric ERAS
Although more common place in adults, ERAS pathways are not the standard in pediatrics. With adaptation behind adult ERAS, pediatric evidence is not as substantiated and less clear to how applicable and effective some protocols are in influencing pediatric outcomes. Slow implementation has been potentially compounded by a misperception that they are not as critical due the shorter recovery and rehabilitation periods in children, even after major surgeries, as many have fewer comorbidities and utilize fewer overall health care costs compared to adults. Due to lack of equipoise for randomization and limited sample sizes, almost all evidence is limited to pre- and post-implementation study designs. These reasons may partially explain, but do not justify the limited pool of evidence. Of notable difference when implemented and compared to common adult ERAS protocols which contain 20+ elements, pediatric protocols only utilize 5-6 on average as described by a recent meta-analysis[16], with more elements increasingly being implemented with recent studies describing 12 to 16 items utilized in certain patient populations[17].

Anesthesiologists Role in Pediatric ERAS Development
With significant variability between and within pediatric institutions in caring for children undergoing surgery, anesthesia providers are uniquely qualified to participate in or lead multidisciplinary efforts to optimize patient care through protocols developed with surgeons, pain specialists, pharmacists, peri-operative nursing, and nurse practitioners. As leaders in pain management and regional/epidural anesthesia/analgesia and the ability to designate short-acting anesthetics, the anesthesiologist stands to be a critical team member in creating standardized protocols. Standardization of practice has the benefit of all teams with consistent education and care for the patient and family. Many times, engaging the family proactively is critical to help motivating participation in their child's care and improving compliance.

Anesthesia Elements in Pediatric ERAS
Anesthesiologists can make greatest contributions in the management of pain, nausea vomiting, euvolemic and normothermia patient states. Preoperatively, avoidance of fasting and administration of complex carbohydrates may earlier return of bowel function postoperatively. As part of regional anesthesia regiments, as described below, multimodal pain management strategies commonly include use of gabapentin for prevention to reduce perioperative and potential for chronic postoperative pain and use of routine non-opioid medications (acetaminophen, NSAIDs). Patient, nurse, or parent controlled analgesia is utilized while emphasis is placed on transition from intravenous to oral analgesics. PONV is a common cause of delayed recovery from surgery in children and hospital readmission[18]. The antiemetic combination of dexamethasone (0.1-0.2 mg/kg) and ondansetron (0.1 mg/kg) has been shown to be effective in children. Low-dose, intravenous naloxone infusions (0.25-1 mcg/kg/hr) or by oral/nasogastric route (10-20 mcg/kg) can be effective in managing opioid-related side effects such as nausea/vomiting, pruritus or ileus. As in adults, increasing evidence suggests that excess perioperative fluid administration may have the same negative effects, highlighting the need for euvolemic maintenance, such as identifying fluid responsiveness and maintaining restrictive or zero-fluid balance strategies. Maintenance of intraoperative normothermia using a forced-air thermal blanket, warming cap, airway humidification device, fluid warmer, and/or increased operating room temperature may benefit coagulation, wound healing, drug metabolism, and reduce surgical site infection.

Regional Anesthesia in Pediatric ERAS
Use of regional anesthesia to reduce or avoid perioperative opioids and side effects is a key tenant of pediatric ERAS to reduce inflammatory and endocrine stress responses, improving gut motility, and reducing insulin resistance. The advent of ultrasound-guided techniques has demonstrated safety and efficacy advantages for both single injection techniques, as well as neuraxial or peripheral catheter placement for continuous local anesthetic infusion. Block techniques in younger children, even in the premature neonate or infant, are highly successful and can address multiple dimensions including decreased stress responses, limiting general anesthetic requirements, and avoidance of postoperative complications such as apnea or prematurity[19]. Large studies have shown the overwhelming safety of regional anesthesia performed after induction of general anesthesia in infants and children. Utility of regional anesthesia, especially continuous epidural nerve blocks in posterior spinal fusion[20] and bilateral paravertebral

catheters in pectus excavatum[21] procedures are a core of these ERAS protocols. Truncal blocks such as transversus abdominal plane blocks, quadratus lumborum, or erector spinae blocks may show to have utility in urologic and abdominal procedures.

Future Directions in Pediatric ERAS

It is recommended that future studies evaluate homogenous populations; separating healthier and sicker populations to better delineate effect sizes. Sicker populations should not be excluded due to comorbidity state, as they hypothetically stand to gain the most from the stress reduction associated with ERAS. Collaborative research studies across will further expedite the advance of more generalizable evidence to support or refute efficacy of ERAS elements, down to the youngest populations, such as that for neonatal intestinal procedures[22]. As reduced length of stay continues to be prioritized by health care systems and as efficiency thresholds are approached, careful consideration has to be taken to avoid compromises in patient and parent acceptability, as well as overall safety and efficacy.

Summary

In summary, enhanced recovery is the cornerstone for reducing hospital length of stay, reducing postoperative complications and potentially increases patient satisfaction. Many successful enhanced recovery programs have been shown to increase quality and reduce cost, thereby increase value of healthcare delivery. Enhanced Recovery will likely become standard of care in the near future and should be embraced by patients, surgeons, anesthesiologists, hospital administrators, medical insurance payers and governments alike.

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Perioperative Troponin and MINS (Myocardial Injury after Noncardiac Surgery)

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Goals of the preoperative assessment are to identify risk factors, predict risk of complications, and recommend measures to minimize that risk. Postoperative myocardial infarction, cardiac arrest, and cardiac death are among the most dreaded outcomes after noncardiac surgery. However, well under half of the patients who suffer a postoperative myocardial infarction have ischemic symptoms suggesting that routine monitoring of cardiac biomarkers may be required to detect these events and allow early intervention. Troponin elevation occurs in approximately 10 to 20% of patients after noncardiac surgery and over 40% with the new 5th generation hsTnT, but until the past few years, were often felt to be of minor importance and were ignored unless the patient met diagnostic criteria for a myocardial infarction. Devereaux and colleagues defined an entity called MINS, myocardial injury after noncardiac surgery, as a troponin exceeding the upper limit of normal, with or without ischemic symptoms or electrocardiographic changes, and excluding major noncardiac causes such as stroke, sepsis, pulmonary embolism, and renal failure. These troponin elevations have been associated with increased 30 day and 1-year mortality rates, raising the question of whether to recommend postoperative surveillance of asymptomatic patients.

A number of issues need to be considered before recommending routine screening including which patients should be screened, whether to obtain troponin preoperatively, postoperatively, or both, what is the short-term risk if the test is not done, what level of troponin warrants an intervention, what investigations or therapies should be initiated if there is an abnormal result, what is the potential for adverse consequences resulting from treatment of an elevated troponin, and ultimately, will the test change management and will that intervention improve outcome.

Reasons for Routine Screening

- Routine screening with postoperative troponin for three days significantly increases the probability of detecting myocardial injury compared to only ordering troponin based on clinical signs or symptoms.
- Elevated or even detectable troponin levels are associated with adverse outcomes.
- Increasing troponin levels have a "dose-related" increase in mortality.
- Detecting asymptomatic troponin elevations can lead to various treatments that may improve outcome.

Reasons Against Routine Screening

- Troponin elevation in a low risk group will be associated with a low mortality rate, and many of these troponin elevations may be secondary to causes other than myocardial ischemia.
- The probability of obtaining an elevated postoperative troponin increases as the patient's clinical risk class increases. Because mortality is highest in patients undergoing vascular surgery, neurosurgery, general surgery, and thoracic procedures, if screening with postoperative troponin is to be recommended, it should be restricted to patients with high clinical risk as well as high surgical procedure risk.
- Detecting asymptomatic troponin elevations can lead to various treatments that may be potentially harmful (antiplatelet agents and anticoagulants) in the wrong setting.

Guideline Recommendations

- ACC/AHA guidelines: "The usefulness of postoperative screening with troponin levels in patients at high risk for perioperative MI, but without signs or symptoms suggestive of myocardial ischemia or MI, is uncertain in the absence of established risks and benefits of a defined management strategy" (Class IIb; level of evidence B). They recommended measurement of troponin levels in the setting of signs or symptoms suggestive of myocardial ischemia or MI (Class I; level of evidence A) but stated there was no benefit in routine screening of unselected patients without signs or symptoms of ischemia (Class III; level of evidence B).
- ESC guidelines: "Measurement of natriuretic peptides and high sensitivity troponin after surgery may be considered in high-risk patients to improve risk stratification (Class IIb; level of evidence B). Pre-operatively and post-operatively, patients who could most benefit from BNP or high-sensitivity troponin measurements are those with METs ≤4 or with a revised cardiac risk index value >1 for vascular surgery and >2 for non-vascular surgery. Post-operatively, patients with a surgical Apgar score <7 should also be monitored with BNP or high-sensitivity troponin measurements, to detect complications early, independently of their revised cardiac risk index values."

- CCS guidelines: "We recommend obtaining daily troponin measurements for 48-72 hours after noncardiac surgery in patients with a baseline risk > 5% for cardiovascular death or nonfatal myocardial infarction at 30 days after surgery (ie, patients with an elevated NTproBNP/BNP measurement before surgery or, if there is no NT-proBNP/BNP measurement before surgery, in those who have an RCRI score >1, age 45-64 years with significant cardiovascular disease, or age 65 years or older) (Strong Recommendation; Moderate-Quality Evidence)."

Management of Troponin Elevations

Because troponin elevation in an asymptomatic patient does not predict a specific type of death, treatment needs to be individualized. Treating these troponin elevations in a similar fashion to myocardial infarctions with antiplatelet therapy and anticoagulation may result in increased bleeding or unnecessary cardiac catheterization and starting beta blockers in the perioperative period may be harmful.

In POISE, patients with postoperative myocardial infarctions who were given aspirin and a statin did better, and there was also a suggestion from a smaller study that intensification of medical therapy (aspirin, statin, beta-blocker, ACE-inhibitor) in patients with postoperative troponin I elevations was associated with improved outcome at 1 year. The MANAGE trial suggested that dabigatran improved the primary efficacy outcome of a major vascular complication, a composite of vascular mortality and non-fatal myocardial infarction, non-hemorrhagic stroke, peripheral arterial thrombosis, amputation, and symptomatic venous thromboembolism with no increase in the primary safety outcome, a composite of life-threatening, major, and critical organ bleeding. However, there were many criticisms of the study including lower patient enrollment, changing outcomes during the trial, definition of bleeding, and significant premature discontinuation of the drug. Additionally, subgroup analysis showed differences in outcomes based on early versus late enrollment and between patients with confirmed MI versus isolated troponin elevation. As noted in the accompanying editorial, the benefit of dabigatran may have been driven by a reduction in non-hemorrhagic stroke with some of the troponin elevations related to paroxysmal asymptomatic atrial fibrillation. The INTREPID study, designed to see if aspirin or ticagrelor would reduce postoperative complications in patients with elevated troponin after noncardiac surgery, was terminated due to enrollment difficulties.

What Should We Do?

Fifth-generation high sensitivity troponin (hsTnT) may be elevated in as many as 20% of patients preoperatively and over 40% postoperatively, thereby significantly increasing the number of patients said to have a complication. Besides potentially subjecting these patients to unproven treatments, it may give the false appearance that hospitals and surgeons using the screening tools had higher complication rates than those who did not screen.

Elevated postoperative troponin may identify patients at higher risk for any adverse event rather than cardiac specific events. In his editorial, Beckman stated that "until a specific strategy or treatment is identified, the possibility of harm in applying standard treatment for type I myocardial infarction, and the potential to divert attention away from the true cause of an adverse event (nonvascular morbid) to a false one (myocardial infarction), routine measurement of troponin may be more likely to cause harm than to provide benefit and therefore should not be used as a screening modality".

There is clearly a need for clinical trials to determine what treatment, if any, can improve outcomes in these patients. While aspirin, statins, and dabigatran may help some patients, there is no consensus on treatment of patients with troponin elevations not meeting criteria for myocardial infarction. Until we have better evidence, we can only speculate as to whether it is beneficial or detrimental to screen patients with postoperative troponins.

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The ASRA Regional and Pain Anticoagulation Guidelines

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Learner Objectives
After participating in this activity, the learner will be able to:

1. Know the changes in the most recent ASRA regional and pain guidelines
2. Understand the differences between the regional and pain guidelines
3. Learn developments in the pharmacologic reversal of the novel oral anticoagulants

The American Society of Regional Anesthesia & Pain Medicine (ASRA) anticoagulation guidelines for both regional anesthesia and interventional pain procedures were updated in 2018.[1,2] Areas of disagreement, in terms of duration of stoppage and reinstitution of the anticoagulants, were lessened. This resulted in less confusion and controversy between the two clinical settings. Differences however will continue because of the higher risks involved in patients with pain (older patients, spinal stenosis, comorbidities, antiplatelet effect of antidepressants) and the surgical nature of the interventions (spinal cord stimulators and intrathecal pumps.)

Aspirin and Non Steroidal Anti-inflammatory Drugs (NSAIDs)
Similar to the ASRA regional guidelines, the patient can continue aspirin when low risk pain procedures are performed. However, the occurrence of reports of spinal hematoma after epidural steroid injection (ESI) in patients on aspirin or NSAIDs led ASRA to recommend stopping these drugs before ESIs, medium- and high-risk procedures. The length of discontinuation depends on the reason for the aspirin intake: 6 days for primary prevention and 4 days for secondary prophylaxis. A study showed the relative safety of doing ESIs in patients on NSAID.[3] However, the lack of large scale studies on pain procedures in patients on NSAIDs made the Writing Committee to use the drug's half-life to guide the duration of discontinuation of the drug before a pain procedure. Five half-lives have been decided to be adequate as this represents 97% elimination of the drug. This range from 1-2 days for ibuprofen, diclofenac, ketorolac, indomethacin, 4 days for naproxen and meloxicam, and longer for namebutone and piroxicam. The drug can be resumed a day after the procedure.

P2Y12 Inhibitors Clopidogrel, Prasugrel, Ticagrelor, and Cangrelor
The ASRA and European guidelines recommended a seven-day stoppage of clopidogrel before regional anesthesia.[1, 2, 4] The Scandinavian guidelines, on the other hand stated that 5 days is adequate.[5] This maybe reasonable since most patients have no platelet inhibition after 5 days, the rest have minimal inhibition.[6] Since a SCS trial entails several days, most pain clinicians stop the clopidogrel for five, not seven, days. If this is the case then a test of platelet activity should be performed to document that platelet recovery is acceptable for the procedure.

Prasugrel causes 90 percent platelet inhibition compared to 60% inhibition by clopidogel. A 7-day stoppage is recommended for medium and high risk procedures. Ticagrelor also cause 90% platelet inhibition. However, its effect is reversible and studies showed that platelet function recovery is adequate after five days of stopping the drug. Prasugrel and ticagrelor can be resumed 24 hours after the procedure as these drugs take effect within 2 to 4 hours. Clopidogrel, if given in its usual 75 mg dose, can be started 12 hours after the pain procedure. Since a 300-600 mg dose of clopidogrel takes effect after a few hours, the loading dose can be started 24 hours later.

Cangrelor (KengrealR) is a new intravenous P2Y12 inhibitor. It is a direct-acting P2Y12 receptor inhibitor with a fast onset and is rapidly reversible, its half-life life is 3-7 minutes.[7] A minimum of 3 hours should elapse before neuraxial procedure is performed; normal platelet function is attained within one hour.

Older Anticoagulants: Warfarin, Heparin, Low-molecular Weight Heparin, Fibrinolytic Agents
Similar to the ASRA regional guidelines, the pain guidelines recommend stoppage of warfarin for 5 days and normalization of the INR before medium and high-risk procedures. Pain procedures should be done 4-6 hours after intravenous heparin. For BID or TID subcutaneous heparin, the interval depends on the dose of the heparin: 4-6 hours for the lower dose and 12-24 hour for higher doses (see table 2). Similar to the ASRA regional guidelines, a 12-hour interval between stoppage of prophylactic dose of enoxaparin and interventional pain procedures is recommended. For therapeutic dose

of enoxaparin and for dalteparin, a 24-hour interval is observed. The new ASRA guidelines on regional anesthesia and pain procedures recommend a 48-hour interval between discontinuation of a thrombolytic drug and neuraxial injection. This number is based on the half-life of the drugs and their 27-hour effect on clotting. There have been no studies on this issue; as pain procedures are elective it should be avoided in this situation.

Table 1: Recommended Intervals between Stoppage and Resumption of the Antiplatelet and Regional Anesthesia or Interventional Pain Procedures

Anticoagulant	Drug Discontinuation and Regional Anesthesia or Pain Procedure	Resumption of Drug
Aspirin	Regional: Continue Pain: 4-6 days	Pain: 24 hours
NSAIDs	Regional: Continue Pain: Based on half-life (see text)	Pain: 24 hours
Clopidogrel	5-7 days	Regional: Immediate, 6 hours for loading dose Pain: 12 hours, 24 hours for loading dose
Prasugrel	7 days	Regional: Same as clopidogrel Pain: Same as clopidogrel
Ticagrelor	5 days	Regional: Same a clopidogrel Pain: Same a clopidogrel

The regional and pain guidelines are basically the same, differences are minor (see text).

Table 2: Recommended Intervals between Stoppage of the Older Anticoagulants and Regional Anesthesia or Interventional Pain Procedures

Anticoagulant	Regional Anesthesia	Pain Procedure
Warfarin	5 days, INR (< 1.2)	5 days, INR (< 1.2)
IV heparin	4-6 hours	6 hours
Subcutaneous heparin, BID-TID	4(6) -12-24 hours*	6-24 hours**
Enoxaparin, prophylactic dose	12 hours	12 hours
Enoxaparin, therapeutic dose	24 hours	24 hours
LMWH, dalteparin	24 hours	24 hours
Fondaparinux	No recommendation***	4 days (5 half-lives)
Fibrinolytic agents	48 hours	48 hours

*Regional: The lower number is for lower doses (5000 heparin sc), the higher number is for higher doses (12 hours for 7500-1000 sc; 24 hours for 10000 sc per dose or >20,000 heparin sc 24h total dose)

**Pain: The lower number is for low- risk procedures, the higher number is for intermediate and high-risk procedures (SCS and IT pumps).

***Single pass, atraumatic placement, avoid indwelling catheters

A clot is stable at approximately 8 hours[8] hence resumption of the anticoagulant is empirical since it takes time for it to achieve maximum effect. The one-hour interval between neuraxial injections and resumption of heparin was based on a study that showed the absence of spinal hematoma when the interval was at least an hour.[9] The longer intervals after high-risk pain procedures is due to the surgical nature of the interventions (spinal cord stimulators, intrathecal pumps). Fibrinolytic agents are usually administered on an emergency basis, ideally the anesthesiologist should be informed so the neuraxial catheter can be removed before its administration.

Table 3: Recommended Intervals between Regional Anesthesia or Pain Procedures and Resumption of the Older Anticoagulants

Drugs	Regional Anesthesia -> Resumption of Drug	Pain Procedure -> Resumption of Drug
Warfarin	6 hours	6 hours
IV heparin	1 hour	2-24 hours
BID-TID subcutaneous heparin	1 hour	2-6 hours*
LMWH, prophylactic/ therapeutic dose	4 hours	4-24 hours
Fondaparinux	(No recommendation)	6-24 hours*
Fibrinolytic agents	(Emergency situation)	(Emergency situation)

The numbers for regional anesthesia are based on published studies (heparin) or per FDA (LMWH).
Warfarin: The interval is empirical, since warfarin takes time to take effect (6-8 hours), and to assure that bleeding stopped.

*For pain, the 6-hour time is based on the 8-hour time it takes for a clot to stabilize and the 2-hour time it takes for the onset or peak effect of the anticoagulant.

*The lower number is for low- risk procedures, the higher number is for intermediate and high-risk procedures (SCS and IT pumps). The 24-hour interval is the usual recommendation after surgery.

Novel Oral Anticoagulants
Dabigatran is a direct thrombin inhibitor while rivaroxaban, apixaban and edoxaban are Factor Xa inhibitors.[8] The discontinuation of the NOACs is based on their half-lives, from two to five half-lives where 25 and three percent of the drug remains, respectively.[10] The pain guidelines recommend an interval of five half-lives while the regional anesthesia guidelines recommend two half-lives for patients with no/minimal comorbidities and five half-lives in patients with renal problems or those with comorbidities.

Table 4: Recommended Intervals between Regional Anesthesia or Pain Procedures and Resumption of the Older Anticoagulants

Drug	Drug Stoppage and Pain Procedure	Resumption of Drug	Reversal
Dabigatran	Regional: 5d, 3d (CrCl > 80 mL/min)* Pain: 4d, 6d (renal patients)	Regional: 6h Pain: 24h	Dialysis; activated charcoal within 2h; idarucizumab
Rivaroxaban	Regional: 3d Pain: 3d	Regional: 6h Pain: 24h	Activated charcoal within 8h; four-factor PCC
Apixaban	Regional: 3d Pain: 3d	Regional: 6h Pain: 24h	Activated charcoal within 3h
Edoxaban	Regional: 3d Pain: 3d	Regional: 6h Pain: 24h	

*Regional anesthesia is not recommended in patients on dabigatran whose CrCl is< 30 mL/mi.

For resumption, the 6-hour time is based on the 8-hour time it takes for a clot to stabilize and the 2-hour time it takes for the onset or peak effect of the anticoagulant.

Monitoring of the NOACs include the dilute thrombin time or ecarin clotting time for dabigatran and ant-Xa assays for rivaroxaban (some use PT as a rough indicator of rivaroxaban activity), apixaban, and edoxaban. The new reversal agents are idarucizumab for dabigatran[11] and andexanet alfa for the Factor Xa inhibitors.[12]

CHADS2 Scoring System

The CHADS2 scoring system helps assess the risk of venous thromboembolism and stroke in patients with atrial fibrillation.[13] In this system, one point each is given for the presence of congestive heart failure, hypertension, age 75 years or older, diabetes and 2 points for history of stroke or transient ischemic attack. A CHADS2 score of 2 or 3 was shown to increase the stroke rate per 100 patient-years by a factor of 4 and 5.9 respectively.[14] A patient with a CHADS2 score of 3 should encourage the use of a LMWH bridge therapy, after discontinuation of the anticoagulant, with stoppage of the LMWH 24 hours before the procedure. This assures continued anticoagulant coverage of the patient up to a reasonable time prior to the regional anesthesia or procedure. Finally, the anticoagulant should be reinstituted as early as noted above.

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The Development, Use, and Limitations of Standards, Guidelines and Best Practices

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Learner Objectives

After participating in this activity, the learner will be able to:

1. Know where to look for guidance for specific diagnoses, disease processes, procedures, and various other situations.
2. Describe the differences between standards, guidelines, practice parameters, best practices, and other forms of guidance.
3. Understand the guideline development process, and the limitations of these guidelines.
4. Develop a framework for using and integrating potentially conflicting guidance from multiple sources for an individual patient.

Introduction

Recent years have seen a proliferation of clinical practice guidelines, standards, consensus documents, and other forms of guidance in health care. In many cases these best practices overlap, contradict or conflict with one another; in other cases, there are large gaps in coverage. At best, these standards can help more patients obtain the best care available, but at worst they can result in a "one size fits none" approach to patient care. In addition, while the development and publication of this guidance has proliferated over the past 2-3 decades, the adoption and integration into everyday practice has been slower. One reason may be the magnitude of the often conflicting and confusing guidance that may be relevant for an individual patient. Clinicians often are not even aware of their existence, or may not know how to apply conflicting guidance This session will help the clinician think about how to utilize the guidance available to provide better outcomes for individual patients.

Key Takeaways

The number of perioperative guidelines and other parameters continues to increase. While this theoretically should provide more clarity to providers and better care for patients, this is not always the case.

Providers need to be aware of standards, guidelines, and other best practices, know when they apply, and be able to integrate them when they overlap or conflict with each other. Ultimately this should assist in the formulation of an individualized plan for each patient.

Types of Guidance

While the term “clinical practice guidelines” is frequently used, there are multiple types of guidance available. The term “standard” is infrequently used, presumably because it implies “standard of care” which has medical legal implications. The terms advisory, alert, statements, guidance statement, expert consensus, expert opinion, protocol, best practice, appropriate use criteria (AUC), and recommendations are all used. There are no precise and widely agreed upon definitions of what these terms mean. For convenience, the terms guidelines and guidance will be used throughout most of this presentation.

The Institute of Medicine (IOM) defines clinical practice guidelines as "statements that include recommendations, intended to optimize patient care, that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options".

Where to Look for “Guidance”

- Guideline Central - https://www.guidelinecentral.com/
- ECRI guidelines trust - https://guidelines.ecri.org (Requires free registration)
- Medscape https://reference.medscape.com/features/guidelines
- Specialty Societies!!—large source of guidelines
- Canadian Anesthesiologists Society
- Useful document with large list of guidelines: https://www.cas.ca/English/Page/Files/97_2019_Guidelines_To_The_Practice_Of_Anest.pdf
- American Society of Anesthesiologists https://www.asahq.org/standards-and-guidelines
  - o Standards
    - “These standards apply to anesthesia care and basic monitoring and are intended to encourage quality patient care.”
  - o Practice guidelines
    - “These practice guidelines are evidence-based and developed using a rigorous process that combines scientific and consensus-based evidence.”
  - o Advisories and alerts
    - “The practice parameters provide guidance in the form of requirements, recommendations or other information to improve decision-making and promote quality outcomes for the practice of anesthesiology.”

- o Statements (position)
  - "Tap into the expertise of ASA by reviewing these opinions, beliefs and medical judgments developed by the committee members."
  - (Some of which are "statements on standard practice")
- o Expert Consensus Documents (advisory, definition, guidelines, protocol, principles)
  - "These include policies, positions, principles, suggestions, and definitions to promote the practice of anesthesiology."
- o Work products from ASA committees https://www.asahq.org/standards-and-guidelines/resources-from-asa-committees
  - "The following work products and resources have been made available by ASA committees. They have not been approved by ASA's Board of Directors or House of Delegates and do not represent an ASA Policy, Statement or Guideline."

- ASA Brain health https://www.asahq.org/brainhealthinitiative/tools/clinicalguides

Development Process

- Structured - not a smoke-filled room
- Based on a review of evidence - "The foundation is a systematic review of the research evidence bearing on a clinical question, focused on the strength of the evidence on which clinical decision-making for that condition is based." (Up to Date)
- Produces an expert consensus based on evidence - A set of recommendations, involving both the evidence and value judgments regarding benefits and harms of alternative care options, addressing how patients with that condition should be managed, everything else being equal.
- There are now "guidelines for guidelines"

Conclusion

- Many forms of guidance available
- Be aware of what is available
- Varying quality, evaluate for yourself
- Treat the patient, not the guidelines

Table 1: Comparing the elements of clinical practice guideline development between the Institute of Medicine (IOM) and the Guidelines International Network (G-I-N).

IOM	Guidelines International Network (G-I-N)
Standard 1: Establishing transparency	1: Composition of Guideline Development Group
Standard 2: Management of conflict of interest	2. Decision-making Process
Standard 3: Guideline development group composition	3: Conflict of Interest
Standard 4: Clinical practice guideline – systematic review intersection	4: Scope of a Guideline
Standard 5: Establishing evidence foundations for and rating strength of recommendations	5: Methods
Standard 6: Articulation of recommendations	6: Evidence Reviews
Standard 7: External review	7: Guideline Recommendations
Standard 8: Updating	8: Rating of Evidence and Recommendations
	9: Peer Review and Stakeholder Consultations
	10: Guideline Expiration and Updating
	11: Financial Support and Sponsoring Organisation

Criteria for trustworthy clinical practice guidelines

Standard	Comments
Transparency	Guidelines should include an explicit description of process and funding.
Conflict of Interest	Conflicts of interest for the guidelines development group should be managed by reporting, exclusion, and divestments.
Members of the guidelines development group	The group should be multidisciplinary and balanced.
Review of the literature	The guideline should be based on systematic reviews of the literature.
Rating strength of evidence and recommendations	Each recommendation should be accompanied by the underlying reasoning, potential benefits and harms, the evidence and its quality, the contribution of values and experience, rating of the level of confidence in the evidence and the strength of the recommendation, and differences of opinion regarding recommendations.
Presentation of recommendations	The guideline should state precisely the recommended actions, when they should be performed, and how they could be measured for evaluation of compliance.
External review	The guidelines should be reviewed by the full spectrum of relevant stakeholders. The general public should have an opportunity to review the guidelines before they are final.
Updating	Guidelines should state the date of publication and evidence review and be updated when new, clinically important evidence is available.

Based on data from the consensus report: Clinical Practice Guidelines We Can Trust. Institute of Medicine of The National Academies. Report available at: http://nationalacademies.org/hmd/Reports/2011/Clinical-Practice-Guidelines-We-Can-Trust.aspx

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GRADE for practice guidelines

Standard	Clarity of risk/benefit	Quality of supporting evidence	Implications
1A Strong recommendation High quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Consistent evidence from well performed randomized, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.	Strong recommendation, can apply to most patients in most circumstances without reservations
1B Strong recommendation Moderate quality evidence	Benefits clearly outweigh risks and burdens, or vice versa	Evidence from randomized, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other form. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate.	Strong recommendation, likely to apply to most patients
1C Strong recommendation Low quality evidence	Benefits appear to outweigh risks and burdens, or vice versa	Evidence from observational studies, unsystematic clinical experience, or from randomized, controlled trials with serious flaws. Any estimate of effect is uncertain.	Relatively strong recommendation; might change when higher quality evidence becomes available
2A Weak recommendation High quality evidence	Benefits closely balanced with risks and burdens	Consistent evidence from well performed randomized, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk.	Weak recommendation, best action may differ depending on circumstances or patients or societal values
2B Weak recommendation Moderate quality evidence	Benefits closely balanced with risks and burdens, some uncertainty in the estimates of benefits, risks and burdens	Evidence from randomized, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other form. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate.	Weak recommendation, alternative approaches likely to be better for some patients under some circumstances
2C Weak recommendation Low quality evidence	Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens	Evidence from observational studies, unsystematic clinical experience, or from randomized, controlled trials with serious flaws. Any estimate of effect is uncertain.	Very weak recommendation; other alternatives may be equally reasonable

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https://www.uptodate.com/contents/overview-of-clinical-practice-guidelines/print 23/24

*GRADE can be implemented with either three or four levels of quality of evidence. UpToDate implements three levels and uses numbers and letters to represent strength of recommendation and quality of evidence respectively.

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Transfusion Therapy Variation: Are We Making Progress?

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Introduction

Decades ago large variations in the indications for and timing of RBC transfusion were observed among several major surgeries including total knee and total hip replacement surgery and coronary artery bypass graft surgery (CABG) patients.[1,2,3] The variation seen in these reports was not explained by patient characteristics or surgical variables. Instead the differences seemed driven by differences in provider and institutional preferences. In other words this observed variation appeared unwarranted. The presence of significant variation in transfusion rates implied that the best practice had yet to be identified, and that indications for transfusions were not consistent among providers.

Frankly, there was nothing more than a longstanding belief for RBC transfusion is that giving back blood will reverse the ill effects of anemia. For example, belief still applied in this era was the "10/30" rule which originated from suggestions to decrease risk among poor anesthesia candidates made by Adams and Lundy in 1942.[4] This "rule" was not based on solid evidence, merely on clinical observation and experience. Yet this rule persisted for decades.

In the 1990s and early 2000s there was still an incomplete understanding of the risks of anemia, the risks and potential benefit of RBC transfusions. Several RBC transfusion guidelines were published by the National Institute of Health (1988), the American College of Physicians (1992), the Blood Management Practice Guidelines Conference (1995), as well as the American Society of Anesthesiologists (1995).[5,6,7] Some criticized these guidelines as an ineffective approach to improving the delivery of health care. More likely these transfusion guidelines from this era were ineffective because there was not clear evidence of the risks of anemia relative to the risks of RBC transfusion. All were well intended to optimize the use of RBC transfusions, but fundamentally limited by the available evidence in the literature at the time.

As a result, clinicians in this era could continue to adopt different approaches to RBC transfusion practice based on their beliefs and personal experiences. Observations of variation in RBC transfusion in the 1990s continued to show large variations in the indications for and timing of RBC transfusion have been documented for many years among coronary artery bypass graft (CABG) surgery patients.[8,9] Importantly, this variation continued to not be explained by patient or surgical variables, but rather by differences in provider and institutional preferences.[10]

Clinical Trials of RBC Transfusion to treat Anemia

This all changed dramatically in 1999 with the randomized trial by Dr. Hebert and colleagues; The Canadian Transfusion Requirements in Critical Care, or TRICC trial.[11] This is the first prospective randomized trial of RBC transfusion therapy. The TRICC trial evaluated a restrictive strategy of maintaining hemoglobin between 7 and 9 g/dL versus a liberal strategy of maintaining hemoglobin between 10 and 12 g/dL among critically ill patients without active bleeding. This study showed that the restrictive strategy was "at least as effective" and possibly superior to the liberal transfusion strategy." Furthermore, subgroup analysis showed an association of improved 30-day survival in patients younger than 55 years old or those with APACHE II scores lower than 20 managed with the restrictive strategy.

Several additional patient populations have been randomized in trials with a similar approach to determine the impact of a restrictive strategy for RBC transfusion. A prospective trial of liberal (greater than 10 g/dL) vs. restrictive (less than 8.0 g/dL) strategies among high risk patients after hip surgery was completed in 2011.[12] Similar to the previously mentioned trial, there was no outcome benefit, as measured by death or inability to walk without assistance, to patients from a more liberal approach to transfusion. Nearly 97 percent of patients in the liberal group were transfused with RBCs. In the restrictive group, far less blood was administered, and only 40 percent of these patients were exposed to RBC transfusions.

In 2013 a similar structured trial was performed on patients with acute upper gastrointestinal bleeding.[13] Compared to the liberal transfusion strategy (hemoglobin threshold was 9 g per deciliter), a restrictive strategy (hemoglobin threshold was 7 g per deciliter) significantly improved outcomes in this patient population. There was a significant 45% relative risk reduction in the primary outcome of 45 day mortality. Significantly fewer bleeding events and other adverse outcomes (e.g. transfusion reactions and pulmonary edema) occurred among patients in the restrictive strategy arm.

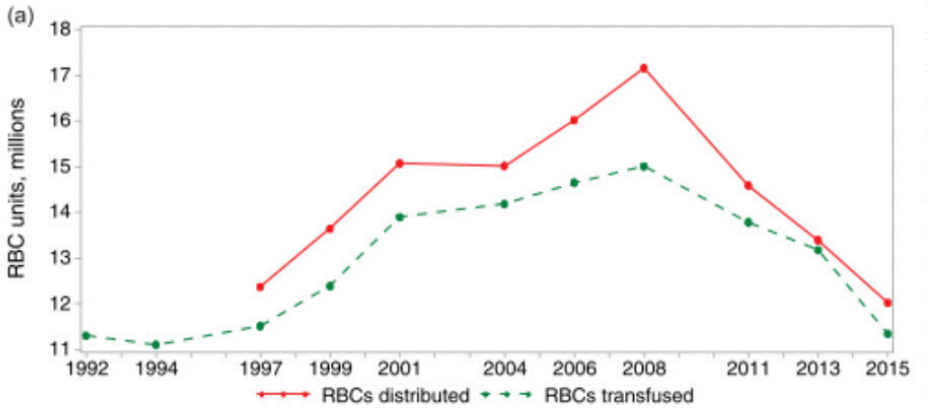

Figure 1. National Red Blood Cell Distributions and Transfusions: 1989 - 2015.
Source: American Association of Blood Bankers 2017 Nationwide Blood Collection and Utilization Survey Report.

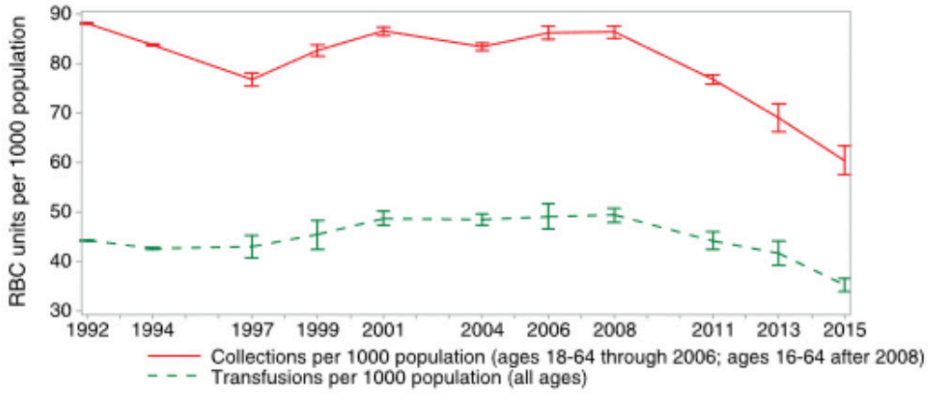

Figure 2. National Red Blood Cell Collections and Transfusions adjusted per 1000 population: 1989 - 2015.
Source: American Association of Blood Bankers 2017 Nationwide Blood Collection and Utilization Survey Report.

A prospective trial of RBC transfusion during cardiac surgery was completed in Brazil.[14] Among 500 patients undergoing cardiac surgery with CPB, a restrictive transfusion strategy of tolerating anemia to a hematocrit of 24% was just as efficacious as a more liberal goal of maintaining hematocrit above 30%. The rate of RBC transfusion was 47 percent vs. 78 percent in the restrictive versus liberal groups. In 2015, Murphy et al randomized cardiac surgical patients with a postoperative hemoglobin level of less than 9 g per deciliter to a restrictive transfusion threshold (hemoglobin level <7.5 g per deciliter) or a liberal transfusion threshold (hemoglobin level <9 g per deciliter).[15] The primary outcome, serious infection or ischemic event, occurred in 35% of the patients in the restrictive-threshold group and 33% of the patients in the liberal-threshold group which was not statistically significant. They concluded that use of a restrictive threshold for the transfusion of red cells after cardiac surgery in adults was not significantly different compared to the liberal threshold for reducing postoperative morbidity and costs. Most recently, in 2017, Koch et al. randomized cardiac surgical patients to a transfusion threshold of 24% versus 28%.[16] The primary endpoint was a composite of mortality and postoperative morbidities. There was no detected statistically significant difference in outcomes at interim analysis, supporting the conclusion that aggressive blood conservation efforts in cardiac surgical patients is warranted.

Updated Guidelines

Today we are better positioned to optimize our use of RBC transfusions than we have been in the past. More recent guidelines are benefiting from the greatly improved evidence now available. But in 2005 another observational study demonstrates that variation continues across institutions in Canada despite new knowledge about the benefits and risks of RBC transfusions.[17] A comprehensive guideline was developed in 2011 by the Society of Thoracic

Surgeons, the Society of Cardiovascular Anesthesiologists and the International Consortium for Evidence Based Perfusion for the cardiac surgery population.[18] More recently, the American Society of Anesthesiologists developed a set of guidelines in 2015 for the perioperative setting.[19] By understanding the current evidence regarding the treatment of anemia with RBC transfusion, current guideline are more evidence based and may be expected to drive significantly decreases in the local, regional, and national variation currently witnessed for transfusions.

Transfusion Utilization in the US

The American Association of Blood Bankers 2011 Nationwide Blood Collection and Utilization Survey Report describes the current status of blood utilization in the United States.[20] Key findings include that for the first time in two decades the annual number of transfusions has started to decrease. Figure 1 describes the overall distribution and transfusion of RBCs nationally in the United States. These data clearly show that the transfusions began to total volume of RBC transfusions began to decrease in the 2008 time period after many years of growth. Figure 2 shows RBC collections and transfusions adjusted for population over time. These data demonstrate the decrease adjusted for a population basis.

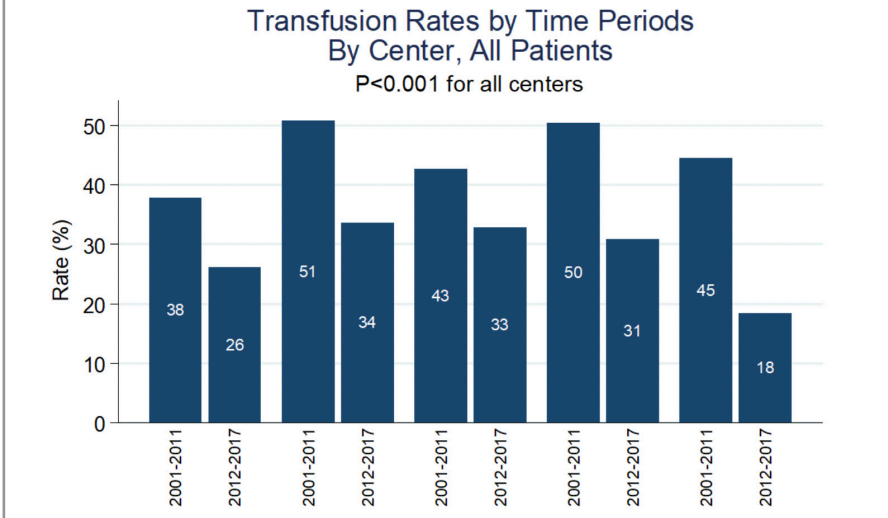

Figure 3. Transfusion rates by time periods for 5 Centers in Northern New England.

Transfusion Therapy Variation; Are we making progress?

Recently, data from Maryland for patients undergoing isolated coronary artery bypass (CAB) and isolated aortic valve replacement (AVR) on cardiopulmonary bypass from 2011 to 2014 was analyzed for variation across the 10 Maryland consortium (MCSQI) hospitals.[21] Unadjusted intraoperative RBC transfusion rates at the 10 centers ranged from 13% to 60%; postoperative RBC transfusion probabilities ranged from 16% to 41%. When stratifying patients by preoperative hematocrit quartiles, significant variability in intraoperative transfusion probability was seen among all quartiles. They concluded that significant variation in intercenter RBC transfusion practices exists during this time period for both intraoperative and postoperative transfusions, even after risk adjustment, among Maryland centers.

Another statewide collaborative examined RBC transfusions in Michigan.[22] They identified all patients undergoing CABG (n = 16,568) or PCI (n = 94,634) at each of 33 centers from 2010 through 2012 in the state of Michigan and compared perioperative RBC transfusion rates for CABG and PCI at each center. As expected, RBC transfusion was more common after CABG (mean 46.5%) than PCI (mean 3.3%), with wide variation across centers for both (CABG range from 26.5% to 71.3, PCI range 1.6% to 6.0%). They observed that RBC transfusion rates were significantly correlated between the CABG and PCI at individual hospitals in Michigan, independent of patient case mix. These data suggest that institutional culture remains a persistent and driving factor for RBC transfusions practice in this state collaborative even during the time period of 2010 to 2012. This collaborative also surveyed these 33 nonfederal Michigan cardiac surgical programs about the relationship of observed inter center RBC transfusion variation with blood management practices for isolated coronary bypass procedures during 2013.[23] The programs were divided into two groups, low and high transfusion rate centers for this study. There was significant variation in rate of RBC transfusion from 0.8% to 26.3% across these centers. No statistical differences in organizational practices were identified between the two groups regarding the blood management committee; the presence of available red blood cell units within the operating room and the frequency of auditing and feedback about blood management. These authors concluded that efforts to reduce variation in 1- to 2-unit, intraoperative transfusions may benefit from evaluating other determinants, including organizational culture and provider transfusion practices.

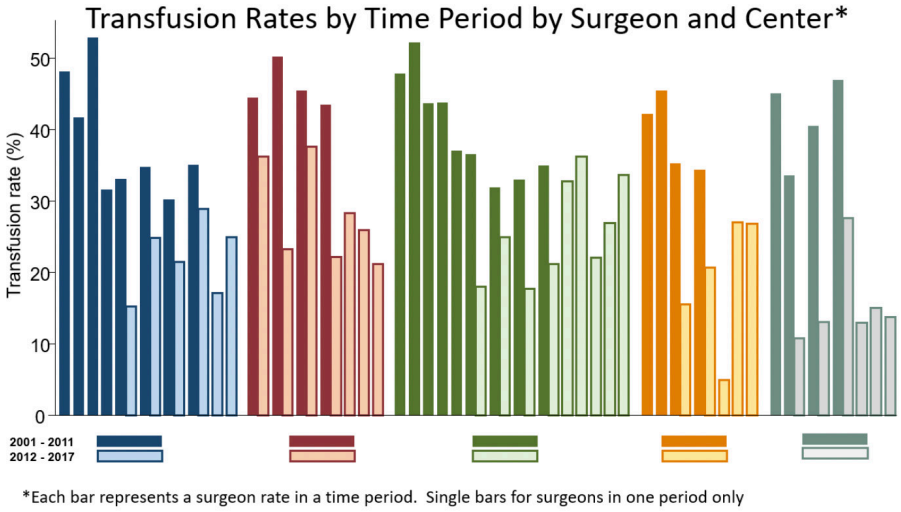

Figure 4. Transfusion rates by time periods for surgeons grouped by center (same color bars represent a center) during isolated CABG in Northern New England. Surgeons with less than 100 isolated CABG during time period excluded. Not all surgeons were working during both time periods.

These recent data from both the Maryland and Michigan registries illustrate ongoing wide variation in RBC transfusion practice in the current decade. Another regional collaborative, The Northern New England Cardiac Disease Study Group (NNE) has collected full data on RBC transfusions since 2001 and these data continue to be collected presently. From this cohort, 51,993 patients who underwent CABG, Valve or combined CABG and Valve surgery were identified with complete data (1,497 (2.7%) patients were excluded). From these date we looked at two time periods. Since 2001 when the NNE identified optimizing RBC transfusion during cardiac surgery as a priority for improving outcomes, there has been a continual quality improvement effort on the topic. This has included plenary sessions, site visits and lectures at annual quarterly NNE regional meetings, local center specific multidisciplinary teams, use of electronic medical record systems to drive improvement through evidence based "hard stop" ordering. In addition, the teams worked on improved management of anemia, reducing blood loss peri-operatively, use of anti-fibrinolytics, perfusion strategies to reduce intra-operative hemo-dilution during cardiopulmonary bypass, and consideration for cell saver management.

Over the two time periods the NNE saw significant reductions in RBC transfusions for all cardiac surgery patients at each of the 5 centers with adequate surgical volume to include in the cohort (see Figure 3.) This pattern was also seen among the subgroup that had isolated CABG surgery as well. Variation across the 5 centers persisted even though each center significantly reduced their rate or RBC transfusion (38 to 51% versus 18 to 34%). They also saw significant reductions in the amount of blood used by surgeon. Seventeen surgeons had more than 100 isolated CABGS and worked during both time periods. Only 4 of these surgeons did not significantly reduce their rate of transfusion though all of these 4 surgeons had a trend of reduced transfusion rate. Variation at the surgeon level also persisted (25 to 54% versus 12 to 42%) for surgeons working in both periods.

Figure 4 illustrates the rate of RBC transfusion for surgeons stratified by medical center and include any surgeon with adequate volume (more than 100 cases) in either time period. Some surgeons only had sufficient volume to be in one of the 2 time periods. This illustrates the rate of RBC transfusion for any active surgeon in both time periods with adequate volume to be included in the analysis. This analysis also shows significant reductions in the rate of RBC transfusion but still we observe significant variation across the active surgeons in each time period at each of the centers.

The IMPROVE collaboration (Maritime Cardiovascular Quality Initiative, Michigan Society of Thoracic and Cardiovascular Surgeons, Northern New England Cardiovascular Disease Study Group, and Providence Health and Services Cardiovascular Disease Study Group) RBC transfusion variation across 56 centers was assessed from 2008 to 2012.[24] This analysis focused on the most recent 200 patients who received 0, 1, or 2 units of RBC transfusion during the index admission at each of the 56 centers. Significant variation in the number of RBC units used existed across regions (zero units, 70% to 84; one unit, 5% to 11%; two units, 9% to 18%). These authors observed that transfusion of small volumes of RBC transfusions varied across geographic regions. These data suggest that differences in regional practice environments contribute to ongoing variability in RBC transfusion rates.

Conclusions

Based on the most recent available evidence there are significant reductions in overall use of RBCs nationally, and regionally that have been accomplished. However, reductions in variation are not being observed as a part of these improvements. This suggests that ongoing preferences, at the regional, hospital, surgeon levels, still persist and are driving the improvements in RBC utilization over time.

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What is The Magic Number? Blood Pressure Thresholds in the Operating Room, ICU and Beyond

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Introduction

Despite surgical patients being sicker, intraoperative anesthesia-related mortality is better than before and currently stands at about 1 in 100,000 patients[1,2]. However, 30-day postoperative mortality is 1-2%[3,4] and is about 1,000 times more common than anesthesia-related intraoperative mortality. If mortality within 30 days after surgery were considered a disease, it would be the third leading cause of death in the United States[5].

Associations between Intraoperative Hypotension and Myocardial and Kidney Injury

Hemodynamic control has always been an essential goal of anesthetic management. With the ready availability of sensitive biomarkers such as cardiac troponin, and accurate minute-by-minute hemodynamic details from tens-of-thousands of patients from electronic medical records, estimation of complex correlations is much easier now than ever before.

There is a strong association between intraoperative hypotension and mortality.[6] Risk increases substantially when the minimum mean arterial pressure maintained for ten minutes is less than about 70 mmHg (Fig. 1).[7] There are similarly strong associations between hypotension and myocardial and kidney injury.[8] The threshold for myocardial injury is a mean arterial pressure of about 65 mmHg (Fig. 2A). The threshold for renal injury appears to be even greater, perhaps near 75 mmHg.[8]

There are also strong associations between hypotension and myocardial (Fig. 2B) and renal injury when mean arterial pressure is expressed as a percentage of baseline clinic pressures. However, changes from baseline are not more predictive than an absolute threshold of 65 mmHg which is easier to use clinically. A third of all hypotension, defined by mean arterial pressure <65 mmHg, occurs between anesthetic induction and surgical incision. Post induction hypotension is significantly and comparably associated with both myocardial and kidney injury before and after incision.[9] This insult is clearly preventable with safe, and appropriate anesthetic drug titration.

Hypotension may simply be a marker of underlying illness rather than a mediator of harm. Similarly, patients who become hypotensive during surgery are also likely to become hypotensive postoperatively, and it might be the postoperative hypotension that causes harm. Fortunately, at least some randomized data are now available, that help elucidate a signal to causality rather than much of the large amounts of observational association analysis.

Futier and colleagues compared tight vs. minimal intraoperative blood pressure control (n=298).[10] High-risk patients were randomized to minimal blood pressure control (ephedrine for systolic pressure <80 mmHg or <40% below baseline) vs. a norepinephrine infusion to maintain systolic pressure within 10% of baseline values during and for four hours after surgery. The primary outcome, a composite of systemic inflammatory response syndrome and/or at least one organ failure, occurred in 56/147 patients in the norepinephrine group vs 75/145 patients in the minimal control group: relative risk 0.73 [95% CI: 0.56, 0.94]. The investigators also reported that there were fewer sepsis cases and that the duration of hospitalization was shorter with tight blood pressure control.

A notable aspect of the trial is that the intervention threshold in the minimal control group was quite low. Most anesthetists intervene well before systolic pressure reaches 80 mmHg.[11] A higher intervention pressure presumably would have reduced the observed 25% benefit. The actual difference in mean pressure was small, just 6.5 mmHg. The investigators do not report the amount of hypotension below critical thresholds, which is probably when harm occurs.

Postoperative Myocardial Injury & the Contribution of Hypotension

Myocardial infarction is the leading cause of attributable post-operative death, accounting for a quarter of all mortality, far exceeding major bleeding (14%) and sepsis (9%). More than 90% of myocardial infarctions within the initial 30 postoperative days occur within two days after surgery.[12] Myocardial infarctions in the post-operative period are usually silent, with minimal clinical manifestations. They also differ from non-operative infarctions in apparently being largely caused by supply-demand mismatch, thus being considered Type 2 infarctions.[13] Most also do not have electrocardiographic or echocardiographic evidence of ischemia, and thus do not meet criteria for myocardial infarction specified in the 4th Universal Definition. However, mortality associated with asymptomatic troponin elevations is almost as high without symptoms as with symptoms — indicating that isolated troponin elevations should be taken seriously.[12]

Ward Hypotension and Myocardial Injury
Ward hypotension is usually less severe but more sustained because vital signs are measured only infrequently, compared with the more profound but short-lasting intraoperative hypotension.

In patients recovering from abdominal surgery on the general care ward, postoperative hypotension (mean arterial pressure <65 mmHg for ≥15 minutes) has been shown to occur in about one fifth of patients and not to be recognized by routine vital sign assessments in about half of the cases. Interestingly, episodes of hypertension, with mean pressures >110mmHg lasting at least 30 minutes were observed in about 40% of patients in the same cohort and almost always went unrecognized by routine assessments.[14]

Patients who become hypotensive during surgery are the same ones who are most likely to become hypotensive postoperatively, making it difficult to statistically isolate independent contributions. Intermittent hypotension is frequently missed on the wards, because monitoring protocols are mostly based on four or six hourly spot-checks. Here the extent and duration of unrecorded hypotension may be making a critical difference in outcomes that we are as yet unaware of.

A sub-analysis of the POISE-2 trial concluded that hypotension, defined as systolic blood pressure less than 90 mmHg (intraoperative, postoperative day-of surgery and for the first four postoperative days) was significantly and independently associated with the composite outcomes of myocardial infarction and death within 30 days. For example, during the remaining day after surgery, each 10 minutes of hypotension increased the odds 3% (95% confidence interval 1, 5%, P<0.001). (Fig. 3).[15]

Hypotension in Intensive Care Units
Critical care patients are an especially vulnerable population. These patients are inherently unstable, hypotension is frequent. Hypotension in critical care patients is thus not only common but may also be especially damaging.

There is increasing evidence for an association between hypotension in critical care patients and serious complications. For example, a recent analysis of 2,918 postoperative critical care patients evaluated the association between the lowest recorded mean-arterial pressure and a primary composite of myocardial injury (defined by 4th-generation troponin T ≥0.03 ng/ml without a non-ischemic cause), and in-hospital mortality at 7 days. There was a strong nonlinear (quadratic) association between the lowest mean arterial pressure and the primary outcome of myocardial injury after noncardiac surgery or mortality, with estimated risk increasing at lower pressures. For example, the risk of myocardial injury after noncardiac surgery or mortality was an estimated 23% higher at the 25th percentile (78 mm Hg) of lowest mean arterial pressure compared with at the median of 87 mm Hg, with adjusted hazard ratio (95% CI) of 1.23 (1.12-1.355; p < 0.001). (Fig. 5B) Post hoc analyses showed that the relationship between ICU hypotension and outcomes depended on the amount of intraoperative hypotension.[16]

Acute kidney injury is far more common than cardiac injury in critical care patients, and the severity of AKI is independently associated with in hospital mortality. In the same study of 2,918 postoperative critical care patients, there was a linear relationship between hypotension and acute kidney injury over the entire range of minimal daily pressures from 110 to 50 mmHg, with an adjusted hazard ratio of 1.27 (95% CI, 1.18-1.37; p < 0.001). (Fig. 5C) This association was much stronger when analysis was restricted to stage 2-3 injury only.[16]

In patients with septic shock, Badin et al. showed that a mean pressure exceeding 72-82 mmHg was needed to prevent acute kidney injury.[17] Others have also concluded that a similar MAP >73 mmHg is needed to prevent progression to kidney injury in patients with severe sepsis.[18] Both duration and severity of hypotension matter: for example, it takes an hour of exposure to 80 mmHg to equal even a few minutes below 70 mmHg. Interpretation of sepsis studies is complicated by the fact the sepsis per se causes hypotension, and worse sepsis presumably causes most hypotension and has the worst outcomes.[19] Distinguishing sepsis severity from the independent effects of hypotension is challenging and it is likely that all such analyses suffer a degree of residual confounding.

There are clearly many causes of delirium in critical care patients,[20] but hypotension may contribute. Aldemir and colleagues screened 818 critical care patients daily for 10 days and reported an association between systolic pressure <80 mmHg and delirium.[21] Delirium is difficult to assess and reported differences from one study to another may in part be explained by how and when and how frequently delirium was evaluated.

In most units, care of septic patients is generally guided by the Surviving Sepsis Guidelines. A strong recommendation, based on moderate-quality evidence, is to titrate vasopressors to an initial MAP target of 65 mmHg during resuscitation of septic shock.[22] The largest trial supporting these guidelines randomized 776 patients to high (80-85 mmHg versus low (65-70 mmHg) MAP targets in patients with vasodilatory septic shock.[23] The

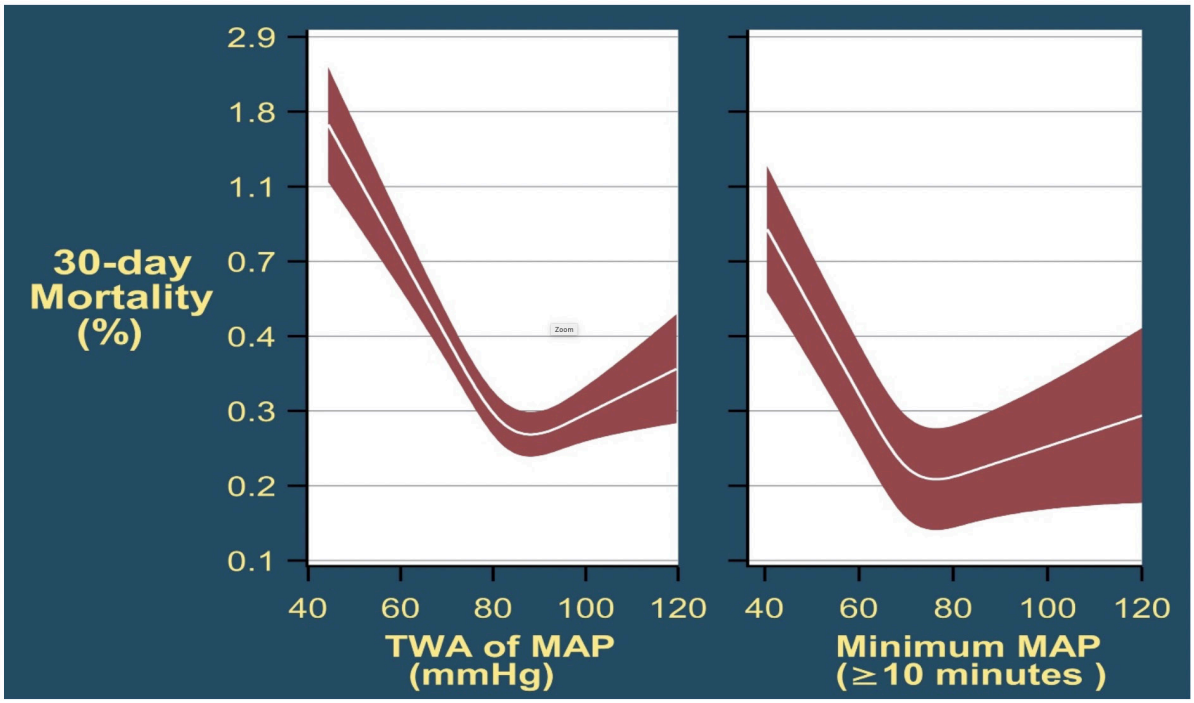

Fig. 1 Mortality in the 30 post-operative days as a function of time-weighted average (TWA) mean arterial pressure or lowest mean pressure maintained for at least 10 minutes. With permission from Mascha et al: Intraoperative mean arterial pressure variability and 30-day mortality in patients having noncardiac surgery. Anesthesiology 2015; 123: 79-91

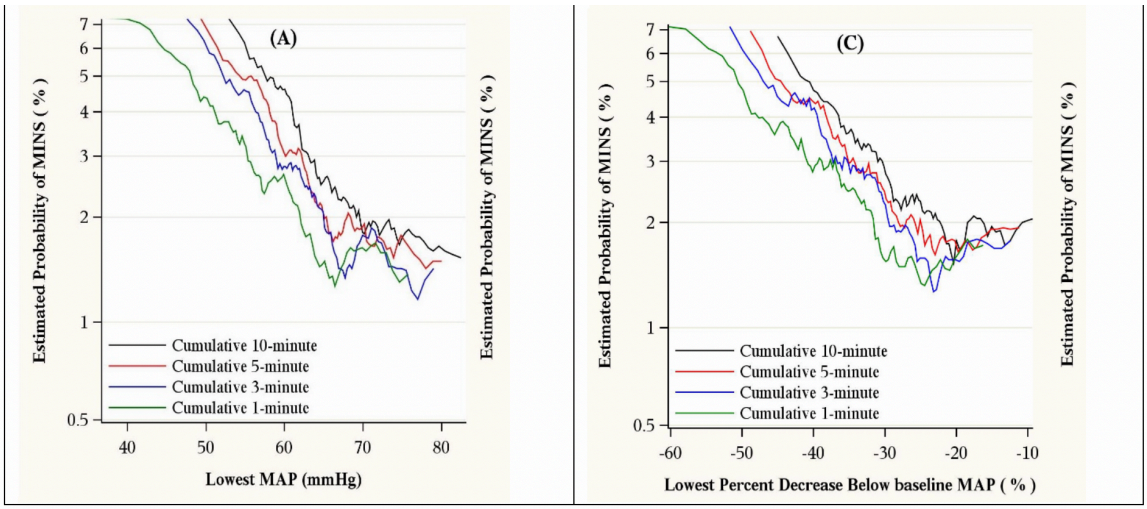

Fig. 2 The left graph (A) shows the relationship between the lowest cumulative absolute mean arterial pressure maintained for 1, 3, 5, and 10 minutes and myocardial injury. The right graph (B) shows the relationship between the lowest cumulative relative mean arterial pressure maintained for 1, 3, 5, and 10 minutes and myocardial injury. Both were highly predictive, but relative thresholds were not more predictive than absolute thresholds which are easier to use. The relationships were generally similar for acute kidney injury (not shown). With permission from Salmasi, et al: Relationship between intraoperative hypotension, defined by either reduction from baseline or absolute thresholds, and acute kidney and myocardial injury after noncardiac surgery: A retrospective cohort analysis. Anesthesiology 2017; 126: 47-65.

investigators had difficulty obtaining the targeted pressures, but did maintain good inter-group separation (85-90 mmHg vs. 70-75 mmHg). A further limitation is that clinical myocardial infarctions were only observed in only 9 patients which precluded reliable assessment of this important outcome. Atrial fibrillation was more common in patients assigned to higher blood pressure, possibly consequent to greater catecholamine exposure. There was no significant overall difference in renal injury but in a pre-planned sub-group analysis, patients with chronic hypertension who were assigned to the lower pressure target had more renal injury and more often required renal replacement therapy. Other smaller randomized trials also report that higher blood pressure targets are associated with more cardiac arrhythmias, more vasopressor use, and similar lactate, regional blood flow, and mortality compared with lower blood pressure targets.[24-27]

Recently, Maheshwari and colleagues reported outcomes from nearly 9,000 septic adults in 110 ICUs across the United States. For every one unit increase in TWA-MAP < 65 mmHg, the odds of in-hospital mortality increased 11.4% (95% CI 7.8%, 15.1%, $p < 0.001$); the odds of AKI increased 7.0% (4.7, 9.5%, $p < 0.001$); and the odds of myocardial injury increased 4.5% (0.4, 8.7%, $p = 0.03$). For mortality and AKI, odds progressively increased as thresholds decreased from 85 to 55 mmHg. The earliest indication of a harm was at a threshold of a MAP of 85 mmHg. (Fig.4)[28]

Summary and Conclusions

Available data suggest that mean-arterial pressures well above 65 mmHg may be needed to prevent hypotensive organ injury in postoperative critical care patients, including those who are septic. If anything, the general paradigm of a MAP of 65 mmHg as a 'one-size fits all' recommendation would need some serious rethinking. In contrast, 65 mmHg or slightly greater appears sufficient during the intraoperative period.[8,29] The most obvious explanation other than a decreased metabolic demand during the intra-operative period, is that intensive care patients have coexisting insults including extreme sympathetic stimulation, fluid shifts, and often pre-existing and subsequently superimposed organ system injury.

The harm threshold on surgical wards remains unknown but may well prove to be somewhere between the pressures required during surgery and those required in critically ill patients. An essential element to improve detection of harm associated with hypotension would be improved granularity of hemodynamic data that is monitored and collected in these avenues.

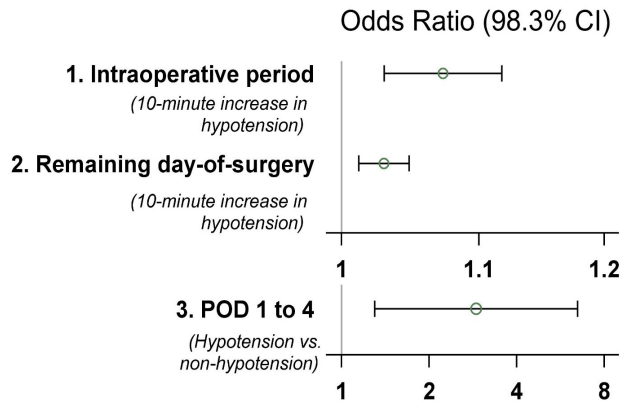

Fig. 3

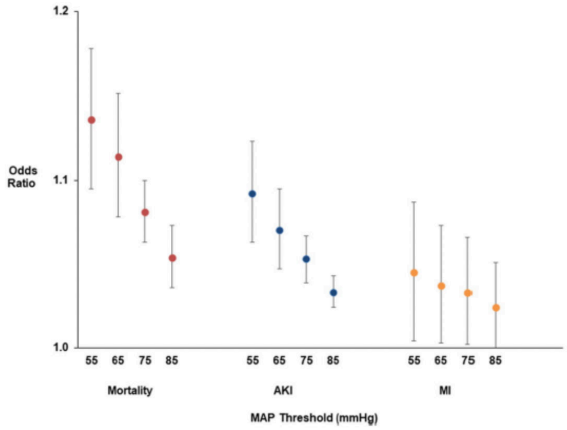

Fig. 4 Association of hypotension exposure with in-hospital mortality, AKI and myocardial injury. Adjusted odds ratios and 95% confidence intervals for a 1 mmHg increase in TWA-MAP, below different thresholds are shown for the primary outcome of in-hospital mortality and secondaryoutcomes of acute kidney injury and myocardial injury. With permission from Maheshwari K, et al: The relationship between ICU hypotension and in-hospital mortality and morbidity in septic patients. Intensive Care Med. 2018 Jun;44(6):857-867.

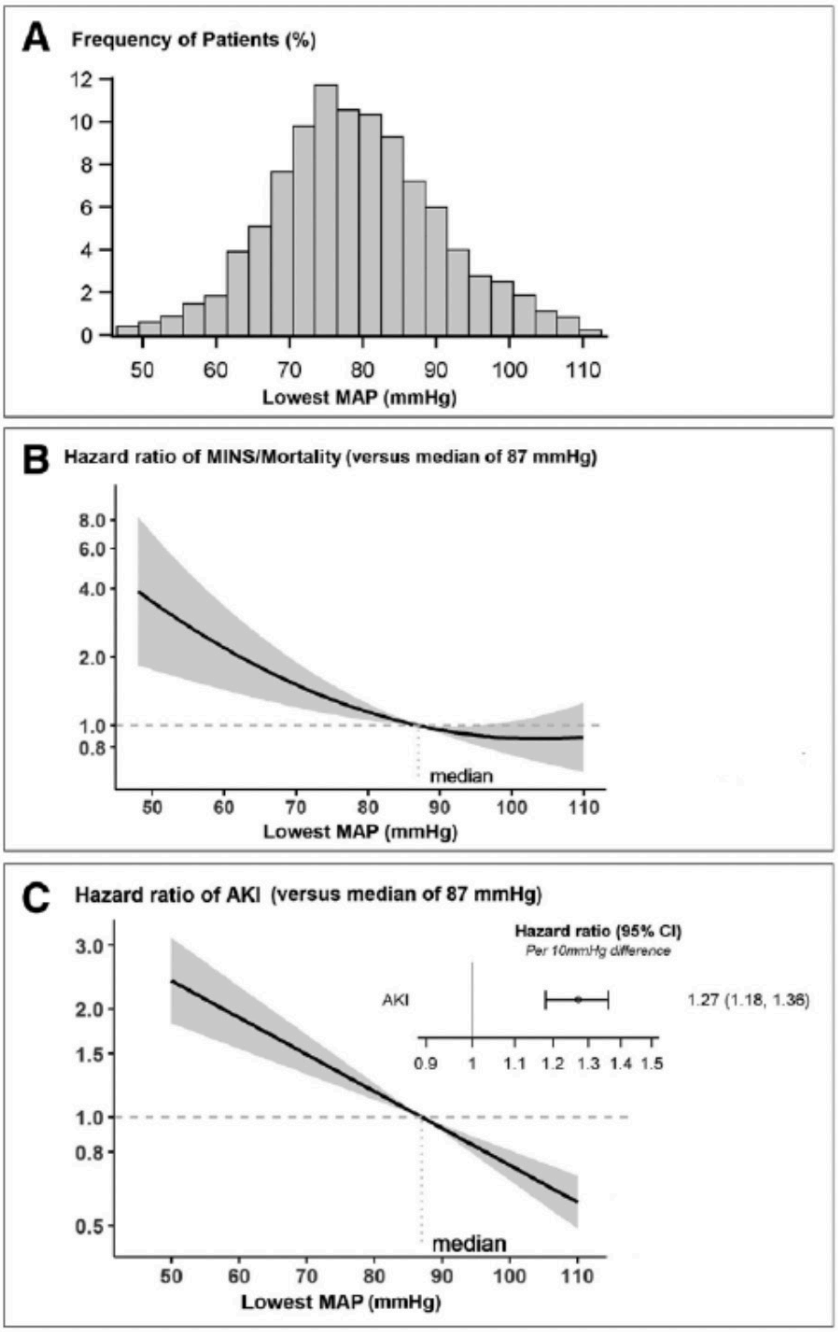

Fig. 5 Distribution of lowest mean arterial pressure (MAP) during ICU stay and its association with myocardial injury after noncardiac surgery (MINS)/mortality and acute kidney injury (AKI). **A**, The distribution of lowest MAP during ICU stay. **B**, Hazard ratio of MINS/mortality comparing to median lowest MAP of 87 mm Hg. The *solid line* and *shaded area* present the estimated hazard ratio and its 95% CI. **C**, Hazard ratio of AKI comparing to median lowest MAP of 87 mm Hg (*left*), and for 10 mm Hg difference in lowest MAP (*right*). The *solid line* and *shaded area* present the estimated hazard ratio and its 95% CI. With permission from Khanna AK, et al: Association Between Mean Arterial Pressure and Acute Kidney Injury and a Composite of Myocardial Injury and Mortality in Postoperative Critically Ill Patients: A Retrospective Cohort Analysis. Crit Care Med. 2019 Apr 10.

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