REVIEW COURSE LECTURES

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RCL-01
SOCCA: The Tele-Vision: Taking Care to the Patient and Expanding the Scope of the Intensivist

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LEARNER OBJECTIVES

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

1. Identify opportunities in Tele-ICU to improve patient care around the hospital;
2. Review Tele-ICU outcomes in remote locations;
3. Examine internal and external barriers to advancing the Tele-Critical Care agenda; and
4. Discuss how to expand the reach of the Intensivist beyond the boundaries of the ICU.

OBSERVATIONAL ICU IN THE ED

Up to 58 percent of emergency department (ED) admissions result in an ICU admission[1].

Increasing volume and acuity of critically ill patients presenting to emergency departments with time-sensitive pathophysiology who need ICU care is a fact of daily life in busy ED's. This is occurring with concurrent increased hospital crowding and delays in ICU bed availability. Delay in care in the form of ICU stabilization and ongoing resuscitation has been associated with poor clinical outcomes for critically ill patients[2]. The increasing number of trained EM-Intensivists are now developing a new subspecialty in Emergency Critical Care to provide early diagnosis, resuscitation and stabilization in specialized units in the ED for critically ill patients. Those critically ill patients with undifferentiated pathology, who require further diagnostic evaluation and work-up or who may have initially responded to resuscitation but remain at risk for acute decompensation following admission to a general care floor. These units are designed for acute, time limited intervention prior to patients being admitted to traditional ICU's for ongoing critical care needs and for acutely decompensated patients who can have their pathophysiology reversed in a timely fashion (e.g.: heart failure secondary to missed dialysis, DKA or reversal of overdose requiring a few hours of mechanical ventilation). Early literature on these units have found that these ED ICU's were occupied by patients who may not benefit from ICU admission and were housing palliative care patients[3]. While this may not be the patient population that the ED-Intensivists want to look after, this does open up an opportunity to address critically ill patients in multiple organ failure, who are transferred to academic centers for higher levels of care, to be able to better assess their care needs for resuscitation and goals of care. Utilizing this space for thorough assessment, appropriate resuscitation or goals of care discussion prior to admitting them to an ICU may be in the patients and the hospitals best interest. To be able to do so with a virtual intensivst (either in the ED or in an ICU outside of the ED) via Tele-ICU would make this an opportunity to leverage existing resources at academic hospitals.

TELE-ICU

The promise of Tele-ICU's to address critical care staffing shortages by leveraging scarce intensivist resources to patients in distant locations to impact ICU mortality and length of stay, thus reducing cost of care and increasing ICU capacity, remains largely unfulfilled.

SCCM Adult Critical Care Statistics[1]:

- 20 % of acute care admissions will be admitted to the ICU
  - 55,000 critically ill patients cared for per day in ICU
- 30% of all ICU admissions will require mechanical ventilation
- In 2010 there were 77 809 ICU beds, increased 15 % in 5 years
- Average LOS 3.8 days but with huge variability
- Average mortality rate ranges from 10-29%
- 35% shortfall of intensivists by 2020 with increasing demand for critical care services

There is a myriad of reasons for the slow adoption of Tele-ICU's, which include everything from high cost to implement and operationalize the system, payment struct°ure for the services provided, hospital culture, credentialing and licensing barriers, change management and physician autonomy coupled with mixed evidence on effectiveness[4,5].

The capital cost to establish comprehensive teleICU capabilities (monitoring, two-way audio-visual connectivity, access to electronic medical record and staffing) are estimated to be around $90,000 per ICU bed with an added $53,000 per ICU bed per year for annual operating costs. The question often arises as to whether the health outcome improvements warrant this cost, particularly in light of the fact that there is no direct billing from providers for the care delivered. A recent study reviewing the cost-effectiveness of Tele-ICU services found that hospitals with fewer resources and minimal access to intensivists would benefit the most from these services[6]. The caveat to that would be the fact that the service would probably be cost-prohibitive to these smaller hospitals. An ad hoc model to provide care on consultation in smaller community hospitals may be a solution for them to reap the benefit of evidence-based care and best practices provided by an intensivst, but without the prohibitive cost of a comprehensive Tele-ICU system. For a community hospital to realize the benefit of this system to reduce ICU mortality, LOS and cost-per-case, a number of conditions need to be in place

i.e. there are engaged, on-site physicians, the remote intensivist has shared decision-making authority and access to the remote electronic medical record, and there is adequate staff training to perform the care required by these patients e.g: dialysis, advanced mechanical ventilation techniques, etc. The organizational and structural changes along with the change management needed to adapt this technology and practice into a community hospital is not insignificant and the barriers are high to successfully implement this model.

Barriers to establishing a remote Tele-ICU ad-hoc consult/co-management model in a community hospital:

- Administrative:
  - Cost
  - Licensing
  - Credentialing
  - EMR access
  - On-site requirements for remote physicians
  - No designated ICU medical director with authority over workflow
  - Top down initiative
- Technical:
  - No monitoring or alerting
  - Rudimentary robot for audio-visual communication
  - Wi-Fi and other technical mishaps
  - Not scalable with different EMR's and connectivity issues
- Clinical:
  - Physician culture and acceptance – threat to their autonomy
  - Different standard of patient care – academic vs. community ICU
  - Best practices (Lung protective ventilator strategies, nutrition, early mobilization)
  - Protocol driven care (electrolyte replacement, glycemic control)
  - Communication/consultation between providers
  - Complexity of care with multiple consultants
  - Difficulty accessing and navigating the EMR
  - Incomplete medical information available to the remote intensivist
- Remote Intensivist:
  - Work flow not sustainable due to taking it on as a secondary responsibility
  - Poor work-life integration – high level frustration and burn-out
  - Liability

RAPID RESPONSE TEAMS

Rapid Response Teams (RRT's) have been nearly universally implemented in North America since the Joint Commission recommended implementation of these teams in 2008. This recommendation arose from a landmark report in 1999 from the Institute of Medicine (IOM) "To Err is Human"[7], which identified failure to rescue acutely deteriorating patients on general care floors contributed to the 98,000 preventable deaths in hospitals each year. In 2005, the Institute for Healthcare Improvement (IHI) launched the 100,000 Lives Campaign[8] to reduce the morbidity and mortality of patients being treated in our complex, but flawed healthcare systems. One of the six initiatives of The Campaign was to deploy Rapid Response Teams when patients were first noted to decline. The other five initiatives included evidenced based care for acute myocardial infarction, reporting adverse drug events, prevent central line and surgical site infections and ventilator-associated pneumonia. Interestingly the last 5 initiatives were all associated with process initiatives such as implementation of bundles of care or implementing a medication reconciliation process, but there was no direction given nor scientific research behind the deployment of RRT's. There was no white paper or process map detailing what constituted acute clinical decline and how was it measured, how did you activate the RRT, what personnel should be on the RRT and what the outcome metrics of success were nor how they should be measured.

The published data around RRT's ability to impact patient outcomes remains a mixed bag (both in quality of studies and inter-study comparability) and clinicians are still struggling to implement scientifically sound, but financially feasible RRT interventions which impact patient safety and outcomes in 2018. There are very few randomized, prospective studies with most of the evidence we have gleaned is from before-and-after studies and a few large meta-analyses. A systemic review of the literature by Bradford Winters, et al [9] showed a small number of high and lower quality studies suggesting reduced rates of cardiopulmonary arrests out of the intensive care unit and only 18 studies that examined barriers to implementation and activation of RRT's. An early meta-analysis of the literature by Chan, et all[10] demonstrates this decrease in out of ICU cardiopulmonary arrests did not result in an improved overall mortality in adult patients, but may have impacted pediatric patients.

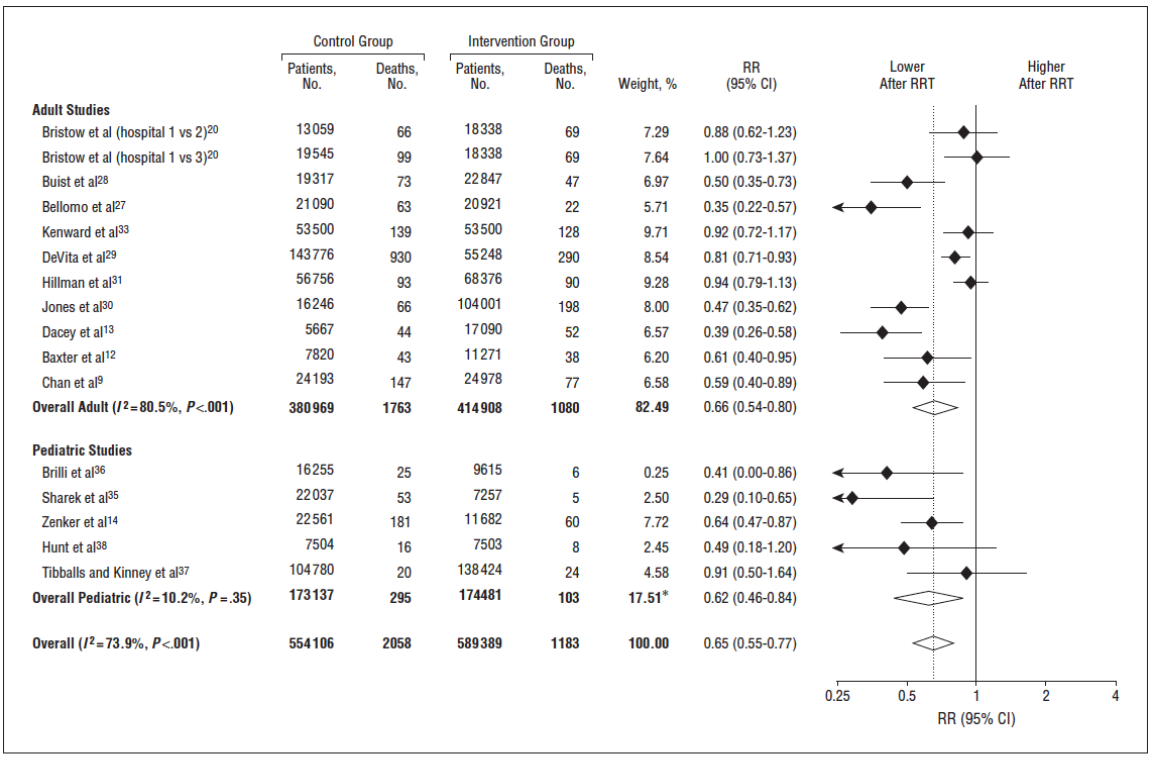

Figure 2. Pooled relative risks (RRs) of cardiopulmonary arrest outside the intensive care unit for adults and children after rapid response team (RRT) implementation. CI indicates confidence interval. *Number owing to rounding error for each of the individual pediatric studies.

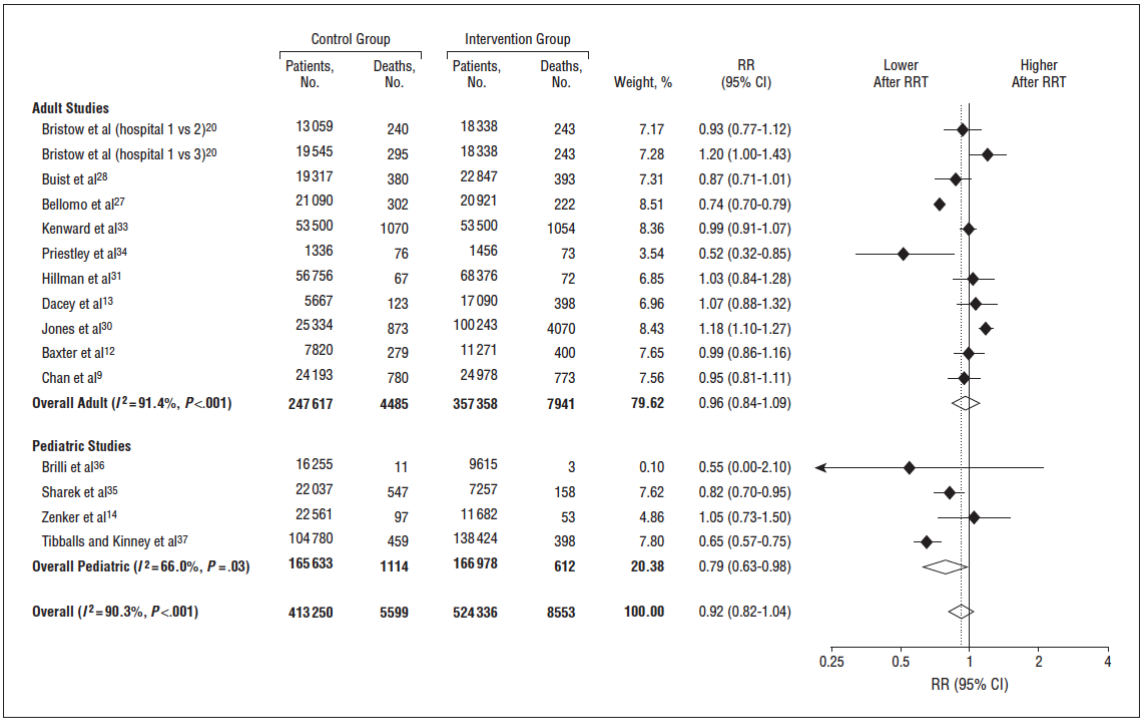

Figure 3. Pooled relative risks (RRs) of hospital mortality for adults and children after rapid response team (RRT) implementation. CI indicates confidence interval.

The variability on RRT effectiveness stems from a number of factors which need to be addressed to improve effectiveness and timeliness in identifying patients who are acutely deteriorating, minimize the barriers to initiating an RRT response, standardizing the personnel who respond to these patients and optimizing the process to manage in pace or rapidly escalate care to the ICU for stabilization. This team should have a governance and quality improvement arm to address education, policy and procedures, as well as review real time data regarding effectiveness, cost and outcomes.

The components that make up a Rapid Response System include:

Afferent Arm:
- Physiologic triggers (may be single/multiple variable alert, early warning systems)
- Bedside nurse/physician/family member recognizes deterioration
- Mobilizes RRT

Efferent Arm:
- Physician/Intensivist led team vs. Nurse led team
- Other team members (respiratory therapy, administrators, pharmacists)

Governance Arm:
- Education
- Policy
- Procedures

Quality Improvement Arm:
- Data collection, analysis
- Process improvement and iteration of policy and process and cost

EARLY WARNING SIGNS FOR CALLING	THE RAPID RESPONSE TEAM at 1-1111
Staff Concerned/Worried	"DOES NOT LOOK/ACT RIGHT," gut instinct that patient is beginning a downward spiral
Change in Respiratory Rate	RESPIRATORY RATE is < 8 or > 30
Change in Oxygenation	PULSE OXIMETER decreases below 90% or there is an INCREASE IN 02 requirements >8L
Labored Breathing	BREATHING BECOMES LABORED
Change in Heart Rate	HEART RATE changes to < 40 or > 120 bpm
Change in Blood Pressure	SYSTOLIC BLOOD PRESSURE drops below 90 or rises > 200
Chest Pain	Complains of CHEST PAIN
Hemorrhage	Develops uncontrolled bleeding from any site or port
Decreased Level of Consciousness	Becomes SOMNOLENT, DIFFICULT TO AROUSE, CONFUSED OR OBTUNDED
Onset of Agitation/Delirium	Becomes AGITATED OR DELIRIOUS
Seizure	Has a SEIZURE
Other Alterations	Any other changes in mental status or CNS Status

Example of Early Warning Signs for Activating the Rapid Response Team.

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RCL-02
Perioperative Cardiac Risk Assessment and Management: The Internist's Perspective

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LEARNER OBJECTIVES

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

(1) Explain the ACC/AHA algorithm for perioperative cardiac risk assessment;

(2) Identify various tools and calculators to assess risk of postoperative cardiac complications;

(3) Judge appropriate evidence-based decisions as to when further cardiac tests are indicated; and

(4) Assess the evidence or lack thereof for risk reduction strategies including revascularization and medical therapy.

The goals of preoperative cardiac consultation are to identify a patient's risk factors, assess severity and stability of comorbid conditions, provide a clinical risk profile for informed and shared decision-making, determine the need for additional testing or changes in management, and make recommendations to optimize the patient's medical condition prior to surgery. This may occasionally involve cancelling a case, switching to a lower risk procedure, or opting for a non-surgical option such as chemotherapy, radiation therapy, or palliative care. The purpose is not to "clear" a patient for surgery which implies a guarantee that there will be no complications.

Risk assessment is dependent upon patient factors including functional capacity, cardiac conditions, and surgery specific risk. There are no evidence-based criteria mandating when a consultation is required and by whom, and these decisions are often left to the discretion of the surgeon or anesthesiologist. These decisions are often dependent on the evaluating physician's experience, knowledge, and comfort level, and often lead to different opinions as to whether or not certain tests are indicated preoperatively. The patient's regular internist or cardiologist are also more familiar with the patient than the anesthesiologist, and this knowledge may also result in different opinions or recommendations.

There are multiple society guidelines for perioperative assessment and management. The American College of Cardiology/American Heart Association (ACC/AHA) guidelines are the ones used most frequently in the United States. The European Society of Cardiology (ESC) guidelines are similar but somewhat more liberal in their recommendations, whereas the Canadian Cardiovascular Society (CCS) guidelines differ dramatically. This discussion will focus primarily on the ACC guidelines.

RISK ASSESSMENT

Procedural risk has typically been divided into low, intermediate, and high-risk groups with estimated 30-day major adverse cardiac event (MACE) rates of less than 1%, 1 to 5%, and greater than 5% respectively. The ACC guideline algorithm combines procedural risk with the patient's clinical risk factors to estimate overall risk and divides patients into low risk of MACE (<1%) or elevated risk (>1%). They recommend using the Lee Revised Cardiac Risk Index (RCRI), Gupta myocardial infarction or cardiac arrest calculator (MICA), or the American College of Surgeons Surgical Risk Calculator (ACS-SRC), the latter two being derived from the NSQIP database. It is important to understand the definitions of risk factors and complications in each as they are different. The patient's activity level is estimated using a cutoff of >4METS for adequate exercise capacity.

Biomarkers such as brain natriuretic peptide (BNP) or NT-proBNP that are elevated preoperatively, postoperatively, or both are associated with increased risk of postoperative cardiac complications, and when used in conjunction with the RCRI may improve predictive accuracy. Troponins have also been evaluated preoperatively and postoperatively, and an elevated troponin has also been associated with an increased risk of postoperative complications. At this time their use in preoperative risk stratification is unclear, although the CCS guidelines recommend them.

The ACC algorithm for patients with CAD uses a basic stepwise approach that includes:

1) Urgency of surgery – if emergent, proceed to surgery with no further testing;

2) History of recent ACS - postpone elective surgery for further evaluation and management as per clinical practice guidelines;

3) Estimate of combined procedural and clinical risk using one of the calculators – if low risk, proceed to surgery;

4) Estimate of functional capacity if elevated risk – if >4METS, proceed to surgery;

5) Consider noninvasive testing (NIT) if elevated risk and <4METS if the results will change management as noted above; otherwise proceed to surgery.

This last step is where physicians often feel uncomfortable and where internists/cardiologists may differ from anesthesiologists as

to the need for further testing. Keep in mind that any intervention will result in delaying surgery for weeks to months. There is no indication for assessment of LV function to predict risk in patients with CAD. These tests (resting ECHO or nuclear imaging) are indicated for patients with dyspnea of unknown etiology, with heart failure and worsening symptoms, or with suspected severe valvular heart disease.

RISK REDUCTION STRATEGIES

Once a patient has been identified as being at high risk, risk reduction measures should be implemented to prevent postoperative complications These include coronary revascularization or medical management.

CORONARY REVASCULARIZATION

Two randomized controlled trials evaluated the efficacy of prophylactic coronary revascularization in addition to optimal medical therapy in patients undergoing noncardiac surgery. The coronary artery revascularization prophylaxis (CARP) trial randomized 510 patients with stable cardiac symptoms scheduled to undergo elective major vascular surgery to medical therapy with or without revascularization. There was no significant difference in the rate of mortality or myocardial infarction between groups at 30-day follow-up, and no difference in the primary endpoint of mortality (22 vs 24%) at a median time of 2.7 years following randomization. The DECREASE V pilot trial studied 101 high risk vascular surgery patients who had markedly abnormal dobutamine stress echocardiograms with multiple abnormal segments. A similar group of patients in an earlier study failed to show a benefit with prophylactic beta blockers. DECREASE V also failed to demonstrate improvement in short or long-term outcomes with the addition of revascularization to optimal medical therapy.

Because of the high procedural risk associated with CABG, it was thought that PCI might be better. Early studies with PCI and bare metal stents (BMS) showed an increase in MACE and major bleeding if the patient underwent noncardiac surgery within 30 days of stent placement which subsequently led to the recommendation to wait at least 4 weeks after BMS insertion to complete the course of dual antiplatelet therapy (DAPT) and to wait 14 days after balloon angioplasty. Drug-eluting stents (DES) were also found to be associated with increased MACE and bleeding if the noncardiac surgery was performed within 3-6 months of stent placement. This finding along with reports of stent thrombosis led to an AHA recommendation to continue uninterrupted DAPT for a minimum of 12 months. The most recent ACC guidelines shortened these requirements to 6 months of DAPT and to only 3 months if the risk of delaying surgery outweighed the risk of stent thrombosis. Surgery should be performed on aspirin if not DAPT. The ESC suggested that it might even be safe after a minimum of 1 month if necessary. Evidence suggests that the newer generation drug-eluting stents are safer than first generation and may require shorter durations of DAPT. However, stents placed in the setting of an acute MI carry a higher risk of thrombosis and require a longer duration.

The ACC guidelines recommend coronary revascularization as per guidelines in the non-surgical setting but not prophylactically just to get the patient through surgery as there is currently no evidence for reduced postoperative complications. However, if a patient had previously undergone coronary revascularization and is asymptomatic, CABG may be protective for at least 4-6 years.

If surgery needs to be performed before completion of the recommended duration for DAPT, ideally both drugs should be continued perioperatively. However, in those situations where this cannot be done, aspirin should be continued. If antiplatelet agents need to be discontinued, the recommendations are to stop prasugrel 7 days before, clopidogrel 5-7 days before, ticagrelor 5 days before, and aspirin from 3-7 days before surgery.

MEDICAL THERAPY

Beta-blockers

Significant controversy exists surrounding the studies of prophylactic beta-blockers to reduce postoperative cardiac complications. Early studies by Mangano, using atenolol, and Poldermans, using bisoprolol, and titrating the dose to control heart rate showed a benefit. Three subsequent studies (DIPOM, MAVS, POBBLE) using metoprolol started the morning of or day before surgery but not titrating the dose showed no benefit. The POISE trial randomized over 8,000 patients to a high-dose of metoprolol-ER was associated with a significant reduction in nonfatal MI but at the expense of increased stroke and total mortality. There was significantly more bradycardia and hypotension in the metoprolol group. Despite criticism over the dose of metoprolol, subsequent use of prophylactic beta-blockers decreased markedly. Another of the DECREASE trials from the Poldermans group again used bisoprolol titrated to control heart rate and showed a more modest reduction in MI and death than the previous trial in vascular patients. However, the validity of these trials has been questioned after Dr. Poldermans was fired due to questions of scientific integrity.

The ACC guidelines recommend continuing beta-blockers in patients already on them as preoperative withdrawal is potentially harmful. They also say that beta-blocker initiation may be reasonable for patients with ischemia on a stress test and may be considered for patients with 3 or more RCRI risk factors (2 or more for the ESC guidelines). They make no recommendation as to which beta-blocker to use whereas the ESC suggests atenolol or bisoprolol over metoprolol. If beta-blockers are started, they should not be started on the day of surgery.

Statins

In addition to lowering cholesterol, statins have a number of pleotropic effects including reducing inflammation which may help stabilize plaques and prevent plaque rupture.

There are limited RCTs using prophylactic statins before noncardiac surgery, and 2 of them are DECREASE trials from the Poldermans group. A small study of 100 patients randomized to atorvastatin 20

mg started 2 weeks before vascular surgery versus placebo showed a reduction in a composite cardiovascular endpoint 6 months later. DECREASE III used fluvastatin XL 80 mg started a month before vascular surgery and showed a significant reduction in MI and death at 30-days after surgery. DECREASE IV, using the same protocol for intermediate risk patients, showed a statistically insignificant trend towards reduced MI and death. Many observational studies have reported beneficial effects associated with perioperative statin use, including reductions in postoperative cardiac complications and death. It appears that statins have potential to reduce postoperative cardiac complications with very little downside. There is no evidence of increased rhabdomyolysis or significantly increased liver enzymes, and only one study found a slightly higher risk of renal injury associated with the use of high-dose statins.

The ACC guidelines recommend continuing statins in patients already on them, say it is reasonable to start the in patients undergoing vascular surgery, and may be considered in patients with other indications for them such as coronary artery disease, diabetes mellitus, or hyperlipidemia.

Clonidine

POISE-2 randomized 10,010 patients to clonidine, aspirin, both, or neither. It demonstrated that prophylactic clonidine did not reduce postoperative MI or death but was associated with an increase in hypotension and nonfatal cardiac arrest. The ACC guidelines recommend against starting it preoperatively, but it should be continued in patients already taking it.

Aspirin

The aspirin arm of POISE-2 failed to show a reduction in postoperative MI or death but was associated with a small but statistically significant increase in major bleeding. Patients with recent stents who had not completed their course of DAPT were excluded as were patients undergoing carotid endarterectomy. However, a subgroup analysis of patients who had previously undergone PCI and completed their DAPT found that in contrast to the overall study results, these patients had a significant reduction in postoperative MI with no significant increase in bleeding.

The ACC guidelines recommend continuing aspirin in patients with prior stents and those on it for secondary prophylaxis if the risk of a thrombotic event outweighs the risk of bleeding.

Renin-angiotensin system antagonists

The use of these drugs perioperatively is controversial. Many anesthesiologists prefer to have patients withhold these drugs on the morning of surgery based on reports of hypotension with induction of anesthesia. However, there is no hard evidence that this increases the risk of MI or death.

The ACC guidelines say it is reasonable to continue them, but if they are stopped preoperatively, they should be restarted as soon as possible postoperatively assuming hemodynamic stability of the patient.

SUMMARY

There are few large scale RCTs in perioperative medicine, and many areas remain controversial. Perioperative cardiac risk assessment and management is a combination of art and science based on clinical experience, observational studies, and expert consensus opinion. Using the ACC guidelines will help guide physicians and hopefully standardize care as much as possible, hopefully resulting in improved outcomes for patients undergoing noncardiac surgery.

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RCL-03
What's New with the Management of Vasodilatory Shock in the ICU?

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LEARNER OBJECTIVES

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

1. Identify evidence of the duration and extent of hypotension during the intraoperative and postoperative period that affects outcomes;

2. Describe how low blood pressure will influence the brain, heart and kidney hypoperfusion syndromes;

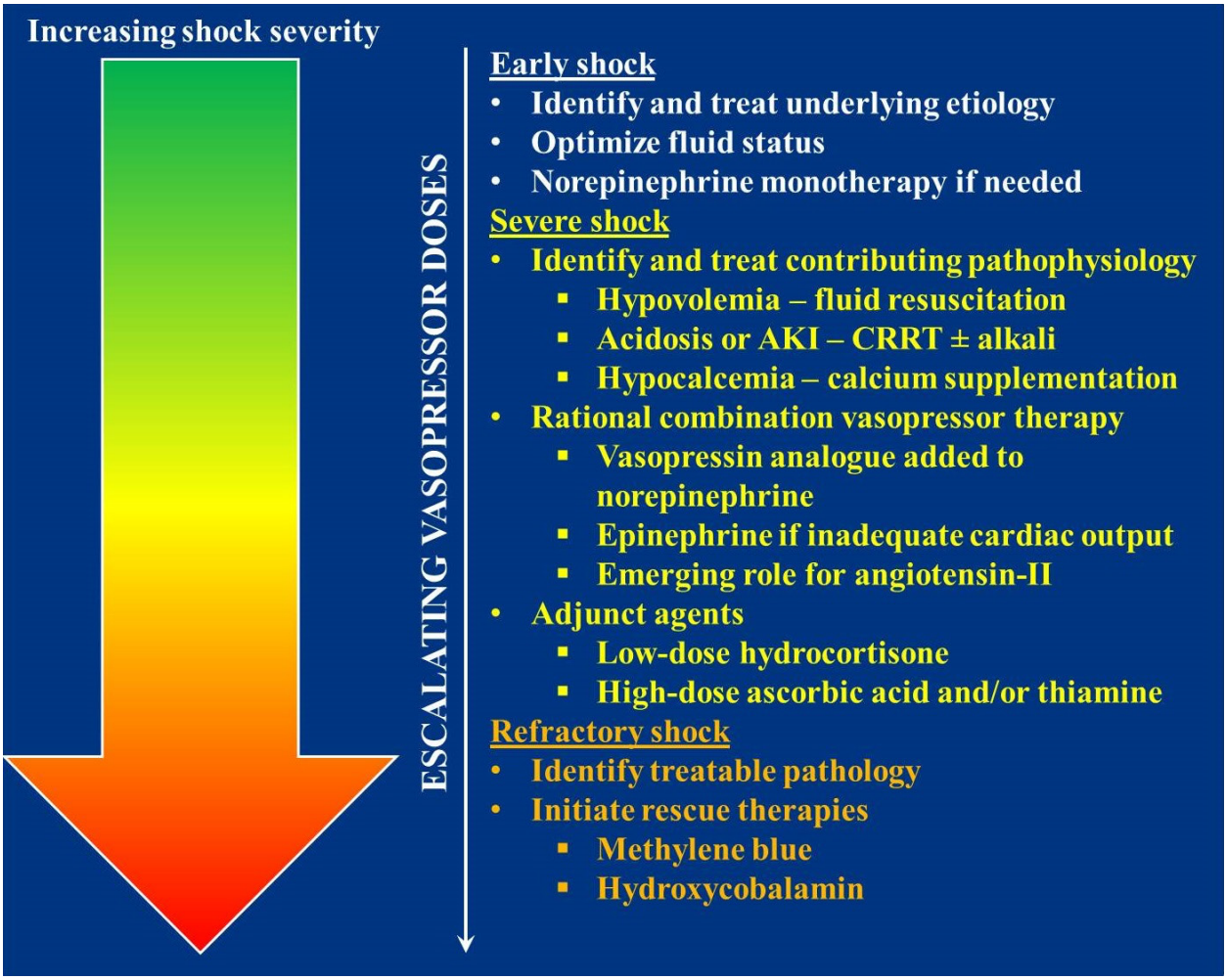
3. Formulate a plan for prioritizing different vasopressors and their usage in vasodilatory shock states in the ICU; and

4. Identify the mechanism of action, physiology and clinical perspectives with the newer vasopressors in refractory vasodilatory shock.

Vasodilatory shock, also known as distributive shock is by far the most common flavor of shock. Septic shock constitutes >90% of vasodilatory shock, though non-septic etiologies are also common, including acute pancreatitis and post cardiopulmonary bypass vasoplegia. The downstream manifestations of shock are hypotension and tissue hypoperfusion leading to inadequate cellular oxygen utilization.[1, 2] Even brief periods of hypotension with a mean arterial pressure (MAP) of <65 mm Hg in the intra-operative period can lead to renal and myocardial injury, and mortality.[3] Once MAP reaches <55 mm Hg one full minute of an exposure to hypotension, this is enough time to be associated with significantly worse outcomes. The threshold MAP associated with adverse outcomes is as yet unclear in critically ill patients admitted to the ICU, and likely depends on the baseline blood pressure and other patient characteristics.[4] The most recent Surviving Sepsis Campaign Guidelines define this threshold using a MAP of <65 mm Hg.[5] Hypotension in critically ill patients is often multifactorial in etiology and is a consequence of pathological vasodilation, impaired cardiac performance, hypovolemia, sedation, processes of care, and worsening morbidity due to underlying pathology. There is recent evidence to support a higher MAP to prevent organ system injury in the ICU. These thresholds are as high as a MAP of > 90 mmHg and have been consistently seen in both the postoperative critically ill population and a more heterogeneous septic ICU population.[7] A cautionary reminder, prior to interpretation of these numbers is that all of this data comes from large registry analysis, and that it remains exceedingly difficult to control for both known and unknown confounders in a population of very sick patients as in the ICU.

Vasodilatory shock that requires escalating doses of vasopressors and remains unresponsive to these interventions is associated with significant mortality and morbidity due to a multitude of factors.[1, 6] An optimal combination and dosing of vasoactive medications, thresholds for defining severe or refractory shock and role of rescue therapies remains to be determined.[6] The current vasopressor toolbox is centered around escalating high doses of catecholamines, supported at varying thresholds by more catecholamines or vasopressin and vasopressin analogues. This poverty of pressor choices may be associated with poor outcomes, largely because high dose catecholamine loads have been seen to be independent predictors of morbidity and mortality.[8,9] Recently, there has been renewed interest in the renin angiotensin aldosterone axis (RAAS), as a physiological regulator of vasomotor tone, blood volume and blood pressure, via the downstream product of RAAS, known as Angiotensin II. The safety and efficacy of Angiotensin II was shown in a randomized, double blind, placebo-controlled trial in patients on high dose standard of care vasopressors and high output vasodilatory shock. This led to subsequent approval of the compound by the FDA. The addition of Angiotensin II to the vasopressor toolbox will serve to offer additional new mechanistic options to intensivists as they deal with severe vasodilatory shock in critically ill patients. This Review Course Lecture will highlight the pathophysiology, risk factors, evaluation and management of refractory vasodilatory shock in the ICU and provide the audience a suggested algorithm to manage this frequent cause of hypotension in the ICU. (Fig.1)

Figure 1: Suggested algorithm to manage shock of increasing severity in the ICU.



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RCL-04
Anesthesia for Children with Inborn Errors of Metabolism: Opening Up the Black Box

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LEARNER OBJECTIVES

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

(1) Describe a broad conceptual overview of the different types of inborn errors of metabolism (IEM);

(2) Identify the pathophysiological nuances involved contextualized to the dysregulation of the normal metabolic pathways;

(3) Assess the perioperative considerations for children with IEMs; and

(4) Identify the anaesthetic complications in patients with IEM including catastrophic metabolic decompensation.

Although individually rare, inborn errors of metabolism (IEMs) are collectively common in the pediatric cohort, with a combined incidence of 1:800 live births. IEM is an umbrella term that encompasses a large group of genetically heterogeneous, inheritable disorders, that are progressive and have multi-systemic sequelae. IEM may be caused by the aberrations of carbohydrate, amino acids, organic acids or lysosomal metabolism and storage; arising from the failure of a discrete step or steps in a metabolic pathway.

The obstruction of a metabolic pathway may manifest as either an accumulation of potentially toxic substrates or a critical deficiency of energy production and utilization. IEM can present in both elective or emergent contexts, having profound ramifications for the Anesthesiologists as many are associated with a difficult airway, respiratory dysfunction, cardiac abnormalities (both structural and electrophysiological), risk of neurological sequelae (including refractory seizures), aspiration of gastric contents, hematological dyscrasias and metabolic dysfunction resulting in metabolic acidosis.

Due to the vast disparateness and heterogeneity of IEMs, exquisite knowledge is neither necessary or tenable. Rather, a basic conceptual understanding of the pathophysiology involved and moreover, proficiency for the safe management of a crisis such as an acute metabolic decompensation can help vitiate adverse outcomes. The session will first outline the common metabolic pathways associated with IEM, followed by a focused and evidence-based framework for the perioperative management of these patients.

RCL-05
Neurologic Complications Associated with Neuraxial Regional Anesthesia

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LEARNER OBJECTIVES

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

1. Identify factors that may predispose patients to neuraxial injury associated with a regional anesthetic;
2. Differentiate those conditions that demand immediate diagnosis and select the proper diagnostic modality;
3. Evaluate the controversial role of corticosteroids and cerebrospinal fluid drainage as therapeutic intervention; and
4. Assess critically the emerging concerns over the possible contribution of spinal stenosis, blood pressure control, and pre-existing disease to these injuries.

The American Society of Regional Anesthesia and Pain Medicine (ASRA) updated its practice advisory on neurologic complications associated with regional anesthesia and pain medicine in 2015.[1] The advisory is based on extensive literature review, analysis, and collation of recommendations by an international group of experts that includes regional anesthesiologists, pain medicine specialists, neuro-anesthesiologists, and neurologists. This Review Course Lecture focuses on complications that are specific to operating room or acute pain medicine applications of neuraxial anesthetic techniques.[2] These complications include 1) needle- or catheter-induced spinal cord trauma, 2) patients with pre-existing neurologic diseases, particularly spinal stenosis, 3) spinal cord ischemia, and 4) cauda equina syndrome (CES).

Attendees should be cognizant that the complications discussed herein are extremely rare — often on the order of only several incidents for every million blocks performed. There are no randomized controlled trials that address events this rare. Consequently, the recommendations offered are derived from large registry data, small case series, pathophysiologic inferences, and expert opinion. The recommendations are neither intended to supersede individual physician judgement, nor should they be construed as standard of care.

Needle- or Catheter-Induced Spinal Cord Trauma

Direct trauma to the spinal cord from needles or catheters is a distinctly rare event — about 5 per million neuraxial blocks as reported in Moen et al's Swedish study.[3] Contrary to expectation, direct needle-to-spinal cord contact is inconsistently heralded by pain or paresthesia, although injection of substances into the spinal cord typically causes pain. Minor paresthesia from direct spinal cord contact is relatively frequent and rarely if ever associated with injury. More intense sensations should prompt withdrawal of the needle or catheter and/or no further drug injection. If the painful sensation resolves and is not associated with neurologic signs, physician judgement becomes paramount in weighing the risk-to-benefit of proceeding with a neuraxial block versus general anesthesia. In theory, if the spinal cord has been entered, application of potentially toxic local anesthetic or adjuvant agents might be best avoided. If the paresthesia persists and/or the patient demonstrates signs of neurologic injury, immediate magnetic resonance imaging (MRI) should be obtained to rule-out spinal cord penetration. Based on studies that show inconsistent benefit with high dose methylprednisolone administration in traumatic spinal cord injury, some practitioners may elect to implement this intervention, especially after consultation with neurology or neurosurgical colleagues.

PRE-EXISTING NEUROLOGIC DISEASE

The wisdom of performing neuraxial anesthetic techniques in patients with pre-existing neurologic disease has long been debated, but the rarity of these disease processes and any associated perioperative neurologic injury precludes definitive recommendations regarding anesthetic management. The relatively large number of pre-existing neurologic conditions, and variations in suggested anesthetic management, make specific recommendations beyond the scope of this review. Instead, participants are referred to the practice advisory's in-depth discussions by Kopp et al.[4] In general, the decision to do a neuraxial anesthetic on a patient with pre-existing neurologic disease should be predicated on the specific disease state and its relative stability in the individual patient, as well as the known benefits of a neuraxial technique versus the theoretical risks of causing a new or worsening neurologic deficit. Based on animal studies, potentially beneficial modifications of regional anesthetics include limiting the total local anesthetic dose, particularly by using lower concentrations, avoiding vasoconstrictive additives such as epinephrine, and for epidural analgesic techniques, preference for neuraxial opioids that are devoid of neurotoxic effects, rather than local anesthetic.

With regard to specific disease states, the practice advisory notes the following: First, there are data to suggest that the provision of spinal anesthesia in patients with sensorimotor neuropathy or diabetic polyneuropathy may result in a slightly increased risk for new or progressive neurologic deficits. Second, neuraxial anesthetics in patients with complex closed spinal dysraphisms is not advised. Third, for obstetrical patients with multiple sclerosis, epidural analgesia is considered safer than intrathecal techniques, but with the knowledge that multiple sclerosis is known to have a higher rate of relapse during the postpartum period. Fourth, although a peripheral nervous system disorder, practitioners who

perform neuraxial anesthetics should be aware of postsurgical inflammatory neuropathies (PSIN). These patients present hours to days after surgery with mono- or poly-neuropathies that may or may not be within the distribution of the surgery or anesthetic. Timely diagnosis of PSIN is important because its course can be improved by immunomodulation therapy.

SPINAL STENOSIS

Perhaps the most relevant pre-existing neurologic disorder is spinal stenosis. (Figure 1) Degenerative spinal canal disease is prevalent, particularly in the elderly population, where 19% of patients in their sixties meet radiologic criteria for severe spinal stenosis. Unfortunately, many patients and their physicians are unaware that they have significant spinal canal narrowing. In recent years, large population studies have confirmed what decades of case reports had suggested, that is, an association of spinal stenosis with perioperative neuraxial injury. This linkage has been established for CES, spinal cord ischemia, and epidural hematoma / abscess. For example, about a third of Swedish patients who developed epidural hematoma after a neuraxial anesthetic were discovered to have previously undiagnosed, age-related spinal stenosis. The frequency of epidural hematoma was 1:200,000 for young women that received epidural analgesia for labor, but 1:3,600 for elderly women having total knee arthroplasty under a neuraxial anesthetic. Many of the older women had significant degenerative disease of the spine.[3]

The association of spinal stenosis with neuraxial injury does not prove a causal relationship, which becomes important when deciding whether to recommend a neuraxial anesthetic for patients with this common diagnosis. The ASRA practice advisory recommends that practitioners consider the benefits of neuraxial anesthesia versus the inherent risks associated with spinal stenosis, especially in two circumstances. First is patients with known severe spinal stenosis, based on spinal imaging and/or development of spinal claudication symptoms with minimal activity. This concern may be especially relevant when the location of spinal stenosis coincides with the intended level of neuraxial block placement. Second are patients with co-morbidities that either further encroach upon an already narrowed spinal canal (such as non-neutral surgical positioning like lateral flexion or lumbar hyperlordosis), or conditions that could reduce oxygen delivery to the spinal cord (such as anemia, hypocapnia, abdominal or thoracic insufflation, sickle cell anemia, or ankylosing spondylitis).

SPINAL CORD ISCHEMIA

Perioperative spinal cord ischemia or infarction in the setting of a neuraxial anesthetic is an extremely rare event that is often attributed to low blood pressure, the use of vasoconstrictors, or direct needle trauma to the spinal cord vasculature. The latter two explanations are fallacious. Normal dose epinephrine does not compromise spinal cord blood flow (SCBF). Regarding needle injury, the posterior spinal arteries are redundant and thus damage to one is unlikely to cause significant injury, while the anterior spinal artery cannot be injured directly without penetrating the spinal cord and thus being associated with MRI evidence consequent to that trauma. Injury to segmental arteries or radicular arteries is possible, but requires either a needle that is misdirected laterally or an intentional lateral-based approach to the neuraxix. (Figure 2)

The issue of blood pressure management and spinal cord ischemia is less clear. Autoregulation of SCBF parallels cerebral blood flow (CBF). (Figure 3) Contemporary understanding suggests that the lower limit of autoregulation (LLA) is closer to 60 – 65 mmHg mean arterial pressure (MAP) than it is to 50 mmHg, varies widely in humans, and correlates poorly with baseline blood pressure or history of hypertension. Recent studies have linked MAPs 30% to 40% below baseline, over prolonged periods of time (probably 20 minutes or longer), with increased risk of perioperative cerebral stroke, myocardial injury, or renal failure. Because SCBF mirrors CBF, it is reasonable to apply the same concerns to blood pressure management during neuraxial blockade, especially because there are few reasons to allow MAPs during neuraxial anesthesia to drop below 20% of baseline. Nevertheless, the rarity of spinal cord ischemic injury and the inconsistency of documented prolonged hypotension in the limited case reports of its occurrence argues for a heightened level of concern in patients with co-morbidities that place them at risk for spinal cord ischemia. Such co-morbidities can cause diminished oxygen delivery to the spinal cord, which can be worsened by low spinal cord perfusion. Co-morbidities include mechanical conditions such as severe spinal stenosis, non-neutral positions, or ankylosing spondylitis. Other conditions that reduce oxygen delivery include anemia, hypocapnia, intra-abdominal or intra-thoracic insufflation, abnormal spinal vasculature, or embolic phenomena.

Although treatment is often futile, suspected spinal cord ischemia should prompt institution of normal to slightly elevated MAP. Consideration may be given to cerebrospinal fluid (CSF) drainage to improve spinal cord perfusion (MAP minus CSF pressure). The ASRA practice advisory recommends against the use of steroids for ischemic spinal cord lesions. Management of these patients is best done in consultation with neurology or neurosurgery colleagues.

CAUDA EQUINA SYNDROME

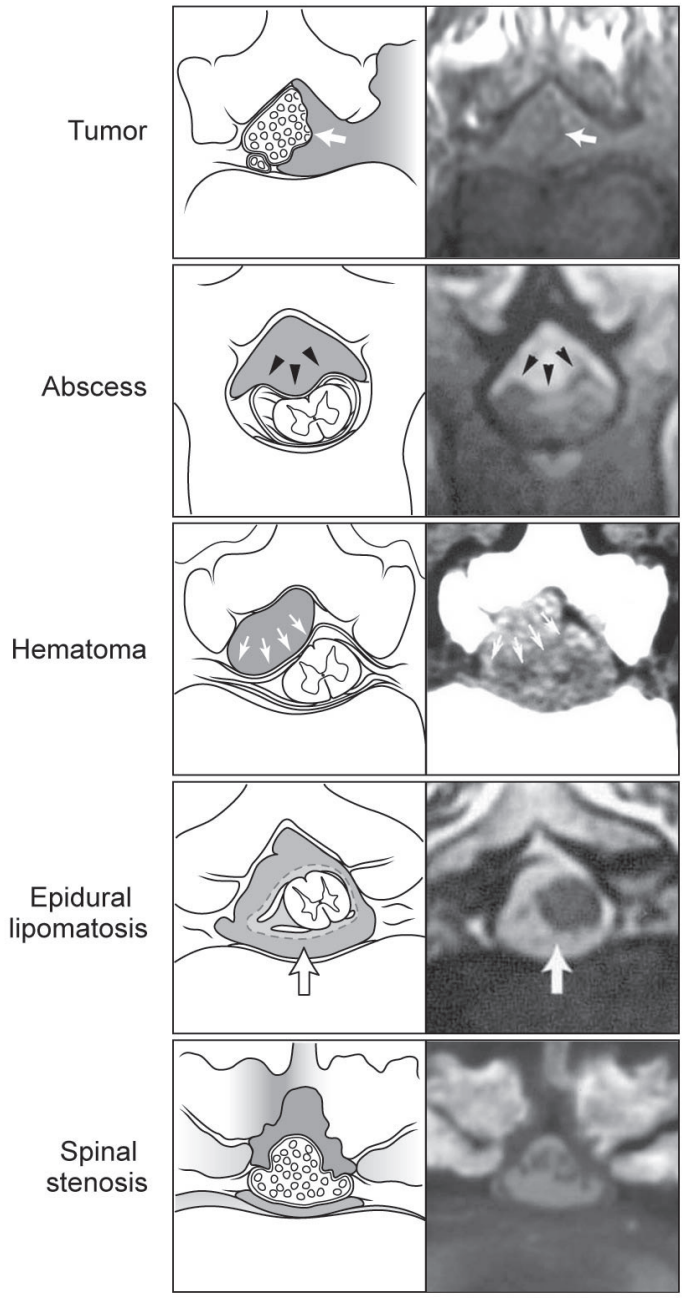
Cauda equina syndrome is quite rare — about 2 per million neuraxial anesthetics.[3] Other than from mass lesions such as an extruded disc or hematoma (Fig. 1), CES has few known risk factors – supernormal doses of intrathecal local anesthetics, maldistribution of those local anesthetics within the sacral area of the spinal canal, and spinal stenosis. Yet these three factors probably account for less than a third of (non-mass lesion) cases. Rather, most CES is idiopathic and associated with normal indication for the block, normal local anesthetic dosing, and pristine imaging studies after the insult. Current theory suggests that idiopathic CES may be the result of neurotoxicity from extreme sensitivity to normal clinical doses of local anesthetic. An alternative explanation is that CES is a manifestation of neuro-inflammation in response to anesthetic drugs, surgery, needle or catheter placement, or factors yet unknown. There is no treatment for CES; recovery is unpredictable, but seldom complete.

DIAGNOSIS AND TREATMENT

Neurologic injury associated with neuraxial anesthesia constitutes a diagnostic emergency, the goal of which is to rapidly rule-out a surgically-correctable mass lesion. If an MRI is not immediately available, computed tomography (CT) can diagnose most significant intra-spinal masses. If the spinal cord is compressed by blood, pus, or degenerative material (Fig. 1), surgical decompression should be accomplished within 8 to 12 hours of symptom onset to optimize any chance of full recovery. The absence of an identifiable mass leads to the presumptive diagnosis of CES or spinal cord ischemia. Especially if performed early after symptom presentation, MRI may not show signs of spinal cord ischemia or infarction until a day or more after the insult. As noted previously, treatment of conditions that do not compress the spinal cord is often futile, differs according to the suspected etiology, and is best conducted in conjunction with expert neurologic consultation.[5]

Figure 1.

From Neal & Rathmell, 2013.[6] Used with permission.



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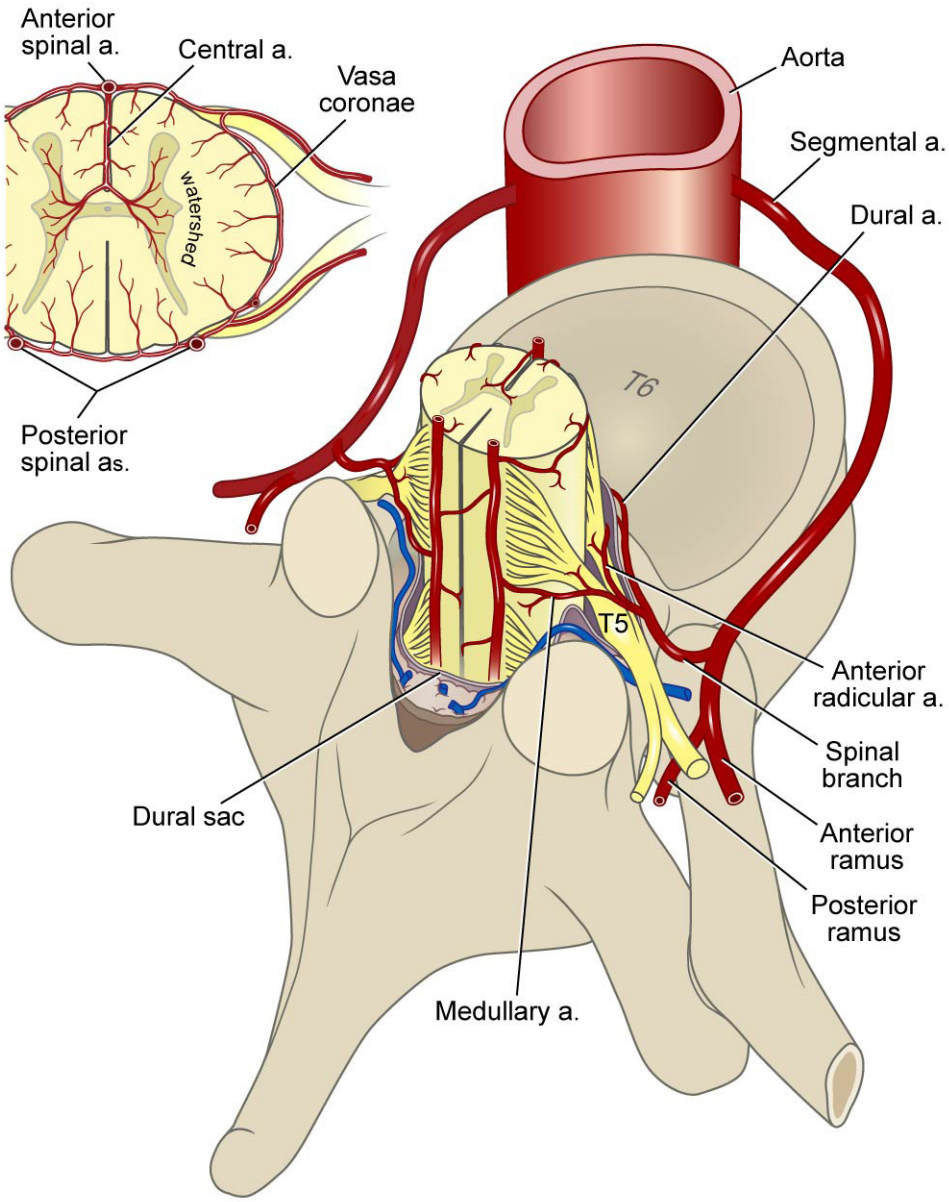

Figure 2.

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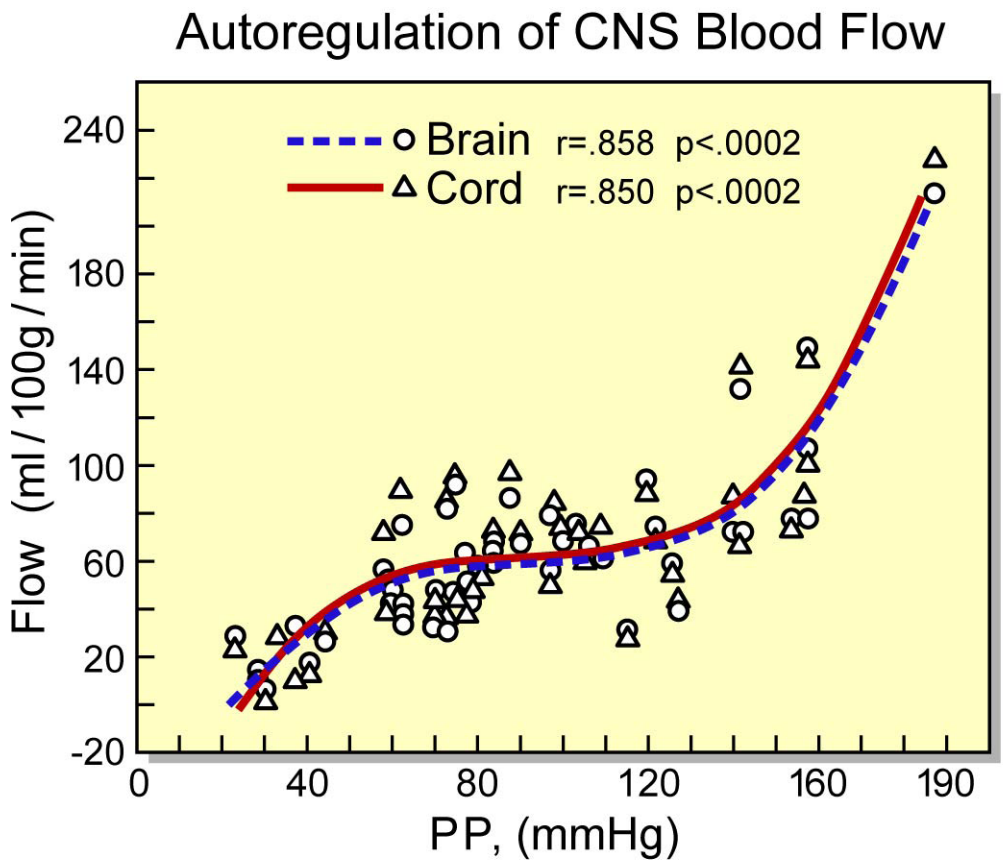

Figure 3.

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RCL-06
SOCCA: Heart Failure with Preserved Ejection Fraction (HFpEF) as a Perioperative Risk Factor

Aalok K. Kacha, MD, PhD, Assistant Professor, Department of Anesthesia and Critical Care, The University of Chicago Medicine, Chicago, Illinois

LEARNER OBJECTIVES

This lecture will provide an overview of heart failure with preserved ejection fraction with a focus on physiology and implications for anesthetic management. A brief introduction of these topics and selected references are included below.

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

1. Identify severe heart failure as a risk factor for overall mortality;
2. Describe the peri-operative risks of heart failure with reduced ejection fraction vs heart failure with preserved ejection fraction;
3. Interpret pre-operative testing of cardiac function for patients with heart failure with preserved ejection fraction; and
4. Propose strategies for management of decompensated patients with heart failure with preserved ejection fraction.

DEFINITION

Heart failure (HF) with preserved ejection fraction (HFpEF) is a heterogeneous disorder and there is variability in how it is defined. The 2013 heart failure guidelines developed by the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines note that heart failure is a disorder of ventricular ejection or filling and has a varied clinical presentation. Heart failure can exist with a range of left ventricular ejection fractions (EF). Heart failure with reduced ejection fraction (HFrEF) is known as systolic HF and associated with an EF ≤ 40%. HFpEF is defined as heart failure with EF ≥ 50%. There is an intermediate group of patients with EF 41-49% which share many characteristics of HFpEF and are often excluded from HFrEF clinical trials.[1]

CLINICAL IMPORTANCE

Approximately half of all patients admitted with HF have HFpEF. A single institution study of over 4500 patients discharged with a diagnosis of HF and a documented EF over a 15-year period reported that 53% of patients had HFrEF and 47% of patients had HFpEF.[2] An analysis of patients enrolled in clinical trials, which often exclude patients with decompensated HF, demonstrated that the outcomes of patients with HFpEF are better than those of patients with HFrEF.[3] The reported mortality rate for HFpEF is in the range of 50 per 1000 patient-years as compared to approximately 110 per 1000 patient-years in with HFrEF. Importantly, the rate of death and hospitalization is higher in patients with HFpEF compared to similar patients with hypertension.

Most clinical trials have focused on HFrEF and the few clinical trials of interventions in HFpEF have not shown a mortality benefit, so treatment options for this disease remain limited. Given the incidence and prognosis of HFpEF, it is important for the anesthesiologist to have an understanding of this disease as our understanding of the mechanism and treatment of HFpEF evolve over time.

DIAGNOSIS AND EVALUATION

The diagnosis of HFpEF presents a challenge as the signs and symptoms of HF are non-specific. These include dyspnea, fatigue, and fluid retention. These may result in reduced exercise tolerance, pulmonary edema, abdominal vascular congestion, and/or peripheral edema. Patients suspected to have HF should be evaluated with echocardiography. Patients commonly demonstrate left ventricular hypertrophy and diastolic dysfunction, but these may be present in patients without HF and absent in patients with HFpEF. Evaluation of natriuretic peptides is recommended for the diagnosis of HF, although some patients with HFpEF may not have elevated levels.[4,5] The European Society of Cardiology 2016 guidelines also recommended confirming either left ventricular hypertrophy, left atrial enlargement, or diastolic dysfunction for the diagnosis of HFpEF.[4] Invasive hemodynamic measurements including right heart catheterization, at rest, and with exercise may be required as the response to exercise is abnormal.

COMORBIDITIES

Risk factors for HFpEF include hypertension, obesity, and diabetes. As these conditions are common in surgical patients, their recognition as risk factors for HFpEF is vital. Atrial fibrillation and pulmonary hypertension are common in patients with HFpEF. Pulmonary hypertension may be absent at rest and develop with exercise, limiting functional capacity of patients. This characteristic reinforces the importance of functional capacity in the pre-operative assessment. Pulmonary hypertension is venous and often associated with decreased left atrial compliance, but may include a slight increase in pulmonary vascular resistance.[6] Given the potential anesthetic and procedural consequences of pulmonary hypertension, the recognition of a potential for a dynamic, clinically relevant increase in filling pressures in patients with HFpEF may be warranted.

PHENOTYPE & PATHOPHYSIOLOGY

There are multiple clinical presentation phenotypes that have been identified in patients with HFpEF. These include lung congestion, chronotropic incompetence, pulmonary hypertension, skeletal muscle weakness, and atrial fibrillation.[7] The management of each of these may assist in treating patients with HFpEF. These conditions may share a common pathologic connection with a role for systemic inflammation resulting in multiple end-organ effects in the pulmonary vasculature, skeletal muscle, and kidneys. Coronary endothelial inflammation may trigger increased interstitial collagen deposition and myocardial fibrosis.[6,7]

MANAGEMENT

To date, there is no therapy for HFpEF which has demonstrated a reduction in mortality. Spironolactone for HFpEF reduces the rate of heart failure admissions.[8] In the major trial of sprinolactone for HFpEF, a subgroup analysis which excluded trial patients from Russia and Georgia suggested there is a reduction in cardiovascular death.[9,10] Current management of HFpEF includes diuretics to improve symptoms, although the pathophysiology of diastolic dysfunction includes a sensitivity to excessive decreases in left ventricular preload.[11] Many therapies used for HFrEF have not shown similar benefit in trials of patients with HFpEF, including angiotensin receptor blockers,[12,13] digoxin,[5] nitrates,[14] and sildenafil.[15] Preliminary work suggests that neprilysin blockade has a favorable hemodynamic effect in patients with HFpEF and a study to assess clinical benefit is underway (NCT01920711).[16,17] A trial to assess whether inhaled nitrite improves exercise capacity in patients with HFpEF is planned (NCT02742129).[18] The introduction of an interatrial shunt with an implanted device to reduce left atrial pressures has shown to reduce PCWP during exercise in patients with HFpEF and is undergoing further study (NCT03088033).[19,20] There are no trials on the acute peri-operative management of HFpEF, but the use of diuretics to relieve congestive symptoms is likely warranted. Fluid management is a challenge, as patients have an increased sensitivity to preload to maintain cardiac output but are susceptible to decompensation with excess fluids. Additionally, given the potential for changes in pulmonary pressures with exercise and possible chronotropic incompetence, it is likely that patients with HFpEF may tolerate surgical stresses less well than patients without HF.

PERI-OPERATIVE OUTCOMES

There are few studies of the effects of HFpEF on peri-operative outcomes. Outcomes of patients with HFpEF, defined as an EF ≥ 50%, who underwent isolated coronary artery bypass grafting (CABG) has been investigating in the Swedish Web-system for Enhancement and Development of Evidence-based care in Heart disease Evaluated According to Recommended Therapies (SWEDEHEART) registry.[21] Outcomes included all-cause mortality and readmission for HF. The registry included 41,906 patients who underwent CABG from 2001-2013. Of these, 4672 patients had HF, 1216 with HFpEF & 3456 with HFrEF. During the mean follow-up time of 6 years, 19.0% of patients died. Patients with HF demonstrated increased mortality: no HF and pEF: 13.2%; no HF and rEF: 24.6%, HFpEF: 33.9%, HFrEF: 42.9%. Additionally, HFpEF has been indentified as in independent risk factor for mortality and post-operative shock after CABG.[22] The effect of HFpEF on outcomes in patients undergoing non-cardiac surgery remains an area in need of study.

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RCL-07
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) Formulate a plan for airway management for cesarean delivery;
2) Describe the role of supraglottic airway devices in the obstetric airway;
3) Discuss advantages and dsadvantages of video aryngoscopy in obstetric anesthesia; and
4) Formulate aplan to exchange a supraglottic airway device with an endotracheal tube.

Difficult 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 technology, and the widespread use of guidelines and algorithms have significantly contributed to a safer environment for airway management in the parturient. This has resulted in decreased anesthesia related morbidity and mortality.[2] 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). Five thousand cases of general anesthesia (GA) for cesarean delivery (CD) were identified. Within that cohort, there was an incidence of failed intubation of 1:553 cases. In patients with a failed intubation, there were no hypoxemic arrests.[3] Using Mckeen's definition for failed intubation in obstetric patients [4] ("*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. retrospectively reviewed airway management for CD's 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). [5]

GA is the fastest approach to reliably anesthetize a patient for a category 1 CD. [6] 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. [7] In a recent systematic review of meta-analyses, Krom et al. 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). [7] Reluctance to convert an inadequate neuraxial anesthetic to a GA frequently results in maternal pain/discomfort and emotional distress. This leads to decreased patient satisfaction and increased liability for the anesthesiologist [2,7].

With the declining rate of general anesthesia 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 CD's in the United States are performed under GA. The implication of this statistic is that there are anesthesia residents graduating without hands-on experience performing a GA for CD. [8,9] 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. [10]

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. [11]

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. The American Society of Anesthesiologists (ASA) practice guidelines for management of the difficult airway recommends considering video-assisted laryngoscopy as an option for the initial approach to intubation. based on the anesthesiologist skill and preference. [12]

There are many *reports* of the successful use of videolaryngoscopes as rescue devices in obstetric patients. [13-16] Comparative studies in the obstetric population, however, are lacking. A retrospective analysis by Aziz et al. reported the successful use of the GlideScope to intubate the trachea in all patients on the first attempt[14] Shonfeld et al. described the successful use of the C-MAC in 27 patients and the Airway Scope has been described to intubate two patients for unscheduled intraoperative awake endotracheal intubation during CD. [15] [17] Technological advances have been

made in the design of several videolaryngoscopes. The McGrath Series 5 laryngoscope has an adjustable blade length that may offer an advantage when intubating an obstetric patient as breast engorgement may interfere with placement of the laryngoscope. The laryngoscope blade of King Vision portable videolaryngoscope can be inserted separately and, once positioned in the oropharynx, the monitor can be attached. Pharyngeal trauma has been reported with videolaryngoscopes requiring a stylet to facilitate intubation. [18] The increased upper airway tissue friability seen in obstetrical patients might make them more prone to this complication.

A potential disadvantage of videolaryngoscopy is the longer time required to intubate the trachea as compared to conventional laryngoscopy. [19, 20] The prolonged period of apnea may be problematical in the obstetric patient who desaturate quickly due to increased oxygen consumption and decreased functional residual capacity. To date, there is no evidence that this longer period of apnea is of any clinical significance.

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) (LMA's Mask Airways and Non-laryngeal Mask Airways) 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. 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.

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.

THE ROLE OF ULTRASONOGRAPHY IN MANAGING THE OBSTETRIC AIRWAY

Recently, Ahuja et al. described the use of airway sonography to assess dynamic airway dimensional changes in preeclamptic patients. [11] Ultrasonography can be used to reliably locate the cricothyroid membrane to facilitate front-of neck access should it be necessary. [21]

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. [22] The ASA practice guidelines for the management of the difficult airway emphasize the importance of a "pre-formulated extubation strategy". [12] 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 which included planning, preparing, and executing tracheal extubation; including post-extubation follow up. [23]

THE VORTEX APPROACH

Recently, the Vortex concept was developed by Chrimes as a visual cognitive aid to help implement difficult airway management algorithms. [24] Currently, there are no reports of implementing the Vortex approach in obstetric anesthesia.

CONCLUSIONS

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 in managing the difficult airway in obstetric anesthesia. With further technological advances and operator comfort, 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. There are serious and nearly insurmountable ethical concerns with studying obstetric difficult airway management in prospective, controlled, randomized trials. Thus, the decision of whether or not video laryngoscopes should be used as a primary airway device in obstetric patients undergoing GA is not likely to be evidenced-based anytime soon.

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RCL-08
LVADs & Noncardiac Surgery: What To Do When They Come to Your Operating Room

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LEARNER OBJECTIVES

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

(1) Describe the increasing incidence of and reasons for LVAD patients presenting for noncardiac surgery;

(2) Identify LVAD console parameters and construct a framework to manage intraoperative hemodynamic perturbations based on these parameters;

(3) Apply current evidence and expert opinion regarding optimal intraoperative hemodynamic monitoring for LVAD patients undergoing noncardiac surgery; and

(4) Formulate an understanding of perioperative anticoagulation management for LVAD patients undergoing noncardiac surgery.

Over the last decade in the United States alone, well over 22,000 mechanical support devices have been implanted, with the vast majority consisting of left ventricular assist devices (LVADs).[1] An LVAD is a pump designed to assist a failing left ventricle, thereby extending the patients' life. Although many indications exist for LVAD implantation, this discussion will focus on patients receiving implantable continuous flow LVADs as either a "bridge to transplantation" (i.e. LVAD supports the patient until a cardiac transplant is available) or "destination therapy" (i.e. LVAD is implanted to improve a non-transplantable patient's quality and quantity of life until death). With the survival after LVAD implantation currently being 81% at 1 year, 70% at 2 years, and 49% at 4 years, the number and frequency of LVAD patients presenting to operating rooms for noncardiac surgery (NCS) will continue to increase.[1-8]

LVAD PHYSIOLOGY

Modern day LVADs are continuous flow devices that function by continuously pumping blood from the left ventricle to the aorta.[9,10] It follows that depending on factors such as loading conditions and LVAD settings, the patient can be either pulsatile or non-pulsatile. Table 1 summarizes important LVAD parameters displayed on the LVAD console. In general, as the speed of the LVAD is increased, blood flow through the LVAD similarly increases. This results in greater unloading of the left ventricle, a decrease in pulsatility, and a decrease in aortic valve opening. These parameters can be used in context with patients' other vital signs and physical examination to interpret hemodynamic pertubations encountered perioperatively (Figure 1).

LVADS AND NONCARDIAC SURGERY

With the increase in both the number of LVAD implantations and survival after LVAD implantation, the need for NCS in this patient population has risen.[1-3,6,8] All surgical specialties have seen LVAD patients presenting for NCS. Additionally, although ideally cared for in hospitals familiar with LVAD patients, emergent operations or circumstances preventing patient transfer may require perioperative management for NCS by anesthesiologists previously unaccustomed to caring for LVAD patients. Several recent retrospective series have reviewed single institutions' experiences in caring for LVAD patients undergoing NCS.[2-8,11]

PERIOPERATIVE MANAGEMENT CONSIDERATIONS

LVAD Logistical Considerations

Continuous flow LVADs are able to be fully powered by portable batteries. However, in the perioperative period, LVADs should be connected to a definitive power source so that they are not reliant on depletable batteries for power. Additionally, the LVAD should be connected to a console so that the LVAD parameters (Table 1) are displayed and can be utilized in interpreting hemodynamic pertubations (Figure 1).

Blood Pressure Monitoring

Controversy exists regarding the optimal method of accurately determining and documenting blood pressure (BP) in continuous flow LVAD patients perioperatively. Of commonly employed noninvasive blood pressure (NIBP) modalities, Doppler determination of blood pressure is the most reliable, resulting in a blood pressure reading in over 90% of attempts, compared to only approximately 50% with traditional automated BP cuffs.[12,13] BP determination with manual auscultation or manual palpation is highly unreliable, as each has been shown to be successful in less than 15% of BP attempts.[12] Doppler BP determination entails utilization of a manual BP cuff and a Doppler probe to determine during manual BP cuff deflation at what BP Doppler signals become audible. This typically is performed on the upper extremity using the brachial artery. Recent series of LVAD patients undergoing NCS have reported use of invasive arterial line BP monitoring in 0-72% of patients.[2-8] However, in the largest series to-date that utilized arterial line BP monitoring in only 20% of anesthetics, blood pressure monitoring gaps of 20 min or more were noted in the majority (55%) of anesthetics.[6,14] It follows that my recommendation, especially if one lacks familiarity caring for these patients, is to utilize invasive arterial line BP monitoring in LVAD patients requiring general anesthesia.[14] In cases involving monitored anesthesia care such as gastrointestinal endoscopy,

noninvasive BP determination is likely sufficient, but resources and a plan to ensure reliable and accurate BP determination must exist should NIBP modalities fail.

Defibrillation and Cardioversion

Device manufacturers of modern continuous flow LVADs have advised that transcutaneous defibrillation or cardioversion is safe and can be performed in patients with these devices.[9,10] However, traditionally lethal cardiac rhythms such as ventricular fibrillation that would result in certain cardiac arrest in patients without LVADs *may* be hemodynamically tolerated in LVAD patients. It follows that perfusion should be assessed prior to defibrillation in LVAD patients. Assessments of perfusion in the operating room may include BP, capnography, pulse oximetry, capillary refill, cerebral oximetry, etc.

Chest Compressions

Recent American Heart Association guidelines support the use of chest compressions in select LVAD patients if necessary.[15] If cardiac arrest is suspected, the function of the LVAD should be immediately verified by auscultating for the LVAD hum. In the highly monitored perioperative setting where rapid changes in hemodynamics commonly occur, if the LVAD is functioning, other treatments to mitigate hemodynamic pertubations such as vasoactive medication and fluid administration should be utilized before chest compressions.

Anticoagulation Reversal

The modern day LVAD manufacturers typically recommend anticoagulation with warfarin for a target international normalized ratio (INR) of 2-3 and antiplatelet therapy with at least aspirin.[9,10] With respect to reversal of anticoagulation and antiplatelet therapy prior to elective procedures in LVAD patients, multidisciplinary consultation with the patient's LVAD cardiologist, surgeon, anesthesiologist, and/or other experts in anticoagulation is recommended to formulate an anticoagulation/antiplatelet continuation or cessation plan. Given the significant morbidity and mortality involved with LVAD thrombosis, proceeding with NCS with full or partial anticoagulation is recommended if possible. In cases of emergent life-threatening bleeding requiring operation (e.g. intracranial hemorrhage, severe intraabdominal bleeding, etc.), reversal of anticoagulation is recommended.

Cardiac vs. Noncardiac Anesthesiologist

Recent series on LVAD patients undergoing NCS all report that the majority (53-100%) of these patients are safely being cared for by noncardiac anesthesiologists.[2,3,5-8] It follows that more important than the formal training of the anesthesiologist is an in-depth understanding of LVAD physiology and the perioperative considerations relevant to this patient population. With the ongoing rise in the number of LVAD patients and their need for NCS, LVADs will continue to become more commonplace for noncardiac anesthesiologists.

SUMMARY

The number of patients with LVADs in increasing due to increased implantation trends and improved long-term survival. NCS in this patient population will continue to increase. Paramount to successful management of LVAD patients presenting for NCS is an in-depth understanding of LVAD physiology and the perioperative considerations inherent to these patients. With this knowledge, noncardiac anesthesiologists can safely and successfully care for this challenging yet rewarding patient population.

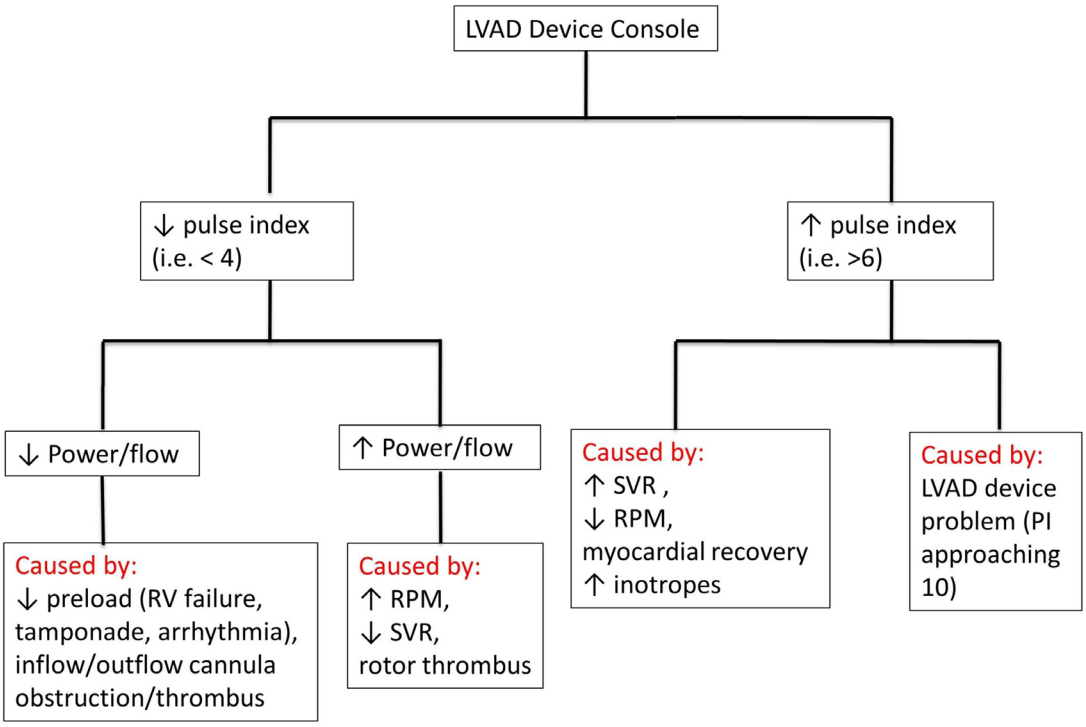

Figure 1 – Clinical interpretation of LVAD parameters

Table 1 – LVAD Parameters

LVAD Parameter	Explanation
Speed	The number of revolutions per minute at which the LVAD is functioning
Power	The measured power in watts that the LVAD is requiring for the set speed. Significant elevations in power may occur with LVAD pump thrombosis.
Flow	The *calculated* blood flow through the LVAD, which is determined algorithmically from speed and power (and in some LVADs the patient's inputted hemoglobin). False elevations in flow may occur in the setting of LVAD thrombosis.
Pulse Index	The *calculated* variability in LVAD flow during the cardiac cycle.

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RCL-09
Cerebrospinal Fluid Drainage Catheters in Endovascular and Open Aortic Surgery

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LEARNER OBJECTIVES

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

1. Identify the indications of CSF drainage catheters in endovascular and open aortic surgery;
2. Describe the safe steps in insertion and management of CSF drainage catheters;
3. Differentiate prophylactic from therapeutic CSF drainage; and
4. Identify CSF drainage catheter related complications, including measures to prevent and manage these complications.

INTRODUCTION

The incidence of spinal cord injury (paraplegia/paraparesis) after open and endovascular thoracic and thoracoabdominal surgery varies largely across studies (1-30%), [1-3] with most studies documenting an incidence between 3-9%.[4-7]

RISK FACTORS FOR SPINAL CORD INJURY AFTER THORACOABDOMINAL AORTIC ANEURYSM (TAAA) REPAIR AND THORACIC ENDOVASCULAR AORTIC REPAIR (TEVAR)

Risk factors for spinal cord injury specific to TAAA repair include prolonged aortic crossclamping, interruption or ligation of intercostal and other spinal collateral vessels, extensive aortic aneurysms (Crawford types I and II), advanced age, diabetes mellitus, and emergency surgery. Risk factors for spinal cord injury specific to TEVAR include long segment endograft deployment in the thoracic aorta, occlusion or injury to major vessels contributing to the collateral circulation of the spinal cord (left subclavian/external iliac/hypogastric) and preoperative renal insufficiency. Risk factors for SCI shared between both approaches (open and endovascular) include severe atherosclerosis of the aorta, previous abdominal aortic aneurysm repair (open or endovascular), and perioperative hypotension. [8]

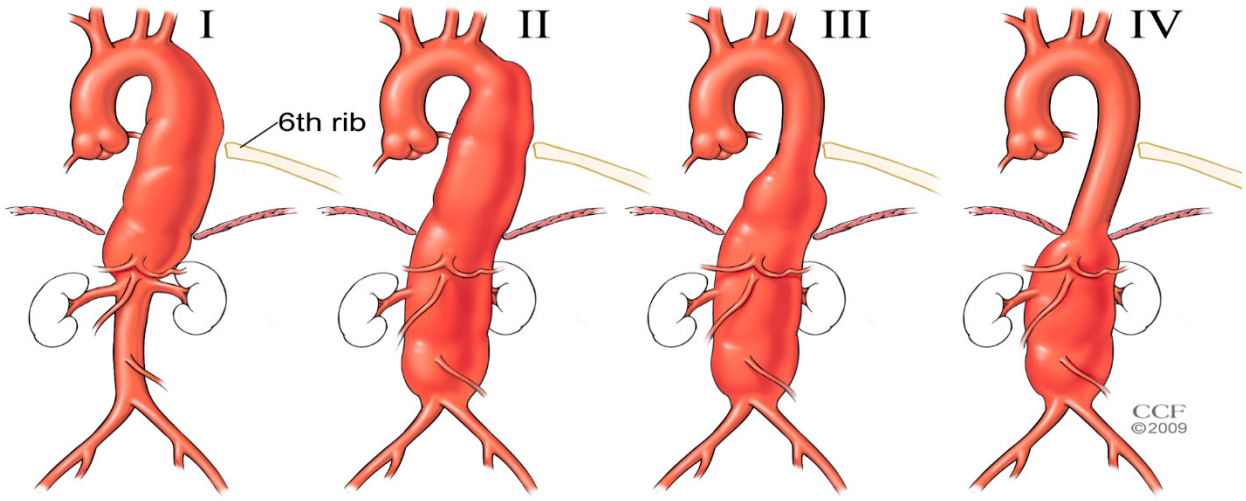

Figure 1: Crawford classification of thoracoabdominal aneurysms

BLOOD SUPPLY TO THE SPINAL CORD (FIGURE 2) AND MECHANISM OF SPINAL CORD INJURY

Cerebrospinal fluid (CSF) drainage theoretically increases spinal cord blood flow by decreasing CSF pressure resulting in an increased spinal cord perfusion pressure.

Spinal cord perfusion pressure is defined as distal mean aortic pressure minus CSF pressure (or central venous pressure whichever is greater).

The blood supply of the spinal cord is made up of two posterior spinal arteries (originating from the vertebral or posterior inferior

cerebellar artery) and one anterior spinal artery. From the caudal end, the anterior spinal artery receives arterial collateral supply from the internal iliac artery and its branches, the middle sacral artery and the inferior mesenteric artery, while the thoracic portion of the anterior spinal artery is supplied by radicular branches of the intercostal arteries.

The largest of the radicular branches, the artery of Adamkiewicz (arteria radicularis magna), arises directly from the aorta at T9–T12 in the majority of cases, but can arise anywhere between T5 and L5. Prolonged aortic crossclamping and interruption of the blood supply to this vessel during TAAA surgery or exclusion of this artery during aneurysm stenting can result in paraplegia.

Other postulated mechanisms for are the occurrence of hypoperfusion as a result of hypotension as well as thrombosis or embolization of the arteries supplying the anterior spinal artery. The injury seen after ischaemia of the spinal cord (anterior spinal artery syndrome) is manifested by loss of motor function and pinprick sensation and preservation of vibratory and position sense.

Evidence of Efficacy of CSF drainage in TAAA and TEVAR

Several randomized trials and a metaanalysis have documented the efficacy of prophylactic CSF drainage (to a pressure of 10 mmHg) in reducing the incidence of spinal cord injury after open thoracoabdominal repair (type I and II). [5,6,9] Evidence to support the efficacy of lumbar CSF drainage in decreasing the incidence of spinal cord injury after TEVAR comes from prospective observational and retrospective trials. [10,11] There are also multiple reports of reversal of paraplegia after institution of CSF drainage in patients undergoing TEVAR.[12,13] In light of proven efficacy in the open thoracic repair literature, it is unlikely that randomized controlled trials will be conducted to prove the efficacy of lumbar CSF drainage in reducing SCI. It is important to note that not all study results support the use of CSF drainage for the reduction in SCI in patients undergoing TAAA and TEVAR. [3,14,15]

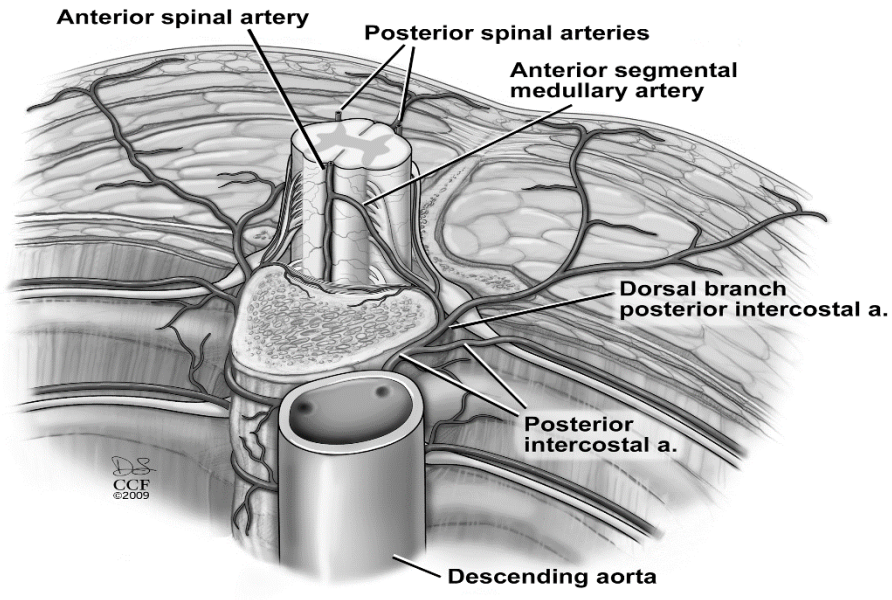

Figure 2: Blood supply of the spinal cord

Table 1: Common Indications of CSF drainage catheters in TAAA and TEVAR (based on risk factors associated with a higher incidence of SCI)

Complication	Incidence	Prevention	Management
Postdural Puncture Headache	2.3% to 9.7% [18,19]	-Use an evidence based approach for choosing CSF drainage catheters -Avoid repeated dural access -Maintain catheter for 48 hours	Epidural blood patch
Drain Failure	7.8% [18]	-Teams experienced in insertion and management -Training -Fluoroscopic guidance	Appropriate troubleshooting following insertion
Neuraxial Hematoma	3.2% [20]	-Use ASRA guidelines -Check coagulation profile -Avoid repeated attempts -Consider radiologic/ultrasound guidance	-MRI (increased signal intensity on T2 images) -Neurosurgical consultation -Emergent decompressive laminectomy and evacuation of hematoma
Bloody Spinal Fluid During Insertion	5% [18]	-Use a midline approach -Follow ASRA guidelines -Check coagulation profile	-Delay anticoagulation by at least 60 minutes -Monitor color of CSF drainage -Consider postponing case (discuss with surgical team)
Intracranial Bleeding (Subarachnoid/Subdural/intracerebral)	2.8 to 3.5% [18,19]	-Avoid overdrainage -Ensure appropriate guidelines for zeroing of transducer and for amount of drainage	-Stop drainage -Brain Imaging -Evacuation of hematoma

Retained Catheter Fragment	1.8% [21,22]	-Identify the correct technique for placement -Special care with guidewire reenforced catheters -In case resistance is encountered during removal, ask patients to take same position used for insertion	-Imaging -Neurosurgical consultation for surgical retrieval of foreign body
Infection (meningitis)	0.2 to 1.2% [21,23]	-Full barrier precautions using surgical gowns and masks. -Alcohol based chlorhexidine solution -Care in an ICU setting -Maintain a closed drainage system -Avoid keeping CSF catheters for >72 hours	-CSF Gram stain and culture -Remove catheter -Antibiotics
Mortality	0.6% [18]	All of the above	All of the above

TEVAR:
Planned long segment thoracic aortic exclusion especially involving T6-T12
Prior open or endovascular abdominal aortic surgery

TAAA SURGERY:
Crawford Type I and II aortic aneurysm (figure 1)
Crawford Type III aortic aneurysm especially with prior open or endovascular aortic surgery

INSERTION AND MANAGEMENT OF CSF DRAINAGE CATHETERS

Lumbar CSF drainage catheters are typically placed by the anesthesia team preoperatively under local anaesthesia through a 14 G Tuohy needles using special CSF drainage kits. Based on institutional preferences, CSF drainage catheters can also be placed under fluoroscopic guidance by the interventional radiology team a day prior to the scheduled surgery. The latter option requires patients to remain in the hospital in a monitored (intensive care unit) setting. CSF drainage catheters can be placed while patients are either in the sitting or lateral decubitus position. Each position has advantages and disadvantages. Regardless of position, care must be taken to avoid seepage of a large amount of CSF during placement of the catheter. In the author's institution, CSF drainage catheters are placed preoperatively while patients are awake to ensure that any pain is communicated during the introduction of the needle and catheter. Other institutions place CSF drainage catheters after induction of general anesthesia and position patients in the lateral decubitus position for placement. [1,16] Following identification of the subarachnoid space, the CSF drainage catheter is advanced 10–20 cm into the subarachnoid space under strict aseptic conditions and are taped to the patient's back. Incorrect insertion steps can cause catheter fracture and increase the incidence of retained catheter fragments. Care should be avoided to avoid kinking of the catheters during taping and a trial of 'passive' drainage of CSF after the patient is in the supine position ensures free flow of CSF when drainage is initiated. [17]

PROPHYLACTIC VERSUS THERAPEUTIC CSF DRAINAGE

Prophylactic drainage of CSF to a pressure of 10 mmHg is typically done by connecting the catheter to a closed drainage system set to a pressure of 10 mmHg, so that any rise in CSF pressure above 10 mmHg results in drainage of CSF into a sealed collection system. The CSF pressure can also be intermittently transduced through a primed transducer tubing system that is not connected to a pressurized flush system.

Caution should be taken to ensure that the zero point of the

transducer is set at the patient's phlebostatic axis (i.e. the approximate location of the right atrium, found at the intersection of the midaxillary and a line drawn from the fourth intercostal space at the right side of the sternum)

Since CSF overdrainage carries its own risks (see below), therapeutic CSF drainage to a lower CSF pressure (as low as 5 mmHg) is only undertaken if the patient develops spinal cord injury (paraparesis or paraplegia) perioperatively as evidenced by clinical examination or MEP monitoring. The CSF drainage catheter is typically left in place for 48–72 hours and gradual increase in CSF pressure as well as capping of the catheters for several hours prior to the catheter's removal is recommended. This is done to allow CSF re accumulation and to evaluate the onset of any paraparesis or paraplegia prior to actual CSF drainage catheter removal. If patients develop any lower extremity neurological deficits, reinstitution of CSF drainage is undertaken, vasopressor therapy is initiated to raise mean arterial pressure and serial neurological examination are performed for evidence of reversal of neurological deficits. In these cases, gradual increase in CSF pressure (and gradual weaning of vasopressor therapy) may avoid recurrence of neurological deficits and allows time for 'adaptation' of the remaining collateral circulation.

CSF DRAINAGE CATHETER RELATED COMPLICATIONS

Cerebrospinal fluid catheter related complications include nerve injury during insertion, bleeding with compressive neuraxial (spinal or epidural) hematoma formation, overdrainage with resultant subdural or intracerebellar hematoma (temporal downward herniation with kinking of the posterior cerebral artery resulting in an acute brain infarction or death) infection with resultant meningitis, and retained catheter fragments. CSF catheter-related drainage complications can be reduced by following strict guidelines for the perioperative management of these catheters including during their introduction, maintenance and removal.

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RCL-10
Neurological Complications of Cardiovascular Diseases

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LEARNER OBJECTIVES

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

(1) Examine the diagnostic approach to a cardiac surgical patient who does not "wake up" after successful cardiac surgery;

(2) Distinguish how to diagnose and manage infectious central nervous system (CNS) complications in the patient with cardiovascular disease; and

(3) Discuss the diagnosis and management of cardiovascular complications and sequelae of primary neurological illness.

INTRODUCTION

Neurological complications of cardiovascular disease encompass a core groups of diagnosis that have significant impact on morbidity and mortality when not recognized early and intervened upon in a timely manner. We shall focus on broad etiologic categories and review some of the updates in the literature. These include the following:

1. Non-convulsive seizures and non convulsive status epilepsy (NCSE)
2. Acute Ischemic Stroke in the perioperative period
3. Infective Endocarditis and Brain Abscess
4. Neurogenic Stunned Myocardium (NSM)
5. Post-operative Cognitive dysfunction (POCD)

Considerations in a patient with delayed emergence after cardiac surgery

Delayed emergence from anesthesia is encountered on an incidental basis in the practice of Anesthesiology. The majority of patients in this cohort of outliers fall into a category of pharmacologic causes (i.e. residual effects of medications administered in the perioperative period), metabolic abnormalities (electrolytes, glucose, etc.). Severe abnormalities of gas exchange such as hypercarbia can be responsible for in these causes as well. [1] Once we go beyond the interval of hours of not emerging from anesthesia in an unanticipated manner, we have to look into more significant and frequently organic causes of altered neurological status. Emergence after cardiac surgery is frequently gradual and in the ICU. The immediate attention tends to be on stabilization of hemodynamic and cardiac function before weaning and emergence from anesthesia. The timelines can be further confounded by sedation practices in the ICU, types of surgical procedures, (e.g. deep hypothermic circulatory arrest etc.) need for continued sedation while dealing with postoperative complications (e.g. bleeding etc.) Once the case is evident that we are potentially dealing with a central nervous system etiology, CT scans can get done in an expeditious manner. It maybe very helpful in the rapid diagnosis of a intracranial hemorrhage but less so in the case of ischemic injury if sufficient time has not elapsed since before the CT is obtained. An MRI - which is highly sensitive to detecting ischemic injury, maybe not be practical if the patent has a PA catheter in place, or unstable hemodynamics or transport for longer windows of time maybe challenging. One must consider the role of EEG in the obtunded patient especially if the initial imaging cannot satisfactorily explain the neurological exam. Seizures in the perioperative critically ill patient can frequently be non convulsive in nature and therefore are not detectable without EEG monitoring. The diagnosis requires a high index of suspicion and continuous EEG monitoring.[2]

Non convulsive status epilepsy or NCSE continues to be a diagnostic challenge in the inpatient population. Neurologists often say, "It is one of those diagnosis that is hard to find if you are not looking for it". It can be especially challenging in the post surgical patient population. The overall incidence of NCSE in the ICU patient population with a decreased level of consciousness as being between 8-20% [3]. The morbidity and mortality increases with a delay in recognition and effective management of NCSE. The incidence of postoperative seizures in a contemporary series of adult patients undergoing cardiac surgery was reported to be about 1.2% [4]

The goals in the management of NCSE are seizure control, diagnosis of underlying cause, and life-supporting therapies. [5] It is imperative to get the neurologist involved to help guide therapy for NCS, especially since the patients may frequently need rapid escalating doses and number of AED's to control seizure activity under continuous EEG guidance. Its worth noting that Ketamine has been used successfully to treat SE. It is postulated that as the duration of status epilepsy is prolonged, GABA agonists (benzodiazepines, barbiturates, and propofol), may become less effective at controlling seizures. This is due to the internalization and subsequent decrease in the density of GABA-a receptors at the synaptic membrane. This is in contrast to NMDA receptors, which are recruited to the membrane. [6] NCSE is a diagnosis where early recognition can have a significant impact on improving overall patient outcomes.

Acute Ischemic Stroke (AIS):

The risk of AIS can range from 2-17% in in patients and in the perioperative period. [7] New high-quality evidence has produced

major changes in the evidence-based treatment of patients with acute ischemic stroke (AIS) since the publication of the "Guidelines for the early management of patients with acute ischemic stroke" in 2013. [8]

There are certain recommendations that have stood the test of time since the early AHA guidelines from 2013. These include the following:

1. The outcomes in AIS are superior when patients are admitted to a specialized Stroke/ Neurocritical care center.
2. Aspirin started within 24 hrs. of the event
3. Intravenous r-tPA administered within the correct window of time. (within the extended time window of 4.5 hours since onset of symptoms)
4. Early decompressive craniectomy for malignant cerebral edema in large vessel / hemispheric strokes.

The 2015 recommendation was revised to include patients who should receive mechanical thrombectomy for large vessel occlusion specifically the internal carotid artery or MCA–M1 segment occlusions. The current recommendations are based on the analysis of 5 randomized controlled trials (the combined analysis was part of the HERMES study (Highly Effective Reperfusion Evaluated in Multiple Endovascular Stroke Trials), which included the 5 trials MR. CLEAN, ESCAPE, REVASCAT, SWIFT PRIME, and EXTEND-IA) [8] More recent data has provided some encouraging strategies for endovascular intervention in patients who were late or just beyond in the traditional time window. Data from the DAWN trial supports the extension of the time window for mechanical thrombectomy in select patients with large anterior circulation vessel occlusion between 6 and 24 hours from last known normal. [9]

Endovascular intervention is truly a game changer in the care of AIS patients. Every effort must be made to have patients with suspected perioperative AIS be evaluated by the Stroke team for endovascular intervention at the earliest.

Brain Abscess:

The overall incidence of brain abscess ranges from 0.4 to 0.9 cases per 100,000 population. [10] Although this is a relatively rare diagnosis, missing it can have significant impact on morbidity and mortality. It is worth noting that increasing cohorts of patients in the developed world who present with a brain abscess are immunosuppressed pts. (e.g. HIV, post transplant or pharmacologically immunesuppressed). The diagnosis of a brain abscess is challenging given that the most frequent symptom is headache and more serious or neurocentric symptoms (including focal deficits, altered level of consciousness) and even fevers are frequently absent on presentation. The symptom can evolve as the abscess enlarges or the surrounding edema increases. Brain abscess can have varied etiologies and can be caused by bacteria, mycobacteria, fungi, or parasites (protozoa and helminths). The common etiologic agents are outlined in table 1.

Management: The choice of initial antimicrobial therapy should be based on the organisms that are the most likely cause of the disease (see table 1), the patient's predisposing condition, on patterns of antimicrobial susceptibility, and on the ability of the antimicrobial agent to penetrate the abscess. It is worth noting that more than 25% of all abscesses are polymicrobial in nature. The key is to start antimicrobial therapy as soon one suspects a brain abscess. The only possible exception is imminent neurosurgery to drain and send intraoperative cultures (if the time frame is hours and the patient is clinically stable). One must consider the PCR-based 16S ribosomal DNA sequencing in culture negative cases to allow for better anti-microbial targeting. [11] The duration of antibiotics are typically in the 6-8 week range. With the use of modern stereotactic neurosurgical techniques, almost any brain abscess that measures at least 1 cm in diameter can be accessed at this time. Stereotactic aspiration can be both of diagnostic significance and therapeutic as well.

Immunocompromised patients	
HIV	Toxoplasma, Nocardia, Mycobacterium, Listeria
Neutropenia	GN Bacteria, Aspergillus, Mucor
Post Transplantation	Aspergillus, Candida, Mucor, Nocardia spp., T Gondii
	Contiguous spread
Penetrating trauma	Staphylococcus aureus, Enterobacteracea, Clostridium spp.
ENT infections	Streptococcus sp. Bacteroides, Enterobactericae
	Hematological spread
Lungs sources	Fusobacterium, Bacteroides, Streptococcus
Endocarditis	Staphylococcus aureus, Streptococcus spp.
Congenital heart disease	Streptococcus spp. & Hemophilus Spp.
Dental	Mixed (fusobacterium, Bacteroides, Prevotella, Streptococcus)

Table 1: Common organisms associated with brain abscess

Infective Endocarditis:

Infective Endocarditis (IE) is a diagnosis familiar in cardiovascular ICU's. Neurological complications tend to be the most significant extra cardiac complications with significant impact on morbidity and mortality. [12] The cerebral complications of IE include ischemic lesions (most frequent), parenchymal hemorrhagic lesions, meningitis, encephalopathy (including sepsis related), cerebral microbleeds, mycotic aneurysm and brain abscess. The risk of cerebral involvement is high in the early disease course and can be frequently neurologically silent. This is common in left sides valvular lesions of both native and prosthetic valves.

Early echocardiography remains central to the diagnosis and management of IE. Frequently TTE and TEE are done in many patients initial evaluation and to provide complementary information. Cerebrospinal imaging should be performed in all patients with IE or contiguous spread of infection who develop severe, localized headache, neurological deficits, or meningeal signs to evaluate for mycotic aneurysms or intracranial bleeds. [13] Bain MRI may reveal cerebral abnormalities in up to 80% of patients, including cerebral embolism in 50% of mostly asymptomatic patients. [14]

It is worth noting that IE can occur in the absence of positive blood cultures with cultures remaining negative in 2 to 7 percent of patients with IE. The global incidence of culture negative endocarditis is reported on a wide range from 2% to 70%. Numerous explanations have been provided for this wide range including the increased incidence of fastidious zoonotic agents (eg, *Bartonella* spp, *Coxiella burnetii*, or *Brucella* spp) causing human infection in developing countries, the differences in microbiologic techniques, and, perhaps, the availability and widespread use of antibiotics without prescription in some countries. [15]

The advent of neuroimaging and recognition of neurological complications is key since this influences the management strategies including timing of surgery. Mycotic aneurysms (MA) occur most frequently in the intracranial arteries secondary to the septic embolization of vegetations to the arterial vasa vasorum or the intraluminal space leading to the intimal spread of infection. These MA frequently occur at major vascular branching points following flow dynamic characteristics. [13] CT angiography or MR angiography maybe a good test to evaluate for MA in IE patients with a high degree of suspicion. Frequently patients with MA can present with severe headaches; "sterile" meningitis with erythrocytes or xanthochromia in CSF.

Timing for cardiac surgery is a frequent question for the neurointensivist/ neurologist. Clinical judgment is still critical and must balance cardiac indications versus the perceived risk of exacerbation of neurological injury by intracerebral hemorrhage,

hypotension, anticoagulation for CPB further embolization from cardiopulmonary bypass, and diffuse cerebral ischemia from altered vasoregulation. Patients with severe cardiac decompensation and severe mechanical cardiac lesions should be operated on emergently or urgently unless the neurological status (eg, coma, large intracranial hemorrhage) precludes heparinization or when meaningful neurological recovery is very low. [13] The decision to operate, and the optimal timing of surgery, as well, in this complex subset of patients should be based on a team approach including infectious disease, cardiology, cardiac surgery, neurology and intensive care teams.

Neurogenic Stunned myocardium (NSM):

Myocardial effects secondary to a neurological trigger can range from hemodynamic instability, EKG changes, and acute LV dysfunction requiring inotropic and vasoactive medication support. This sequence of events frequently follows injury to the insular cortex and hypothalamus (bleeds more than ischemic events) that triggers a catecholamine storm that can have direct and indirect effect on the myocardium. [16] The most significant sequelae constitute the spectrum of myocardial wall motion abnormalities and LV functional changes called stunned neurogenic myocardium. These include impaired LV contractility, low ejection fractions and pattern of wall motion abnormalities that are similar to the apical ballooning or Takotsubo cardiomyopathy and inverse or reverse Takotsubo syndromes. The inverse Takotsubo pattern is more common in the NSM population. [16, 17]

When LV wall motion abnormalities do not correspond with coronary vascular territories, discrepancies exist between the magnitudes of troponinemia, acute EKG changes and echocardiography findings following an acute neurologic event favor a neurogenic origin of cardiac dysfunction. [17] These dramatic changes tend to grossly improve with support over days but complete or near complete resolution can take several weeks.

Postoperative Cognitive dysfunction after cardiac surgery:

Postoperative cognitive dysfunction (POCD) is a decline in cognitive function from preoperative levels, which has been frequently described after cardiac surgery. It refers to deficits in cognitive domains of attention, concentration, short-term memory, motor dexterity, and psychomotor speed - commonly tested modalities included tested in the battery for POCD. [18]

The psychomotor testing is frequently based on seven tests with nine subscales outlined in the consensus statement on the Assessment of Neurobehavioral Outcomes after Cardiac Surgery. [19]

The precise etiology of POCD in patients undergoing CABG remains unknown but a widely held theory focused on the pivotal role of cerebral micro emboli from CPB in the pathogenesis of POCD. Implying that perhaps avoidance of CPB reduces the barrage of microemboli and thus may result in lower POCD. This however has not consistently been shown to be true in multiple studies at this time. [19] This inconsistency in trial results confounds the potential explanation of a complex pathophysiologic process by a single hit hypothesis.

Another relative unique challenge in studying POCD is that there is significant variability between tests, intervals of testing and the actual tests included in the assessments as noted in a number of previously published studies. [19, 20] The interpretation of literature on POCD is challenging due to numerous methodological limitations, difference in definition of POCD used in studies and the lack of data from control groups. [20]

Two recent trials evaluating biomarker changes post anesthesia exposure- the ARCADIAN and CAPACITY studies shone some new light into the pathophysiology of POCD. [21] Neurofilament light, Tau proteins (Hyperphosphorylated tau) are some of the candidate biomarkers being evaluated in the POCD domain. It is worth noting that biomarkers have promised much and delivered less in clinical practice whether it is traumatic brain injury, acute kidney injury or now POCD. The promise of biomarkers offers an attractive and tantalizing solution that is yet to be widely seen in the POCD cohort. The current data does not answer whether a biomarker bump is sufficient to call alarm to general anesthesia exposure. It remains a fascinating data point that may have more significance as future data emerges.

CONCLUSION

The spectrum of neurological complications in the cardiac surgical patient poses a unique set of challenges to the perioperative physician/ intensivist. Early recognition of abnormalities, seeking expert opinion (for possible endovascular and focal surgical interventions) and aggressive intensive care management can lead to positive outcomes in this complex patient population.

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RCL-11
Perioperative Management of Hyperglycemia for Noncardiac Surgery: Who, How and Why?

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A large body of evidence has established the association between hyperglycemia and increased risk of perioperative morbidity and mortality, in patients with and without diabetes. The risk of postoperative complication is related to the severity of hyperglycemia both on admission, and during the hospital stay. Trials examining surgical patients demonstrate better outcomes in non-diabetic patients when their blood glucose (BG) target is achieved as versus diabetic patients controlled to the same glycemic range. However, optimal glucose management during the perioperative period is widely debated. Recent randomized controlled trials using conventional glycemic targets do not demonstrate the significant risk of hypoglycemia, as seen in prior studies using insulin to maintain tight blood glucose control. Substantial evidence indicates that correction of hyperglycemia (BG > 180mg/dL) with insulin administration reduces hospital complications and decreases mortality in cardiac and general surgery patients.[1]

LEARNER OBJECTIVES

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

(1) Discuss the impact of long and short-term glycemic control on the perioperative period;

(2) Understand the outcome differences in the diabetic and non-diabetic population suffering from hyperglycemia in the perioperative period; and

(3) Screen elective surgical patients for risk of hyperglycemia and make pre-operative treatment recommendations regarding home hypoglycemic regimens; and

(4) Interpret recommended blood glucose targets and discern the risks/benefits of the various hyperglycemia treatment options.

Prevalence of Hyperglycemia and Diabetes in Surgical Patients

Perioperative hyperglycemia is reported in 20-40% of patients undergoing general surgery.[2] A recent report examining point-of-care blood glucose testing in three million patients, across 575 American hospitals, reported a prevalence of hyperglycemia (BG >180 mg/dl) as 32% in both intensive care (ICU) patients and non-ICU patients. Providers are most suspicious for the development of hyperglycemia in patients with a known diagnosis of diabetes; however, 12-30% of surgical patients who develop elevated blood glucose levels in the hospital do not have a history of diabetes before surgery.[4] Patients without a known history of glucose intolerance, whose blood glucose levels are elevated during hospitalization, exhibit a state labeled as 'stress hyperglycemia.'

Pre-Operative Testing

Poor preoperative glycemic control is associated with an increased rate of complications and reduced long-term survival after surgery.[2] Optimizing preoperative glucose management may improve outcomes; however, no prospective randomized studies have established ideal pre-operative diabetes control as a means to improve clinical outcomes. Retrospective studies suggest that acceptable long-term glycemic control may vary according to type of surgery. At this time, data is inconclusive identifying the optimal HgbA1C that justifies surgical delay. The Joint British Diabetes Societies 2016 Summary on *Management of Adults with Diabetes Undergoing Surgery and Elective Procedures* suggests consideration for referral in elective surgery patients with HgbA1C > 8.5%.[21] In patients with known diabetes, pre-operative HgbA1C predicts insulin responsiveness in hospitalized medicine patients and may help tailor a personalized insulin regimen for day of surgery and inpatient care.

The American Diabetes Association (ADA) recommends screening for diabetes in patients ≥ 45 years old, or in those who are overweight/obese (BMI ≥25kg/m2 or 23kg/m2 in Asian Americans) with one other risk factor (Table 1).

Table 1. ADA Risk Factors for Type 2 Diabetes

ADA RISK FACTORS for Type 2 DIABETES [18]
First-degree relative with diabetes
High risk race/ethnicity (African-American, Latino, Native American, Asian American, Pacific Islander)
History of cardiovascular disease
High density lipoprotein level < 35mg/dL and/or triglycerides > 250mg/dL
Women with polycystic ovary syndrome
Physical inactivity
Clinical syndromes associated with diabetes (severe obesity, acanthosis nigracans)

Studies examining stress hyperglycemia reveal that patients labeled as "non-diabetic" are often undiagnosed diabetics or pre-diabetics. Cross-sectional and longitudinal studies have shown that between 30-60% of these patients have impaired carbohydrate tolerance or diabetes on oral glucose tolerance testing after hospital discharge. Furthermore, 60% of patients admitted with new hyperglycemia had confirmed diabetes at 1 year.[18] Measurement of HbA1c in patients with hyperglycemia during hospitalization provides the opportunity to differentiate patients with stress hyperglycemia from those with diabetes who were otherwise undiagnosed. It has previously been demonstrated that patients without a formal diagnosis of diabetes are less likely to be treated with insulin when hyperglycemic as versus their diabetic counterparts.[2] While not yet proven, identifying at-risk patients in the pre-operative period may improve hospital and provider adherence to testing and treatment regimens with the goal to improve surgical outcomes.

PREOPERATIVE HYPOGLYCEMIC REGIMENS

Oral Agents

Treatment recommendations for perioperative home medication use in type 2 diabetics are generally categorized on the extent of the surgical procedure, length of pre and post-operative fasting, type and frequency of daily medication, and state of metabolic control prior to surgery.

There is a lack of randomized controlled trials demonstrating the role of oral medication prior to surgery. Most oral anti-diabetic agents are generally recommended through the day prior to surgery with certain medications also endorsed on the day of surgery. General recommendations are made in Table 2 and include:

- Sulfonylureas and insulin secretogogues should be discontinued the day of surgery to limit the risk of perioperative hypoglycemia.[20,21]

- Metformin may be used on the day of surgery in patients expected to resume a normal diet shortly following the procedure. If the procedure includes contrast dye or the patient has reduced renal function (GFR < 60 milliliters/minute, mL/min), metformin should be held on the day of surgery.[20]

- Sodium-glucose cotransporter-2 (SGLT-2) inhibitors have been associated with the rare complication of euglycemic diabetic ketoacidosis in surgical patients. The American Association of Clinical Endocrinology (AACE) recommends that these agents be held 24 hours prior to surgery.

- Dipeptidyl-peptidase 4 (DPP-4) inhibitors, when compared to a basal-bolus insulin regimen in non-cardiac surgery patients, have recently been shown to effectively and safely manage blood glucose during hospitalization.[54] Continuation of DPP4 agents on the day of surgery is recommended.

- Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) enhance pancreatic insulin secretion when a glucose load is delivered to the gut. This limits significant hypoglycemia associated with these agents.. Exendatide use in cardiac surgical patients (HgbA1C < 8.0%) recently revealed that at the dose studied, there was not a difference in the number of patients who achieved target blood glucose range versus placebo infusion. However, the amount of insulin required in the exenatide group was decreased, and the time to start insulin delayed. Currently, there is little data regarding perioperative use of these agents in non-cardiac surgical patients.

- GLP-1 RAs slow gastric emptying, which may be of concern in both pre and post-operative patients. Evidence suggests that with routine use of these agents (versus acute administration), tachyphylaxis develops to the GLP-1 effect on gastric emptying. Continuation of these agents on the day of surgery is likely safe and is recommended by the Joint British Diabetes Societies.[23]

Table 2. Perioperative Non-Insulin Medication Recommendations

Medication	Day Before Surgery	Day of Surgery if: 1. Normal oral intake anticipated same day AND 2. Minimally invasive surgery	Day of Surgery if: 1. Reduced post-operative oral intake OR 2. Extensive surgery, anticipated hemodynamic changes or large fluids shifts
Secretagogues Sulfonylureas (glimepride, glyburide, glipizide) Metglitinide (nateglinide, repaglinide)	Take*	Hold	Hold
SGLT-2 Inhibitors -gliflozin (canagliflozin, empagliflozin)	Hold	Hold	Hold
Thiazolidinediones -glitazones (pioglitazone, rosiglitazone)	Take	Take	Hold
Metformin	Take §	Take §	Hold
DPP-4 Inhibitors -gliptins (sitagliptin, saxagliptin, linagliptin)	Take	Take	Take
GLP-1 Receptor Agonists - exanatide, liraglutide, lixenatide, dulaglutide	Take #	Take	Take #

* If the patient is undergoing a bowel prep, hold secretagogue therapy
§ Hold if patient having a procedure with IV contrast dye administration or GFR < 60 mL/min
# Consider holding if concern for gastric emptying or gastrointestinal surgery

Insulin

Patients with type 2 diabetes treated with insulin should continue their home regimen, with appropriate modifications the day prior to and day of surgery.

- Reduce the patient's basal insulin (glargine or detemir) by approximately 20-25% of normal dose the evening before surgery, or day of surgery if patient administers morning insulin.
- Evening doses of premixed formulations should be reduced by 20-25% the day before surgery,28 and by 50% the morning of surgery. Morning of surgery insulin should be held in patients with type 2 diabetes and fasting glucose < 120 mg/dl. Premixed insulin has been shown to result in more episodes of hypoglycemia in surgical patients than basal plus bolus insulin.
- Patients starting a clear liquid diet, or undergoing bowel prep the day before surgery, can administer their rapid-acting insulin. Half21 to full dose is recommended based on patient blood glucose measurement. Rapid-acting (meal) insulin should be held when the patient begins NPO status. Administration of meal-time insulin in NPO hospitalized surgical patients, has been associated with hypoglycemia under anesthesia.

GLYCEMIC TARGETS

Glycemic targets recommended by several organizations are shown in Table 3. Less aggressive blood glucose targets (140-180mg/dL) are largely recommended by multiple societies to minimize risk of harm. At this target, randomized controlled clinical trials demonstrate that the risk of hypoglycemia is significantly reduced as versus intensive insulin therapy used to achieve lower physiologic ranges (80-110mg/dL). However, emerging studies support more personalized blood glucose targets with non-diabetic patients potentially demonstrating greater outcome benefit at 110-140mg/dL. Similarly, diabetic patients on oral agents versus insulin may require varied targets to optimize outcomes; continued research will elucidate if more personalized targets improve surgical care.

INTRAOPERATIVE GLYCEMIC MANAGMENT

Insulin therapy is recommended in the perioperative period for both diabetic and non-diabetic patients with hyperglycemia (>180 mg/dL).[17] Depending on the patient, type of surgery, and length of NPO status, hyperglycemia can be treated with subcutaneous (SC) rapid-acting insulin analogs or with an intravenous infusion of regular insulin. There have not been large trials examining the use of rapid-acting SC insulin in the operating room. Based on the pharmacokinetics of these fast-acting, shorter-duration medications, patients undergoing ambulatory surgery are appropriate candidates for their use.[20] The onset time of rapid-acting insulin analogs is between 15-30 minutes and they peak in 1-1.5 hours; this limits the risk of 'insulin stacking' which is associated with repeated doses of SC regular insulin. Inpatient procedures of short duration (≤ 4 hours operating room time) may safely allow the use of rapid-acting SC insulin analogs, particularly minimally invasive surgeries with expected hemodynamic stability and cases that allow early resumption of oral intake. Advantages of SC rapid-acting insulin analogs include ease of administration, low rate of hypoglycemia, and efficacy in correcting hyperglycemia. Algorithms are available that recommend subcutaneous insulin dosing regimens to treat intraoperative hyperglycemia. Dose

Table 3. Society Guidelines for the Treatment of Inpatient Hyperglycemia

	Operating Room, PACU	ICU	Non-ICU
SAMBA[20]	Recommend SC rapid-acting insulin analog ***Treatment goal:*** Intraoperative blood glucose levels <180 mg/dL		
AACE[43]		***Treatment goal:*** 140–180 mg/dL. 110–140 mg/dL may be appropriate for select patients, if achievable without significant risk for hypoglycemia.	***Treatment goal:*** If treated with insulin, pre-meal glucose targets <140 mg/dL, with random glucose levels <180 mg/dL.
Society of Critical Care Medicine[44]		Insulin infusion recommended; suggest protocols minimize glycemic variability. ***Treatment goal:*** Maintain glucose <150 mg/dL for patients in ICU and absolutely < 180mg/dL.	
ADA[18]		***Treatment goal:*** 140-180mg/dL 110–140 mg/dL may be appropriate for select patients, if achievable without significant risk for hypoglycemia.	***Treatment goal:*** 140-180mg/dL Lower target goal (< 140mg/dL) may be appropriate in select patients. Higher range acceptable in terminally ill and those with severe comorbidities
Society of Thoracic Surgeons[45]	Adult cardiac surgery patients: ***Treatment goal:*** Recommend glucose <180 mg/dL during surgery with monitoring every 30-60min.	Continuous insulin infusion ***Treatment goal:*** BG < 180mg/dL in ICU Certain patient populations* should have BG ≤ 150mg/dL.	Transition insulin infusion to SC analogue ***Treatment goal:*** BG < 180mg/dL in peak postprandial state, ≤110mg/dLin fasting and pre-meal states.
Joint British Diabetes Societies[21]	Manage type 2 diabetic patients with short starvation period via modification of their home medications. Insulin infusion recommended for others. ***Treatment goal:*** Insulin infusion for BG > 12mmol/L (216mg/dL) x 2 consecutive measurements. Monitor hourly. Target 6-10mmol/L (106-180mg/dL). Up to 12mmol/L (216mg/dL) acceptable.	***Treatment goal:*** For patients on a VRII, acceptable range 6-10mmol/L (106-180mg/dL). Hourly BG monitoring.	***Treatment goal:*** 6-10 mmol/L (108–180 mg/dL) in patients on a glucose-lowering agent. An acceptable hospital range = 3.5-12 mmol/L (63–216 mg/dL). 3.5mmol/L does not require treatment in the awake patient.

SAMBA: Society for Ambulatory Anesthesia; AACE/ADA: American Association of Endocrinologists and American Diabetes Association joint guidelines; ADA: American Diabetes Association; PACU: post-anesthesia care unit; ICU: intensive care unit; IV: intravenous; SC: subcutaneous
* Mechanical ventilation > 3 days, intraaortic balloon pump, left ventricular assist device, need for inotropes, anti-arrythmics, dialysis or continuous veno-venous hemofiltration

adjustments based on expected insulin sensitivity are recommended when dosing subcutaneous insulin in the operating room.[29]

A variable rate intravenous (IV) insulin infusion should be considered in patients undergoing procedures with anticipated hemodynamic changes, significant fluid shifts, expected changes in temperature, predicted use of inotropes, or lengthy operative times (>6 hours). These operating room variables alter subcutaneous insulin absorption and distribution. Due to unreliable pharmacokinetics, this may result in either persistent hyperglycemia or hypoglycemia. For these same reasons, hyperglycemia in critically ill patients or those undergoing cardiac surgery, insulin should be given via continuous IV infusion. The short half-life of IV insulin (less than 15 minutes) allows flexibility in adjusting the infusion rate in the event of hemodynamic changes, poor tissue perfusion or acid-base disturbance. The ideal protocol uses current and previous glucose values to calculate rate adjustments. Hourly blood glucose testing is recommended for these patients; electronic alert systems in the operating room have demonstrated increased provider adherence to testing and treatment of blood glucose.

Hypoglycemia

Hypoglycemia (BG < 70mg/dL) is the most common risk of insulin treatment in the hospital, and is associated with poor clinical outcomes and mortality.[8] Because hypoglycemia may go unrecognized under anesthesia, providers can be reticent to use insulin in the operating room. Data demonstrates that the probability of hypoglycemia increases significantly when glycemic goals are aggressive[7,8] Studies examining insulin use on the surgical ward in non-critically ill patients report an incidence of hypoglycemia (BG < 70mg/dL) and severe hypoglycemia (BG ≤ 40mg/dL) of 23.1% and 3.8% respectively. A retrospective review of severe hypoglycemia in the operating room found only 17 events in the anesthetic records of 80,379 patients.[30]

Patient risk factors associated with inpatient hypoglycemia are listed in Table 4. Conservative blood glucose target ranges,[7] frequent monitoring, perioperative provider communication, and treatment algorithms that base insulin dosing not just on current blood glucose level but also on previous values and insulin sensitivity,[34] jointly reduce the risk of intra and post-operative hypoglycemia.

Table 4. Patient Risk Factors Associated with Inpatient Hypoglycemia (BG < 70mg/dL)
Type I Diabetes
Use of sulfonylureas and metglinides on hospital admission
Interruption of enteral/parenteral nutrition
Age ≥ 70 years (decreased stress regulatory mechanisms and/or failure to perceive hypoglycemic symptoms)
Renal insufficiency (consider insulin dose reduction in patients with GFR < 45ml/min)
Sepsis
Liver failure
Low albumin levels, malnutrition
Dementia, delirium, frailty

FUTURE DIRECTIONS

Recognizing the risks of hypoglycemia, the ease of oral versus injectable therapy and the magnitude of the patients affected by diabetes in the United States, insulin therapy alternatives (i.e., oral antidiabetic agents) are actively under investigation in surgical patients. The use of DPP4 inhibitors both alone and in addition to basal insulin, have been shown to decrease the number of correctional insulin doses required in the post-operative period.[7] The Linagliptin Surgery trial (NCT02004366) compared DPP4 inhibitors to insulin therapy in 280 general surgery patients with type 2 diabetes. Compared to basal insulin therapy, DPP4 inhibitors show equal efficacy in treatment of mild to moderate hyperglycemia, but result in significantly less hypoglycemia (12% vs. 2%). Given its success in treating patients with known diabetes in the hospital, DPP4 inhibitors are currently being studied as an agent to decrease the frequency and persistence of hyperglycemia in diabetic patients undergoing cardiac surgery (NCT02556918). Further evaluation is also examining their role in preventing stress hyperglycemia in surgical patients without diabetes. Studies in both cardiac surgery (SITACABG nonDM, NCT02443402) and non-cardiac surgery (NCT02741687) are underway with results pending.

New research is also emerging in surgical patients investigating the role of GLP-1 receptor agonists. In an outpatient setting, GLP-1 RAs have been demonstrated to provide greater improvement in HgbA1C control than DPP4 agents, with both drug classes resulting in minimal hypoglycemia. Exenatide is currently being explored for its possible role in non-ICU surgical patients as a sole agent or given in addition to basal insulin therapy (NCT02455076). Should research reveal that these agents modify the hyperglycemic state in diabetic (and/or non-diabetic) patients undergoing surgery, with minimal risk of hypoglycemia, these agents may be embraced as part of surgical care pathways.

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RCL-12
Perioperative Venous Thromboembolism: A Review

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LEARNER OBJECTIVES

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

1) Assess the enormous magnitude of the problem of perioperative venous thromboembolism (VTE) and its affect on health care costs;
2) Identify the basic pathophysiology of deep vein thrombosis and pulmonary embolism;
3) Discuss the key role anesthesiologists can play in its prevention;
4) Demonstrate 2 interventions that can immediately be introduced into practice at no cost to reduce the incidence of VTE; and
5) Identify the role of genomics in predicting VTE risk.

There is a growing trend in modern anesthesia care to expand the envelope of our responsibility to include the entire perioperative period, usually considered as that time interval from decision for surgery to 30 days post-hospital discharge. This general concept of the anesthesia provider as a perioperative physician is embedded in the perioperative surgical home model as defined by the ASA. Anesthesia departments are including the term "perioperative care" in their titles, and new training guidelines include more internal medicine and perioperative care exposure[1]. The traditional interpretation of anesthesia responsibility as ending once the patient is discharged from the post-anesthesia care unit *is simply no longer valid*. Implicit within the PSH model is the inference that the care anesthesiologists provide during the preoperative, intraoperative and postoperative periods markedly affects *long term* patient outcome[2]. By our interventions (or lack there of) we impact the frequency of such major postoperative complications as surgical site infections, chronic postoperative pain, cognitive impairment, pulmonary and cardiac dysfunction and possibly even cancer metastasis following resection of a primary tumor[2-6]. We also play an important but perhaps less appreciated role in the prevention of deep vein thrombosis and pulmonary embolism[7,8]. These two postoperative complications are often combined under the single heading "venous thromboembolism," as they are considered different manifestations of the same pathophysiological mechanism. According to the venerable classic textbook on the subject by Hume, Sevitt and Thomas[9], "It is our belief that venous thrombosis and pulmonary embolism are basically one disease, the latter being the most serious complication of the former."

VTE is an important cause of postoperative morbidity, mortality and unplanned hospital readmission and for which the potential for major risk reduction exists[10]. In fact, VTE is *the major cause of hospital-related mortality*, responsible for approximately ten percent of all hospital deaths, a figure that dwarfs the incidence of traditional anesthesia-related mortality. Some estimates of overall VTE mortality rates place these above those for breast cancer[10], myocardial infarction or stroke[11]. Raskob et. al., in an extensive review, commented on the worldwide prevalence of the problem, noting that VTE "causes a major burden of disease across low-, middle-, and high-income countries[12]." It is evident that the role of the the perioperative physician takes on profound importance with respect to minimizing the frequency of surgically-associated VTE, considered *the most preventable* of the major postoperative complications[13,14-16]. This review presents a summary of the pathogenesis of surgically- provoked VTE and the important role of the perioperative physician in reducing its incidence. Some of the important questions we address include:

- What are the primary provocations for perioperative venous thromboembolism? What is the underlying pathophysiology?
- Potent anticoagulant drugs such as rivaroxaban or low molecular weight heparin have often been touted as superior to anti-platelet drugs for surgical VTE prophylaxis even though many orthopedic surgeons utilize aspirin for the majority of their patients. Recent studies have questioned the benefit of potent anticoagulants as the primary means of VTE *prevention*. Indeed, there is evidence that all-cause mortality may be greater with the potent anticoagulants. As aspirin is associated with a lower incidence of bleeding and infectious complications, the rational behind these two different regimens needs clarification. Might the orthopedic surgeons have the weight of current evidence on their side?
- VTE incidence increases in a non-additive fashion with additional risk factors.Individuals with the Factor V Leiden mutation have a 7-fold increased risk of VTE and individuals taking hormone contraceptives have a 4 fold increased risk of VTE. However, patients with both risk factors have a 30 fold increased risk of VTE[17]. Bovill et. al. have also discussed a potential synergistic effect resulting from the presence of multiple genetic risk factors[18]. Is there a sound pathophysiologic basis for these findings?
- Of the numerous risk factors are associated with VTE in the surgical patient, which should be of greatest concern to the perioperative physician?
- What role do microvesicles and neutrophil extracellular traps play in the increased risk of VTE in the oncological surgical patient?
- Are simple and safe interventions available to the perioperative physician that may be introduced

preoperatively and/or intraoperatively or postoperatively with the potential to reduce VTE risk?

In traditional medical literature, dating back at least 50 years, VTE has been described in terms of "Virchow's Triad." This consists of 3 conditions, the presence of all of which are seeming required to initiate thrombogenesis: (1) venous stasis (2) changes in blood coagulability and (3) vessel wall damage. Such a simplified explanation of VTE pathogenesis does little to guide the perioperative physician in providing effective interventions. It is much more useful to discuss pathogenesis in terms of current understanding of the detailed processes involved.

1. *Stasis*: *VTE is initiated by venous stasis*. This is the critical *provocation* which ultimately *leads to thrombus formation*. Although VTE can occur in the absence of stasis, with respect to surgical procedures, it is *only* those procedures wherein stasis occurs (that is procedures involving either general or neuraxial anesthesia) that are associated with VTE. Furthermore, by "stasis" we mean either (1) lack of pulsatile flow secondary to elimination of the venous calf muscle pump (2) reduction in total blood flow secondary to the effects of surgery and anesthesia on cardiac function and venous return or (3) a combination of both factors. The lack of pulsatile flow in particular leads to hypoxia of the large venous valve cusps, causing *activation of the valvular endothelium activation, laying the groundwork for clot formation*[8,17].
2. *Fibrin formation: Venous stasis ultimately leads to thrombin generation and the formation of fibrin threads adjacent to the endothelial surface. This is a consequence of the stasis-induced hypoxia of the valvular endothelium, triggering expression of the cell adhesion proteins P and E selectin, which in turn attract tissue factor bearing monocytes and microvesicles. Von Willebrand factor (vWF) within the endothelium is also activated.* This activated vWF, which is much larger and "stickier" than that normally found in the blood, attracts platelets and neutrophils and promotes the formation of neutrophil extracellular traps (NETS) and expression of P-selectin on the platelet surface[17,19,20]. Increasing evidence suggests that microvesicles also play a prominent role in VTE formation, particularly in patients with malignancies[17]. The fibrin threads and neutrophil extracellular traps ensnare red blood cells, platelets and additional neutrophils.
3. *Clot retraction:* The glutinous mass of cells which is weakly tethered to the valve cusp endothelium contracts and organizes, attracting additional platelets and neutrophils to the nascent thrombotic nidus. Clot retraction is followed by the expression of additional TF sufficient to generate platelet aggregation. The resulting platelet "release reaction" and activated platelets in turn express additional P-selectin, attracting neutrophils, leukocytes and microvesicles triggering TF release and activation of the extrinsic clotting cascade, as well as additional NET formation. Extracellular RNA and DNA simultaneously promote activation of factor X and the intrinsic clotting cascade, further stabilizing the growing coagulum[17].
4. *Propagation:* As the platelets and neutrophils clump, additional thrombin is formed via the extrinsic clotting cascade through P-selectin generated tissue factor on microvesicles and monocytes. Once again, fibrin threads are formed as well as additional NETs by activated neutrophils. The resulting stands of fibrin and NETS ensnare additional red blood cells, platelets and neutrophils. Successive layers rich in fibrin, red blood cells, platelets and neutrophils (red layers), alternate with platelets and neutrophils (white layers), leading to clot propagation and characteristic Lines of Zahn[9]. The process continues layer by layer, with organization diminishing as one moves farther away from the valve pocket[20]. It is also worth noting for that traditionally venous clots are referred to as "red thrombi" whereas clots in the arterial circulation are referred to as "white thrombi," denoting the presence of accumulation of red cells in the former, and the primacy of platelets in the latter. It is also known that patients with a greater number of venous valves are at greater risk of VTE.

With this basic physiologic framework to build upon, we discuss numerous cost effective, readily implemented interventions the perioperative physician may introduce to reduce the distressing high and unchanged incidence of VTE.

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RCL-13
TAS: The Practicalities of Delivering Massive Transfusions in Trauma Resuscitation

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LEARNER OBJECTIVES

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

1) Compare different intravenous catheters and access sites;
2) Discuss the function of rapid infusion devices;
3) Evaluate key targets in hemostatic resuscitation;
4) Apply point-of-care tests to guide resuscitation; and
5) Describe key non-technical skills vital to effective delivery of massive transfusion resuscitations.

INTRODUCTION / OVERVIEW

The principle of hemostatic resuscitation of the bleeding trauma patient is restoration of oxygen delivery while supporting coagulation. It is widely accepted that the early delivery of packed red blood cells (pRBCs), fresh frozen plasma and platelets is key to achieving this[1,2]. Many centers have adopted evidence-based massive transfusion protocols (MTP) to streamline provision of products and improve coordination between clinicians providing direct patient care and laboratory services[3]. Less prescribed is the practical manner in which MTPs are implemented.

THE TRAUMA ANESTHESIA TEAM

During the intraoperative phase of trauma resuscitation, anesthesiology team members need to perform four roles;

1) Team lead: coordinates team activities.
2) Proceduralist: hands on intervention & assessment.
3) Transfusionist: delivers and tracks MTP products.
4) Investigator: runs (& interprets) point-of-care testing / laboratory results.

In resource-rich systems there may be sufficient staff available for each role to be filled by individual staff, in others, or out-of-hours, team members may have to cover two or more. It is vital to ensure the roles are carried out by the attending, resident, nurse anesthetist or technician with the most appropriate practical skillset. Due to the high cognitive load inherent to trauma resuscitations, non-technical skills are also fundamental to optimum performance by team members and a useful framework for these was published by Flin *et al* in 2010[4].

Through discussing key practical and non-technical considerations fundamental to each of the trauma anesthesia roles the following will review key points in the effective delivery of massive transfusions in trauma.

THE PROCEDURALIST

The patient may arrive in the OR with a definitive airway, arterial line and sufficient intravenous access from the emergency department. If not, one or more members of the team will be tasked with performing these practical procedures.

Intravenous Access

A vital step in the resuscitation of the exsanguinating trauma patient is achieving intravenous access capable of infusing blood products at a sufficient flow rate to reverse a volume deficit and maintain tissue perfusion in severely injured patients, despite ongoing blood loss. The Hagen–Poiseuille law, which governs laminar flow rates in non-compressible Newtonian fluids, states that infusion rate is proportional to the internal radius of the intravenous catheter to the fourth power and driving pressure, but inversely proportional to the viscosity of the infusate and length of catheter[5]. This accounts for the fact that short, wide catheters provide the greatest flow rates.

While peripheral cannulae of gauges 16 to 14 will be of great use initially, patients with severe bleeding will require larger bore access and the 9Fr cordis (also known as the Swan Sheath) is widely employed in this instance. At the author's trauma center, the flow rates achievable with the available wide bore access devices were assessed using a Belmont rapid infusion device (RID) and expired pRBCs and FFP in a ratio of 1:1. The best performing device was the 9Fr multi-lumen access catheter (MAC), which is as quick to insert as a cordis and confers the benefit of a second lumen for drug delivery or blood sampling. Although the MAC has the same internal lumen radius as the cordis, it is shorter and lacks the 90-degree angle of the cordis. Some practitioners employ hemofiltration catheters for volume resuscitation lines but although these catheters have an external diameter of 13Fr the internal lumen is only 12G and is therefore not a significant step up from a 14G peripheral cannula, is significantly longer than the cordis or MAC and, due to the separate dilator, insertion takes longer.

Another useful device in trauma resuscitation is the rapid infusion catheter (RIC). This allows upgrading an existing peripheral cannula to a 7Fr device which, during our *in vitro* assessment, out-performed the 9Fr cordis, likely due to its shorter length. *In vivo* the results may have been different as we were unable to account for the downstream pressures within the veins. Peripheral veins are under higher pressure than larger central veins and as such the driving pressure would be much lower for infusions going through peripherally inserted RICs.

Central veins are preferable to peripheral veins for multiple reasons; they are less collapsible in the hypovolemic patient (especially the

subclavian vein), more able to accommodate large volume fluid boluses and catheters placed within them are less likely to become displaced. Many trauma centers preferentially use the subclavian vein, others the femoral as it avoids the risk of pneumothorax. A study by Scalea *et al* (1994)[6] showed no difference in time of insertion or success rates in the subclavian rate compared to the femoral route in a prospective study of central venous access in trauma resuscitations. However, they noted an instance where a patient with a stab wound to the flank received resuscitation via a femoral cordis and on laparotomy it was discovered that blood products had been lost through a retroperitoneal vena caval injury. This highlights the fact that the femoral route should be avoided in patients in whom a venous injury between the diaphragm and pelvis is possible. The femoral route can also be problematic once the patient reaches the OR; it obliges the use of extended patient lines on rapid infusion devices, which can slow infusion rates and checking the insertion site intraoperatively is challenging. Regardless of the device being used, all needleless connectors should be removed as they dramatically reduced flow rates and the patient line length should be kept to minimum.

Non-Technical Skills

Practical procedures require a significant proportion of the practitioner's cognitive bandwidth and therefore the team's overall attention has been reduced, with the potential to reduce reaction times in the face of deterioration in the patient's status. A team behavior employed by London's Air Ambulance to address this is for the proceduralist to declare themselves 'head down'; thus informing other team members that they will need to allocate a greater amount of their attention to the patient's status for duration of the procedure.

Anticipation is also an important aspect of this trauma anesthesia role. Delays caused by not having the prerequisite equipment and drugs readily available are easily avoidable. Participation in daily trauma room checks can facilitate this.

THE TRANSFUSIONIST

The clinician playing the role of transfusionist is responsible for administering checked, warmed blood products at an appropriate rate and ratio. At Zuckerberg San Francisco General, although the team lead determines which products to administer, this role is often given to an anesthesia technician.

Rapid Infusion Devices

There are number of rapid infusion devices available which vary in their complexity and expense. Their principle functions are to pressurize and heat infusate for delivery to the patient. With the more advanced models such as the Belmont or the Thermacor, it is possible to set a specific infusion rate, track the volume administered and deliver boluses of predetermined volume at the highest rate the intravenous catheter being used can achieve. The more widely available Level 1 rapid infuser is less efficient at warming and less capable of removing air than the more advanced RIDs[7].

With ongoing critical bleeding, there are two possible approaches to employing an advanced RID. Increase the infusion rate until hemodynamics improve then back off once hemostasis has been achieved or give repeated boluses with a lower basal infusion rate until the patient stops responding to the challenges (based on Starling's law). The latter carries a slightly higher cognitive burden as the operator needs to consider the response to the boluses and determine the changes to the basal infusion rate. After a bolus is delivered the RID will drop back to its basal infusion rate and if this insufficient to keep up with losses it is easy to fall behind.

Tracking products administered is vital to ensure that the recommended ratios of packed red cells to plasma are maintained. This is often achieved by piling empty units up in separate stacks and regularly counting. At Zuckerberg San Francisco General we developed a tick box form for use during massive transfusions that reduced the mess and increased the ease of product tracking (Figure 1). An even more elegant solution could involve computer-based unit barcode tracking that included a notification if ratios

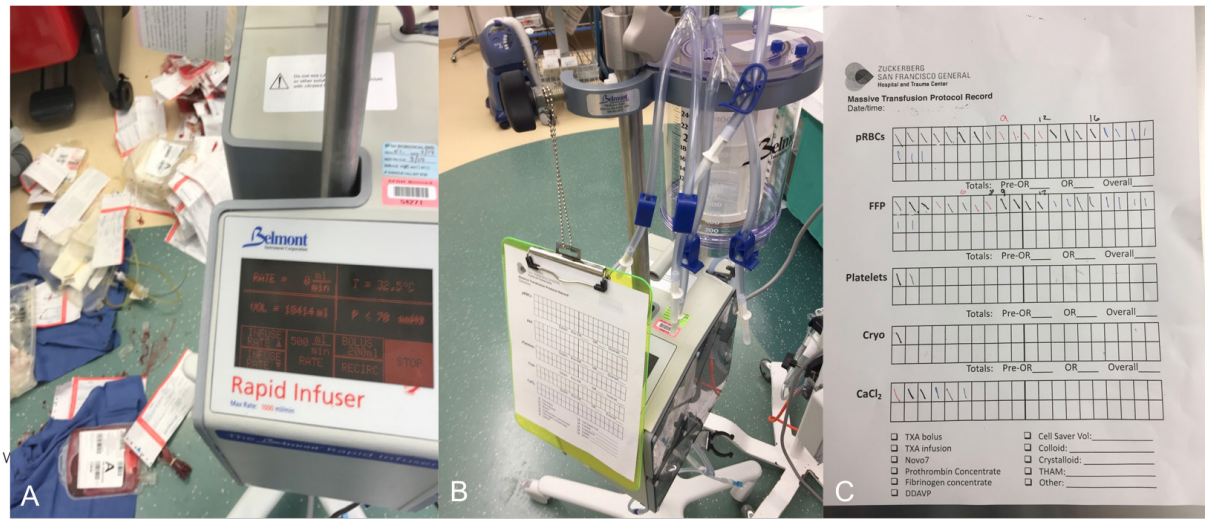

Figure 1: Product tracking before (A) and after introduction of the blood product tracking form (B and C).

Non-Technical Skills
Coordination with blood bank staff and the runner responsible for fetching coolers of blood products is vital in this role. Recruiting the operating room 'float' nurse to assist in product checking will improve team efficiency. Most importantly, accurate anticipation of future product requirements ensures a constant supply while reducing the risk of product wastage.

THE INVESTIGATOR

Point-of-care testing, including blood gas analysis and viscoelastic coagulation tests are integral to targeted hemostatic resuscitation, and conventional laboratory assays remain important. However, blood sampling and running tests are labour intensive, especially if analysers are housed away from the OR.

Baseline testing should occur at regular intervals (usually every half hour) with further sampling triggered by changes in hemodynamic status. During testing, complications of massive transfusions should be actively excluded by ensuring the potassium is not rising and calcium levels not falling.

Non-Technical Skills
Effective closed-loop communication will ensure that results have been disseminated through the team and prevent vital results from being overlooked, while making the team aware that the clinician performing the analysis is effectively 'head down'. Anticipation of testing requirements will also help detect any deterioration early and facilitate a timely cessation to aggressive volume resuscitation.

TEAM LEAD

The anaesthesia lead directs the efforts of the team members, initiating the MTP if not done in the emergency department, guides the resuscitation via goal setting and terminates the MTP as soon as appropriate.

Initiating a Massive Transfusion Protocol
MTPs are triggered by hemodynamically unstable patients who are known or suspected to be hemorrhaging and anticipated to require a large volume of blood products in the coming hours. Classically, the process by which clinicians predict this requirement is to generate a composite image of the patient in front of them in terms of vital signs, laboratory and point of care analysis, imaging findings (e.g. FAST) and the nature of the injury. In a large study utilizing the prospective, observational, multicenter, major trauma transfusion (PROMMTT) study population the parameter most predictive of massive transfusion requirements was INR > 1.5, followed by systolic blood pressure (SBP), base deficit and haemoglobin concentration[8].

Multiple professional bodies have produced guidelines to assist clinicians in predicting the need to initiate an MTP and several scoring systems have been published, the most widely studied being the assessment of blood consumption (ABC) and the trauma-associated severe hemorrhage (TASH) scores. A positive ABC results from the presence of two or more of the following parameters; SBP less than 90mmHg, heart rate greater than 120 beats per min, positive fast and penetrating mechanism of injury[9]. The more complex TASH score incorporates eight variables, a maximum score of 28 and a positive score of greater than 16[10].

Within their validation populations, the ABC and TASH scores have negative predictive values (NPV) of 95% and 94%, and positive predictive values (PPV) of 55% and 57%, respectively[11]. This indicates that both scores identify patients that progress to receive massive transfusions accurately but are less useful in identifying those that will not require a massive transfusion. However, the precision of the ABC score has been shown to less favourable among populations with a low incidence of penetrating trauma, such as Europe and Australia. Pragmatically speaking, the NPV is of greater importance as it far safer to have blood to hand and not need it, than the reverse, especially with the availability of temperature indicators for blood product units to identify those that have been warmed to unsafe levels.

Resuscitation Goals
Targets of resuscitation can be thought of in three broad categories; hemodynamics, metabolic markers of perfusion and coagulation tests, the individual importance of which will vary based on the stage of the resuscitation. Generating a composite image of the patient's current state with data parameters from each of these categories will facilitate more targeted interventions and reduce the risk of over or under resuscitation. Trends over time reveal more than individual readings, while specifically assessing the responses to interventions can provide valuable information. Clinical parameters that provide continuous, real-time data tend to be more useful, especially prior to stabilisation, than those that only give a snapshot, such as laboratory assays, which may be grossly unrepresentative of the patient's current state. Lastly, assessments need to be pragmatic, while a straight leg raise can provide useful information on a patient's volume status at the end of a procedure (foregoing any lower limb or pelvic trauma), it is not practicable intraoperatively.

Conventional hemodynamic (pulse rate and blood pressure) monitoring is easy to initiate, freely available and provides continuous real-time data on the state of the patient. It is especially useful at the start of the resuscitation and during periods with the greatest risk of instability, such as induction of anesthesia and initiation of positive pressure ventilation in the hypovolemic patient. However, a clinical picture based solely on these parameters can easily become obscured by altered autoregulation in older patients, concurrent medications or hemodynamic reflexes to hypovolemia. While the baroreceptor reflex predominates in the bleeding trauma patient this can be mimicked by the response to pain or masked by the bradycardic response to hypovolemia caused by the Bezold-Jarisch reflex or reverse Bainbridge reflex[12,13].

Advanced cardiac output (CO) monitoring can be extremely useful in guiding resuscitation, especially in the instance of continued hemodynamic instability after hemostasis has been achieved, where distinguishing between persisting hypovolemia, reduced cardiac contractility due to acidosis, or vasoplegia from an ischemia-reperfusion effect is challenging but vital. Uncalibrated

pulse contour analysis (PCA) techniques have their detractors but in the time-critical, task-intensive periods of resuscitation can be initiated rapidly and easily and provides continuous, real-time parameters for targeted interventions. Good agreement between PCA and transthoracic echocardiography has been demonstrated among trauma patients[14]. The esophageal Doppler is an alternative minimally invasive CO monitor that has been employed in trauma patients. However, although this device has proven advantages in determining volume status[15,16], it can be difficult and time-consuming to position correctly, shows considerable user variability and is relatively contraindicated in the coagulopathic patient. A focused transesophageal echocardiography exam can provide a detailed assessment not only of the patient's hemodynamic status but also diagnosis of specific injuries[17], but requires a skilled operator and is again relatively contraindicated in coagulopathic patients.

Accompanying the hemodynamic reflexes that attempt to compensate for the fall in oxygen delivery (DO_2) that results from hypovolemia, is an increase in oxygen extraction by tissues. This can be seen graphically in Figure 2 and detected clinically by a fall in central venous saturations ($S_{CV}O_2$). Although not as accurate a measure of whole body oxygen extraction as mixed venous oxygen saturation, which necessitates a pulmonary artery catheter, the trend of $S_{CV}O_2$ has been demonstrated to be useful target in resuscitation attempts[18]. In a porcine model of hemorrhagic shock, a decreasing $S_{CV}O_2$ was more predictive of coagulopathy (as measured by thromboelastography) than pH, lactate, base deficit or mean arterial pressure[19].

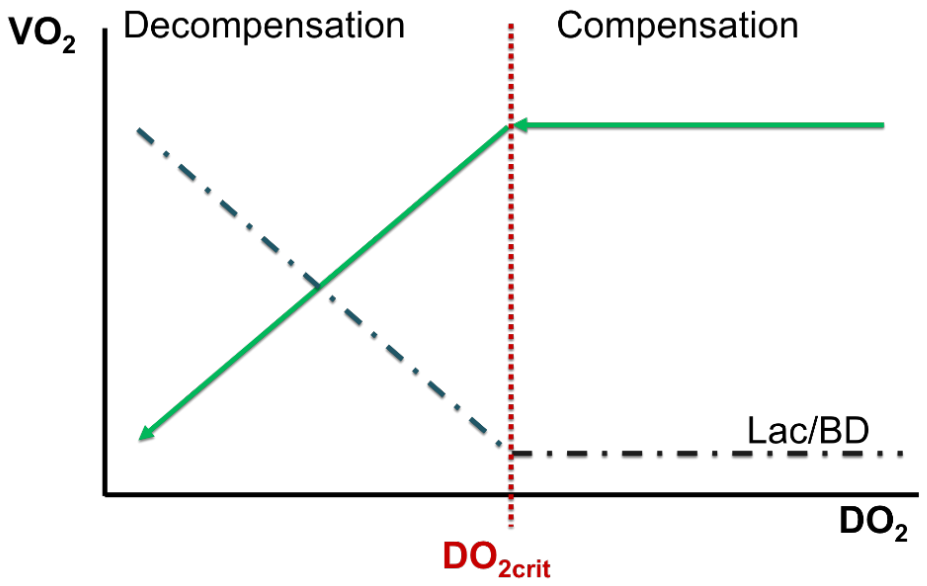

Figure 2: Graphical representation of the relationship between oxygen delivery (DO_2) and oxygen consumption (VO_2). VO2 is initially independent of DO_2 because as DO_2 falls, tissues extract more oxygen to maintain energetic processes and VO_2 remains constant. This compensatory mechanism is finite and once exhausted the critical DO_2 point is reached, beyond which, VO2 becomes dependent on DO_2 and anaerobic respiration increases with a concomitant rise in lactate and base deficit (adapted from Barbee *et al* [2010][20]).

Many centers have integrated point-of-care viscoelastic coagulation analysis into their massive transfusion protocols for the rational administration of clotting products. This was shown to reduce usage of plasma and platelets and improve early and late survival among trauma patients, as compared to a conventional coagulation analysis guided MTP[21]. This approach permits a targeted hemostatic approach, specifically tailored to the response of a patient's clotting systems to the injuries sustained and resulting hypoperfusion.

Lactate and base deficit (BD) remain the key metabolic markers of tissue hypoperfusion and highly correlated with mortality[18]. One instance in which care must taken in the interpretation of elevated levels is in the young adult male who has been assaulted or restrained as the exertion inherent to these situations can cause lactate and BD to rise without underlying hypoperfusion[22]. As with all resuscitation targets, the trend in levels will provide more informative information than single, absolute values.

The field of biosensors and 'wearable tech' has advanced significantly recently, permitting professional sportspersons to adapt training and track improvements more closely to their underlying physiology. Non-invasive devices have been produced that permit quantification of lactate within sweat[23] and expired respiratory gases[24]. While the absolute levels of lactate in sweat are significantly different to venous blood levels, increments in sweat lactate were significantly correlated with those seen in venous lactate during intense exercise[25]. A similar pattern was seen

in lactate levels within exhalation gases[26]. These techniques may represent continuous, real-time means of monitoring lactate, with significant implications for trauma resuscitation.

Terminating a Massive Transfusion Protocol

Terminating a massive transfusion at the correct moment is of critical importance. It can be challenging to distinguish between causes of ongoing hemodynamic instability after hemostasis. Persisting volume deficit will need further blood products but a whole-body ischaemia reperfusion vasoplegia, common after protracted or delayed resuscitation efforts in polytrauma, will need vasopressor therapy.

Over resuscitation results in wastage of a valuable resource and can have significant deleterious effects on the patient beyond the excess exposure to the widely known risks of transfusion. Packed red blood cells, especially older units, contain free heme as part of their 'storage lesion'. This acts as a damage associated molecular pattern and modulates the innate immune system via Toll-like receptors in a similar manner to those released by the original tissue injury and can contribute to the progression to multi-organ failure[27]. Recently this has also been related to excess death in a murine model of pneumonia after major trauma[28].

Guidelines have been produced by several professional bodies and typically include hemostasis with improvement in hemodynamic and/or laboratory results[11]. The major difference in initiating and terminating an MTP is time. Initiating an MTP must be done rapidly with far less data to hand than what is available at the end. Clinicians should therefore generate a gestalt image of the situation with input from the surgical team on hemostasis and a thorough assessment based on the goals outlined above to ensure the patient has been fully resuscitated and only then terminate the MTP.

Non-Technical Skills

Communication, both within and between teams, is key to effective team leadership in trauma anesthesia. It is easy to become remain ensconced in team anesthesia and not coordinate efforts with surgical colleagues. To address this, the trauma team of the British military hospital in Camp Bastion, Afghanistan developed a communication tool based on the World Health Organisation surgical checklist to ensure multidisciplinary participation in team discussions at key points of trauma resuscitation[29]. One unique feature of this was a ten second situation report to be conducted every ten minutes that included the following;

T – Time since start of procedure, temperature of patient

B – Blood pressure, blood product volume given, blood gas results

C – Clotting (ROTEM, surgical hemostasis)

S – Surgical progress and plan

Team leads should set and clarify goals as the resuscitation progresses and ensure team members are comfortable with and capable of performing tasks allotted. Members of the team may be relatively junior and have little experience with the emotional effects of witnessing wounds and treating critical injured patients, they should be supervised closely during the resuscitation for the benefit of patient safety and their education. Debriefings and video reviews including the whole trauma team can help members process the event and improve subsequent performances[29,30].

CONCLUSION

Implementing massive transfusions in trauma resuscitation requires multiple complex tasks to be accomplished in a time-critical fashion, while maintaining vigilant of changes in the stability of the patient. Only through a thorough understanding of the underlying physiological principles and effective team behaviours can these clinical scenarios be managed successfully, and the twin perils of under- or over-resuscitation be avoided.

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RCL-14
ASER: Enhanced Recovery Program: Key Components, Implementation and Outcomes

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LEARNER OBJECTIVES

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

(1) Discuss the changing healthcare landscape and the importance of increasing the value proposition;

(2) List the key components of the enhanced recovery protocol (ERP);

(3) Demonstrate the outcomes of the enhanced recovery strategy; and

(4) Identify barriers and share tips for successful implementation of the ERP.

The population of patients undergoing elective surgery is expanding. It is estimated that worldwide, more than 230 million surgical procedures occur each year. An increasing proportion of these patients, as life expectancy increases, are likely to be high-risk and elderly patients with multiple co-morbidities who present particular challenges to anesthesiologists, surgeons, nursing, and other perioperative care providers.

Despite improvements in surgery and anesthesia, approximately one in five patients experience a complication after major surgery. Complications increase short-term costs and long-term mortality, as well as reduce functional capacity and quality of life.

Perioperative complications can be directly caused by surgery or anesthesia but are more commonly related to or exacerbated by the perioperative care processes that occur during the patient's hospital stay. The optimum perioperative management of patients requires input from a multidisciplinary team.

Fast-track or surgical enhanced recovery pathways (ERP) have been proposed to improve the quality of perioperative care with the aim of attenuating the loss of functional capacity and accelerating the recovery process. The ERP reduces the delay until full recovery after major surgery by attenuating surgical stress and maintaining postoperative physiological functions. The implementation of the ERP has been shown to impact positively in reducing postoperative morbidity, and as a consequence, length of stay in hospital and its related costs.

This presentation addresses the physiological basis of enhanced recovery strategy, outline the components of the enhanced recovery pathway, discuss the implementation strategies and appraise the evidence and outcome of the enhanced recovery recommendations.

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RCL-15
Ultrasound Findings in Intraoperative Anesthetic Emergencies

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LEARNER OBJECTIVES

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

1) Describe how arrests in the operating room may be different from those that occur in the emergency room, in other parts of the hospital, or outside the hospital;
2) Review ultrasound findings in different causes of perioperative arrest, focusing on cardiovascular, respiratory, and anesthetic causes of arrest; and
3) Recall the logistics of performing ultrasound during cardiopulmonary arrest.

Bedside or point-of-care ultrasonography provides real-time patient information to the clinician performing the examination. Unlike a comprehensive examination, the focused point-of-care ultrasound study efficiently and immediately answers clinical questions and may be repeated if conditions change.[1] Point-of-care ultrasound in emergency room patients with undifferentiated shock has been shown to help narrow the differential diagnosis.[2] However, shock, hemodynamic instability, and other life-threatening events in the operating room differ greatly from the emergency room setting. Operative patients usually have known medical histories and witnessed events.[3] Intraoperative point-of-care ultrasonography should thus focus on etiologies of shock that are specific to the operating room environment.

This lecture will first review standard views in the point-of-care, focused ultrasound examination. Then, the epidemiology of intraoperative cardiac arrest will be discussed. Finally, ultrasound findings in shock due to cardiovascular, respiratory, and anesthetic causes will be described and summarized.

REVIEW OF ULTRASOUND VIEWS

The focused transthoracic echocardiographic (TTE) examination includes four basic views: the parasternal long-axis (PLAX), the parasternal short-axis (PSAX), the apical 4-chamber (A4C), and the subxiphoid.[4] The PLAX view allows evaluation of left ventricular (LV) size and function, as well as the right ventricle (RV) and the descending aorta. LV contractility may be estimated visually or assessed semi-quantitatively by fractional shortening using M-mode. The PSAX view may also be used to examine LV contractility and the presence of regional wall motion abnormalities (RWMA);[4] in addition, the interventricular septum (IVS) may demonstrate RV pressure or volume overload in this view.[5] The apical window shows LV and RV size and function, as well as valvular anatomy.[4] M-mode may be utilized in the A4C view to measure the tricuspid annular plane systolic excursion (TAPSE) as a surrogate of RV systolic function.[5] Similar to the A4C view, the subxiphoid view demonstrates LV and RV size and function.[4]

The thoracic ultrasound examination divides each hemithorax into four zones.[6] In each zone, the clinician may assess for lung sliding (movement of the visceral and parietal pleura against each other during respiration), lung pulse (movement or pulses of the pleura due to cardiac activity), and A lines (reverberation artifacts consisting of horizontal lines deep to the pleura).[6] B lines (comet-tail artifacts due to interstitial or alveolar fluid) may also be identified as vertical lines originating from the pleural line and extending to the bottom of the screen. Healthy lung tissue may show a few B lines, especially in dependent areas.[7] The diaphragms appear as hyperechoic lines cephalad to the liver and spleen and can assist with identification of pleural effusions.[6]

Ultrasound of the abdomen often includes the hepatorenal and splenorenal recesses and the bladder to assess for free abdominal fluid.[8] In addition, respiratory changes in the diameter of the inferior vena cava (IVC) may be used to estimate central venous pressure (CVP). Finally, compression ultrasonography can identify the presence of deep venous thrombosis (DVT), particularly in the highest-risk proximal lower extremity veins.[9]

EPIDEMIOLOGY OF INTRAOPERATIVE CARDIAC ARREST

In one single-center, 10-year study, approximately 20 cardiac arrests occurred per 10,000 anesthetics in a 24-hour perioperative period. Peri- and intraoperative cardiac arrests depend on surgical factors such as emergency status and type of surgery, as well as patient comorbidities, with greater risk in older, sicker patients.[10] The incidence of cardiac arrest due to anesthesia is about 0.5 to 1 per 10,000 anesthetics[11] and is often attributed to overdose of medications, hypovolemia, and problems with airway management.[10,12,13]

Survival after cardiac arrest increases in those that are witnessed and with shorter time to initiation of chest compressions.[14] Cardiac arrests in the operating room generally occur in witnessed and monitored patients, and resuscitation starts quickly once cardiac arrest is identified. In addition, these events are sometimes expected and carry a relatively narrow list of potential etiologies. The patient's comorbidites and possible precipitating or causative factors are known, allowing a more focused ability to diagnose and treat the underlying cause of the arrest.[3] Early point-of-care

ultrasound may assist in narrowing the differential diagnosis further and in ruling out reversible causes of arrest.[2]

The causes of intraoperative shock and cardiac arrest may be divided into cardiovascular, respiratory, or anesthetic causes. For each entity, focused, point-of-care ultrasound examination findings will be discussed.

ULTRASOUND FINDINGS IN SHOCK DUE TO CARDIOVASCULAR CAUSES

Cardiovascular causes of shock are divided into *cardiogenic* (which includes acute coronary syndrome [ACS] and rhythm disturbances), *hypovolemic* (including hemorrhagic), *obstructive* (which encompasses cardiac tamponade, tension pneumothorax, acute RV strain due to pulmonary hypertension or pulmonary embolism [PE], intra-abdominal hypertension, air/fat/amniotic fluid embolism, and bronchospasm and auto-positive end-expiratory pressure [PEEP]), and *distributive* (which comprises sepsis, anaphylaxis, spinal shock, and vasoplegia).

Cardiogenic shock

Cardiogenic shock occurs for a variety of reasons, including ACS and arrhythmias. Life-threatening, non-perfusing arrhythmias may occur with local anesthetic systemic toxicity and malignant hyperthermia, but these entities will be discussed in more detail in the section on anesthetic causes of shock.

The TTE in cardiogenic shock shows enlarged, poorly contractile ventricles with possible valvular dysfunction.[15] If the etiology is ACS, regional wall motion abnormalities (RWMA) may be seen in the PSAX view.[4] However, it may be difficult to distinguish acute from chronic RWMAs and to determine whether new wall motion abnormalities caused the arrest or occurred due to ischemia during the arrest.[16] Patients in asystole or true pulseless electrical activity show no ventricular wall motion, while those in a fibrillating rhythm may show ventricular "quivering."[17] Electrolyte abnormalities such as hypo- and hyperkalemia can cause a variety of arrhythmias that may lead to a non-perfusing rhythm (ventricular tachycardia, ventricular fibrillation, pulseless electrical activity, or asystole) and cardiac arrest,[18] which would show absent to minimal or fibrillating ventricular cardiac movement on TTE.

Patients with cardiogenic shock exhibit homogeneous, bilateral, diffuse B lines on the thoracic ultrasound examination[15] due to fluid accumulation in interlobular septa and alveoli. This pattern differs from that of pneumonia (in which B lines may be more localized or unilateral)[6] and of acute respiratory distress syndrome (ARDS) (characterized by heterogeneous, patchy B line distribution). The abdominal ultrasound examination for patients with cardiogenic shock demonstrates a dilated IVC with no respiratory variation, which indicates elevated CVP.[15]

Hypovolemic shock

Hypovolemia is associated with small, hyperdynamic ventricles[15] plus end-systolic LV cavity obliteration on TTE.[5] The thoracic ultrasound is normal with minimal B lines. If the hypovolemic shock stems from hemorrhage, a large hemothorax may be visible on thoracic examination,[15] appearing as an anechoic space cephalad to the diaphragm.[6] Large pleural effusions may surround adjacent lung tissue, leading to compressive atelectasis.[7] Intra-abdominal bleeding may also cause hemorrhagic shock; the abdominal ultrasound would then show free fluid in or around the liver, spleen, and/or pelvis.[8] Hypovolemic shock would result in a collapsible IVC with respiratory variation.[15]

Obstructive shock

Obstructive shock comprises several different diagnoses, all of which obstruct the flow of blood into or out of the heart.[15] Etiologies include cardiac tamponade, tension pneumothorax, acute RV strain, intra-abdominal hypertension, air/fat/amniotic fluid embolism, and bronchospasm and auto-PEEP. The ultrasound findings for each entity will be discussed separately.

Tamponade: TTE demonstrates small, hyperkinetic ventricles surrounded by pericardial effusion.[19] Pericardial effusions lie anterior to the descending aorta on the PLAX view. A pericardial effusion may cause cardiac tamponade when the pressure in the pericardial sac exceeds that in the heart, leading to diastolic collapse of the right atrium (RA) or RV. The best views to detect this phenomenon are the A4C and subxiphoid windows.[4] The thoracic examination will not show B lines.[15] The IVC would be dilated on abdominal ultrasound.[9]

Tension pneumothorax: Similar to the TTE findings in tamponade, the heart has small, hyperkinetic chambers in tension pneumothorax.[15] The thoracic ultrasound examination reveals findings characteristic of pneumothorax: absence of lung sliding and lung pulse, absence of B lines, and the presence of the lung point. If identified, the lung point is pathognomonic for a pneumothorax. It marks the transition from intact visceral and parietal pleura to pneumothorax, and it allows measurement of the size of the pneumothorax. However, no transition point exists with complete lung collapse, which is likely if a tension pneumothorax causes cardiac arrest.[20] The abdominal ultrasound would show a dilated IVC.[9]

Acute RV strain: Severe pulmonary hypertension or a PE may lead to acute obstruction to RV outflow, which then causes RV distension and dysfunction. The characteristic findings on TTE include an enlarged RV with poor function and flattening of the IVS.[21] In the A4C or subxiphoid views, the RV is normally approximately 60% of the size of the LV at the end of diastole; RV end-diastolic size equal to or greater than the LV indicates RV enlargement. Furthermore, the RV takes over the apex of the heart when it is dilated. RV pressure or volume overload also causes flattening of the IVS to form a D-shaped LV in the PSAX view. Low TAPSE measured in the A4C or subxiphoid views indicates decreased RV systolic function as well.[5] In PE, clot may be identified in the RA, RV, or pulmonary artery (PA) on echocardiography.[21] The thoracic ultrasound examination will

not show abnormal B lines.[15] A dilated IVC would be present on abdominal ultrasound. DVT may be identified on lower extremity vascular examination in some patients with PE; a vein with a DVT will show incomplete collapse when pressure is applied with an ultrasound probe.[9]

Intra-abdominal hypertension: Abdominal compartment syndrome or intra-abdominal hypertension due to elevated pressure in the intra-abdominal space may cause obstructive shock by decreasing venous return to the heart as well as increasing RV afterload. The TTE will show a small LV and a dilated, dysfunctional RV. Intra-abdominal hypertension may elicit pulmonary edema formation,[22] which would manifest as diffuse B lines on thoracic ultrasound.[15] Abdominal ultrasound would show a compressed IVC due to increased intra-abdominal pressure.[22]

Venous air embolism: Air introduced into the venous system may embolize to the PA, increasing PA pressures acutely and leading to sudden RV strain. The TTE in venous air embolism (VAE) has findings similar to acute RV strain with a dilated, dysfunctional RV. In addition, air may be seen in the RA, RV, and/or PA.[23] The thoracic examination would likely not show abnormal B lines. The abdominal ultrasound would demonstrate a dilated IVC.[9]

Fat embolism: Long bone or pelvic fracture and intramedullary instrumentation may cause embolization of fat into the systemic circulation.[24] As with VAE, embolic material travels to the PA, leading to an increase in RV afterload, RV dilation, and decreased RV function.[24,25] TTE may also demonstrate echogenic fat globules in the RA or IVC.[24] Thoracic ultrasound would likely be normal. A dilated IVC would be seen on abdominal ultrasound.[9]

Amniotic fluid embolism: Amniotic fluid embolism (AFE) has a variable presentation that may culminate in sudden cardiovascular collapse during or shortly after labor. It is thought that amniotic fluid traverses the uterine veins into the maternal circulation. Available data suggests that TTE in these patients would reveal primarily severe LV dysfunction. A small number of patients may also develop RV dysfunction.[26] Thoracic ultrasound would likely demonstrate abnormal B lines due to cardiogenic pulmonary edema.[15] There may be a dilated IVC on abdominal ultrasound.[9]

Bronchospasm and auto-PEEP: Severe bronchospasm and auto-PEEP due to dynamic hyperinflation of the lungs, or breath stacking, increase RA pressure and obstruct venous return to the heart.[27,28] Lung hyperinflation also raises pulmonary vascular resistance, which may cause RV dysfunction. The TTE likely shows RV dilation and dysfunction with septal flattening.[28] B lines would not be prominent on thoracic ultrasound.[15] A dilated IVC would likely be evident with abdominal ultrasound.[9]

Distributive shock

This category includes sepsis, anaphylaxis, spinal shock, and vasoplegia. It also comprises elevated vagal tone, anesthetic overdose, and hypotensive transfusion reactions, which will all be discussed in more detail in the section on anesthetic causes of shock.

Vasodilation of peripheral blood vessels and low systemic vascular resistance characterize distributive shock. The TTE usually reveals small, hyperkinetic ventricles[15] with decreased end-systolic cavity size.[5] Sepsis may be associated with myocardial dysfunction.[15] The thoracic ultrasound in some cases of distributive shock will be completely normal. If pneumonia is the source of sepsis, however, the thoracic examination shows alveolar consolidation, air bronchograms, and B lines. Consolidated lung resembles liver tissue and is termed hepatization of the lung.[6] The abdominal ultrasound examination shows a collapsible IVC.[15]

ULTRASOUND FINDINGS IN SHOCK DUE TO RESPIRATORY CAUSES

Respiratory causes of shock and arrest consist of tension pneumothorax, severe bronchospasm, and auto-PEEP, all of which have been described above. An additional cause of intraoperative cardiac arrest is a malpositioned endotracheal tube (ETT) and unrecognized esophageal intubation.[13]

With a properly positioned ETT, the thoracic ultrasound examination reveals bilateral lung sliding and diaphragmatic movement. A mainstem intubation only allows ventilation of one lung; the non-ventilated lung will not show lung sliding or diaphragmatic movement with ventilation, but it will demonstrate a lung pulse because the visceral and parietal pleura remain intact. An esophageal intubation, however, leads to lack of ventilation bilaterally. No lung sliding or movement of the diaphragms is visible, but the lung pulse is present in both lungs.[6] In addition, placement of the ETT in the esophagus can be visualized directly with an ultrasound probe over the neck.[6,29] The TTE would be normal, and the abdominal ultrasound examination would likely show a collapsible IVC.

ULTRASOUND FINDINGS IN SHOCK DUE TO ANESTHETIC CAUSES

Anesthetic causes of arrest encompass problems encountered primarily due to iatrogenic interventions such as elevated vagal tone (neuraxial block with high-level sympathectomy, vasovagal reaction), local anesthetic toxicity, malignant hyperthermia, anesthetic overdose, and hypotensive transfusion reactions. Unfortunately, ultrasound examinations during these rare catastrophic events have either not been performed frequently or have not been published or described in depth. The ultrasound findings referred to in the following scenarios are based on the hemodynamic and physiologic changes that are known or thought to occur.

Elevated vagal tone: Several entities culminate in elevated vagal tone, such as vagovagal reaction, oculocardiac reflex, and "high spinal" (neuraxial block with high-level sympathectomy). Cardiac arrest occurs in approximately 7 out of 10,000 spinal anesthetics. Bradycardia and cardiac arrest likely result from dense sympathetic blockade after spinal anesthesia. This sympathectomy leads to peripheral vasodilation with decreased venous return, blocking of cardioaccelerator fibers arising from T1 to T4, and other reflexes that contribute to bradyarrhythmias.[30] The TTE would likely

demonstrate findings similar to distributive shock with normal to hyperdynamic contractility[15] and end-systolic obliteration of the ventricles.[5] The thoracic examination would likely be normal, and the abdominal ultrasound would show a collapsible IVC with respiratory variation.[15]

Local anesthetic systemic toxicity (LAST): Systemic local anesthetics may cause seizures, arrhythmias, and decreased myocardial contractility.[31] Central nervous system symptoms often precede asystole, ventricular tachycardia/fibrillation, or pulseless electrical activity.[32] Ultrasound examination likely appears similar to that of cardiogenic shock, with the TTE showing dilated, poorly contracting ventricles,[15] or possibly fibrillating or non-contracting ventricles.[17] Heart failure would then lead to pulmonary edema and diffuse B lines on the thoracic ultrasound, as well as a dilated IVC on abdominal examination.[15]

Malignant hyperthermia (MH): Uncontrolled calcium release in susceptible patients leads to muscular rigidity and rhabdomyolysis, which can then cause life-threatening hyperkalemia and cardiac arrhythmias.[33] The arrhythmias may manifest on TTE as cardiogenic shock with poorly contractile ventricles[15] or ventricles that fibrillate or remain motionless.[17] If the patient is in cardiogenic shock, pulmonary edema may develop with diffuse B lines on thoracic ultrasound examination, as well as a dilated IVC on abdominal ultrasound due to elevated CVP.[15]

Anesthetic overdose: Overdose of anesthetic medications is one of the most common causes of anesthesia-related cardiac arrest. [10,12,13] Volatile agents and propofol decrease systemic vascular resistance and may cause mild myocardial depression.[31] The TTE would likely be similar to that in distributive shock with normal to hyperdynamic contractility[15] and small end-systolic ventricles.[5] Contractility may be reduced, however, with myocardial depression. The patient would likely have a normal thoracic examination with a collapsible IVC on abdominal ultrasound.[15]

Hypotensive transfusion reactions: Acute hypotension with blood transfusion may occur for a variety of reasons, including hemolysis, bacterial contamination, anaphylaxis, transfusion-related acute lung injury (TRALI), or increased levels of activated bradykinin.[34] These reactions likely cause a distributive shock picture with normal to hyperdynamic cardiac contractility[15] and end-systolic ventricular effacement on TTE.[5] The thoracic ultrasound examination would likely be normal unless the patient develops TRALI with diffuse pulmonary infiltrates.[34] TRALI is associated with heterogeneous, patchy B lines on thoracic ultrasound, similar to ARDS.[35] As with other causes of distributive shock, the abdominal examination would likely show a collapsible IVC.[15]

INTRAOPERATIVE CARDIAC ARREST

Ultrasound evaluation in patients with undifferentiated hypotension or shock may improve the accuracy of the diagnosis and the success of the resuscitation. One protocol for critically ill patients incorporates ultrasound assessment of the endotracheal tube, lungs, heart, aorta, IVC, abdomen, and vasculature, with the patient's clinical presentation dictating the order of individual parts of the ultrasound examination.[29] If the patient has sustained an arrest and is undergoing chest compressions, this series of examinations may not be possible. A different algorithm for performing an ultrasound examination during cardiopulmonary resuscitation (CPR) primarily recommends TTE using the subxiphoid window during the 10-second pulse check to minimize interruption of chest compressions.[17] While transesophageal echocardiography (TEE) allows continuous visualization and monitoring regardless of ongoing CPR, TEE requires more invasive and elaborate equipment[36] and a significantly greater amount of operator training than TTE.[37]

CONCLUSIONS

Shock and cardiac arrest in the operating room differ from those in the emergency department as the patient and precipitating events are known and often witnessed. However, the etiology still requires investigation. Point-of-care, focused ultrasonography examining the heart, lungs, abdomen, and vasculature can assist in narrowing the differential diagnosis and in ruling out certain entities. This discussion has delineated what the ultrasound findings might show in various emergency situations and is summarized in **Table 1**. In the future, further description of rare causes of intraoperative arrests should be published in order for providers to more accurately diagnose and successfully treat patients with life-threatening events unique to the operating room environment.

Table 1. Summary of ultrasound findings in intraoperative anesthetic emergencies.

Pathophysiology	TTE			Thoracic				Abdomen		Vascular
	LV	RV	Other TTE	Lung sliding	B lines	Lung pulse	Other lung	IVC	Other abdomen	
Cardiogenic shock (including ACS, rhythm abnormalities, LAST, MH)	Enlarged, poor function	Enlarged, poor function	Possible RWMA in ACS	+	+++ (homogeneous, bilateral, diffuse)	+		Dilated		
Hypovolemic shock (including hemorrhagic)	Small, hyperkinetic, end-systolic cavity obliteration	Small, hyperkinetic, end-systolic cavity obliteration		+	Normal	+	Possible pleural fluid if hemothorax	Collapsible	Possible free fluid if bleeding	
Obstructive shock										
Tamponade	Small, hyperkinetic	Small, hyperkinetic, diastolic collapse	Pericardial effusion	+	Normal	+		Dilated		
Tension PTX	Small, hyperkinetic	Small, hyperkinetic		None	None	None	Lung point	Dilated		
Acute RV strain (severe pulmonary HTN or PE)	Smaller than RV, normal function	Dilated, poor function, flattened IVS	Clot in RA, RV, PA if PE	+	Normal	+		Dilated		Possible DVT if PE
IAH	Small	Dilated, poor function, flattened IVS		+	Normal/+ (bilateral, diffuse)	+		Compressed		
VAE	Normal	Dilated, poor function, flattened IVS	Intracardiac air	+	Normal	+		Dilated		
Fat embolism	Normal	Dilated, poor function, flattened IVS	Intracardiac fat	+	Normal	+		Dilated		
AFE	Poor function	?Poor function		+	+++ (homogeneous, bilateral, diffuse)	+		Dilated		
Bronchospasm and auto-PEEP	Normal	Dilated, poor function, flattened IVS		+	Normal	+		Dilated		
Distributive shock (including sepsis, anaphylaxis, spinal shock, elevated vagal tone, anesthetic overdose, hypotensive transfusion reactions)	Small, hyperkinetic, small end-systolic size	Small, hyperkinetic, small end-systolic size	Possible myocardial dysfunction with sepsis	+	Normal/+ (localized in PNA; heterogeneous, patchy in TRALI)	+	Possible PNA in sepsis (lung hepatization, air bronchograms), TRALI in transfusion reaction	Collapsible		
Malpositioned ETT	Normal	Normal		None or 1 lung	Normal	+	Unilateral or no diaphragmatic movement, visualization of ETT in esophagus	Collapsible		

Abbreviations: ACS, acute coronary syndrome; AFE, amniotic fluid embolism; DVT, deep venous thrombosis; ETT, endotracheal tube; HTN, hypertension; IAH, intra-abdominal hypertension; IVC, inferior vena cava; IVS, interventricular septum; LAST, local anesthetic systemic toxicity; LV, left ventricle; MH, malignant hyperthermia; PA, pulmonary artery; PE, pulmonary embolism; PEEP, positive end-expiratory pressure; PNA, pneumonia; PTX, pneumothorax; RA, right atrium; RV, right ventricle; RWMA, regional wall motion abnormality; TRALI, transfusion-related acute lung injury; TTE, transthoracic echocardiography; VAE, venous air embolism.

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RCL-16
Blue Babies: How Do They Survive?

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LEARNER OBJECTIVES

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

1) Define nitrate physiology in both the adaptations to, and surgical management of, congenital heart disease;

2) Discuss basic research in anesthesiology and organize the process of building a successful research proposal and its timely execution;

3) Describe new technology like side stream dark microscopy and its scope in anesthesia; and

4) Assess the benefits of building collaborative studies involving multidisciplinary departments.

BACKGROUND

The incidence of congenital heart disease (CHD) is approximately 1/100 live- born children, of which up to 50% will require cardiac surgery at some stage during their life.. Although CHD ranks within the top five causes of infant mortality in most industrialized countries, more than 75% of infants born with critical CHD (requiring surgical intervention to survive) survive to one year of age. Over 80% of cardiac surgical procedures require cardiopulmonary bypass (CPB). While the cardiac surgical and intensive care mortality in children following cardiac surgery is low (2-5% peri operative death rate), major postoperative morbidity is common and translates into an increased rate of long-term mortality, morbidity, and disability [1] Many forms of congenital heart disease result in poor oxygenation of systemic arterial blood. Because immediate surgical correction is not always possible, some babies will be expected to remain blue (cyanosed) for up to several years before complete correction is possible. It is clear that these babies adapt to chronic hypoxaemia in ways that still allow the tissues to receive sufficient oxygen for survival and growth. Adaptive mechanisms include the persistence of foetal haemoglobin, increased cardiac output and polycythaemia. Adaptive changes in vascular tone are likely to also play an important part but have been more difficult to study. Whilst outcomes following surgical interventions continue to improve in children, our understanding of the physiological adaptive mechanisms at play, the impact of cardiopulmonary bypass and the risk factors for neurodevelopmental delay remain incomplete. Recent research on nitrate physiology suggests that nitrate species are key signalling molecules and may play a central role in each of these important areas.

Nitric oxide (NO) is recognised as a fundamental and important mediator in the precise regulation of regional blood flow and several other dynamic biological processes. It's biology and interactions within multiple organ systems (circulatory, gastro-intestinal, neuronal) have been defined over the last decade and its importance in health and disease has been increasingly appreciated by those involved in its basic science [2]. Its role in clinical practice (as a therapeutic agent), on the other hand, has been relatively confined and selective- only partly explained by its expense and difficulties in delivery [3].

The biology of nitric oxide and nitrogen species almost certainly play a role in adaptation to chronic hypoxaemia, as evidenced by studies in adults who have adapted to high altitude hypoxia [4]. These later studies, using a natural experiment design (comparing Tibetan inhabitants with sea-level dwellers), confirm that NO production and the regulation of nitrogen species is significantly altered by chronic exposure to hypoxic environments. These studies suggest that adaptation to chronic hypoxaemia involves much more than simple respiratory and haematological adjustment and that adaptation may be crucially dependent on vascular adjustments mediated through NO biology.

There is little scientific data that define the role of NO in adaptive changes in paediatric cyanotic congenital heart disease [5]. The chronic hypoxaemia experienced by many affected babies clearly stimulates adaptive changes that can extend well beyond the time-frames usually associated with the relative hypoxaemia of intra-uterine life. Our understanding of these adaptive changes is limited but essential to further improvements in clinical outcomes of babies with cyanotic congenital heart disease. A greater understanding of the mechanisms may allow the identification of babies who fail to make appropriate adaptive changes. It may allow early targeted intervention during peri-operative care and a more rational use of drugs such as NO in the peri-operative setting.

THE PHARMACOLOGICAL EFFECT OF NITRIC OXIDE (NO) IN CARDIAC BYPASS SURGERY

Organic nitrates, such as nitroglycerin (also known as glyceryl trinitrate), have been used clinically in the treatment of cardiovascular diseases for more than 150 years, but it was only in the late 1970s that their beneficial effects were shown to be due to the release of NO[6, 7]. NO has since been found to be produced endogenously and to have a key role in the regulation of many physiological processes, including cardiovascular function [8]. Studies have shown that directed delivery of NO during cardio-pulmonary bypass (CPB) has the capacity to reduce the CPB-induced systemic inflammatory response more selectively, with minimal systemic side effects [9]. A small single centre U.S. study reported a reduction in bypass-induced inflammation using the delivery of gaseous nitric oxide (NO) to the bypass circuit [10].

Children randomised to receive CPB with supplemental gaseous nitric oxide had a significantly shortened duration of mechanical ventilation (8.4 versus 16.3 hours; P< .05) and intensive care unit length of stay (53.8 versus 79.4 hours; P < .05) compared with the placebo group. The patients had significantly lower troponin and B-type natriuretic peptide levels postoperatively. In addition, patients treated with NO had a less positive fluid balance, with significantly less diuretic usage, and higher haemoglobin levels postoperatively. This study had important limitations, principally the small number of subjects (n = 16) and focus only a single type of cardiac lesion, tetralogy of Fallot [10].

Royal Children's Hospital Melbourne performed a pilot study using a randomized-controlled trial design to deliver gaseous NO on CPB in 198 children [11]. This pilot study confirms the positive effects on NO reported in the U.S. trial, and demonstrated significantly reduced incidence of low cardiac output state (LCOS) with improved patient outcomes, including lower need for extra-corporeal life support (ECLS), and trends for reduced length of stay, and shorter duration of ventilation. In view of these preliminary results from two studies with similar effect size, a large multicentre trial is currently running in Australia to test the generalizability of these findings to children requiring heart surgery.

Postoperative paediatric cardiac surgical patients are at very high risk of major complications, including cardiac arrest, death, and long-term neurological impairment. Low Cardiac Output Syndrome is the major determinant of poor patient outcomes, translating into prolonged PICU and hospital length of stay, prolonged need for ventilation, higher risk of organ failure, brain damage, and renal replacement. Should the current multicentre trial of NO Nitric oxide administration during paediatric cardiopulmonary bypass impact positively on long-term outcome of patients, there is potential for it to translate into the development of standard clinical indications for nitric oxide use via the oxygenator, during paediatric cardiopulmonary bypass.

CONGENITAL HEART DISEASE AND MICROVASCULAR PERFUSION

Children with CHD undergo changes in their microvasculature as an adaptation to chronic hypoxia [12]. Similarly, following surgical correction of cardiac defects there are changes in vascular performance related to increased oxygen delivery to the tissues [13] Directly visualised indices of micro vascular performance provide a useful and novel insight into overall circulatory performance. Non-invasive techniques such as sidestream darkfield microscanning (SDF) can be used to quantify microvascular perfusion at the bedside. Scolletta et al conducted an observational study which measured microcirculatory and haemodynamic data in 24 children under the age of 5 undergoing cardiac surgery for correction of CHD [14]. SDF imaging of the sublingual mucosa was performed to record the microcirculatory parameters which included total vascular density (TVD, vessels mm−2), proportion of perfused small vessels (PPV, %) and microvascular flow index (MFI, arbitrary units). These parameters of perfusion and blood flow were collected at five different time points starting at induction of anaesthesia through to ICU admission. The study showed that in cyanotic children there was an increase in PPV over time [14].
Apart from peri-operative care for CHD, monitoring of the microcirculation has potential value in the monitoring of critically ill patients. The ability to monitor this change at the bedside through the SDF technology would provide anaesthesiologists and intensivists with information to optimally manage these patients, particularly in critical situations [15].

CURRENT AND FUTURE DIRECTIONS

In an attempt to get greater understanding of the mechanisms impacting vascular function and nitric oxide bioactivity we are developing a programme with the following aims

1. To explore the relationship between nitrogen species – specifically nitrites and nitrates and nitrosyl-haemoglobin and the severity of chronic hypoxaemia in infants born with congenital heart disease.
2. To determine correlations between nitrogen species and objective measures of microvascular flow.
3. Understand changes in NO biochemistry in controls and matched cases that receive exogenous NO during cardiopulmonary bypass

Management of congenital heart disease requires complex care by a multidisciplinary clinical team that includes anaesthetists, cardiac surgeons, intensive care specialists, cardiologists, nurses and perfusionists. This programme represents a rich interdisciplinary collaboration involving the Departments of Anaesthesia, Cardiac Surgery, Cardiology, Paediatric Intensive Care, and the Department of Pathology.

By combining our collective expertise in clinical and basic science we will provide an opportunity to scale up collaborative research that will ultimately improve the outcome and long-term wellbeing of children with congenital heart disease.

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RCL-17
Medicine for Care of Older Persons and Emergency Laparotomy: The Lessons and How We Can Improve Care

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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; and
3. Formulate a care bundle that has been proven to reduce mortality for emergency general surgery.

INTRODUCTION

Aging

The world population is aging. This will be one of the most significant transformations of the 21st C 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 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 speciality 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.

CONCLUSION/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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RCL-18
Safety Reporting, Checklists, and Root Cause Analysis: What Are They Good For? Absolutely Nothing?

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LEARNER OBJECTIVES

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

1) Describe the evolution and application of safety reporting, checklists, and root cause analysis from high-reliability organizations to health care;
2) Identify components of an effective safety reporting system;
3) Summarize essential elements of perioperative checklist implementation; and
4) Assess the effectiveness of actions intended to address hazards identified by root cause analyses.

After several high-profile cases of patient harm were reported in the press (Libby Zion, Betsy Lehman, and Willie King) and the Institute of Medicine's Report *To Err is Human* was published in 1999, a heightened focus on patient safety in health care was launched.[1] More than a decade earlier, researchers at the University of California at Berkeley were investigating a diverse set of industries (aircraft carriers, commercial aviation, and nuclear power plants) which, although seemingly unrelated, all shared a very important factor in common.[2,3] The factor that they all had in common was that their operations very rarely failed. Despite the constant threat of disaster and harm, their day-to-day functioning was safer than would have been expected. The term high-reliability organization (HRO) was used to describe this diverse group of industries bound by their low failure rate, and the functioning of HROs has been what health care has been determined to imitate. A widespread adaptation of safety tools from these HROs followed. Safety reporting, checklists, and root cause analysis are among these tools borrowed from other industries that, to some extent, every practicing anesthesiologist is familiar with. Despite the use of these tools, and although tremendous progress has been made in the almost two decades since the release of *To Err is Human*, health care still lags far behind high reliability industries in the reduction of preventable harm.[4,5,6] This review will focus on how the less than optimal adaptation of safety reporting, checklists, and root cause analysis hinders the utility of these tools in making anesthesia safer for our patients.

SAFETY REPORTING

Incident reporting, as we know it to be in health care, has its roots in aviation. The Aviation Safety Reporting System (ASRS) was designed and implemented by Charles Billings, a flight surgeon and aviation medicine expert.[7] In order to facilitate reporting, it existed within a disinterested third party organization (NASA) rather than within the primary regulatory body (the FAA). Reporting of incidents (as opposed to accidents – events in which harm occurred) was confidential, and the reporter was subject to limited immunity. In health care, it is quite the opposite: reporting is typically to a person in a supervisory role and no such immunity exists. Further, the confidentiality of some safety reporting systems has been challenged, and the threat exists for the discovery of the submitted reports and their use in medicolegal proceedings.

The goal of safety reporting was best summarized by Sir Liam Donaldson in an analogy called the orange-wire test.[8] The essence of the analogy is that an engineer, while inspecting a plane, discovers an orange wire that is frayed in such a way that it suggests a systemic fault, as opposed to routine wear and tear. A report is filed which results in warnings world-wide, and within a few days every orange wire in similar aircraft is inspected and replaced if necessary. The goal of safety reporting should be to inform those who are unaware of a problem, so that further investigation can be performed and corrective action taken if necessary.

Unfortunately, in healthcare, safety reporting often is not as useful. As Lucian Leape indicated in his testimony before congress in 1997, the overwhelming majority of adverse events are not reported.[9] In fact, what typically gets reported is what cannot be concealed. This results in the loss of a large amount of potential data for quality improvement. Reporting, whether considered voluntary or mandatory, still remains essentially voluntary. Many factors affect whether a person reports an event.[10] The fear of punishment, the complexity of reporting systems, workload, and perceived utility of reporting all affect whether a person choses to complete a report. As a result, reports *do not* reliably indicate the incidence of events. According to Charles Billings, safety reporting in aviation was never intended to determine the prevalence of a problem.[7] The presence of two or three reports should suffice for identifying the presence of a problem; for some problems, which pose a high threat to patients, a single report may be enough to indicate that a solution needs to be sought. Another problem with looking at the quantity of safety reports can be thought of as reporting dichotomy, as described by Wachter.[11] On one hand, organizational leadership can be pleased that the number of safety reports has increased, choosing to believe that it indicates the attentiveness to safety and comfort of their staff in reporting events. On the other hand, organizational leadership can also be pleased that the number of safety reports has decreased, choosing to believe that the number of harmful events is decreasing. Clearly, rising and falling numbers of reports cannot both be interpreted as good.

The concept of blame is sometimes tied to safety reporting. Often, instead of a staff member saying, "I will complete a safety report on the event," it becomes "I will write them up." Safety reporting is not meant to be punitive, rather an occurrence is being described so that an investigation can take place and, hopefully,

the likelihood of it happening again will decrease. Repeatedly, the narrative portion of safety reports describe who did (or who did not) do something. Wording such as "forgot to," "failed to," or "supposed to" indicate that a particular person or group is to blame; meanwhile, the reporter is only observing the event from his or her own perspective. What effect does the suggestion of blame in a safety report have on the reviewer of the report? An interesting linguistics study showed two groups of individuals the same videotape of an incident.[12] The two groups then read two different reports of the event they had just witnessed. The group that read the written report of the incident with agentive language (e.g. "He broke the vase") was more likely to assign blame for the incident than the group that read a written report containing non-agentive language (e.g. "The vase broke"), even though both groups observed the exact same video of the incident. Indeed, reading a biased report may cause "cognitive contamination" within the reviewer of the report and hinder an unbiased investigation and the determination of the true cause of the event.

CHECKLISTS

The use of checklists to simplify complex tasks can also be traced back to aviation. The crash of the Boeing 299, killing two experienced test pilots at Wright Field in Dayton, Ohio on October 30, 1935, yielded the design of the first checklist in aviation.[13] More than 65 years later, the first large study was published touting the benefits of a checklist in medicine. The work of Pronovost et al., described how the use of a checklist for the placement of central lines in the ICU resulted in a large and sustained reduction in the rate of catheter-related bloodstream infections.[14] This was followed by the work of the Safe Surgery Saves Lives Study Group and the World Health Organization's release of the surgical safety checklist, which demonstrated a reduction in the rate of death and complications in patients older than 16 undergoing noncardiac surgery in a diverse group of hospitals.[15] Hospitals were smitten with the idea that something so simple and inexpensive could result in a significant reduction in harm to patients.

The gold standard for research had long been the randomized controlled trial. Over time, this definition was amended to include the fact that the results should also be *reproducible*. Within a short amount of time, both the checklists for central line placement and surgical safety became plagued with problems involving reproducing the significant reductions in harm that the original studies seemed to promise.[16,17,18] As it turns out, using a checklist is significantly more complicated than it first appears, and its success, or failure, strongly correlates to its implementation.[19] Implementation science is quite complex and beyond the scope of this review course, however there are several resources listed in the reference section for further study.[20,21,22]

Beyond the implementation of the checklist as a change in an organization's practice, there are factors directly related to checklist design that affect its fidelity. Much of this research is based upon work conducted by NASA scientists.[23] Checklists function best when they are short and contain only the critical steps. They cannot be used as a substitute for training, communication, or vigilance. The checklist should be conducted as a discourse between two people, with a challenge – response format. If the checklist is interrupted, it must be started over. If a particular element cannot be verified, the checklist must be halted until it can be verified. Finally, checklists perform poorly when used as a conversational prompt.[24] For instance, the Safe Surgery Checklist includes the element "What are the critical or non-routine steps?" This item is designed to initiate a conversation with the team. This is a very different item than "Is essential imaging displayed?" which will elicit a binary (yes or N/A) response. The quality of the conversation in response to the conversational prompt element is a better reflection of the safety-mindedness of the team using the checklist. Mandating the use of a checklist alone will not transform a poorly communicating team into a team that shares the same mental model. A checklist is only a sheet of paper which serves as a reminder tool to those who are using it. Its functionality is only as good as the team that is using it, and the introduction of a checklist alone will likely do little to improve safety.

ROOT CAUSE ANALYSIS

The origin of root cause analysis (RCA) is often attributed to engineers at Toyota Motor Corporation.[25] The earliest root cause analysis sessions consisted of asking why 5 times in order to achieve a deeper understanding of the cause of the problem. Although this process added depth to the analysis, it did so without adding to the breadth of understanding, resulting in a failure to consider the complexity of the system in which the error occurred and the likelihood of multiple causes acting in concert. Root cause analysis has evolved to include multiple tools to facilitate the process, including brainstorming, fishbone diagrams, flowcharts, histograms, scatter charts, and process mapping.[26,27] Yet despite the multitude of tools developed to assist with root cause analysis, there is little evidence that the process leads to safer patient care. It is this diversity of tools that causes RCA to become a heterogeneous process which ideally serves two purposes: 1) to inform risk evaluation, or risk acceptability and 2) to determine risk treatment, or risk reduction.[28] Although the RCA process, as employed by the Veterans Health Administration, was successful in accomplishing the first purpose, by shifting the analyses of adverse events toward a search for system vulnerabilities rather than human errors, its ability achieve the second purpose was not clear. [29]

Percarpio et al. identified several problems with the RCA process, including that the motivating factors for conducting RCA are often regulatory in nature, rather than purely safety-driven; near miss events are typically not prioritized for analysis leading to a loss of valuable data; hindsight bias can lead to misinterpretation of the causes; the investigation process often stops at a "convenient" root cause, rather than the correct one; and there is often a lack of action after the RCA has been conducted.[30] Perhaps the biggest Achilles' heel in the RCA process has been implementing an effective solution. The belief exists that a high quality risk evaluation process will naturally lead to a high quality risk reduction plan, which is not necessarily the case.[28] For this to occur, the health care workers responsible for the risk reduction plan would need training in human factors and reliability engineering, which

they often do not have. This results in the proposal of less effective solutions. A recent study examining 302 RCAs over 8 years found that the most commonly implemented solutions were weaker actions, such as additional training and policy enforcement.[31] Not surprisingly, during the study period multiple event types were observed to occur more than once, reflecting the lower quality of the solutions employed. Two reviews of interventions which are more likely to generate more effective solutions are contained in the reference section.[32,33]

SO WHAT ARE THEY GOOD FOR? ABSOLUTELY NOTHING?

Safety reporting, checklists, and RCA *are* good for something. Applied correctly, these tools can assist us in improving safety for our patients. There is no doubt, however, that health care has not made use of these tools as effectively as it might. Safety reports can be made more valuable if they are easy to fill out, limit the user to a brief narrative of the event, and provide feedback to the person submitting the report. Safety reports should never be used to track incidence, and the absence of reports on a given type of event should not be interpreted to mean the absence of that type of event. Checklists are most useful when they are brief, are able to progress uninterrupted by distractions, are conducted between two people using the challenge-response method, and have elements which evoke a binary response. Although the checklist can be used to stimulate the communication of essential information between team members, it likely will not do so unless the entire team is engaged in the safety process. The key to the checklist functioning optimally for this purpose is recognizing that it requires strong implementation and often a change in culture. As Leape points out, it "is not a technical problem that can be solved by ticking off boxes…but a social problem of human behavior and interaction."[34] The quality of the RCA process can be improved by ensuring an adequate depth and breadth of the investigation, the use of investigators with diverse backgrounds, and mindfulness regarding the effect that hindsight bias plays in determining the cause of the event. The interventions selected to address the problems identified by the RCA need to be both effective and sustainable, and audits should be conducted to ensure that the interventions remain in effect. Training in the science of safety and human factors will help those tasked with designing the interventions to be more successful.

THE FUTURE OF SAFETY

Although improving the utility of safety reporting, checklists, and RCA has the ability to improve safety for our patients, it simply isn't enough. Three relatively recent concepts may hold the key to advancing to the next level of improving patient care. The first of these concepts is "safety anarchy," proposed by Sidney Dekker.[35] Anarchy in this sense refers to a group of people being able to have confidence in spontaneous cooperation and the existence of mutuality without hierarchy.[36] Safety anarchy is *not* about the total absence of authority or the absolute freedom of an individual, but rather the idea that safety is an ethical obligation that those in healthcare have, rather than an obligation to rules and regulations.[35] The focus should shift, Dekker argues, from creating more policies & procedures, policing of staff, and metrics to cultivating diversity, motivation, creativity, and autonomy.

So what are organizations to do while not creating more policies, coaching rule breakers, and insisting on more double-checking of staff members' work? They can focus on the second concept: joy at work. Health care providers cannot meet the challenge of providing safer care if they don't find joy and meaning in their jobs.[37] Joy is not the same as happiness; joy refers to the sense of accomplishment and sense of importance in daily work.[38] Threats to joy in the workplace come from a feeling of lack of respect for ones' work, production pressure, the poor design of work flow, and the extent of non-value added work.[38] One "blueprint" for increasing joy in the workplace, which Don Berwick of the Institute for Healthcare Improvement often refers to, comes from Paul O'Neill, former United States Secretary of the Treasury and CEO of Alcoa. O'Neill states that people need to find three things in the workplace: every day they are treated with respect and dignity, they are provided with the tools and are encouraged to give their life meaning through making a contribution to the value created by their organization, and they are recognized and appreciated for what they do. [37, 39]

The final concept is termed Safety-II.[40] Safety-I, the perspective of safety that we are most accustomed to, is the absence of accidents or incidents. It becomes defined as the state where as few things as possible go wrong. Safety-II, rather, focuses on the state where as many things as possible go right. In complex situations, such as those encountered in healthcare, which are dominated by uncertainty and ambiguity, humans respond with variability and adaptation. Instead of this variability and adaptation viewed as a negative quality of a system, Safety-II advocates see this as a necessary resource for things to go right. By examining the care of our patients as something that most commonly goes right, it becomes easier to understand how things occasionally go wrong. Safety-II is not a replacement for our traditional approach to safety (the Safety-I approach), but provides an additional lens for viewing events which will allow for a greater understanding of how everyday actions achieve safety.

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RCL-19
Principles of Lean Management and Systems Engineering for Anesthesiologists

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LEARNER OBJECTIVES

After participating in this activity, learners will be able to:

1) Apply concepts of lean management to quality and efficiency initiatives at their institutions;
2) Prepare a charter to advocate for support to begin a quality improvement initiative;
3) Evaluate the best approach to collect data and confidently and independently analyze results; and
4) Formulate ongoing quality improvement and efficiency projects for their department and institution.

IMPROVING THE VALUE OF HEALTHCARE DELIVERY: A NECESSITY AND AN OPPORTUNITY

The implementation of value-based healthcare initiatives is imperative to improving our healthcare system. While the concept of anesthesiologists as perioperative leaders is not new, anesthesiologists now have the opportunity to lead collaborative perioperative care teams in the redesign of the perioperative process, to maximize our impact on patient outcomes. The application of continuous improvement strategies will result in improved efficiency and quality both in the perioperative period and beyond. This review of lean management strategies aims to provide anesthesiologists with the skills to apply these principles in their current roles within their department and hospital.

> ***"Before you try to solve a problem, define it. Before you try to control a process, understand it. Before trying to control everything, find out what is important."*— W. Edwards Deming.**

WHAT IS LEAN SIX SIGMA?

Lean philosophy centers around identifying and solving problems, with a focus on continuously improving the quality of the process. Lean processes in healthcare seek to identify and reduce waste, decrease cost and improve outcomes while also enhancing the patient experience. The Lean management business philosophy originated in post Word War 2 Japan with the Toyota company. W. Edwards Deming is credited with bringing systems engineering and Lean thinking to the forefront in the United States after appearing in a documentary entitled " If Japan can, Why Can't We?" in 1980. Six Sigma is a separate, related business system which focuses on the production of a defect free product from the process, every time. Often these 2 business concepts are used together. Systems engineering involves the design of a complex system in order to get the best outcomes or product possible. Anesthesiologists are often in prime positions to serve as systems engineers of the perioperative process, skilled in identifying opportunities to create an efficient, well-coordinated process that results in optimal patient outcomes.

THE 8 STEPS TO PROBLEM SOLVING

A structured approach to problem-solving has many benefits. It reduces the amount of time lost in debate, facilitates the identification of the weak points in the process, highlights systemic causes, provides a factual representation of the incident, and allows comparison of what actually happened against what should have happened, at any point in the process.

1. Identify the Problem and Prioritize Opportunities:

The first step of the problem solving process is problem identification. The problem must be clearly defined in order to understand where the opportunities for improvement are within the process. This step will also facilitate a decision about which opportunities should be focused upon first.

Common Tools for problem identification:

- **Observation:** One of the best ways to understand the process is to observe the workplace and speak to the workers. In the words of honorary Toyota chairman Fujio Cho: "Go see, ask why, show respect."
- **An Affinity Diagram** is used to organize facts, opinions and issues into natural groups to help diagnose a complex problem. This tool is most useful when a problem is not well organized. Group members write down their observations about issues and problems on sticky notes, and then post them randomly on the board. The group then silently organizes the notes into groups or themes. Silence during the exercise is crucial to engage both extroverted as well as introverted group members. Notes may be duplicated if the group determines that it belongs in 2 categories. The organized notes are then labeled by category and a diagram of the problem and its components is created.
- **A Cause and Effect Diagram** is also known as an **Ishikawa, or Fishbone** diagram. The purpose of this tool is to help the team move beyond identifying the symptoms of the problem to determining its' root causes. The tool is used for root cause identification only once a focused definition of the problem has been created. It can also be a solution tool for brainstorming ways to prevent future problems. In a process that provides a service (as opposed to creating a product), the traditional "bones" of the diagram are labeled: policies, procedures (steps in a task), plant (equipment), and people. The "head" is where the description of the problem is written.
- **A Pareto Analysis** is used to categorize and stratify potential problems. The Pareto`principle`(also known as the`80/20 rule), suggests that for many events, approximately 80% of the effects come from 20% of the causes. This tool is best

for determining where to first focus improvement efforts, or to identify the issues that contribute to the problem the most. A pareto analysis is conducted by collecting data on different categories of problems and tabulating the scores to determine the total number of problems observed and the total impact. A vertical axis line is drawn to display the total number of categories that were observed, and a bar graph is created to compare the contributions from each category to the problem. As a rule, "other" is avoided as a category label. When it is included, it is placed last in order, even if it is the tallest bar. A cumulative percentage line is drawn to determine which categories combine to contribute 80% of the total effect. A second order pareto analysis further examines the subcategories of the largest original category that was identified.

- **5 Whys:** this technique is used to get to the root of the problem. Asking "Why?" five times in a row facilitates an understanding of the underlying cause of the problem, which may not have been readily obvious.

2. Define the Project

Once the problem is clearly identified, the project must be defined. Creation of a charter will assist in determining the scope, and identifying key stakeholders involved in the process. In the course of charter creation, it is important to determine the key metrics that will be followed. The better the problem is articulated, the better the buy-in from stakeholders.

Key questions to address at this stage in the process include:

- Why is this project important?
- What are the consequences of not dedicating enough resources to this project (morale, patient safety, lack of efficiency with a real financial consequence, etc.)?
- What data is available that illustrates the extent of the problem?

3. Document and Measure Current Reality

Process improvement is a strategic approach to improving products, services and processes. The goal of creating a process map is to understand the actual process in its' current state and to identify the waste, which are areas of opportunity to improve the process. A process is a series of steps that must occur to produce a product or provide a service. All processes have start and end triggers, and a customer; each needs to be identified. Every process involves suppliers, inputs (variation comes from inputs), outputs and customers. It is important to understand which inputs cause the most variation, as well as which ones the team is able to influence. The value of the process occurs by delivering to the customer exactly what they need, when they need it, every time, defect free, in a safe environment, at the lowest cost, and without waste. The value stream map is used to clearly outline roles and responsibilities for all members of the process. Value added as well as non-value added steps are identified to inform the vision of the desired future state. The value stream map will also highlight the resources that are needed to make the shift to the future state. By identifying waste and redesigning the system, existing resources may be redeployed in many cases.

4. Analyze and Identify Muda (Waste/ Overburden)

Waste (Muda) is defined as any activity that takes time, resources and space, but does not address the customer's requirements. To add value, each step must: change the form, fit or function of a product or service, be done right the first time, and be something that the customer is willing to pay for. No process can be entirely free of waste due to the need to meet regulatory requirements, business and employee needs.

Waste comes in many forms:

- **Excess inventory:** any unnecessary supplies or materials that do not support "just in time" delivery.
- **Unnecessary Transportation:** any unnecessary material movement that does not support a lean value stream
- **Over-processing:** effort which adds no value to a product or service
- **Waiting and que time:** idle time in which no value added activities take place
- **Unnecessary motion:** any movement of people which does not add value to the product
- **Defects:** products or services that do not meet customer requirements.
- **Over production:** producing more than is immediately needed
- **Injuries:** work related accidents
- **Unused employee creativity:** missed opportunities for employee-driven improvements (leads to low morale, resignations)

5. Optimize Flow and Remove Friction: the Beginning of the System Re-design

The goal is to optimize the process at each step, such that the product or service is always being worked on without interruption and with minimal waste. The start trigger of the process will be the customer's request, and the end trigger is delivery of the product to the customer. One or two metrics should be selected to track to determine if the re-designed process is successful. Metrics must be in alignment with project objectives and satisfy basic criteria. The selected metrics should be:

- Strategic: focused on the group's priorities and the mission
- Quantitative: provide prevalence, rate of improvement etc.
- Provide the opportunity to adjust and make further improvements
- Provide transparency to leadership as well as those involved in the process in order to drive the priorities, behaviors and desired outcomes
- Inform decision making and next steps
- Ensure work is not simply pushed elsewhere along the value stream

Process metrics are measures of how well the steps of the process are being completed. Outcome metrics are measures of how well the outputs meet their intended purpose.

6. Implement and Validate

Implement the future state process and validate its effectiveness. Generate a list of actions required to address the root cause of the problem, assign a team member as the owner of the action item, and establish a timeline for implementation. Action items should follow the SMART mnemonic. They should be specific, measurable, assigned to one person, realistic and timed. Verify that all actions are completed.

7. Measure and Sustain

Quality data is a strategic asset. There is no one best way to collect data, and depends upon factors such as what you need to know, what resources are available, and how frequently the data must be updated. The data may be continuous or discreet, depending on the metric chosen. Continuous (variable) data can be measured on an infinitely divisible scale or continuum. There are not gaps between possible values (ex: temperature, time, age). Discreet (attribute) data measures attributes or counts. Gaps exist between possible values (ex: smokers vs. non-smokers, categorized data). Examples of time based metrics include: takt time, cycle time, total lead time.

Data and Variation Analysis:

Run charts: graphs which portray the change in data over time, also known as a time series chart. 5 or more points in the same direction usually constitute a trend in the data. A shift, or signal of improvement, is defined by 6 or more consecutive points above the median.

To create a run chart:

1. Plot time along the X axis. Choose the appropriate time increment based on your improvement project.
2. Plot the key measure you're tracking along the Y axis. Note that a run chart becomes more powerful as you add more data points because there will be more opportunities to identify patterns. If you're looking for signs of improvement, usually you need at least 10 data points.
3. Label both the X and Y axes, and give the graph a useful title.
4. Place a line that represents the median of the data on the run chart.
5. Add a goal line, if appropriate. Include annotations for unusual events, changes tested, or other pertinent information.

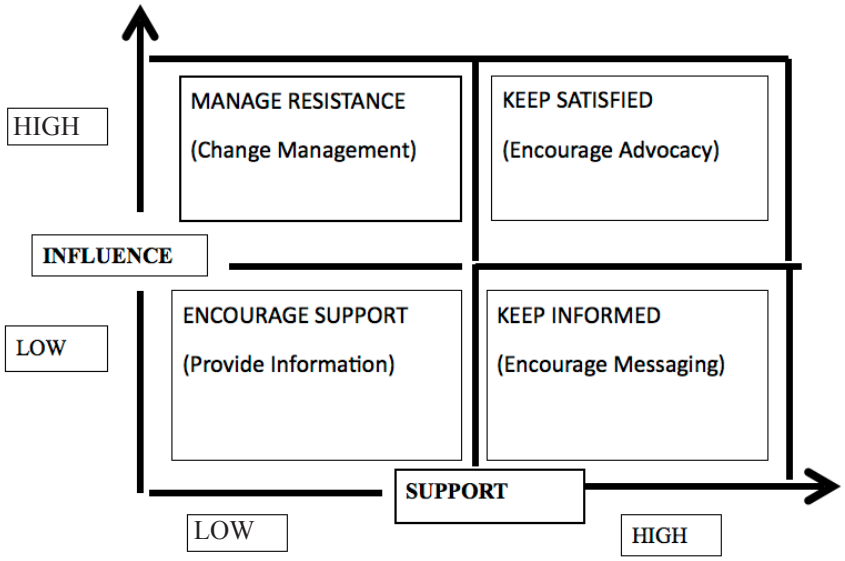
Control charts: display data calculated over time and indicate the range of variation built into a system (control limits).
To create a control chart:

1. Plot the data as described in steps 1-3 above for a run chart.
2. Calculate and place a line to indicate the mean. Add the upper control limit (UCL), which is defined as +3 standard deviations from the mean, and the lower control limit (LCL), defined as -3 standard deviations from the mean. If all points are within the upper and lower control limits, the process is described as "in control". If it contains data points out of the range of variation, it is out of control, or unpredictable. It contains special cause variation that must be explored.

Variation can be related to either a common cause, or a special cause. Common causes are uniform and predictable, stable over time, and remain constant within specified predictable limits. By contrast, special causes are random, unpredictable and unstable over time. The output of a system with special cause variation shows abrupt changes or unexpected patterns or changes in outputs.

8. Communicate and Acknowledge Success

Communicating success of the project requires stakeholder management. Identify all individuals who are involved in, or affected by a process. Communicate with the stakeholders to understand how they can affect and will be affected by the project; inquire about their concerns. Stakeholders can be sorted based on level of support and degree of influence using stakeholder grid, which plots each individual's level of support against their level of influence on the project. Plan to address stakeholder needs and concerns throughout the continuous improvement cycle.



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RCL-20
Women in Medicine and Leadership: Glass Ceiling, Sticky Floors, and Everything in Between

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LEARNER OBJECTIVES

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

1) Appraise and examine the factors leading to the underrepresentation of women in leadership positions in academic medicine;
2) Identify the challenges faced by women in medicine during their careers, including gender biases, lack of mentoring, and work-life balance;
3) Organize and differentiate those challenges in a meaningful framework;
4) Describe and interpret commonly used metaphors in the context of the career paths of women in academic medicine;
5) Appraise an formulat practical approaches to advancing the career of women in academic medicine; and
6) Differentiate and begin to formulate personal, organizational, and societal plans of action to increase the representation of women in leadership positions.

According to a recent report by the Association of American Medical Colleges (AAMC), women in academic medicine are underrepresented in the advanced leadership positions such as deans or chairs. Despite the progress made over the past decade, their career advancement still lags behind their male counterparts [1-3]. Women represent 21% of full-time professors, 16% of medical schools deans and 15% of academic department chairs[1]. The gender-gap is even more pronounced in male-dominated specialties, such as surgery and radiology.

It is recognized that increasing women in leadership is "the right thing to do" and, more importantly, is "the smart thing to do" [4]. In addition to the recognized financial advantages of increased women representation in the C-suite, women may favor a different style of leadership, focused on the "soft" skills that promote a collaborative and potentially transformative environment [5-7]**.** The paucity of women in advanced leadership positions also means there are fewer women who are available to be role models or mentors for the next generation [8]. Without appropriate mentorship, women are less likely to expand their potential, to explore new opportunities, to invest in their "social capital" [3,4] , or to satisfactorily manage their professional and personal lives.

THE GLASS CEILING AND OTHER METAPHORS

It was originally thought that the under-representation of women in advanced leadership positions was caused by a pipeline issue, with fewer women graduating medical schools [9]. However, for the past few decades in the US, close to half of medical school students are women[1]. When discussing women's career paths in academic medicine, a reference is frequently made to the **glass ceiling** [9-11]. This metaphor was first introduced in 1986 to describe the effect of the barriers women faced in the corporate world [12], representing a goal that was visible and yet unreachable. Thirty years later, the same challenges persist: workplace prejudice about women's capabilities, assumptions of reduced availability owing to family demands, and a lack of "sponsors" or mentors to increase visibility [12]. Others theorized that a **sticky floor** slows women faculty's development, with women spending more years than men in lower academic ranks [13]. During the financial crisis, a new phenomenon emerged in which women were placed in leadership positions during risky transition phases in an organization, to walk along the **glass cliff** [14]. The glass cliff appeared in politics as well. First, desirable positions are more often sought and obtained by men than women, leaving women fewer choices. Second, in times of turmoil, people may prefer a women's approach to leadership, focusing on a collaborative and relational leadership style. **Gatekeeping** is at play when men in positions of power prevent the advancement of women[15] and instead, promote those with whom they most identify. The **leaky pipeline**[1] suggests that if fewer women stay in academic medicine, then fewer women are available to assume leadership positions. Uphill struggle, thankless job, and learning to navigate the leadership labyrinth [5] could also reflect some of the experiences of women in academic medicine.

CHALLENGES ON THE CAREER PATHS

Women face "disproportionately bigger challenges" in their careers, when compared to men [2]. Among those challenges are the availability of mentorship, learning negotiation skills, the need to balance work and family life, and presence of gender biases in the workplace.

Those and other challenges can be grouped in four general categories, which were previously used to describe challenges faced by women political activists: environmental, structural, situational and motivational factors [15].

Environmental conditions describe the work environment's acceptance and general support of women in leadership positions, including the presence of gender biases. *Structural factors* refer to the institutional infrastructure needed to achieve advanced leadership positions, such as availability of mentoring, training and workshops, and other resources. *Situational factors* relate to the need to balance family and career, and to the presence of supportive social and family networks. Finally, *motivational factors* can explain the presence or lack of women's interest in pursuing or achieving leadership positions in academic medicine. It is likely that a confluence of several of those factors affect women's career paths.

The most prevalent and most reported challenge remains the presence of gender-biases at work[16]. Shared experiences of women in academic medicine are affirmed by published surveys and interviews spanning the past twenty-five years. Women report perceptions of gender biases for their career advancement such as biased promotion criteria, and fewer professional development opportunities[17]. Even women in leadership positions are not immune to gender-based challenges [4,18] and a sample of women chairs identified gender biases as one cause of women's under-representation in leadership positions [4], which further hinders women's career development.

Dependent-care responsibilities are more likely to affect a woman's career than men's, steering them away from a full-time practice, thereby reducing women's chances for promotion and positions of leadership [1,17,19].

Of the factors described, less is known about women's interest in leadership positions in academic medicine, and their perceptions of what those positions represent and require. Women's ambitions and their interest in leadership seems to be readily replaced by an apprehension of what success would entail [7,20]. This could be partly related to a lack of affirmation and to gender role expectations [21]. However, further exploration of women faculty's perceptions and personal motivation (or lack of) is needed.

TOWARD BETTER REPRESENTATION

It has been cautioned that we may achieve diversity, but we should strive to achieve inclusivity. This is reflected in the types of leadership roles entrusted to women in academic medicine, and to the value attributed to their contributions. The preliminary results of interviews conducted with women faculty at a single large, urban academic center are presented. Based on that research, women are more interested in seeking roles of influence, to effect change, regardless of the leadership position. Administrative tasks are perceived as an obstacle, preventing them from engaging in patient care. Not surprisingly, women want to have a voice, with or without a title. Interventions at the individual, organizational and societal levels are explored. These recommendations could serve as a road map to promote women's involvement in academic medicine and their attainment of meaningful and rewarding leadership positions.

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RCL-21
Biases in Education and Research and Their Impact on Patient Safety

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LEARNER OBJECTIVES

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

1. List the most common biases encountered in education, clinical practice, and scientific research;
2. Define the most common biases encountered in education, clinical practice, and scientific research;
3. Explain how the most common biases encountered in scientific research impact our interpretation of research studies and the quality of care; and
4. Identify their own biases and work to eliminate or reduce their impact on education and clinical practice.

A bias can be defined as an inclination or prejudice for or against one thing, person, or group compared with another, usually in a way considered to be unfair. A bias may be highly individualized and reflect learned behavior or a set of behaviors displayed by a particular individual (i.e. racism, sexism, etc.) Biases can also be systematic, reflecting inherent tendencies of institutions or processes (i.e. publication bias). Biases can have a significant negative impact on our ability to effectively teach and practice medicine, as well as our ability to interpret the scientific literature.

For example, implicit biases involve associations outside conscious awareness that lead to a negative evaluation of a person on the basis of irrelevant characteristics such as race, gender, weight, age, language, income and insurance status. In a 2017 systematic review, investigators found that healthcare professionals exhibited the same levels of implicit bias as the wider population.[1] The authors concluded that there was a strong need for the healthcare profession to address the role of implicit biases in disparities in healthcare. Indeed, the Joint Commission for Accreditation of Healthcare Organizations called for institutions to work to understand, assess and correct biases in healthcare.[2]

This presentation will attempt to review commonly encountered biases in education, research, and clinical care.

THE DUNNING-KRUGER EFFECT

The Dunning-Kruger Effect is a cognitive bias where people of low ability suffer from illusory superiority where they mistakenly assess their ability as greater than it actually is.[3] Individuals displaying this effect will:

- Fail to recognize their own lack of skill
- Fail to recognize the extent of their inadequacy
- Fail to accurately gauge skill in others
- Recognize and acknowledge their lack of skill only after being exposed to formal training in that skill

This cognitive bias was originally described in 1999 when it was observed that participants scoring in the bottom quartile on tests of humor, grammar, and logic grossly overestimated their test performance and ability. Although their test scores put them in the 12th percentile, they estimated themselves to be in the 62nd percentile.[3] It was also observed that more highly skilled individuals often underrate their own abilities, suffering from illusory inferiority.

Since the original description, the bias has been observed in many other fields, including medicine, where it can lead to bad decisions and patient complications. The Dunning-Kruger Effect may be a particular problem for residents and young faculty.[4] Learners with the least amount of knowledge or skill may paradoxically be more likely to evaluate themselves favorably compared with their peers. This phenomenon is particularly relevant in medicine where we rely on self-directed learning not only in many of our undergraduate and postgraduate programs, but in guiding the pursuit of continuing medical education. Residents are probably safest at the beginning of residency when they're scared and know that they don't know what's going on. When they progress through the second year, they begin to feel more comfortable yet may not be aware of all the things they still don't know. The same can be said of new faculty who have never been unsupervised (and completely responsible) before.

The Dunning-Kruger effect should not be mistaken for arrogance. Rather, the Dunning-Kruger effect simply suggests that people of low skill simply do not know how much they do not know.

PUBLICATION BIAS

Publication bias occurs when the outcome of an experiment or research study strongly influences the decision whether or not it is published. In science and medicine, publication is more likely to occur when the results of the study are positive (or show an effect) than when the results are negative (or do not show an effect). In medicine, a typical story would begin with the publication of a large, randomized trial that demonstrates efficacy for a new drug (or device, technique, etc.) Often, such a trial can be sponsored by someone who will directly benefit from the drug (or device). After publication of the large, positive trial, smaller studies that fail to demonstrate efficacy are not published because they are thought to be underpowered or not correctly designed. Selective reporting of clinical trial results may have adverse consequences for researchers, study participants, health care professionals, and patients.

For example, fluoxetine (Prozac®) is an antidepressant in the selective serotonin reuptake inhibitor (SSRI) class that was approved by the FDA in 1986 as a result of a large, randomized, controlled trial. Following the approval of fluoxetine, many other SSRIs were introduced into clinical practice. In 2008, a review of both published and unpublished clinical trials submitted to the FDA regarding the efficacy of SSRIs was published. This review noted that 94% of published trials demonstrated efficacy whereas only 51% of unpublished trials demonstrated efficacy.[5]

Although new drugs, devices, and techniques may be introduced less frequently in anesthesiology than they are in some other fields, publication bias can be observed in the anesthesiology literature. In 2012, De Oliveira and colleagues observed that publication bias was more likely to exist in higher impact factor journals. They reported that approximately 75% of studies published in journals with an impact factor higher than 9.1 had positive results whereas only half of studies published in journals with an impact factor higher than 9.1 were had positive reults.[6] In 2016, Hedin and colleagues noted that publication bias and nonreporting was found in the majority of systematic reviews and meta-analyses published in anesthesiology journals.[7]

SURVIVORSHIP BIAS

Survivorship bias is the error of concentrating on the people or things that made it past some kind of selection process and overlooking those that did not, typically because of their lack of visibility. Survivorship bias is a type of retrospective bias and can result in the false belief that correlation proves causality.

For example, as early as 1973 it was observed that patients who suffered a myocardial infarction (MI) frequently developed premature ventricular contractions (PVCs). Increased PVCs were associated with an increased risk of patient mortality.[8] Thus, physicians assumed that if survivors had fewer PVCs, then treating patients with an anti-arrhythmic that reduced the number of PVCs would certainly decrease mortality after an MI. Indeed, in a 1990 survey, 38% of cardiologists treated asymptomatic PVCs in patients with known coronary artery disease or a history of myocardial infarction. This practice continued until 1991 when a randomized, controlled trial of 1498 patients with PVCs after myocardial infarction demonstrated an increased likelihood of death in patients randomized to anti-arrhythmic therapy.[9]

HINDSIGHT BIAS

Hindsight bias is the tendency, after an event has occurred, to see the event as having been predictable, despite little or no objective basis for predicting it. It can also be known as the "knew-it-all-along" effect or "creeping determinism." In essence, people with knowledge of an outcome tend to exaggerate the extent to which an outcome could have been predicted. Hindsight bias was first reported in medicine in 1981. Investigators divided 75 physicians into 5 groups of 15. Physicians in the first group (the "foresight group") were presented a case history of a frequently encountered clinical problem and asked for the most likely of four clinical diagnoses. Physicians in groups 2-5 (the "hindsight groups") were each given the same clinical problem, but were given the diagnosis. They were then asked what their diagnosis would have been, had they seen the case prospectively. Physicians in the hindsight groups were more likely to select the diagnosis that they were given. The authors reported that implications of this hindsight bias for physicians are substantial: overconfident second opinions, overconfidence in diagnostic accuracy, and inadequate appreciation of the original difficulty of diagnoses.[10]

The implications of hindsight bias on medical malpractice is self-evident. Among physicians, radiologists and pathologists are probably most likely to be victims of hindsight bias in medical malpractice litigation. Practically speaking, if you know that the patient has cancer, seeing a small tumor on a mammogram or finding a single cancerous cell in peripheral smear is simply easier. The American College of Radiologists has taken steps to reduce the risk of hindsight bias in expert witnesses.[11] Hindsight bias is also relevant to anesthesiologists, who often make decisions quickly and in real time.[12]

FUNDAMENTAL ATTRIBUTION ERROR

Attribution theory states that we all attempt to explain behavior by attributing a cause to the behavior. We can explain a person's behavior as a result of either internal factors (personality, disposition) or external factors (environment, situation, etc.). Fundamental attribution error (or fundamental attribution bias) is our tendency to explain someone's behavior as a result of internal factors coupled with our tendency to explain our own behavior as a result of external factors. This particularly true when the behavior is seen as negative.

Although fundamental attribution error can be very difficult to study objectively,[13] fundamental attribution error has been well-studied in business, engineering, and education, but it is understudied in medicine and seemingly unknown to most physicians. For example, in morbidity and mortality reviews or medical malpractice cases, we have a tendency to attribute errors and unanticipated bad outcomes to shortcomings (internal factors) of other physicians as well as to explain errors and unanticipated bad outcomes in our own patients as being the result of extenuating circumstances (external factors). Medical education researchers and policy makers may be guilty of this error in their quest to understand clinical quality. Many authors have suggested that to truly improve clinical quality, we must examine situational factors, which often have a strong influence on the quality of clinical encounters.[14]

CONCLUSIONS

Biases are ubiquitous in medicine and can significantly impact our ability to provide optimal care and educate ourselves as well as our students. Only by identification and understanding can we assess and correct biases and work to improve patient safety and healthcare quality.

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RCL-22
The Trials and Tribulations of ERABS: Implementing ERAS in Bariatric Anesthesia!

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LEARNER OBJECTIVES

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

1) Evaluate the role of ERAS in improving patient safety and outcomes;
2) Appraise the evidence for ERABS–ERAS in Bariatric Anesthesia; and
3) Formulate an ERABS strategy for patients with Morbid Obesity.

The well-established principles of Enhanced Recovery after Surgery (ERAS) were developed to improve perioperative outcomes for patients undergoing a wide variety of elective surgical procedures. The implementation of ERAS in patients with morbid obesity scheduled to undergo weight loss (bariatric) surgery may not yet be consistently practiced and/or widely implemented. This article will revisit the ERAS paradigm and review its implementation in Enhanced Recovery after Bariatric Surgery (ERABS). Future strategies to implement ERAS in patients with morbid obesity undergoing elective surgical procedures will be discussed.

THE ROLE AND SCOPE OF ERAS

The concept of Enhanced Recovery after Surgery (ERAS) was introduced in the 1990's with the primary goal of reducing the length of stay (LOS) in hospital after elective colorectal surgery[1]. The main purpose of ERAS is a multi-disciplinary approach to reduce patient's physiological and psychological stress associated with surgery[2]. The 'elements' of ERAS are interventions that were developed and modified by meticulous research to improve perioperative outcomes [3]. These were then integrated into ERAS pathways and has evolved to include improving patient's functional capacity before surgery. Another aspect of successful ERAS implementation is the reduced patient to patient variability with regards to LOS. Moreover, patients enrolled in ERAS pathways are not only discharged earlier than conventional programs; they do so without increases in readmission rates or emergency room (ER) visits. Overall, the implementation of ERAS benefits both patients and health care systems, with improved resource utilization and cost savings.

As ERAS protocols continue to evolve, it cannot be overemphasized that these interventions need to be implemented together in 'bundles' and the compliance within the pathway needs to be continuously audited. The research supporting ERAS implementation has also moved towards measuring more 'patient-centric' outcomes[4]. For example, for perioperative analgesic interventions, researchers are seeking and reporting outcomes beyond pain scores and analgesic consumption. Early resumption of normal diet and activity with validated quality of recovery and satisfaction scores, amongst others, are the newer benchmarks of ERAS programs [5]. More recently, attention in ERAS has shifted to the preoperative period and patient education is becoming more standardized with potential to r reduce perioperative morbidity and further shorten the recovery period[6]. These 'prehabilitation' strategies are aimed at physically and mentally preparing the patient for their surgery and encouraging them to become 'active' participants in the ERAS pathway[7].

From an organizational perspective, ERAS implementation has directly challenged the traditional 'working in silos' approach to perioperative medicine. Now within ERAS programs, various specialties (notably surgery, anesthesia, nursing, physiotherapy and pharmacy etc.) are working together as teams to further improve patient safety and outcomes. On a larger scale, there have been standardized evidence-based ERAS protocols that have also been adopted at different organizational levels and endorsed by regional, national and international societies (www.postoppain.org). This in turn has led to sharing of protocols and centralized data collection with focus on improving compliance with ERAS implementation (www.erassociety.org/guidelines). Finally, ERAS has spread well beyond colorectal surgery. Over the past three decades, gradually some of the other surgical specialties have attempted to adopt and implement ERAS-like standardized evidence-based protocols, but with variable success. Elective weight loss (bariatric) surgery may be one of the 'newer' additions to the ERAS family, with the introduction of Enhanced Recovery after Bariatric Surgery (ERABS).

CHALLENGES OF IMPLEMENTING ERABS

Over the last decade, weight loss (bariatric) surgery has become a well-accepted and widely available treatment option for patients with morbid obesity. Conservatively estimated annually at over half a million patients, ever increasing bariatric surgery procedures are being performed worldwide. Even at a local or regional level, in many centers (including at this author's), bariatric surgery is more frequently performed than elective colorectal surgery. An important link between ERAS in colorectal and bariatric surgery is somewhat 'historic': many bariatric surgeons (and anesthesiologists) come with a current or previous experience and interest in laparoscopic and minimally invasive surgery. But do these facts, the sheer volume of bariatric surgery and its close relationship to colorectal surgery, make implementing ERABS (ERAS in bariatrics) a foregone conclusion?

The colorectal ERAS experience outlined in the previous section, has had an almost two-decade head-start over bariatrics. This lag may not be adequate to explain the fact that ERABS pathways are not well established and/or less consistently implemented. Early

ERABS studies report the use of protocols that were extrapolated from colorectal studies with a focus on reduced LOS as the primary outcome [8]. These investigators noted both a reluctance of patients and lack of enthusiasm amongst staff, as barriers to implementation of ERABS. Interestingly, they also noted inadequate pain control, nausea and poor oral intake as the major reasons for the visits to ER after discharge. This early experience with ERABS drew attention to the intraoperative anesthetic management during bariatric surgery. Studies reporting the implementation of opioid-sparing multimodal analgesia followed and these demonstrated a significant reduction in both pain scores and rescue analgesic consumption[9, 10]. Further improvements with reduction in postoperative nausea and vomiting were achieved by implementing ERABS protocols that included both opioid free analgesia and intravenous anesthesia [11]. These studies have also established a role for the routine use of non-opioid parenteral analgesics (dexmedetomidine, lidocaine and ketamine) in ERABS anesthesia [12]. Postoperative pain management in ERABS also requires careful and pragmatic application of acute pain pharmacology in patients with morbid obesity [13]. The use of regional anesthesia techniques in bariatric surgery is the subject of ongoing and future research [14]. It is possible that all these interventions may become important to achieving more consistent early oral intake, ambulation and patient discharge with fewer side-effects and better patient satisfaction.

To date, two systematic reviews and meta-analyses of clinical trials in bariatric surgery have been published- they confirm that compared to conventional treatment plans, patients in ERABS pathways have reduced LOS [15, 16]. But as the colorectal experience has suggested, using LOS alone as surrogate for ERAS is woefully inadequate. Future ERABS studies will have to assess patients with objectively measured global recovery and satisfaction scores and reassess their return to preoperative functional status beyond the immediate postoperative period.

One of the emerging challenges with designing research in this field is that if ERABS is considered as 'the standard of care', prospective trials comparing conventional management may not be clinically or ethically justified. Therefore, future research will have to implement all elements of ERABS pathways and compare outcomes to those available from historic pre-ERABS controls. Alternatively, RCTs will have to recruit patients to standardized ERABS pathways and randomize patients in the study arm to a single element or intervention. It is likely that these clinical trials, where all patients irrespective of randomization benefit from the rest of the ERABS pathways, will not be able to demonstrate any additional benefit or improved outcomes for the intervention in the study arm. This ERAS research conundrum is explained eloquently by the 'aggregation of marginal gains theory', where an existing superior performance of an entire bundle cannot be significantly improved any further by any single intervention [17]. Nevertheless, future research is needed, and negative trials will be welcome; these will contribute immensely not only to further refinement of existing ERABS pathways. Directly or indirectly, these studies may also indirectly improve the dissemination of ERABS?

The ERAS Society has published guidelines for bariatric surgery [18]. They have commented on the lack of evidence for many elements and identified the extrapolation of these from other surgical models. It must be appreciated that patients with morbid obesity undergoing bariatric surgery have co-morbidity burden that may preclude direct application of some of the classical ERAS elements. For example, in ERABS, there may be hesitancy to reduce the period of fasting with the provision of liberal preoperative carbohydrate drinks due to the increased incidence of gastro-esophageal reflux disease and diabetes mellitus respectively. While the use of systemic steroids for pain and PONV have also gained popularity in other ERAS pathways, predictably this may also be met with some resistance in ERABS pathways. Conversely, certain other ERAS elements have been pragmatically implemented in the now almost exclusively laparoscopically performed bariatric surgery- avoiding bowel preparation, surgical drains and indwelling catheters. A simple yet comprehensive outline of ERABS principles is required.

One of the major limitations with implementing ERAS in bariatrics is the prevalence of obstructive sleep apnea (OSA) in this patient population. If left undetected and/or untreated, in patients with morbid obesity, OSA is a well-established cause for postoperative respiratory adverse events and delayed discharge [19]. The presence of OSA is therefore often an indication for extended monitoring and will impact other aspects of postoperative care in patients after bariatric surgery [20]. Many centers (including this author's) have implemented rigorous screening and testing for OSA. Elective bariatric surgery is scheduled only after patients are compliant and comfortable with their prescribed CPAP or BiPAP therapy. These are important strategies to not only mitigate the perioperative risks of OSA, it may additionally allow for patients with OSA to also benefit from ERABS pathway implementation and ensure safe early discharge.

FUTURE OF ERABS: EDUCATE, ENGAGE AND EMPOWER THE PATIENT

The ERABS paradigm needs to continue to evolve with research and standardized implementation of evidence-based processes for patients undergoing bariatric surgery. Individual centers need to use protocols and implement these consistently. At a national and international level, these protocols should be shared, and centralized data collection could facilitate comparison. The vast expertise and wide experience, especially in high volumes centers, needs to be converted in good quality evidence. International collaborative efforts need to be encouraged and society level consensus guidelines should be prepared, presented and published. As in ERAS, implementation at this scale should aim to improve clinical outcomes and reduce cost, making ERABS an important example of value-based care applied to elective surgery [21].

But in implementing ERABS, we shouldn't lose focus of the patient and the goal of improving the individuals perioperative experience. One of the strategies to increase the participation of patients in their own ERABS care is to standardize the preoperative education.

Now with the integration of innovative healthcare technology (web-based patient-care mobile apps) into ERABS, patients can be better educated and actively engaged in the entire process. Using prehabilitation models, patients can improve their physical and mental health before surgery. And by measuring their own functional capacity with simple tools like the validated 6-minute walk test and peak expiratory flow rate, they can be empowered to achieve better and clinically relevant outcomes. Additionally, these outcomes can be self measured, reported and monitored using the same web-based apps. Once validated, healthcare providers will be able to collect, analyze and compare the pre and postoperative recovery outcome data more efficiently. Cleary, the future of ERABS should not just rely on only advancing the clinical science, but better integration and implementation of what we already know. ERABS will undoubtedly contribute to the improved the perioperative care of all patients with morbid obesity.

In conclusion, perioperative physicians caring for patients with morbid obesity undergoing elective surgical procedures should focus on better understanding of the pre- surgical preparation, perioperative care and postoperative recovery processes. ERABS teams should aim to implement evidence-based strategies that maximize homeostasis and minimize surgical stress. With all these efforts, patients with morbid obesity should be able to leave the hospitals and return to their normal level of activity and function, not only earlier, but possibly in better health.

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RCL-23
Update on Healthcare Reform: The Impact of MACRA on the Practice of Anesthesia

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LEARNER OBJECTIVES

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

1. Review recent changes in Medicare Access and Chip Reauthorization Act (MACRA);
2. Discuss the impact of advanced Alternate Payment Modal (APM)s and the Merit-Based Incentive Payment System (MIPS); and
2. Discuss strategies to develop a sustainable anesthesia practice.

In 2015, Congress passed the Medicare Access and CHIP Reauthorization Act (MACRA). MACRA had many goals, but its key driver was to "fix" the Sustainable Growth Rate (SGR). The SGR formula was legislation established in the Balance Budget Act of 1997 and utilized by Centers for Medicare and Medicaid Services (CMS) to control Medicare spending for physician and other health care providers' services. The SGR formula was developed to limit Medicare Physician spending based on the GDP growth.[1-2]

MACRA replaced the SGR creating two payment tracks under the Quality Payment Program (QPP).$_2$The goals of the QPP are to promote quality, cost-effective and value-based care, encompassing provider accountability and patient care coordination.[3] MACRA places providers in one of two tracks: the advanced Alternative Payment Model (APM) or The Merit-Based Incentive Payment System (MIPS). Advanced APMs description and qualification criteria have been detailed by CMS.[3] An essential condition for an advanced Alternative Payment Model is that it requires health care entities to accept two-sided financial risk (upside and downside). In order to be a CMS approved advance APM, see Table 1 for what is required.
Most alternative payment models (APM) are not qualified to be advance alternative payment models (APM) because they only have one-sided risk with no downside risk. In other words, when a provider's Medicare spending per beneficiary (MSPB) is lower than the average targeted expenditure benchmark (MSPB), the provider receives some portion of the savings while Medicare receives the remainder of the saving. Providers who are in one-sided risk APMs or ACOs share in saving only and not in losses. In contrast, in the two-sided risk APM, when a provider's MSPB is high and it exceeds the average MSPB targeted benchmark, this will result in losses to the Medicare program as well as to the provider. Worth mentioning, in the two-sided risk APMs providers share in a greater proportion of the savings then the one-sided risk APM providers. Hence this shared loss is referred to as risk bearing. In summary, risk-bearing APMs are CMS qualified as advanced APMs.

Risk adjustment is an essential requirement in order to predict how patients with comorbid conditions contribute to the overall spending, MSPB or savings. QPP performance results can be impacted by comorbid conditions, social economic status, reporting and coding. It is necessary to define risk factors as well as predict individual or group provider cost analysis. If you know the risk profiles of patients and quality performance of providers in their respective communities you can develop programs to optimize care, improve outcomes and design reliable and realistic "episodes of care "innovations. For example, an anesthesiologist who cares for a patient who has been discharged from the hospital for routine laparoscopic cholecystectomy and is readmitted two days after discharge. The anesthesiologist may be unaware of the re-admission, not realizing its significance in terms of quality and performance measures. On the other hand if an anesthesiologist was a participant in a "laparoscopic cholecystectomy episode of care bundle, the significance of that admission takes on a new dimension and relevancy.

Data collection and data analysis should provide real-time accurate patient information that allows clinicians to have a continuous clinical feedback and make mid-stream improvements. Prompt data analysis for quality and cost allows physicians/administrators to negotiate for patients' payment for new models of care based on accurate transparent and realistic cost projection given the patient risk factors and co-morbid conditions. Lastly, how the population of patients is attributed to providers for both cost and quality needs to be accurate and reliable. Attribution can be prospective or retrospective. In prospective attribution patients are assigned in advance, whereas in retrospective attribution patients are assigned after they have been seen by a provider.

Table 1

CMS requirements for Advance APM Qualification
1. Clinicians must use **certified electronic health record** technology
2. The APM pays for covered services "based on **quality measures** comparable to those used in the quality performance category of the **MIPS"**
3. "Either be a *Medical Home Model* expanded under CMMI Center authority; or (2) require participating APM Entities to *bear* more than a nominal amount of **financial risk** for monetary losses"

www.cms.gov 2018

The providers who are participants in the advanced APM track qualify because they have at least 20% of their Medicare patients or 25% of Medicare revenues in an Advance APMs. Large groups, small groups and individual practitioners may seek to join, merge or be acquired by other entities in order to become an advanced APM. The incentive for this includes an immediate 5% payment bonus beginning 2019. Currently less than 20% of all clinicians (Physicians, APRN, PA, Therapist, Podiatrist, and others) participate in advanced APM and between 15-20 % of physicians are in advanced APM. Interestingly enough, a significant percentage of clinicians are exempt from MIPS. (See Table 2 below).

Table 2

Clinicians required to participate in MIPS and exempt from MIPS

	2017	2018
Total number of Part B billing clinicians	**1,380,000**	**1,548,000**
Exempt (low-volume)	**384,000** (Less than $30,000 in Medicare payments per year or fewer than 100 patients)	**540,000** (Less than $90,000 in Medicare payments per year or fewer than 200 patients)
Exempt (A-APM qualifying participants)	Between **70,000-120,000**	Between **185,000-250,000****
Exempt (other reasons)	**285,000**	**315,000**
Required to participate in MIPS	Between **600,000-640,000**	Between **445,000-510,000****

Medpac 2017 Report to Congress
Medicare Advantage beneficiaries which represent just over 31% of all beneficiaries are not considered participants in an advanced APM

Merit-based Incentive Payment System (MIPS)

In 2018, slightly over 500,000 physicians and other clinicians are estimated to participate in MIPS, out of a total of 1.55 million of all Part B billing clinicians. According to the AMA and Medicare, the demographics of physician billing Medicare (under the Physician Fee Schedule) for beneficiaries in 2016 was 589,000 physicians. The remainder of the other health professions (APRN, PA, Therapist and other) billing Medicare was approximately 363,000.[5] The MIPS Quality Payment Program (QPP) is designed to tie payment adjustment to a Quality Performance Score. Quality Performance is based on 6 or more self-selected measures. The final 2018 QPP score components are the following:

CMS 2018 [2-3]

1. Quality (60%)
2. Care Improvement (25%)
3. Advancing information (15%)
4. Cost (10%), (starting in 2018)

The QPP performance measures have two threshold levels, first for avoiding penalty and second in order to receive high performance bonuses. Regulatory performance thresholds. Appendix 3

MIPS program commences with the potential of earning incentive bonuses or penalties of +-4 % in 2019 and progressively increasing or decreasing annually thereafter.

Table 1. Statutory payment updates and incentive payments for physicians and health professionals.

		Jan-June 2015	July-Dec 2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026 and later
A–APM clinicians	Update	0%	0.5%	0.5%	0.5%	0.5%	0.5%	0%	0%	0%	0%	0%	0%	0.75%
	APM bonus						5%	5%	5%	5%	5%	5%		
Other clinicians	Update	0%	0.5%	0.5%	0.5%	0.5%	0.5%	0%	0%	0%	0%	0%	0%	0.25%
	Potential MIPS adjust-ments						0% (-4% to +4%)	0% (-5% to +5%)	0% (-7% to +7%)	0% (-9% to +9%)	0% (-9% to +9%)	0% (-9% to +9%)	0% (-9% to +9%)	0% (-9% to +9%)

Medpac Report to Congress 2017[5]

Anesthesiologist and other specialist are in a unique position to lead, because, many practices have 24 hours in-house coverage and can tailor the hospital systems and EMR to deliver comprehensive quality metrics and cost related feedback. Anesthesiologists have leadership opportunities which impact decision-making in health care systems. This allows hospital based physicians to obtain transparent data and achieve interoperability with healthcare systems. Several models exist for hospital based physician. Anesthesiologists can work as an independent contractors billing directly for services, or they may work under contract as a private group. In addition, physicians can work in a closed system, hospital-employed under various built-in contract incentives for productivity and quality. Large provider groups, especially multi-specialty practices are very attractive for acquisition by hospital systems. Health expenditures have increased in areas where there are increasing mergers and acquisitions of physicians' practices. Small and medium size practices often do not have the infrastructure to collect, analyze and report the data to meets MIPS requirement. There are independent consultant groups that will help physicians navigate the requirements of MIPS QPP. In addition, CMS has provided grant support to assist practices.

A method for specialist to succeed is by understanding how *disruptive innovation* can lead to accomplishing the goals of health care reform, namely, *better patient experience, improved quality and less cost* (Triple Aim IHI). *Disruptive Innovation* is defined as "Innovations that make products and services more accessible and affordable, thereby making them available to a larger population."[16] Specialists can no longer function under MACRA with the same practice pattern as in the traditional "Fee for Service" (FFS) world. Anesthesiologists have actively developed ERAS and Perioperative Surgical Home (PSH). These are examples of transition steps toward bundled payment. The difference is that with ERAS and PSH there is limited participation with fewer providers and most don't bear financial risk.

A *bundle payment*, also commonly referred to as *episode of care payment* or *global payment*, can be defined as a single payment which pays for all or most the individual services for a defined "Episode of Care". Anesthesiologist have been involved in a type of bundle payment structure when they engage in Plastic Surgery combined pricing services in which the Anesthesiologist receive a fixed payment regardless of units of time or procedure complications or resource utilization. Innovations such as the joint replacement bundle (Comprehensive Care for Joint Replacement (CJR)) initiative provide opportunities for surgeons and anesthesiologists to lead in designing high value programs.[8] The CJR is an excellent example of innovation that has resulted in improved quality and decreased cost. CJR initiative demonstrated that, between 2008- and June 2015, there was a 20% reduction in Medicare expenditures as episode expenditures decreased from $26 785 to $21 208 ($P<.001$) for 3738 episodes of joint replacement).[8] This was accompanied by decreased length of stay, readmissions and emergency department visits. Cost reductions in overall hospital savings were 51.2 %(29% of which came from Implants), and there was a 48.8% reduction in Post-Acute Care (PAC).[8] Examples of other Episode of Care Bundles are listed in the Appendix 2

Why are bundle payments good for anesthesiology specifically? Firstly, episode-of-care bundled payments allow anesthesiologists to design specific treatment objectives with patient-centered efficient care. It also offers greater control over cost effective intervention, eliminating low-value care: Secondly, there is the advantage of price transparency for patients and this allows patients to share in decision making regarding their care and out-of-pocket (OOP) costs:. Thirdly, bundled payments can be designed to provide physicians with the greatest versatility to implement creative programing that utilizes the most cost efficient means for a given community and patient demographic (Table 7)

Table 7

Five ways to make bundled payments work for both specialists and patients
• 1. Make bundled payment packages as inclusive as possible of services
• 2. Ensure that quality measurement and improvement is a key component
• 3. It is essential to have feedback to the primary care physicians for continuity of care Look for opportunities form bundled payments
• 4. Preserve patients shared informed decision-making
• 5. Include risk adjustment with data analysis findings

In 2018, an anesthesiologist can remain in traditional Medicare fee-for-service, join an advance APM, and/or be a salaried employee in a health care system or large multi-specialty group. Other options include the opportunity to create a Virtual Group. While the requirements to become an advance APM have been reviewed along with the necessary reporting requirements for MIPS, the reality of the magnitude and distribution of the incentive bonuses and penalties have not been clearly elucidated. The Anesthesiologist Group Practice Check list will enhance Anesthesiologists ability to navigate the changing landscape. A MIPS checklist for Anesthesiologists who engage in innovative leadership in the MIPS Program will allow independent and hospital employed physicians to stay focused and change the trajectory for their practice management.

CMS has defined Virtual Groups as an option for physicians to qualify for MIPS. A Virtual Group have been defined " *as a combination of two or more Tax Identification Numbers (TINs) assigned to one or more solo practitioners, or to one or more groups consisting of 10 or fewer clinicians (including at least 1 MIPS eligible clinician), or both, that elect to form a virtual group for a performance period for a year. A Virtual Group is considered to be an entire single TIN that elects to participate in MIPS as part of a virtual group. The participation is based on tax ID numbers and NPI numbers.*"[8] Performance results are pooled across groups participating within one virtual group. Nothing is changed regarding QPP performance benchmarks or requirements for exemption. There is a CMS Virtual Group election process which has a deadline prior to the year of participation.

Virtual Groups can be formed with different geographic regions and different specialties. Participants in a Virtual Group must meet the low volume threshold and are not participating in advance APMs.[9]

Some potential problems encountered with virtual groups include heterogeneous groups in which one participant scores very low in one category dragging down the other provider performance in that category.[8] The development of virtual groups in some environments may encourages selection and widening health care disparities that may exist with sicker patient populations. It is possible that joining a Virtual Group can be profitable. However, if not well researched, penalties can be enormous as well. So this is a CMS option that has been established for providers who would like to participate in MIPS who desire shared responsibility, flexibility in alignment with other provider and optimizing resource efficiency.[11] When does an anesthesiologist decide to form a Virtual Group or join a Virtual Group or an Advance APM or do nothing?

Part of this decision making is determined by examining the check list (see below) and understanding the specific practice environment. For example, it would be innovative to develop regional pain entities that could be multidisciplinary and have geographic dominance, allowing centers of excellence to perfect quality and reduce expenditures in an entire region. Although this discussion is centered on MACRA this type of innovation would impact the commercial environment as well. Anesthesiologist leadership is valuable in physician led APM and advanced APM.

Anesthesiologist Group Practice Checklist
❑ Optimize Care –Quality Monitor Program
❑ Data Collection and Analysis
❑ Reporting-System reporting vs Qualified Clinical Data Registry (QCDR)
❑ Feedback-Strategic Intervention-Clinical and Financial
❑ Innovations-Disruptive Innovation Value Proposition
❑ Patients- Case Mix and Risk Analysis
❑ Providers-Designing Culture (Specialties specific High Value services that contribute to Population Health)
❑ System-Analysis of Health System, Consolidation and divestiture
❑ Health Care Reform/Political Environment Assessment Analysis
❑ Community and Population Evaluation
❑ Marketing

RECENT UPDATE MACRA MIPS

Medicare Payment Advisory Commission (MEDPAC) recommended getting rid of MIPS in its January 2018 meeting and replacing it with the Voluntary Value Program. The rationale behind this recommendation was that reporting the performance measures was burdensome and costly for physicians, the initial payment adjustments would be too small to influence outcome and "*scores are not comparable among clinicians because each clinician will get a composite MIPS score reflecting a mix of different, self-chosen, measures.*"[2] The proposal aims at getting rid of MIPS reporting and using claims data focusing on population measures to evaluate **ALL** physicians, specialist and primary care included. The proposed Population Health measures include mortality, patient experience (surveys), readmission rates, emergency room visit and healthy days at home. These Population Health Measures would be aggregated in a defined geographic region. The Population Health measures would be implemented for Virtual Groups as well as other FFS providers. In the Medpac proposal, the providers not participating in advance APMs would have the choice of;

a. Joining an advanced APM, or

b. Joining a Virtual Group or

c. Remain in Medicare traditional "fee for service".

For the latter, (those choosing to remain in FFS), MEDPAC discussed recommending a reduction in the Physician Fee Schedule of 2% annually. The payment incentives in the former would be determined by regional Population Health measures. Many physician practices have little impact on improvement of regional Population Health Measures such as hospital readmission rates, mortality and emergency room visits.

In summary there are gargantuan changes in the Medicare quality payment system in the near future. Anesthesiologist are positioned to assume leadership in the development of Bundle initiatives, create innovated clinical pathways, and comprehensive value-driven care. Most importantly, Anesthesiologists need the infrastructure required to produce a robust data base with ongoing data analysis that direct quality initiatives development, creating a radical transparent environment with finger-on the-pulse feedback. The culture of practicing anesthesia is a multiple level paradigm and as with other specialties, it demands close collaboration with every service that intersect with patients' quality and cost.

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Appendix 1

Examples of advance APM's at the 2018 are the following:
1. Bundled Payments for Care Improvement Advanced Model (BPCI Advanced)[6]
2. Comprehensive Care for Joint Replacement (CJR) Payment Model (Track 1 - CEH-RT)
3. Comprehensive ESRD Care (CEC) Model (LDO arrangement)
4. Comprehensive ESRD Care (CEC) Model (Non-LDO arrangement Two-sided Risk Arrangement)
5. Comprehensive Primary Care Plus (CPC+) Model
6. Medicare Accountable Care Organization (ACO) Track 1+ Model
7. Medicare Shared Savings Program Accountable Care Organizations —Track 2
8. Medicare Shared Savings Program Accountable Care Organizations —Track 3
9. Next Generation ACO Model
10. Oncology Care Model (OCM) (two-sided Risk Arrangement)

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Appendix 2

Episode of Care Bundles	
Acute MI	Chest Pain
Amputation	CABG
Atherosclerosis	Diabetes
Back and Spine except fusion	Esophagitis, gastroenteritis
Cardiac Arrhythmia	GI Hemorrhage
Cardiac Defibrillator	GI Obstruction
Cardiac Valve	Pacer
Cellulitis	Pacer Device Replacement
Cervical spine fusion	Percutaneous
COPD	Stroke
CHF	Removal of Orthopedics Devices
Combined Anterior and Posterior Cervical Fusion	Renal Failure
Fractures	Transient Ischemic Attacks
Joint Replacement	Sepsis

Appendix 3

	2017	2018
Regulatory performance thresholds (points out of 100)		
MIPS performance threshold	3 points	15 points
MIPS exceptional performance threshold	70 points	70 points
Estimated impact for MIPS clinicians		
Share receiving a negative adjustment	5%	3%
Share receiving a neutral or positive adjustment	95%	97%
Share receiving MIPS exceptional performance bonus	N/A	74%

Medpac Report to Congress March 2018

RCL-24
SPA: Perioperative Pain Management in Children with Sleep-Disordered Breathing: A Difficult Balancing Act

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LEARNER OBJECTIVES

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

1) Review the epidemiology of OSA and pain symptoms;
2) Discuss the pathophysiology of OSA and acute pain states;
3 Discuss the mechanisms underlying opioid-induced respiratory depression;
4) Formulate a unifying hypothesis for pain-related behavior, hypoxia and opioid side effects;
5) Choose analgesic options for OSA patients; and
6) Discuss the importance of preoperative screening for OSA as a risk factor for PACU pain requiring intervention.

About 6 million children undergo surgery every year in the United States. Unfortunately, postoperative pain remains a major cause of morbidity after these procedures with an estimated incidence as high as 80%, particularly following otolaryngology procedures. Obstructive sleep-disordered breathing (oSDB) is increasingly prevalent in the general population with a consequent increase of its component symptomatology among children undergoing surgery and anesthesia. It is a clinical diagnosis characterized by obstructive abnormalities of respiratory pattern; or the adequacy of oxygenation/ventilation during sleep, and include snoring, mouth breathing, and breaks in breathing. oSDB encompasses a spectrum of obstructive disorders of the upper respiratory tree that increases in severity from primary snoring to obstructive sleep apnea (OSA). Daytime symptoms associated with oSDB may include inattention, poor concentration, hyperactivity or excessive sleepiness.
The most frequent surgical procedure for which oSDB is a prominent feature is adeno-tonsillectomy (T&A), which is among the commonest ambulatory surgical procedures performed in children. T&A is also often associated with moderate to severe postoperative pain with almost 20-60% of patients having documented moderate to severe pain upon recovering from anesthesia in the PACU.

Opioids have long been the cornerstone of perioperative pain therapy, but their use is often associated with significant side effects. Indeed, use of opioids for treating acute and chronic pain has increased dramatically in the last two decades. One of the enduring dilemmas in the care of ambulatory pediatric surgical patients is the high prevalence of obstructive sleep disordered breathing (SDB) which is known to be associated with increased rates of opioid-induced respiratory depression.

Compounding this therapeutic dilemma is the observation that obstructive SDB may be associated with enhanced nociception because of chronic systemic inflammation. Thus, on the one hand these patients may have overall heightened pain sensitivity while on the other they have hypoxia-induced amplified sensitivity to the respiratory depressant effects of opioids. This has resulted in a pervasive culture of opiophobia in the care of children with SDB. To this end, practitioners often withhold or administer lower intraoperative doses of opioids out of concern for delayed recovery from general anesthesia and opioid-related respiratory depression. An unintended consequence of this practice is that patients undergoing painful surgical procedures are at increased risk of postoperative pain requiring treatment upon recovery from anesthesia in the post-anesthesia care unit (PACU).

This review course lecture will comprehensively examine three clinically-relevant questions:

- Is SDB associated with enhanced nociception?
- Does SDB matter in non-ENT surgical procedures?
- Is respiratory sensitivity the same as analgesic sensitivity? Stated another way, is it sound clinical practice to give small intraoperative dose of opioids to children with SDB? Does this practice inadvertently increase the likelihood PACU analgesic intervention?
- Is personalized analgesia a feasible goal?

Final perspectives

The findings of the present report have several implications for research and perioperative care of children particularly regarding measures designed to ameliorate postoperative pain among children with SDB. First, there appears to be compelling evidence that when describing early postoperative pain in children, SDB should be considered. Future studies may examine genetic and pharmacologic differences between children with or without SDB symptoms to assess differences in the perioperative handling of opioids and other analgesics between children with and without SDB symptoms.

Lastly, pediatric postoperative pain is a complex process that may be determined by clinical phenotypes (such as SDB), systemic inflammation and other as yet undetermined variables. Practitioners need to be aware of the possibility of SDB in children undergoing surgical procedures and the fact that in addition to its association with increased acute respiratory complications, SDB may be an important predictor of early postoperative pain and need for PACU analgesia.

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RCL-25
SASM: Postoperative Respiratory Depression: Who? When? How? Knowledge that Anesthesiologists Should Have

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LEARNer OBJECTIVES

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

1. Evaluate the risk factors of postoperative respiratory depression;
2. Assess the timing of postoperative respiratory depression;
3. Appraise the case reports of death or near-death reports of respiratory depression;
4. Evaluate whether postoperative oxygen therapy is friend or foe; and
5. Examine the evidence of support for oximetry and/or capnography.

Opioid-induced postoperative respiratory depression (OIRD) is a serious complication that can lead to permanent morbidity and mortality. Though the incidence of critical OIRD, as assessed by respiratory depression/arrest requiring naloxone reversal, is approximately 1 per 1,000 anesthetics, the rate of prolonged postoperative hypoxemia appears to be very common affecting up to 20% of hospitalized postsurgical patients. Traditional methods of postoperative monitoring, such as intermittent vital sign checks, appear ineffective in detecting cases of OIRD, leading to tragic "Dead in Bed" events, which have occurred even shortly after reassuring nursing assessments. One reason is that vital sign checks can awaken somnolent patients and increase oxygen levels, masking pending potentially lethal OIRD. Improved strategies for postoperative monitoring for OIRD are being developed including continuous pulse oximetry with telemetry, bedside capnography, and impedance plethysmography. However many questions regarding optimal monitoring to detect OIRD exist. For example, application of supplemental oxygen delays the onset of hypoxemia secondary to hypoventilation which can potentially result in dangerous levels of hypercarbia. The optimal duration of monitoring for OIRD is also not known. Sleep architecture is disturbed for several postoperative nights; however, it appears that the majority of cases of OIRD occur within the first 12 postoperative hours, the exception being special circumstances associated with OIRD following administration of epidural and intrathecal opioid analgesics.

There has been increased understanding of patient and procedural factors associated with OIRD. The best appreciated patient risk factor is obstructive sleep apnea (OSA). Opioids and other sedating medications can worsen the upper airway obstruction in OSA during sleep as well as blunt increased respiratory drive in response to raising levels of arterial carbon dioxide. Different phenotypes of OSA are being described, and different presentations may incur varying degrees of risk. Patients with OSA are frequently not diagnosed and appear to be even higher risk for OIRD. All surgical patients without a prior assessment for OSA should be screened (e.g. with an assessment tool such as STOP-BANG) preoperatively and have their perioperative management tailored accordingly. Other important comorbid conditions with associations with OIRD include cardiovascular diseases, neurologic disorders, and frailty. Chronic use of opioids and benzodiazepines may be associated with increased risk. Recent evidence suggests that chronic use of gabapentin and pregabalin are associated with a six-fold increased risk for postoperative OIRD. Several important perioperative factors have been identified to increase risk of OIRD during anesthesia recovery. These include use of longer acting anesthetic agents (e.g., isoflurane), benzodiazepines, and higher doses of opioids. Interestingly, preoperative gabapentin, used as a non-opioid analgesic, is also associated with increased risk of OIRD during anesthesia recovery. OIRD during anesthesia recovery is noteworthy, as afflicted patients have a five-fold increased risk for critical OIRD events on postoperative wards. Following anesthesia recovery, patients who develop OIRD often are administered higher doses of opioids and other sedating medications.

Emerging evidence is providing clinicians with better understanding of this important postoperative complication and driving evidence based guidelines from the ASA and SASM. Recognition of the important association between OSA and OIRD has led to recommendations that all surgical patients are queried about a history of OSA and if negative undergo a preoperative assessment. Awareness of other aspects of OIRD and other risk factors will be critical in developing other management strategies.

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RCL-26
Advanced Teaching Skills for the OR: How to Teach Effectively when Faced with High Clinical Workload and Lack of Time

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LEARNER OBJECTIVES

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

(1) Describe the current and relevant teaching theories, including the adult learning theory and the Dreyfus model;

(2) Explain the development of clinical decision-making by residents;

(3) Identify potential obstacles to teaching in the fast-paced, high-pressure environment of the OR; and

(4) Describe simple approaches to optimize the curriculum, as well as effective techniques to improve teaching without compromising quality of care.

Teaching in the fast-paced, high-pressure environment of the operating room (OR) can be very demanding. High clinical workload and lack of protected time represent major obstacles to education and are unlikely to change in the near future;[1-7] thus, the educator-anesthesiologist must learn teaching strategies that are effective and time-efficient. The goal of this review is to provide an overview of the relevant teaching theories, highlight potential teaching obstacles, and provide effective techniques to improve teaching without compromising quality of care.[8]

I. CURRENT AND RELEVANT EDUCATIONAL MODELS

Multiple educational models have been described. The two outlined below are particularly relevant to the educator-anesthesiologist:[1, 2, 9-13]

Adult Learning Theory (ALT)[14] promotes self-direction in learning.[14, 15] The central idea of the ALT is that as the person matures, they develop a drive and desire to learn as well as assimilate responsibility for their own training. Therefore, the energy and motivation comes from the trainee. Consequently, the educator should:

- Promote *independent learning*. Example: Provide educational materials and encouragement to read independently.
- Focus on knowledge with practical relevance. Example: Concentrate on topics relevant to *current patient care*, thereby demonstrating the *practicality of such knowledge*.
- Promote a respectful learning environment and treat the learner as a colleague. Example: Solicit learner opinions when appropriate.

Dreyfus and Dreyfus model

The Dreyfus and Dreyfus model describes the progression from a novice learner to master across sequential stages of increasing complexity: Novice, Advanced Beginner, Competent, Proficient, Expert, and Master.[5, 16] The tenets that drive this process are: familiarity with recurrent clinical presentations, prioritization, and development of fast, intuitive, pattern-recognition approach to clinical situations.[2, 5, 6, 9, 10, 16] The *novices* approach a skill with a primarily rule-based and context-free mindset. Exposure to clinical work facilitates (Table 1):[5, 6, 16]

1. Recognition that many clinical presentations are "copies" of prior patients allowing quick, efficient, and safe treatment by using a pattern-recognition approach without textbook consultation.
2. Developing "own" idiosyncratic anesthesia techniques ("illness scripts").
3. Developing the ability to prioritize and see the "big picture".

II. EFFECTIVE AND TIME-EFFICIENT TEACHING TECHNIQUES FOR THE OR

The key to productive and time-efficient teaching in the OR is to spend the limited time effectively. Research has shown that this can be best accomplished with a simple 3-step-approach:[17-19]

Step 1: Identify the learning needs of the particular resident

Step 2: Focus teaching on those resident specific requisites only (*e.g., limited and rapid teaching)*

Step 3: Finish strong with feedback to ensure that the learning needs have been met and reinforced

This *"target an educational need, teach only that need, and then make sure you got your message across!"* reduces the time required for OR teaching by focusing only on what is lacking, and not what the learner already knows, or is not prepared for (increasing "teaching productivity").[17-19]

Step 1: Identify the learning needs of the particular resident.

A. Asking questions is a very quick and effective way to assess learning needs.

B. Observation is a simple yet effective tool that can be performed anytime and anywhere. It is an efficient tool to identify a wide range of requisites: interpersonal

interactions, physical examination, technical skills (iv- placement, A-line or central line placement, intubation, etc.).

C. It is important to note that most faculty are using both techniques already, whether they realize it or not. The learner is often unaware that these moments are educational opportunities, running the risk of perceiving questions and observations in a negative manner.[2] For example,

- Observation by the attending could have a counter-productive effect by making the resident think "Is my attending going to take the procedure away from me?!" Similarly,
- Well-meant questions, like "Did you give the patient the 2mg of midazolam?" can be perceived negatively by the learner: "Did I do something wrong?"

What needs to happen instead is to purpose questions and observations as educational opportunities — they must be "disclosed" as an educational activity.

Step 2: Teach only the identified needs

Once the specific learner's needs have been identified, teaching should focus on addressing only those requisites:

A. One-Minute Preceptor Model (1-MP)[20-24]

The 1-MP model is a well-established teaching method in educational literature. It includes 4 steps:

- Step 1: Obtain a commitment from the learner regarding a clinical problem. For example: You are called to the OR because of bradycardia. On arrival, you ask the trainee "What do you think is going on?" (providing insight into the learner's reasoning).
- Step 2: Probe for supporting evidence focusing on the learner's clinical reasoning, e.g., *"What led you to that conclusion?" or What would you like to do now for this patient?"*
- Step 3: Teach a general principle, based on the identified learner's strengths/needs.
- Step 4: Brief feedback

B. The Think Aloud Approach[25, 26]

Here the expert reports aloud to the learner what s/he was thinking when making a particular clinical decision. This teaching method is considered by some clinicians as possibly the most powerful tool in clinical reasoning education. Typically, it only requires a few minutes of the attending's time to review step by step his/her decision making methodology.

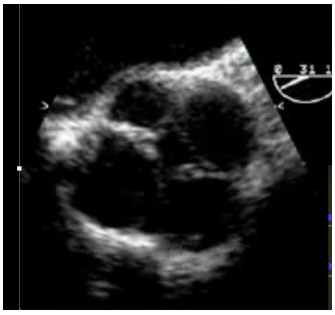
C. "Activated" Demonstration Model[19]

This is an excellent method to address deficits in technical skills. In the "Activated" Demonstration Model the tables are turned and the learner observes the master clinician:

- Step 1: "Disclose" as an educational activity; No procedure will be taken away from the learner
- Step 2: Tell the learner what to focus on. - This is a key step!
- Step 3: Following the demonstration, "activate" the learner by asking them to clearly describe what they observed to verify they "got the teaching point"
- Step 4: Offer the resident an opportunity to repeat the just demonstrated activity to reinforce the teaching point.
- Step 5: Provide brief feedback

D. The Aunt Minnie Model[27]

This is a very effective technique to teach pattern recognition introduced in the 1940s by Dr. Ben Felson, a radiologist at the University of Cincinnati. The model is based on the observation that *"A case with radiologic findings so specific and compelling that no realistic differential diagnosis exists." - If someone walks like Aunt Minnie, talks like Aunt Minnie, and looks like Aunt Minnie, then it's Aunt Minnie![27-29]* It can be a very powerful method in promoting rapid pattern recognition. Example #1: *Attending: What is this?*



E. Focused "Teach General Principle" Model

This old-fashioned model can be more time-efficient and effective,[2, 8] by dividing the deficits into urgent or non- urgent categories:

- Urgent needs refer to deficits that if not corrected ASAP could endanger a patient.
- On the other side, there are many non-urgent knowledge needs. For example, if the resident doesn't know the molecular effect of epinephrine it is unlikely that a patient will be endangered. Thus, this learning need can be covered at any time, especially, when acute demands have diminished in the case.
- Obtain the learner's undivided attention. One well-established approach is taking over the case (and saying this out loud) so that the learner can focus fully on just learning.
- Provide clinical pearls in context of the current patient
- Limit teaching to learner's requisites only and limit teaching time to 10-15 minutes per "episode". – Less is more.

Step 3: Finish strong with feedback to ensure that the identified learning needs have been resolved

Providing meaningful feedback is a critical, but challenging skill.[30-35] The old-fashioned "feedback sandwich" is so widespread that most learners are familiar with its methodology. So, while the teachers are pointing out the positive things they observed, the learners are not paying much attention. They are waiting for the "meat" of the feedback. Thus, the interested reader might consider the new sandwich: "ask-tell-ask":[36, 37]

- ASK: General questions, for example What do you think about today? How did you do?
- TELL: Opportunity to be positive, agree with resident assessment, for example "You are correct, this was not a great intubation", and even build up the resident "I think your intubation was better than you described. You did well."
- ASK: Focus on future aspects: So, what are you going to do differently next time?

Overall, the new Ask-Tell-Ask sandwich is more interactive and less confrontational.

III. SUMMARY: ADVANCED TEACHING SKILLS - HOW TO TEACH UNDER PRESSURE?

Let's conclude this review by providing a simple set of Guidelines for Practical Application: [1, 2, 9, 10]

- **Get buy-in from the resident**
  a. Establish educational context
  b. Ask about learner's past experiences & current rotational goals
  c. Identify learning needs
  d. Be aware of idiosyncrasies (resident vs. you)
- **Maintain buy-in**
  a. Be interested
     i. Pay attention to what they do and their approach to clinical thinking (talk about it)
  b. Teach identified needs (no more than 1-3 points)
     i. Clinical context; clinical pearls
     ii. Get commitment - Probe for evidence
     iii. Wait for the right moment
  c. Explain your decision-making process
  d. Don't be defensive. Be the expert – and set the stage.
- **Finish strong**
  a. Solid feedback (Ask-Tell-Ask), so they remember you did it!
  b. Go over teaching points; Review what they learned; Ensure teaching-productivity
  c. Appreciate learner's efforts / work

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RCL-27
The Adult Patient with Congenital Heart Disease Presenting for Noncardiac Surgery

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LEARNER OBJECTIVES

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

(1) Identify the diverse epidemiology of Adult Congenital Heart Disease (ACHD);

(2) Discuss perioperative risk assessment of ACHD; and

(3) Describe perioperative anesthetic considerations of ACHD.

EPIDEMIOLOGY

Advances in pediatric cardiac surgical and medical care have led to increased survival of patients with congenital heart disease (CHD). Marelli et al reviewed in 2007 and then in 2010 the administrative database in Quebec and showed that the percent of patients with CHD has been steadily increasing from 1985 to 2000 and continued to increase from 2000 to 2010 in both pediatric and adult patients. He also pointed out a steep increase between 2005 and 2010 in adult patients, mostly in adults above 26 years, leading to a change in the adult/children ratio (66/34 vs 54/46). In the year 2000, the prevalence was 11.89 per 1000 children and 4.09 per 1000 adults, whereas in 2010, the prevalence was 13.11 per 1000 children and 6.12 per 1000 adults. In addition, the number of geriatric (≥65 years) patients with CHD is increasing. In a population-based Canadian study, the prevalence of CHD was found to be 3.7 per 1000 in geriatric adults and 4.2 per 1000 in 18- to 64-year-old adults. Webb et al estimates that adults currently comprise 22–26% of the total CHD population worldwide.

PATIENTS ABOVE 60

The 15-year survival beyond age 65, as shown by Afilalo et al is 56%, with 67% for patients with severe lesions, 55% for patients with shunts, and 58% for patients with valvular lesions. Nine independent predictors of increased all-cause mortality were identified and in descending order of magnitude were: dementia (hazard ratio [HR]: 3.24; 95% CI: 1.53 to 6.85), gastrointestinal bleed (HR: 2.79; 95% CI: 1.66 to 4.69), chronic kidney disease (HR: 2.50; 95% CI: 1.72 to 3.65), heart failure (HR: 1.98; 95% CI: 1.65 to 2.38), diabetes mellitus (HR: 1.76; 95% CI: 1.45 to 2.13), chronic obstructive pulmonary disease (HR: 1.67; 95% CI: 1.31 to 2.12), cancer (HR: 1.43; 95% CI: 1.17 to 1.76), myocardial infarction (HR: 1.40; 95% CI: 1.07 to 1.83), and male sex (HR: 1.33; 95% CI: 1.13 to 1.55). In addition, more recently, Tutaral et al have shown an increase in the number of patients above 60 years of age from less than 50 in 2000 to above 300 in 2012. The increase was 12-fold for simple cases and 6-7 fold in patients with moderate-severe complexity. The numbers of interventions, length of hospitalization, and outpatient clinic visits were significantly higher in patients ≥60 compared with patients aged between 20 and 60 years. Patients ≥60 years of age with moderate or severe congenital heart defects had also worse survival prospects than their age- and gender-matched comparison population.

DIFFERENT SETUPS FOR TREATING ACHD

Caring for an anticipated aging adult congenital population with increasingly numerous coexisting medical problems and risk factors currently occurs in adult and pediatric hospitals. However, when surgery becomes necessary, a congenital pediatric heart surgeon best serves these adult patients. Founded in 1991, the Canadian Adult Congenital Heart (CACH) Network advocated for a regional approach to ACHD care. Some countries in Europe (e.g., Britain, Sweden, Germany, Belgium, the Netherlands, Switzerland, and Spain) have also developed specialized ACHD centers. In Europe, the term "Grown-up Congenital Heart Disease" (GUCH) is often used instead of ACHD. An example in Boston in the US, the Boston adult congenital hearts (BACH) follows the adult patients with CHD. These patients continue to present to children's hospital for diagnostic and interventional catheterization and surgical procedures while followed closely by the adult cardiologists. In a recent study, Nasr et al utilizing the Healthcare Cost and Utilization Project (HCUP) database compared the cost associated with CABG in non-CHD and CHD patients. In addition, they characterized the risk profiles and risk factors associated with increased cost in the two groups. CHD patients had higher costs, complication rates, and mortality than their non-CHD counterparts undergoing CABG surgery. In addition, despite being younger, CHD patients had significantly higher comorbidity scores than non-CHD patients.

RISK ASSESSMENT

As adults with CHD age, acquired co-morbidities, coronary artery disease, and heart failure become strong predictors of poor outcome. The most common cardiovascular problems encountered in adults with CHD as described by Webb et al include arrhythmias, coronary artery disease, heart failure, pulmonary hypertension, infective endocarditis and pregnancy related issues. In addition, ACHD patients continue to be afflicted by increased mortality in comparison with the general population, as they grow older. Diller et al have shown that survival in the entire ACHD was significantly worse with standardized mortality ratio (SMR) of 2.29 (CI 2.08-2.53) compared to an age gender matched sample from the general population in the UK. In fact, the greater the complexity of the lesion, the higher the SMR is; such as in Eisenmenger syndrome (12.79), fontan (23.4) and complex CHD (14.13). Although the equivalent ages for simple lesions are comparable or only slightly

(and nonsignificantly) elevated compared with those of the general public, patients with complex, univentricular, or uncorrected lesions had highly elevated values. For example, an average ASD 40yo is comparable to a 42yo. However, a Fontan 40-year-old patient had mortality rates comparable with those expected in a 75-year-old individual. These numbers are useful for counseling patients.

MORTALITY COMPARED TO THE GENERAL POPULATION

A retrospective review of data on all adult patients with CHD under active follow-up at the Royal Brompton Hospital, London between 1991 and 2014 showed that the highest mortality rates were observed among patients with complex ACHD, Fontan physiology, and Eisenmenger syndrome. The data also provides an overview of causes of mortality and especially the causes of death in ACHD patients: heat failure, pneumonia, sudden cardiac death, and cancer. With increasing patient age and simple CHD, the proportion of patients dying because of cardiac reasons despite the inclusion of acute myocardial infarction decreased and, proportionally more patients died because of competing non-cardiac causes. However, in moderate and complex CHD, the ACHD patients continue to die from cardiac causes.

PERIOPERATIVE CONSIDERATIONS FOR NON-CARDIAC SURGERY

The ACHD are at a higher risk than the general population. Maxwell et al compared ACHDs undergoing non-cardiac surgery with a non-ACHD matched cohort. Inpatient mortality was 4.1% in the ACHD cohort versus 3.6% in the non- CHD cohort, and the odds ratio of perioperative morbidity for ACHDs was 1.44. There are probably many different strategies to approach ACHD perioperatively. The main points to remember include the potential need for endocarditis prophylaxis or so-called bubble precautions, invasive monitoring, fluid status, goals for the hemodynamic management, residual defects (eg. mitral valve regurgitation following atrioventricular repair), the typical long-term problems of the CHD lesions and the patient disposition following the procedure. In addition to patient factors, the type of surgery may play a role. Recently, Liu et al have defined the intrinsic cardiac risk of operations showing that operations may carry an intrinsic cardiac risk, independent of patient characteristics with high variation within the low, intermediate and high-risk categories.

CONCLUSION

Advances in pediatric cardiac surgical and medical care have led to increased survival of patients with congenital heart disease (CHD). As patients with CHD survive into adulthood they are at risk of developing the same disease processes as their adult counterparts without CHD. When ACHD present for non-cardiac surgery, in addition to a routine preoperative assessment, multiple factors should be considered including the cardiac lesion, residual defects, other co-existing diseases, the type of procedure, hemodynamic goals and disposition.

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RCL-28
SAGA: The Dementia Brain: Considerations for Anesthesiologists

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LEARNER OBJECTIVES

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

(1) Summarize important behavioral differences of common neurodegenerative disorders encountered preoperatively;

(2) Identify areas of the brain vulnerable to cortical (Alzheimer's disease, Frontotemporal dementia) versus subcortical (small vessel vascular dementia, Parkinson's disease with and without dementia);

(3) Discuss potential interactions between neurodegenerative disease relative to anesthesia mechanisms; and

(4) Discuss intelligently how pain management and medication management may differ for each behavioral profile.

DEMENTIA IN YOUR ANESTHESIA PRACTICE

People aged 65 and older currently represent 8.5% of people (617 million) worldwide. By 2050, this percentage will double (reaching 1.6 billion). People aged 80 and older will triple between 2015 and 2050, growing from 126 million to 447 million (National Academy of Medicine statistics). Increasing age is associated with worsening of health status, increased utilization of healthcare systems, and reduced independence. Unfortunately, with the aging population comes an increase in neurodegenerative disorders. For all of these reasons, population and aging related disorders such as cerebrovascular disease, Alzheimer's disease, and Parkinson's disease, will become a significant strain on economies, health systems, and social structures worldwide.`

Coupled with the exponential growth of older adults is an increased need or desire for surgical interventions that include anesthesia. At least 26-33% of individuals will be presenting with early signs of dementia that will have been undiagnosed.[1] They shall arrive into the preoperative environment relatively unaware or denying the presence of their cognitive impairments.[2] Patients with dementia will arrive at your doorstep in larger numbers over the next 25 years.

WHY CARE?

Delirium and post-operative cognitive decline are two of the most frequently discussed domains within the anesthesia literature and at conference events. Yet, remarkably, we have no answers about which anesthesia medications are most concerning or how the actual surgical stress accelerates brain changes, if at all. Despite countless animal studies and increasing numbers of human investigations, the underlying biological mechanisms of changes remain unsolved.

Yet, a contributing risk factor is repeatedly shown throughout the literature. Preoperative cognitive weaknesses as well as frailty are significant predictors of delirium and mortality.

Anesthesiologists can play a pivotal role in reducing the strain of dementia on pre and post-operative care. Anesthesiologists should be at the forefront of learning about the aging brain, dementia, and other neurodegenerative pathologies. Equipped with at least fundamental knowledge about the brain and brain-behavioral profiles associated with normal versus abnormal aging, anesthesiologists will have the essential skills necessary to recognize concerning behavioral profiles that predict poor post-operative outcome such as delirium. Preventative interventions can include prospective pre-operative optimization, anesthesia care planning, and post-operative monitoring and consultation with appropriate allied health colleagues.

Until we know more about which anesthetics may be most appropriate for patients with reduced cognitive function and different neurodegenerative disorders, it is important anesthesiologists know the basics of dementia, learn to recognize characteristics of dementia in undiagnosed patients so that identifying risk for delirium is feasible and accurate. This will change our response to delirium from reactive to proactive.

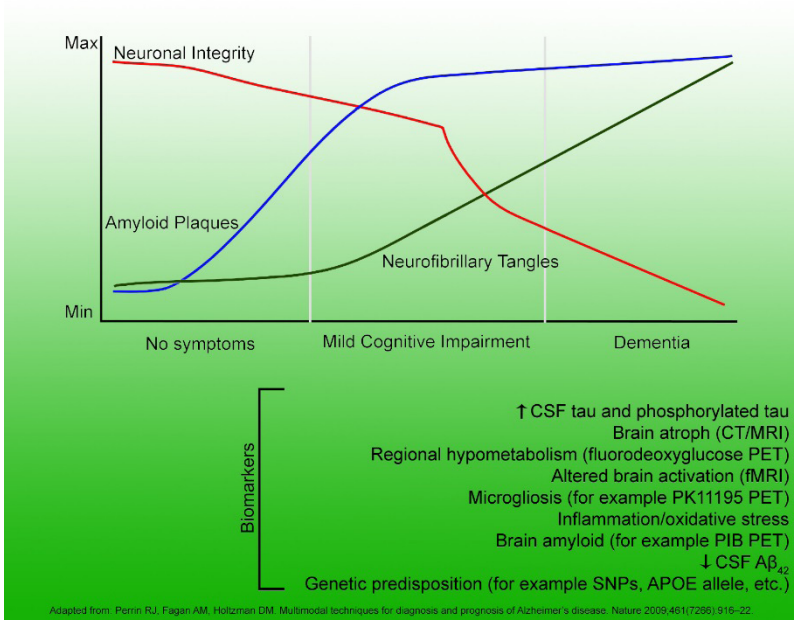

Figure 1. Adapated figure from Perrin, Fagan, Holtzman (2009). Multimodal techniques for diagnosis and progrnosis of Alzheimer's disease. Nature, 461)7226: 916-22.

Normal Aging, Mild Cognitive Impairment, and Dementia

Normal aging involves retention of cognitive abilities that are consistent with demographic, educational, and occupational status. Normal aging is associated with slower processing speed and fluid reasoning relative to younger age groups, but functioning remains at average levels relative to same age peers. Functional abilities (driving, medication management, etc.) remains unchanged relative to younger years.

Mild cognitive impairment (MCI) is considered the prodromal phase of dementia.[3] MCI was initially used to specifically define the prodromal phase into Alzheimer's disease. More recently, evidence suggests that MCI represents the prodromal phase for any form of dementia including vascular dementia, Parkinson's disease dementia, and frontotemporal dementia.

Classification: A patient classified with MCI has typically been given a structured interview by a trained neurologist or neuropsychology and has met formal criteria based on neuropsychological testing. Impairment is one standard deviation or lower relative to their aged peers in one or two cognitive domains. There is no impairment in functional status; independent activities of daily living (driving, finances, and medication management) are reported to be intact.

Common types of MCI include: MCI single domain amnestic (indicating a specific impairment in learning/memory with all other cognitive domains are average or higher), MCI single domain non-amnestic (specific impairment in another domain such as executive functioning which includes processing speed, working memory, inhibitory functions, or higher cortical planning and abstract reasoning, with average scores on learning and memory), MCI multiple domain amnestic (memory and at least one other domain shows impairment), and MCI multiple domain non-amnestic (if memory domain was not impaired and more than one non-memory domain was impaired).[4,5]

Outcome: A diagnosis of MCI does not necessarily mark an individual as destined for dementia. The criteria used to define a patient as MCI is important. When patients are classified by neuropsychological methods researchers have found these patients to be more diagnostically stable (less than 1% revert back to normal), progress to dementia, and have greater correspondence with AD biomarkers (APOE allele four, cerebrospinal fluid hyperphosphorylated tau, beta-amyloid) than did those classified by other criteria.[6] Figure 1.

Dementia is classically defined as impairment in two or more cognitive domains with one of these domains involving learning/memory functions, combined with impaired functional status (changes in driving behavior, financial/medication management, etc.). Behavioral profile, type of cognitive impairment, medical status, and information about comorbidities provides diagnostic information on primary disease location, possible pathology, and consequently dementia diagnosis. These dementias are described in the sections later.

Diagnostic and Statistical Manual of Mental Disorder Diagnoses Pertinent to MCI and Dementia: Within the DSM-V there are two terms you should know, as some physicians use these terms in place of MCI or dementia.

Mild Neurocognitive Disorder is a clinical diagnosis based on evidence (self-reported, objective measures) of modest cognitive decline from a previous level of performance. The changes can be within domains of complex attention, executive functioning, learning and memory, language, perceptual-motor, or social cognition). Change in function is based on: 1.) Concern based on self-report of the individual or a knowledgeable informant; or 2.) A modest impairment in cognitive performance preferably documented by neuropsychological testing (note that this diagnosis does not require a certain standard deviation of decline). These cognitive changes cannot interfere with capacity to function independently. These cognitive changes cannot occur exclusively in the context of delirium. These changes cannot be explained by another mental disorder. Classification of Mild Neurocognitive Disorder involves disease specification (i.e., Alzheimer's disease, Frontotemporal dementia, vascular disease, etc.). Practitioners then specify if the patient has active behavioral disturbances (psychotic symptoms, mood disturbance, agitation, apathy, and other behavioral symptoms).

Major Neurocognitive Disorder involves evidence of significant decline from a previous level of performance in one or more cognitive domains (complex attention, executive functioning, learning and memory, language, perceptual-motor, social cognition). Change documentation is based on: 1.) Concern of the individual or a knowledgeable informant; or 2.) a substantial impairment in cognitive performance ideally based on neuropsychological testing. Contrary to Mild Neurocognitive Disorder, the individual has to have cognitive deficits that interfere with independence in everyday activities. The cognitive disorder cannot exclusively occur in the context of delirium. The severity if specified as mild (difficulties with instrumental activities of daily living such as housework, managing money), moderate (difficulties with feeding, dressing), or severe (fully dependent).

GRAY, WHITE MATTER, BRAIN CHANGES WITH NORMAL AGING

Brain integrity decreases with normal aging and even more markedly for neurodegenerative pathologies. Cross sectional studies show that older age involves reduction in whole brain volume and increases in cerebrospinal fluid.[7] Within the brain, white matter volume declines during the middle age years. Cortical gray matter loss occurs later.[8] The most common white matter changes observed in normal aging involves leukoaraiosis[9] (LA). Cognitively well older adults have LA within one percent or less of their white matter.[10] LA is dominant around ventricles (called periventricular LA). For cognitively well adults, LA is less prominent in the deep white matter or near the cortex. Pathological burden can differentially develop within the gray and white matter tissues. The pattern of changes combined with cognitive profile and other biomarkers differentiates normal aging from early disease pathologies. Figure 1.

THE DEMENTIA TYPES AN ANESTHESIOLOGIST WILL MOST OFTEN ENCOUNTER

Before we discuss the types of dementia, the most common form of dementia is mixed dementia; i.e., mixed dementia syndromes often consist of Alzheimer's disease and some other neuropathological substrate.[11] This represents more than 50 percent of cases. Research suggests that Alzheimer's and vascular pathology represent the most common dementia types.[12,13] When we consider cognitive function, however, patients with primary memory deficits show reduced hippocampal volume, while individuals with more dysexecutive/frontal profiles show more leukoaraiosis in the deep regions of the white matter.[14]

Alzheimer's Disease (AD): Between the years of 2010 and 2050, the number of people with AD is expected to triple.[15] Approximately 50 to 80 percent of individuals diagnosed with Alzheimer's disease have significant small vessel vascular disease, and can be considered a mixed dementia. More "Pure" Alzheimer's disease will present with some of the following characteristics:

Behavioral profiles: The classic cognitive profile is considered a "cortical" profile where impairment involves changes to the gray matter cortex and less change to the subcortical white matter and gray matter subcortical nuclei. Associated with these disruptions are changes in learning new information (inability to retain new information after a short filled time delay). As the disease progresses, prominent word retrieval, and reduced naming of common objects emerge. Attention, mental flexibility, and abstract reasoning remain unchanged largely until the moderate stages of the disease.

Clinical pearls:

a. Individuals with Alzheimer's disease can converse well, hide their impairments, retain excellent eye contact, and show excellent attention and problem solving skills.

b. Impairments will not surface until you ask pointed orientation questions, conduct a learning/memory test, or ask them to name objects.

c. Primary motor skills including gait and balance remain intact until the later stages of the disease.

d. On cognitive screeners such as the clock drawing test, individuals with AD may only draw a circle or draw a circle and put in the number, but improve substantially on the copy condition.

e. One three-word memory, recall could be all or none of the words depending on severity of disease stage.

Associated Imaging markers: Structural neuroimaging is used routinely in clinical practice but primarily for the exclusion of other pathology. Advances in automatic analysis, however, are helping us to identify neuroanatomical regions of atrophy. The entorhinal cortex is one of the first neuroanatomical regions to show Alzheimer disease pathology,[16] with more than half of adults between 56 and 60 years shown to have neurofibrillary tangles

in at least the entorhinal region of the brain. Then, the pathology progresses to the inferior frontal regions, and to the lateral temporal and parietal regions. The cortical disease progresses in an outward fashion until the pathology arrives at motor and sensory regions.

Cholinergic System: Acetylcholine is an important part of cortical activation, arousal, and cognitive functioning. Cell bodies of neurons that provide cholinergic innervation to the cortex reside within the basal nucleus of Meynert (BNM) – which is anterior to the thalamus and basal ganglia.[17-19] Cholinergic axons linking BNM and cortex are mostly unmyelinated[20] and thus more vulnerable to aging-related vascular changes in the brain as well as pathologies of AD and small vessel vascular dementia.

Biomarkers Markers/ PET: There have been advances with the measurement of amyloid-beta peptide (Abeta, Aß), total tau (t-tau), and hyperphosphorylated tau (p-tau) within the cerebrospinal fluid for patients with Alzheimer's disease.[21] Also used is positron emission tomography (PET) to image amyloid deposition. These measurements have improved our classification of AD in the prodromal and preclincial phases, but remain elusive for collection due to the invasiveness of CSF and cost/access of PET studies.[22]

Anesthesia Considerations: It is unknown if individuals with AD respond differently to anesthetics. Hypothetically, disrupted cholinergic production and pathological disease infiltration into the cortex may disrupt frontal-parietal communication, anesthetic metabolism, and/or anesthetic response. Because patients with memory impairment have been shown to have higher rates of delirium,[23] these patients warrant close monitoring and referral for inpatient geriatric monitoring, if possible.

Vascular dementia (VaD): Prevalence of VaD is rapidly increasing. It is the second most common form of dementia, only trailing behind Alzheimer's disease (AD).[24] This high prevalence rate is due to hypertension, hypercholesterolemia, and diabetes. There are two main categories of VaD: small-vessel vascular dementia and large-vessel vascular dementia Note: There is controversy as to whether VaD represents a distinct dementia subtype of a co-morbid occurrence with other dementias. For example, Schneider et al., (2009) observed mixed AD/ vascular neuropathology in approximately 50 percent of their autopsy sample. For this reason, you may sometimes see reference to the AD/VaD spectrum disorders.

Behavioral Profiles: VaD is traditionally termed a subcortical dementia, such that the disease largely impacts the white matter fibers connecting cortical gray to subcortical gray matter. The most disrupted circuits are those connecting frontal to subcortical regions as well as frontal-parietal connections. Behaviorally, this manifests as a "dysexecutive syndrome".

Clinical pearls:

a. Small vessel vascular dementia:
   i. Patients with small vessel VaD will have insidious (slowly progressive) cognitive changes over time.
   ii. Slower processing speed, more impulsiveness, more distractibility, production of perseverations (doing the same thing over and over), have difficulty sustaining attention over time.
   iii. Source memory errors; recalling the incorrect information that he heard from another recent source.
   iv. May have gait/balance impairments.
   v. Higher rates of depressive symptomatology.
   vi. Common clinical errors on screening: Clock drawing to command may have hands to the 10 and the 11, rather than 11 and 2; produce similar errors on command and copy conditions.[25]
   vii. Three word memory recall: Could be variable; patients may recall all or none of the words.

b. Large Vessel vascular dementia (also called Multi-infarct dementia):
   i. Shows a step wise cognitive decline; decline with first stroke, followed by cognitive stability, followed by stroke and consequent decline, etc.
   ii. Can have a variety of cognitive and emotional profiles depending on stroke lesions.
   iii. Would be at higher risk of additional stroke and cognitive change.

Associated imaging markers: Leukoaraiosis (LA) is common. Individuals with signs of small vessel vascular dementia or mixed AD/VaD show LA comprising 3% of white matter volume, on average, with some individuals showing up to 24%[10,14]. For patients with small vessel vascular dementia, these changes occur around the ventricles but also the deeper white matter, and are often accompanied by lacunea within the thalamus and caudate nucleus. These changes are often accompanied by widening ventricles, and overall brain integrity volume loss.

Biomarkers: The features of white matter disease are the most frequently cited as important neuroimaging biomarkers. Hypertension and presence of at least one APOE epsilon4 allele has shown to present with more subcortical and deep white matter disease and cognitive profile of small vessel VaD.[26] White matter lesions are also hypothesized to represent disruption to the blood brain barrier and induced neuroinflammation.[27]

Anesthesia Considerations: Anesthesiologists may wish to be particularly attentive to hemodynamic variability and anesthesia factors (e.g., isoflurane) that may alter blood brain barrier integrity as well as cholinergic function.

Parkinson's disease and Parkinson's disease dementia
Parkinson's Disease (PD) impacts at least 1.5 million people in the United States alone; its prevalence increases with age, and most diagnoses occur over age 60.`PD itself is not a dementia. However, the majority of PD patients who survive more than 10 years after the onset of PD will eventually develop dementia.[28] Cognitive and motor symptoms result in reduced quality of life, nursing home placement and increased mortality.`` The rate of dementia in PD is higher (25-40%) than that of the general population. It is now recognized that prodromal forms of dementia in PD (PD mild cognitive impairment; PD MCI) exist, although the occurrence varies widely based on age, disease duration, and disease severity.[29,30] Cognitive impairments can occur across various cognitive domains, but impairment in a single domain is most common.

Behavioral Profiles: Parkinson's disease is most known by its motor symptoms and is diagnosed by these symptoms (unilateral resting tremor, rigidity, or gait instability). Accompanying these motor symptoms, however, are disruptive cognitive, emotional, and autonomic disruptions.

Clinical pearls:

a. Individuals with Parkinson's disease have compromised processing speed; slow learning for new information, slower than normal word retrieval, slower problem solving. If provided with additional time, however, non-demented individuals with PD will perform at the same level as their age and education matched peers.
b. Disease progresses to include reduced mental flexibility, distractibility.
c. Memory and problem solving difficulties can occur as the disease progresses through cortical regions.
d. With increasing cognitive impairment in PD: Watch for errors on clinical screening, impaired learning and retention for new information
e. Patients with PD can be asked to engage in clinical screening tests that require motor testing, as their tremor should be primarily "at rest" (not an action based tremor).
f. On clinical screening with the clock drawing test, individuals with PD (non-demented) should perform normally on command and copy. Due to processing speed limitations, patients with PD may take more time to complete the drawing, however. Some patients may show micrographic clocks (small clocks) this is more common with increasing cognitive impairment.
g. Three-word memory recall may miss one word (2/3 correct).

Associated imaging markers: Volumetric MRI studies of risk factors have also shown mixed results, with some reporting that individuals that convert from PD-MCI to PDD show smaller volumes in frontal cortex and caudate nucleus,[31], while others report these individuals show thinning in temporoparietal regions.[32] Increased freewater also occurs within the substantia nigra.[33]

Biomarkers: On imaging, you can see reduced pigmentation in the substantia nigra. There may be reduced volume in the putamen and caudate nucleus.[34,35] Pathologically: Neuronal intracytoplasmic filamentous inclusions, referred to as Lewy bodies (LBs), are frequent in the substantia nigra and are considered the histological hallmark of PD. Evidence is also accumulating, however, that the brains of non-demented PD patients contain abnormalities within the neuronal support cells, specifically the glial (astrocyte and oligodendroglial) cells that are responsible for myelination of the axonal processes, production of neurotropic factors, and regulation of iron metabolism. Abnormalities of these neuronal support cells have been linked to a mutation of NACP/ α-synuclein - a presynaptic protein whose physiological role is associated with synaptic function.[36-38] NACP/ α-synuclein-positive glial inclusions and LBs have been identified even in the intact white matter of the cerebrum, cerebellum and spinal cord of deceased PD patients. Additionally, PD staging criteria report infiltration of pathology from the nuclei brainstem to the gray matter of frontal cortex, with suggested pathways following ventral (temporal) and medial dorsal subcortical gray to frontal streams.[39]

Anesthesia Considerations: Individuals with PD are vulnerable to delirium even after outpatient surgical procedures. For inpatients, much concern is the consistency of their levo-dopa medication management during the time of hospitalization[40] and maintaining appropriate sleep-wake cycles.[41] Preliminary pilot studies suggest individuals with PD may be at greater risk for processing speed and inhibitory function slowing after orthopedic surgery.[42]

Diffuse Lewy Body (DLB): DLB accounts for approximately 1-2% of the 65+ population[43] and approximately 5% of all dementias over the age of 75.[44] Individuals with DLB can mimic individuals with Parkinson's disease and Alzheimer's disease. Indeed, Diffuse Lewy Body disease can be misdiagnosed as Alzheimer's disease early in their disease course.[45] For DLB, cognitive impairment is primary and then followed by motor disorder symptoms mimicking parkinsonism. DLB is a disorder with alpha-synuclein deposition/ Lewy Bodies that infiltrate throughout the subcortical and cortical regions. There is a higher rate of mortality after diagnosis; The median time from estimated first cognitive symptoms to death was 7.4 years (interquartile range 5.7–10.2).[46]

Behavioral Profiles: The primary feature involves cognitive waxing and waning, balance instability, and a history of first symptoms involving cognition/sleep disorder followed by motor symptoms.

Clinical pearls:

1. Sleep disturbance and particularly REM sleep disorder with vivid dreaming and night thrashing may precede DLB for years.
2. Visual hallucinations, can occur with vibrant color
3. Cognitive waxing and waning; will appear attentive one minute and distracted or staring off into space the next minute; transient episodes of consciousness
4. A history of falling or balance difficulties; falls may be backwards

5. Depression and anhedonia are common
6. Constipation
7. More common in males
8. On cognitive screening measures, look for impaired clock command and copy. Clock drawing would be slow, disorganized, and show errors on hand placement.
9. Three word memory performance would be compromised.

Associated imaging markers: Reduced volumes in hippocampus, putamen, caudate nucleus, and larger ventricles. Reduced gray matter thickness throughout the brain. EEG abnormalities may be observed, metabolic decrease in the cortex. Decreased striatal 123I-FP-CIT binding is associated with nigral dopaminergic cell loss[47] but with higher Tau and cortical Lewy Body load particularly in the temporal cortex.[48]

Anesthesia Considerations: Due to the widespread of Lewy Bodies throughout the brain, confusion needs monitoring. Delirium is a significant risk factor.

Frontotemporal Dementia (FTD): is used as the umbrella term for a main group of dementing syndromes that present histopathologically with neuronal loss, prominent microvacuolar spongioform change, and gliosis within the frontal and temporal regions of the brain.` This combination of features combined with the usual absence of tau-positive intraneuronal inclusions (Pick-bodies) differentiates the FTD group from that of another frontal disorder termed Pick's Disease.[49] In addition, FTD histology is also absent of neurofibrillary tangles or amyloid plaques thereby distinguishing itself, at least histopathologically, quite clearly from that of AD. The three most commonly discussed FTD subtypes are Progressive Non-Fluent Aphasia (PNFA), Semantic Dementia, and FTD dyexecutive/ behavioral syndrome. ***Due to the complexity of these subtypes, the imaging and biomarker perspectives will not be discussed.***

Behavioral Profiles: Each FTD type is associated with patterns of cortical degeneration and behavioral presentation. Progressive non-fluent aphasia types present with impaired speech production; Semantic Dementia with reduced comprehension and word finding difficulties. Patients with dysexecutive / behavioral profile will show impaired social skills (imipaired affect, inappropriateness, and executive dysfunction).

Clinical pearls:

1. PNFA: Broca's like aphasia profile; non-fluent speech, yet intact attention and comprehension, intact learning/memory; most patients with PNFA normal clock drawing with variable three-word memory.

2. SD: Will not appear to understand some of your words (even simple nouns), will have difficulty naming objects, can be confused for Alzheimer's disease; clock drawing could be compromised at command due to semantic difficulties; copy may be compromised due to visuoperceptual/spatial limitations which also accompany SD.

3. Social/Behavioral: Impulsive, socially inappropriate, personality changes are reported, in appropriate jocularity, inappropriate sexual behavior, etc. Clock drawing may should impulsivity and poor planning errors.

Anesthesia Considerations: These dementias can behaviorally mimic stroke patients at times. Anesthesiologists are encouraged to be aware of preoperative comprehension, speech, and executive function limitations in their patients and potential changes post-operatively; potential increased signs of speech of language disruption and increased lability and confusion post-operatively relative to pre-operative baseline. It is unknown how these patients accelerate in symptomatology.

Cognitive/Brain Reserve, Dementia, and Surgery with Anesthesia

Figure 2. Cognitive / brain reserve is defined as the a form reserve supply that allows some people to cope with progressing neurodegenerative pathology or successive neuronal insults.[50,51] Higher cognitive reserve is related to psychosocial and experiential factors (e.g., greater educational attainment) and genetic factors (e.g., childhood intelligence). Brain reserve can be indicative of pathology. It has been theorized that individuals can remain at above a critical threshold due to cognitive or brain reserve until some combination of factors (e.g., brain damage, neuronal stress) summates to accelerate symptom manifestation (threshold theory).

These models have been applied to explain the expression of neurodegenerative disorders including Parkinson's Disease,

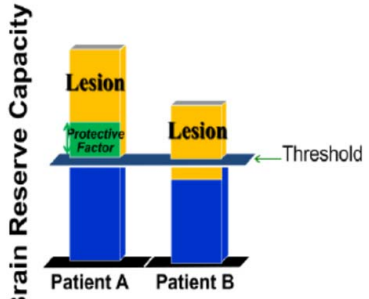

Figure 2. Modified from Satz [50] Patient A has greater "reserve" (e.g., greater brain size relative to intracranial volume, greater education, etc) relative to Patient B. Both patients experience a "lesion" or biological challenge or stressor. Only Patient A with the greater reserve, however, remains above the critical threshold of cognitive impairment. In contrast, Patient B with less pre-operative "reserve" falls below this critical threshold and demonstrates significant cognitive change. In the event of an additional lesion, Patient A may eventually develop cognitive impairment. The aggregate effect of the two lesions eliminates his remaining reserve; he now presents with clinical symptoms of cognitive impairment.

Alzheimer's disease, vascular dementia. The hypothetical threshold model is shown in Figure 2. These concepts have been applied to the topics of post-operative cognitive decline/dysfunction and delirium.[52]

It remains unknown if individuals with MCI or dementia have disease acceleration after surgical procedures with anesthesia. Studies prospectively following patients with neurodegenerative disorders are extremely rare.[42] This is largely due to the challenges of screening and enrolling large numbers of patients for prospective follow-up. Recent pre-post operative biomarker research does show, however, increased Tau protein and neurofilament light at 48 hours surgical procedures.[53] Whether anesthesia type alters these markers remains uncertain.[54]

ANESTHESIA AND THE DEMENTIA BRAIN

One of the difficulties in assessing the effects of anesthetic on the demented brain is the fact that an anesthetic whether regional or general anesthesia is rarely delivered without a concomitant surgical procedure as the two almost always occur together. Surgery injury causes a stress response via activation of endocrine, metabolic, and inflammatory responses. The inflammatory response is activated not only locally at the wound site but more importantly triggers an inflammatory systemic response which has the potential to be harmful to the brain.[55,56] Attempts to separate out surgery as a risk factor have been difficult as anesthesia administration is typically required to perform a major surgical procedure and thus challenges in research have included attempts to have an appropriate control group that did not require a surgical procedure. In one retrospective study that attempted to control for surgical procedure, patients undergoing coronary artery bypass grafting (CABG) surgery were compared to patients who had known cardiovascular disease requiring a percutaneous transluminal coronary angioplasty intervention.[57] In this study, those patients who underwent CABG survey had an adjusted risk of dementia of 1.7 compared to patients who underwent the percutaneous procedure up to 6 years after the procedure.

Anesthetic Effects

Numerous studies have been performed trying to understand the impact of anesthetics on the demented brain. Many of these studies utilize basic science models with fewer studies in humans. Due to the extensive literature on this topic, only a few additional key points concerning anesthesia will be covered in this portion of the handout.

Agents that are used to produce the desired effects of general anesthesia which include loss of consciousness and memory function while preventing pain and patient movement decrease the release of acetylcholine (Ach) and cholinergic transmission.[58] Although some reports on anesthetic agent such as isoflurane have suggested that it may have properties that protect against neurotoxicity,[59] other reports have concerns about its potential neurotoxicity. In human neuroglioma cells, isoflurane produced neurotoxic effects including inducing caspase activation, extracellular accumulation of Aß, and cell death.[60] In addition, commonly used volatile anesthetic agents, isoflurane and sevoflurane, have been shown in mice models to increase amyloid accumulation and induce apoptosis.[61] Sevoflurane has also been associated in mouse models with an increase in Aß[62] as well as increased tau phosphorylation;[63] both of these represent key protein biomarkers in the most commonly found form of dementia, Alzheimer's disease. A newer volatile anesthetic, desflurane, which differs from isoflurane and sevoflurane, has been shown in human neuroglioma cells to not activate caspase-3 or impact amyloid precursor protein (APP) processing or Aß accumulation nor in mice to cause learning or memory impairment.[64] In humans, comparing spinal anesthesia to general anesthesia with isoflurane or desflurane, isoflurane but not desflurane increased cerebrospinal levels of Aß proteins.[65] Propofol in a rat model has not been shown to impact Aß via its precursor protein APP[66] and may have inhibitory actions for isoflurane Aß oligomerization.[67]

Neuromuscular Blocking Agents

Neuromuscular blocking agents are often utilized intraoperatively. For treatment of dementia as for example with Alzheimer's disease, patients are often administered cholinesterase inhibitors to promote cholinergic transmission activity. The cholinesterase inhibitors may result in bradycardic side effects and can prolong the duration of succinylcholine. In patients treated with cholinesterase inhibitors reversal of nondepolarizing neuromuscular blocking agents may benefit from the avoidance of anticholinergic medications for use as reversal and may benefit from the use of newer reversal agent sugammadex[68] which work by a different mechanism.

Pain Management

Pain management throughout the perioperative period for patients with dementia is especially important as pain and its management may further impair cognitive functioning.[69] In addition, inappropriate pain management can contribute to the development of postoperative delirium.[70]

Postoperative Delirium and the Demented Brain

For postoperative delirium, dementia represents one of the the most significant risk factors and also determines its severity.[71-73`] Delirium is described in the Diagnostic and Statistical Manual of Mental Disorders as representing an acute condition that involves a transient alteration in consciousness and cognition that develops over a short period of time that rapidly onsets and typically has a fluctuating course.[74,75`] Patients with a history of delirium are at risk of a future episode of delirium. The risk of delirium can vary with the type of dementia; the risk of recurrence of delirium is much higher with those with a history of delirium with DLB compared to Alzheimer's disease as a cause of dementia.[76`] Recognition of postoperative delirium represents a medical emergency as it can lead to increased morbidity and mortality.` Cognitive impairment prior to surgery is a well-established delirium risk factor.[6-8]

Anesthesiologists can play a pivotal role in reducing postoperative delirium through optimizing perioperative care fo the patient with dementia. Although a comprehensive discussion is beyond the scope of this handout, it is important for anesthesiologists to recognize the factors that predispose a patient to delirium and can be precipitating. In addition, it is important to identify drug-related contributing factors including drugs that may be used for treatment of dementia and those that have high anticholinergic property (Ref Pervin). Recognition of the impact of medications utilized in the perioperative period is also an important consideration in attempts to decrease the incidence of delirium in the patient with dementia. Anesthesiologists are also crucial in the early recognition and delirium treatment which involves searching for underlying causes as well as providing changes in the environment and behavioral support as well as pharmacological treatment when needed.`

MORE QUESTIONS THAN ANSWERS

Anesthesiologists have a pivotal role in care of the patients with dementia and given the increasing incidence of dementia with the aging population, those providing anesthesia for older adults will

invariably have a patient presenting with dementia for anesthesia perioperative management. The anesthesiologist's assessment begins with preoperative recognition of the signs of normal aging compared to the presentations with the various forms of dementia. Although there are many questions about anesthetics impacts on the brain with dementia, more and more information becomes available about optimal choices for management through out the perioperative period. Identifying those patients at risk for delirium and being proactive in those patients management to decrease and ideally prevent postoperative delirium with perioperative management remains a key in management of this patient population.

Some Terms Defined

Leukoaraiosis	A radiological term literally meaning 'White' (LEUKO) 'changes' (ARAIOSIS) seen on MR/CT brain images. In histological material, LA is primarily associated with ischemia of the white matter induced by narrowing of intracranial vessels. It occurs in 15 to 65% of adults, with a three-fold increase in older relative to younger adults. Prominent feature of small vessel vascular dementia. In large amounts (on average 3% of the white matter), LA associates with reduced frontal function.	
Lacunae	Small holes from infarcts, typically seen within the caudate nucleus and thalamus, but also common in the deep white matter of the brain. More common in small vessel vacular disease.	
Entorhinal cortex	The gateway into a key memory structure – the hippocampus - and can be seen best in the coronal brain slices. Shown to have cellular layer loss and/or thinning in early stages of Alzheimer's disease.	
Basal nucleus of mynert	Located in the ventral portion of the bilateral frontal regions; believed to be necessary for acetylcholine production.	
Vascular Cognitive Impairment	vascular disease could result in significant cognitive impairment without necessarily reaching true dementia	
Vascular Cognitive Disorder	Global diagnostic term that ranges from VCI to VaD, although this term has recently been relegated only to cases with significant cognitive impairment with no dementia	
Lacunar state	a syndrome first proposed by Marie P (1901) and Ferrand J (1902) to characterize behaviorally impaired (what kind) patients with diffuse white matter softening (particularly in the frontal lobe), and the presence of lacunes in subcortical gray matter	
subcortical dementias	(i.e., vascular dementia, Parkinson's disease) describes a pattern of cognitive impairment involving difficulty in executive functioning as well as personality/ emotional changes	
cortical dementia,	(e.g., AD, FTDs) - with its hallmark changes to specific cortical gray matter regions that disrupt 'higher' functions such as memory, language, abstract reasoning, problem solving	

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