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RCL-01
ECMO (Extracorporeal Membrane Oxygenation): Implications for Anesthesia and Critical Care

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LEARNER OBJECTIVES

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

1) Discuss principles and different modalities of ECMO;
2) Describe the indications and contraindications for ECMO;
3) Discuss common clinical problems and complication of ECMO;
4) Describe ECMO outcomes and data;
5) Evaluate perioperative implications of ECMO.

SYLLABUS

Extracorporeal membrane oxygen (ECMO) or extracorporeal life support (ECLS) has been used for many years to support patients with respiratory or combined cardiac and respiratory failure. Initial success in the neonatal and pediatric patient population was followed by disappointing results of the first adult trials. Since the 1980s, ECMO technology and management and generally critical care have changed dramatically. Although only one larger randomized controlled trial for adult ECMO exists, adult ECMO has now become an accepted treatment option for both cardiac and respiratory support.

Respiratory failure patients are usually supported with veno-venous ECMO (VV-ECMO), a modality that removes blood from the inferior vena cava (IVC) (and sometimes the superior vena cava (SVC)) and returns blood to the right atrium and subsequently into the right ventricle. In rare cases, patients with primary pulmonary pathology require veno-arterial ECMO (VA-ECMO), such as in acute pulmonary embolism or other cases in which the pulmonary vascular resistance is elevated or right ventricular dysfunction is present. Common indications for VV-ECMO include acute respiratory distress syndrome (ARDS), primary graft dysfunction (PGD) after lung transplantation, and pneumonia. Cannulation strategies are either bilateral femoral venous, femoral and jugular venous, or double-lumen jugular cannulation.

Patients with cardiac or combined cardio-respiratory failure are generally supported with veno-arterial ECMO (VA-ECMO). In a parallel fashion, blood is removed from the venous circulation and returned to the arterial circulation. Several approaches exist, including central cannulation where venous blood is drained from the right atrium and returned into the ascending aorta (typically in the setting of post-cardiotomy heart failure) and various forms of peripheral cannulations, where most commonly blood is drained via a femoral vein and returned via a femoral artery. The most common indication for VA-ECMO is acute cardiogenic shock due to acute myocardial infarction, fulminant myocarditis, an exacerbated cardiomyopathy, or refractory ventricular arrhythmias.

Modern ECMO technology includes the use of closed heparin-bonded circuits and centrifugal pumps. This has led to a reduction in heparin requirements to keep these systems from clotting. Given that much of the thrombotic circuit complications are due to platelet adhesion and aggregation, heparin is typically administered via IV infusion with a goal aPTT of 60-80 seconds or an activated clotting time (ACT) of 180-220 seconds. Again, given the improvements in ECMO technology over the years, these goals are much lower compared to historical systems that could only be safely operated with an ACT greater 400 seconds.

Critical for the application of either ECMO modality is the observation of aforementioned indications and also contraindications such as a progressive and non-recoverable disease process in combination with a non-candidacy for organ transplantation or durable assist device. Other common contraindications are severe neurologic injury or intracerebral bleeding, an unrepaired aortic dissection, and other absolute contraindications to anticoagulation. It is quite important to determine clear goals at the time of or immediately after initiation of ECMO, especially in the patient population requiring VA-ECMO for cardiac support. Once the decision is made that this patient cannot be treated with other less invasive temporary support devices and requires ECMO, an exit strategy should be discussed. Potential treatment plans include bridge-to-evaluation (needs to be readdressed within hours), bridge-to-recovery (most common strategy in patients with respiratory failure on VV-ECMO), bridge to transplant (poor outcomes for patients on VA-ECMO being bridged to heart transplantation), and bridge-to-durable device (only available for heart failure patients).

There are side effects, phenomena, and complications that are typical for either VA- or VV-ECMO and then some that are part of ECMO in general. Bleeding events are among the most common general complications of ECMO and there is often a fine line between adequate anticoagulation and thromboembolic events. Limb ischemia or low-flow state is a devastating complication of peripheral VA-ECMO, but can be greatly reduced by standardization of cannulation procedures including the insertion of a distal perfusion cannula. North-south syndrome describes a phenomenon of relative upper body hypoxemia in the setting of peripheral VA-ECMO and cardiac recovery, but ongoing pulmonary failure. With improving native cardiac function, but poorly functioning lungs, de-oxygenated blood is ejected primarily into the coronary arteries and the cerebral branches of the aortic arch. Adjustment of ventilator settings or change to VV-ECMO can usually remedy this problem. In contrast, ventricular distention occurs in the setting of cardiac failure with very poor ventricular function or absence of native ejection. In this case, lack of contractility ultimately results in ventricular distention, stasis and possible thrombus formation, and pulmonary edema or even hemorrhage. Low-dose inotropic therapy or mechanical venting of the left ventricle can help avoid distention and a subsequent increase in wall

tension and perfusion, which can impair cardiac recovery. A classic phenomenon observed in patients on VV-ECMO is recirculation, which describes the portion of oxygenated blood coming from the ECMO circuit and instead of going into the patient's right ventricle is returned into the circuit via the drainage cannula. This is often related to cannula position and pump flows, but has become less frequent with the use of double-lumen venous cannulas.

Randomized-controlled trials are lacking for the use of VA-ECMO in cardiac failure, however with improved technology and a growing number of large cardiac centers embracing ECMO technology, it appears to be a well-accepted modality for acute cardio-pulmonary support. Some case series and case-control studies investigating the use of VA-ECMO for acute cardiac failure show promising results, however the morbidity and mortality remain considerable with a roughly 40% survival to de-cannulation rate for VA-ECMO cardiac support patients as reported by the Extracorporeal Life Support Organization (ELSO). In contrast, one modern-day randomized-controlled trial exists looking at VV-ECMO for patients with acute respiratory failure from ARDS showing a reduction in mortality in the ECMO group, however this study has been widely criticized for its methodological flaws. It did however convincingly show that mere referral to a specialized ECMO center is associated with better clinical outcomes. Subsequent smaller trials have confirmed the center volume to positive patient outcome relationship. There are at least two well-designed ongoing trials on the use of ECMO in patients with ARDS.

More recent, the use of ECMO has further expanded. VA-ECMO is now used in the setting of cardio-pulmonary resuscitation (CPR) and results are promising considering the historically poor outcomes of patients undergoing CPR. Patients with end-stage lung disease and exacerbation of their chronic lung disease, particularly patients with cystic fibrosis, are now successfully bridged to lung transplantation with the help of VV-ECMO. This not only allows those patients to be liberated from the ventilator, but also facilitates caloric intake and mobilization in this very vulnerable patient population.

In sync with the national trends analyzed and published by ELSO, anesthesiologists and critical care physicians will see an increasing number of patients on ECMO. Anesthesiologists generally become involved in the management of these patients during initiation of ECMO, providing anesthetic care, making hemodynamic and respiratory adjustments, and often providing image guidance for cannula placement or assessment of cardiac structures. Subsequently, many of these patients need anesthetic care for other procedures all the way to ECMO de-cannulation, which often requires vascular repair at that time. Knowledge of ECMO principles, technology, and physiologic response can help anesthesiologists to adequately manage these patients, particularly in critical situations, for example acute hemorrhagic complications, weaning from ECMO, or critical limb ischemia. Last but not least, critical care anesthesiologists will also encounter more and more ECMO-supported patients on all types of intensive care units.

In summary, ECMO is a support, not a treatment measure and should be performed in specialized centers only. Despite its increasing use and improving technology, it remains resource-intensive and can cause serious complications. It is however often the only viable option for patients who have failed conventional management and cardiac or pulmonary failure is potentially reversible. Finally, there is a definite need for randomized-controlled trials.

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RCL-02
SOCCA: Perioperative Ultrasound

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Funding related to this topic: Departmental only.

LEARNER OBJECTIVES

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

(1) Identify clinical situations, in a practice like one's own, where diagnostic imaging with ultrasound by an anesthesiologist can provide support in pre-operative risk assessment and anesthetic planning;

(2) Demonstrate how diagnostic imaging with ultrasound by an anesthesiologist can support clinical decision-making and problem-solving for many different common acute perioperative patient problems;

(3) Demonstrate that diagnostic imaging with ultrasound by an anesthesiologist can support clinical decision-making, particularly in the setting of acute perioperative cardiovascular collapse or cardiopulmonary resuscitation; and

(4) Demonstrate how relatively basic ultrasound education, training, and practice, combined with access to both relatively simple, portable as well as advanced, sophisticated ultrasound imaging devices in the perioperative practice setting can be organized and conducted effectively in order to introduce and maintain this diagnostic modality option in clinical perioperative practice.

INTRODUCTION/OVERVIEW

To use ultrasound constructively in one's own perioperative anesthesia practice requires a number of things. One needs some basic understanding of how ultrasound works and how to acquire and save images, images that can be interpreted. One needs access to appropriate ultrasound equipment, and a working familiarity with this equipment. One needs be prepared when confronted with preoperative patient issues such that the anesthesiologist (or a collegue) can produce diagnostic ultrasound imaging as a supplement to the physical examination and preoperative evaluation. Not only looking for possible cardiac findings, but also, for example assessing pre-operative gastric volume. Ultrasound can be used to advantage in facilitating a number of planned procedures, of which vascular cannulation is one example. Ultrasound can be used to establish diagnoses perioperative when unplanned but common patient problems occur, including cardiovascular or respiratory insufficiency or identification of a full urinary bladder is another. Ultrasound can be used to facilitate emergency management, including identifying airway anatomy, sources or regions of bleeding/blood collection, pneumothorax, and heart conditions and activity in a pulseless patient. Implementation of ultrasound as a diagnostic tool in one's perioperative practice requires some investment in learning how to acquire and interpret some images, as well as organizing access to an appropriate ultrasound machine and probe. Finally, ultrasound imaging to facilitate acute or emergent patient management requires a dedicated pair of eyes, and cannot be done reliably by the same person who is managing the patient. This review course lecture is not addressing ultrasound and regional anesthesia.

Why ultrasound?, Structure and motion

In our anesthesia (and intensive care medicine) practices, we manage patient vital functions. Diagnostic ultrasound can help us to examine patients at any point in the perioperative period. It is an extension of the physical examination, and can demonstrate structure and motion (function) which we otherwise cannot directly visualize. With relatively modest investments in education and equipment, anesthesiologists can themselves (with ultrasound) visualize the heart, lung, vessels and flow, body spaces and internal organs.

What is ultrasound? What are some of the common artifacts?

Ultrasound images are based on sound waves which come from the probe and are reflected back from tissue, stationary or moving, and resolved in time and space to one, two, or three dimensional images in approximately realtime. Sound waves are transmitted well by densities where there is a lot of water, and are reflected by air or other dense structures (no penetration of sound waves through air in the body-including air in the pleura). Bits of collagen in tissue produces 'speckles', or high intensity reflections. Common artifacts can include 'drop out' behind impenetrable tissue, or reflections of very solid (reflective) items projected into an area where they are not (for example, a moving catheter). But, artifacts can typically be learned and recognized. Tissue that is moving (blood or other moving organs) can be assessed for velocities. Vessel and chamber sizes can be measured accurately. This allows resolution of flows and flow patterns in the circulation.

Routine Perioperative Diagnostic Questions (Where Ultrasound Might be Used to Advantage)

Together with reviewing available patient records, taking a history, and performing a physical examination, a focused and relatively simple ultrasound assessment can be used to corroborate cardiovascular health or dysfunction. For patients with recent changes in symptoms, such as dyspnea or exercise tolerance, or for whom there is a suggestive physical finding, an ultrasound examination by the anesthesiologist can provide support and motivate further and more detailed pre-operative patient evaluation (other testing or imaging). When very high patient cardiovascular risk is identified in this way, such as previously undetected or accelerating heart failure, there is an opportunity, in the patient's best interest, to revisit and potentially re-evaluate the perioperative management, including possibly the type and extent of surgery, and also post-operative planning.

There are many signs of heart failure that might be seen on echocardiography, related to chamber size, wall motion, and

flows. With simple beside ultrasound, an anesthesiologist can observe a hypocontractile ventricle, a pattern of pulmonary hypertension and right heart overload, pulmonary edema ('comet tails' or B lines with lung ultrasound) or other relevant findings. Obvious heart valve disease can be readily apparent both by examining the structure and motion of valves and chamber sizes, as well as abnormal flows through valves (flow restrictions or valve incompetence).

There may be other aspects of a patient where an anesthesiologist preoperatively may use ultrasound to advantage, potentially to evaluate airway anatomy (front of neck) which may appear otherwise difficult to identify, if concerned about potential for need for a surgical airway. One can scout anatomy for impending vascular access procedures, if it is known that there is a specific challenge for that patient. Even for healthy elective surgical patients, knowing their preoperative gastric content volume is relevant, and this is easily assessed with ultrasound. This review will not address ultrasound use in regional anesthesia.

Planned Procedures (Where Ultrasound Might be Used to Advantage)

Once a patient is anesthetized, confirming endotracheal tube placement is possible with ultrasound, and for cuffed tubes, this can be facilitated by inflating the endotracheal tube cuff with saline. Ultrasound is used commonly to support vascular cannulation, optimally through pre-procedure assessment of the anatomy, and then ultrasound-guided needle and catheter entrance into the vessels, to try to limit complications. Intraoperatively, in anticipation of potential bleeding or other fluid losses, transthoracic or even transesophageal ultrasound can be used to perform serial measures of vessel (inferior vena cava, vena cava superior with TEE,for instance) and chamber sizes and motion. The anesthesiologist can measure cardiac output (cross sectional area of the aortic outflow track and systole velocity integral during allows calculation of ejection flow during systole (stroke volume), and this times the heart rate equals cardiac output). Measured right atrial pressures can be related to observed heart chamber sizes, as well as movement of the interatrial septum can help guide intraoperative fluid management (to help to avoid hypovolemia or hypervolemia). After the surgical procedure, when no urinary bladder catheter has been placed, a quick ultrasound assessment of the amount of urine in the bladder can be performed.

Special Procedures

There are a number of special procedures where ultrasound (among different imaging methods) is crucial for guidance of the procedure itself. In the perioperative, catheterization lab, or interventional suite context, these include trans-vascular valve, or other cardiac or vascular prosthesis placements. These fall within the realm of cardiology, cardiothoracic anesthesia, and radiology, where ultrasound is already used routinely, and will not be addressed in this review lecture.

Urgent Problem-solving

Probably the implementation of ultrasound by the anesthesiologist that can have the greatest impact and patient benefit is for rapid diagnostics when a patient intraoperatively is found to be pulseless. There need to be some rapid determinations to identify the cause and appropriate remedies, all during chest compressions. Correct diagnostic information is vital for emergent problem solving. If the heart chambers are filled with blood, but are not contracting (ventricular fibrillation or asystole), that is useful, possibly confirmatory information. If the heart is unexpectedly 'empty', and there is no readily identified cause (for example, unintended prolonged high airway pressures), unrecognized bleeding might be a cause. Ultrasound images of the heart can be acquired from a subcostal position without interrupting chest compressions. Diagnostic imaging is also collected in the few seconds during "analysing ECG" phases for a semi-automated defibrillator. There should be no pause in chest compressions just for ultrasound imaging. With the traditional surgical FAST examination, large amounts of blood free in the abdomen can be quickly identified with ultrasound. If there is a dilated and hypocontractile right ventricle and normal left ventricular motion, though very underfilled, then acute pulmonary embolism should be considered as a potential cause. Suspicious collections of pericardial fluid, with collapsing right heart chambers, can awaken suspicions of filling restriction or tamponade. These types of general ultrasound cardiac image patterns are important to recognize for a pulseless patient.

Unexplained hypotension can be assessed by quick ultrasound imaging of the heart to identify either underfilled heart chambers or obvious ventricular dysfunction. Ultrasound can be a complement in the hemodynamic assessment. A pneumothorax can be quickly detected in a supine patient where in health one normally sees lung and visceral pleura sliding on parietal pleura with breathing, but when air is in the pleura, sound waves are not transmitted through and beyound. Pleural fluid and atelectatic lung can be detected, where a patient has oxygenation problems. Even pulmonary edema signs can be detected by ultrasound.

If in an emergent "can't intubate can't ventilate" situation, and while moving towards a front of the neck airway, when anatomy is difficult to identify, ultrasound has been used to help locate the cricothyroid membrane. Of course, this should be practiced before-hand in quiet and controlled (simulated) conditions, if one wants to be able to rely on this anatomical localization in an emergency.

It is also necessary to recognize that in an urgent or emergent patient situation, if ultrasound diagnostics are to be used, then the person working to acquire and interpret images will lose their situational awareness for the whole patient and the potentially dynamic patient changes in condition. When urgent ultrasound needs to be used, it should be a different person who maintains overall medical direction for the patient while acquiring images. Calling for help during an intraoperative emergency may mean also calling for a rapid beside ultrasound diagnostic resource.

Practical Solutions, Basic Daily Practice

In order to begin to use ultrasound in one's daily practice, the methods for imaging, and confidence in interpreting images, must be already up and coming. It should be recognized that starting to use a new imaging and diagnostic

method requires some support locally, ideally in the form of a friend/colleague who is very skilled with ultrasound, as a reference person. Images should be archived if possible, though this function may be limited in some of the hand-held ultrasound devices. Early on, one may limit focus to imaging where one can be confident, and then expand the realm of diagnostic interest ambitiously but carefully. It is rewarding to work collaboratively, in order to acquire more ultrasound experience and expertise. One may need to present obvious gains (emergent, live-saving diagnostics, urgent problem solving) to hospital leadership, to support investment in ultrasound equipment which can be made available and stationed close to perioperative patients.

Incorporating bedside ultrasound into one's routine may increase one's workload for learning and also practical workload at the bedside. But, rapid and reliable images, which provide explanations for rapid patient deterioration, are irreplacable. Those who have incorporated ultrasound imaging into their anesthesia and intensive care practice can now not imagine practicing without it.

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RCL-03
Blood Components and Blood Derivatives

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LEARNER OBJECTIVES

- After participating in this activity, the learner will be able to:
  (1) Recall when to order modified blood components such as packed red blood cells (PRBCs) and platelets
  (2) Evaluate the rationale why plasma is no longer indicated for emergent warfarin reversal
  (3) Describe why activated coagulation factor concentrates are necessary to reverse the new oral anticoagulants in the absence of a specific antidote

Blood Products and Their Modifications

For the last several decades, component therapy has replaced allogeneic whole blood for transfusion, with rare exceptions. Routinely used blood components include packed red blood cells (PRBCs), plasma, commonly known as fresh frozen plasma (FFP), cryoprecipitate (CRYO) and platelets (random or apheresis) (Table 1)[1]. While the most common source of PRBCs is from a volunteer whole blood donation that is separated into the various components, blood centers may choose to collect PRBCs by apheresis from specific donors. Independent of the method used, the same provisions listed in the table apply. Plasma is a generic term that encompasses FFP, which is the product frozen within 8 hours from the donation, and PF24, frozen with 24 hours of the phlebotomy. PF24 is the most commonly available plasma product in the United States for approximately 10 years. FFP and PF24 have similar composition and the same indications. When thawed at 30-37 C, FFP and PF24 may be relabeled as thawed plasma to be issued for transfusion within 5 days. CRYO is the concentrate of proteins that precipitate when FFP is thawed at 1-6 C, it is resuspended in saline, and frozen within 1 hour of preparation. The supernatant of the FFP unit used for CRYO preparation is called plasma cryoprecipitate-reduced, and its only use is as replacement fluid during therapeutic plasma exchange for thrombotic thrombocytopenic purpura.

Only PRBCs and platelet products are considered cellular products and may be modified, such as leukoreduced or irradiated. In addition, PRBCs may be washed. Indications for such modifications are in table 2. The designation of blood products as "CMV-negative" also only applies to PRBCs and platelets, and refers to units from donors without prior exposure to the virus as evidenced by negative CMV serology. Nowadays, leukoreduction has almost completely replaced the need for CMV-negative units since CMV is harbored by leukocytes, which are significantly (up to 99.99%) removed by leukofiltration (especially when performed pre-storage at the blood collection facility). Jehovah's witness patients do not accept any blood product, but may accept blood derivatives such as albumin and plasma-derived coagulation factor concentrates such as the prothrombin complex concentrate (PCC) described below for emergent reversal of warfarin anticoagulation. In addition, they are likely to accept coagulation factors prepared by recombinant technology such as factors VIII and IX concentrates for the treatment of hemophilia A or B, or recombinant factor VIIa. Several other alternatives to blood components for patients with severe anemia are available and discussed elsewhere in the literature[2].

Reversal of Oral Anticoagulants in Emergencies

Warfarin

As the oldest anticoagulant in clinical use (approximately 60 years), warfarin continues to save lives through its antithrombotic properties, but pose risks of bleeding due to its unpredictable dose-response[3,4]. Furthermore, when faced with a hemorrhaging patient on warfarin or someone anticoagulated that must have an emergent surgical procedure, reversal of its effect needs to be quick and reliable. The American College of Chest Physicians (ACCP) has changed its recommendation regarding management of these patients thanks to the availability of a 4-factor PCC approved by the FDA in April of 2013 (KCentra®)[5]. Unlike previously available 3-factor PCCs, KCentra® has all 4 procoagulant factors II (prothrombin), VII, IX and X, and also the natural anticoagulants protein C and protein S. The multicenter randomized, prospective, controlled phase IIIb trial used to approve KCentra® by the FDA, enrolled 212 patients to compare the new product with plasma (plus vitamin K in both arms) for urgent warfarin reversal for acute bleeding[6]. KCentra® yielded hemostatic efficacy as measured by adequacy of stopping a major bleed assessed at 24 hours from the start of infusion 72.4% of the time compared with 65.4% with plasma. However, while 62.2% of patients receiving KCentra® experienced INR reduction to ≤1.3 at 30 minutes post-infusion, only 9.6% of those receiving plasma did. The effect of KCentra® was achieved with 87% lower volume (105 mL +/-37 mL versus 865 mL +/- 269 mL) that was 7-times faster than the time needed to transfused the several units of plasma (24 minutes versus nearly 3 hours). Thus, 4-factor PCC is the standard of care in the emergent reversal of warfarin anticoagulation.

Direct oral Anticoagulants (DOACs)

Since the end of 2010 when dabigatran (Pradaxa®) was approved, there have been 3 other new drugs introduced in the United States market, all extensively studied and with excellent safety profile: rivaroxaban (Xarelto®; 2011), apixaban (Eliquis®, 2012) and edoxaban (Savaysa®, 2015)[3,7]. Although warfarin is still the most commonly prescribed, the number of patients receiving one of the DOACs is steadily increasing. Despite their increased cost, all have improved reliability and do not require routine laboratory monitoring, highly sought qualities for a drug[8]. For perioperative physicians, several recommendations have been published regarding the management of patients on one of the DOACs

in preparation for a surgical procedure[9,10]. The European Society of Anaesthesiology and the French Working Group on Perioperative Haemostasis (GIHP) recommend their discontinuation approximately 2-3 half-lives prior to procedures with anticipated low risk of bleeding, and 5 days from one with medium or high bleeding risk. In addition, it is important to consider the specific drug the patient is taking, as well as his/her renal function. In the recent review by Levy, the reader can learn more about this subject.

For reversal of DOACs, refer to table 3 for information on the mechanism of action of each drug, the role of laboratory tests and suggested reversal strategies. Considering that the DOACs "block" or "inhibit" clotting instead of causing factor deficiencies as warfarin does, their reversal must take this fact into account. For this reason, plasma transfusion is ineffective to overcome the inhibition by any of the DOACs and should never be used. Only dabigatran, however, has a specific antidote, a monoclonal antibody (idarucizumab) that binds to the drug and prevents it from binding to thrombin. For the other 3 DOACs, all direct factor Xa inhibitors, the practice remains variable and includes PCCs as well as the activated PCC FEIBA®, which contains a high concentration of activated factor VIIa and smaller amounts of activated factors II, IX and X. The only current approved indication of FEIBA® is management of bleeding due to hemophilia in patients with inhibitors, or those with a rare autoimmune condition called acquired hemophilia.

In the last 6 years, physicians have had to become familiar with several new anticoagulants that may pose challenges in the perioperative period. It is essential to understand their benefits and risks, and to manage them effectively when reversal is necessary.

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Table 1: Blood Components Summary

Blood Component	Special Precaution Regarding ABO and Rh	Storage and Shelf-life	Composition	Usual Dose
PRBCs	Must be ABO-compatible; Rh negative to Rh negative patients to prevent anti-D formation or when anti-D detected in antibody screen	1-6 C for 42 days in additive solution (AS-1, AS-3, AS-5); 1-6 C for 35 days in CPDA-1; if washed, expires in 24 hours; if irradiated, expires in 28 days	Red blood cells with hematocrit ~55% (in AS) or ~80% in CPDA-1	One unit at a time unless ongoing bleeding to increase hemoglobin by 1 g/dL
Plasma, thawed	Must be ABO-compatible; Rh not important	2-6 C for 5 days (frozen kept at -18 C for 12 months)	All coagulation factors at 1 unit/mL; mostly water	10-15 mL/Kg of body weight to increase factor levels by 10-15%
CRYO	May not have to be ABO-compatible; Rh not important	Room temperature for 4-6 hours (frozen kept at -18 C for 12 months)	Fibrinogen (150-250 mg/single unit), Factor XIII, von Willebrand factor, Factor VIII, fibronectin	10 single units or 2 pooled units for adult with hypofibrinogenemia
Platelets	May be ABO-incompatible (preferably low titer anti-A or anti-B); Rh identical to prevent anti-D; if anti-D detected in antibody screen, safe to give Rh positive unit	20-14 C with continuous gentle agitation for 5 days; irradiation does not change expiration date	5.5 x 1010 platelets per random unit (from whole blood); 3.0 x 1011 platelets per apheresis unit	4-6 random units or 1 apheresis unit to increase platelet count by 30,000-50,000/microliter

Table 2: Reasons and Indications for Modifications of Packed Red Blood Cells or Platelets

Modification and why to order it	Who should receive it
Leukoreduction (LR): Decreases risk of febrile reactions, HLA alloimmunization, and CMV transmission (LR-products considered CMV-safe) by decreasing white blood cells to <5 x 106 cells/unit	Varies by institution; many use "universal leukoreduction" of all PRBC and platelet inventory; common indications include: 1. Intrauterine and neonatal transfusions; 2. Chronically transfused patients such as those with sickle cell disease or bone marrow failure such as during chemotherapy or myelodysplastic syndrome; 3. Immunosuppressed patients such as those with lung transplants in whom CMV-infection may be severe
Irradiation: Inactivates donor lymphocytes to avoid TA-GVHD with gamma or x ray irradiation of the unit	1.Fetuses receiving intrauterine transfusions; 2. Premature or low birth weight newborns and those with HDFN; 3. Patients with congenital immunodeficiencies, especially of T cells (such as DiGeorge syndrome); 4. Patients with hematologic malignancies or solid tumors or who have received fludarabine; 5. Peripheral blood stem cell/marrow transplant recipients; 6. Products from first-degree relatives; 7. Crossmatched or HLA-matched platelets; 8. Granulocyte components (rarely used)
Washing: Reduces plasma proteins such as IgA, anti-A or anti-B, or potential allergens to avoid allergic or anaphylactic reactions	1. Patients with previous severe allergic (i.e. anaphylactic) or repeated transfusion reactions to PRBCs; 2. IgA-deficient patients; 3. Neonates with renal failure and hyperkalemia

Abbreviations: CMV- cytomegalovirus; TA-GVHD - transfusion-associated graft-versus-host disease

Table 3: Recommended Reversal Strategies for Oral Anticoagulants (in order of approval by FDA)

Drug name/Half-life	Mechanism of action and laboratory test(s)	Reversal comments
Warfarin (Coumadin)	Vitamin K-antagonist: causes deficiencies of prothrombin (II), Factors VII, IX and X, and proteins C and S - Prolongs PT causing high INR	Must replace low factors; plasma too diluted; for emergent reversal (major/life-threatening bleeding or prior to major surgery), give 10 mg of vitamin K by slow IV injection (mixed in minimum 50 mL and given over at a rate not exceeding 1 mg/minute and 4-factor prothrombin complex concentrate (PCC; KCentra®); dose dependent on INR and urgency of reversal: for emergent reversal: INR 2-<4: 25 units/Kg (maximum 2500 units) INR 4-6: 35 units/Kg (maximum 2500 units) INR >6: 50 units/Kg (maximum 2500 units)
Dabigatran (Pradaxa®) (elimination half-life: 12-17 hours; significantly longer in patients with decreased renal function – 80% excreted by the kidneys)	Direct thrombin inhibitor (DTI) – Thrombin Time very sensitive (prolonged) when dabigatran in circulation (not quantitative); PT and PTT not useful	If ingested in last 1-2 hours, consider activated charcoal; for emergent reversal, order the monoclonal antibody idarucizumab (Praxbind®) specific for dabigatran, 5 g IV once (2 x 2.5 g vials); for refractory bleeding, consider hemodialysis or a second dose of idarucizumab
Rivaroxaban (Xarelto®) (elimination half-life: Healthy: 5-9 hours; elderly: 11-13 hours; longer in patients with decreased renal function - 67% renal elimination)	Direct Xa inhibitors – Anti-Xa test useful to confirm drug in plasma (not quantitative); PT and PTT not useful because the drug effect is quite variable on the different assays used in hospital laboratories (i.e., the same patient's blood sample may yield a normal and an abnormal result if tested in 2 laboratories using different methodologies and reagents	No specific inhibitor such as that available for dabigatran (see above); reversal peptide being evaluated by FDA but not yet approved; no evidence-based guidelines for reversal in emergencies; consider activated prothrombin complex concentrate (aPCC or FEIBA®) at 50 units/Kg (used in author's institution); others use PCC (KCentra®) at 50 units/Kg; activated charcoal may be useful to inactivate apixaban if ingested in last 2-6 hours
Apixaban (Eliquis®) (elimination half-life: 12 hours, range from 7 to 15); longer in patients with decreased renal function - 33% renal elimination)		
Edoxaban (Savaysa®) (elimination half-life: 10-14 hours); higher in patients with decreased renal function – 50% renal elimination)		

Abbreviations: PTT – Partial thromboplastin time; PT – Prothrombin time;

RCL-04
How to Decide if Neuraxial Anesthesia is Safe in the Face of Possible Hematologic Contraindications?

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This lecture will provide an overview of the current data on potential hematologic contraindications to obstetric neuraxial anesthesia. A brief introduction of these topics and some related references are included below.

The goal is to enable the anesthesiologist to:

(1) Appraise the relative risks and benefits of neuraxial analgesia and anesthesia in obstetric patients with thrombocytopenia;
(2) Propose a rational plan for anesthetic management;
(3) Relate the impact of the new VTE thromboprophylaxis BUNDLE guidelines to the anesthetic management of obstetric patients,
(4) Apply existing tools to make decisions regarding neuraxial anesthesia in these patients;
(5) Evaluate Factor FXI, von Willebrand, and other factor deficiencies in obstetric patients and the impact on the candidacy for neuraxial analgesia or anesthesia;
(6) Differentiate between the available hematologic testing devices and test results (e.g. thromboelastography, ROTEM, fibtem; aPTT, anti-Xa levels) to identify appropriate clinical applications when evaluating the risk of epidural hematoma in obstetric patients.

INTRODUCTION

Although the consequences can be devastating, spinal epidural hematoma (SEH) associated with obstetric neuraxial blockade is a rare event with an incidence of 1:200,000-250,000[1] compared to the incidence in the general surgical population (e.g. 1: 3,600 in elderly females undergoing orthopedic surgery).[2,3] The hypercoagulability of pregnancy and associated increase in platelet aggregation, fibrinogen, and coagulation factors including factors II, VII, VIII, IX, X, XII, vWF, coupled with a compliant epidural space contribute to this favorable outcome. When abnormalities of the hematopoietic system do occur, the obstetric anesthesiologist must decide whether or not it is safe to proceed with neuraxial anesthesia. Knowledge of the primary hematologic disorder, the relevant pregnancy-related physiological perturbations, and the available published data allows the clinician to make informed decisions.

Thrombocytopenia

Thrombocytopenia in pregnancy is defined as a platelet count of less than 150 x 109/L.[4,5] Gestational thrombocytopenia, which accounts for approximately 70-80% of the pregnancy-associated cases, is typically a benign disorder with platelet numbers > 70 x 109/L.[4] Platelet function is usually preserved and therapy is rarely needed.[6] Idiopathic thrombocytopenia purpura (ITP) accounts for approximately 5% of thrombocytopenia cases, and has an autoimmune etiology.[6] Although platelet function is generally excellent, platelet numbers in ITP in pregnancy have been reported to be as low as 2 x 10^9/L). Therapies to enhance platelet production include corticosteroids, or intravenous gamma globulin (IVIg). Thrombocytopenia can also be associated with the hypertensive disorders of pregnancy, particularly severe preeclampsia, and HELLP syndrome. These disorders feature not only a decline in platelet numbers but also a decrement in platelet function of unclear etiology.

Historically, hematologic societies have suggested that >80 x 109/L is a safe platelet count at which to place or remove an epidural catheter in an otherwise healthy patient with ITP. Anesthesia societies have refrained from endorsing specific recommendations. Recently, investigators have combined their institutional cases with the published cases of neuraxial anesthesia in obstetric patients with thrombocytopenia to yield SEH risk estimates. With no cases of SEH, at a platelet count of ≥75 x 10^9/L, the calculated 95% confidence intervals were 0-0.6%.[7,8]

VTE Thromboprophylaxis

In the face of the growing U.S. incidence of VTE in obstetric patients, recent initiatives have expanded the thromboprophylaxis recommendations for pregnant and newly postpartum women.[9] Key components include "adjusted dosing" by weight [(for low molecular weight heparin (LMWH)] and by trimester [(for unfractionated heparin (UFH)]. It is reassuring that a recent systematic review of published cases between 1952-2016 and the Anesthesia Closed Claims Database (1990-2013) found no cases of obstetric SEH in the setting of thromboprophylaxis and neuraxial anesthesia.[10] Quantitative interpretation of these findings is limited, however, by lack of data on the total number of obstetric neuraxial procedures (the denominator) and data on cases with higher doses of UFH.

The newly updated American Society of Regional Anesthesia (ASRA) guidelines now suggest waiting 4-6 hours after a low dose (5000U) of subcutaneous UFH, before undertaking a neuraxial procedure (or withdrawing an epidural catheter).[1] For obstetric anesthesiologists, these simultaneous events have the potential to make balancing the relative risks and benefits of neuraxial versus general anesthesia increasingly complex.

In response, a multidisciplinary taskforce with SOAP, ASRA, and hematologic experts have collaborated to synthesize the available recommendations, and provide a tool-kit of clinically relevant tactics and decision aids.

These tools, and the corresponding background data, will be presented in the lecture.

Factor Deficiencies

For risk related to neuraxial anesthesia, factor deficiencies can be grouped into 3 categories: 1) disorders in which the factor levels increase in pregnancy (e.g. Type 1 von Willebrand's disease)[11] 2) disorders where the factor levels decrease but may be responsive to factor replacement (e.g., FXIII deficiency)[12-14] and 3) disorders where functional factor deficiencies may pose an increase risk of SEH with neuraxial anesthesia irrespective of therapy (e.g. type 3 von Willebrand's disease).

Factor XI deficiency, which can pose a high risk of bleeding in both the mother and the fetus, can be particularly challenging, as the factor levels do not necessarily correlate with bleeding risk.[15,16]. Although, factor XI deficiency is not necessarily an absolute contraindication to neuraxial anesthesia,[16] there is no consensus as to what constitutes a safe factor level for neuraxial anesthesia.

During the lecture, a clinically relevant approach to stratifying patients with factor deficiencies, based on perceived risk of SEH, will be discussed.

Assessing the Risk of Spinal Epidural Hematoma-Laboratory Tests

There is currently no standardized test to assess the risk of SEH with neuraxial anesthesia. Current practice guidelines suggest monitoring the aPTT, particularly when patients are on high dose anticoagulants, to assess adequate coagulation prior to neuraxial anesthesia.[17] However, aPTT levels are attenuated in term pregnancy.[18] Whereas anti-factor Xa assays may be more reflective of the anticoagulant effect of LMWH or UFH, the test is typically not readily available. In addition, unless the levels are undetectable, it is unclear how to apply the anti-factor Xa assay to decisions about the safety of neuraxial anesthesia. For some of the more common factor deficiencies, such as von Willebrand's disease, there is consensus around safe factor levels for neuraxial anesthesia. For many other bleeding disorders, this consensus does not exist.

Some investigators have used thromboelastometry (ROTEM) or thromboelastography (TEG) to assess the maternal coagulation profile in obstetric patients receiving anticoagulants or factor replacement therapy.[11,19] These point-of-care test results have the advantage of being available in less time than standard laboratory tests of coagulation. Several studies report reference range TEG values for pregnant patients.[20,21] Of the measured variables, the r time appears to have the best correlation with heparin anti-factor Xa activity in vivo in the presence of anticoagulants.[22] In vitro investigations reveal that TEG r times are very sensitive in the setting of anticoagulants and pregnancy.[23,24] However, safe ranges for TEG r times for performing neuraxial block in pregnant or newly postpartum women with thromboprophylaxis have not been established.

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RCL-05
Regional Anesthesia in Improving Outcomes

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Since the discovery of cocaine medical practitioners have recognized the profound benefits that regional anesthesia can provide for patient care. Significant benefits including pain relief[1] together with a reduction in other adverse effects have led to a dedicated use of regional techniques in many centres around the world over the last 100 years[2].

In recent decades many studies of the highest quality have demonstrated the perioperative benefits of regional anesthesia on improved pain control (both acute and chronic), reduction in nausea and vomiting, improved mobility and improved organ function[3].

Recent years have seen the development of methods to further increase efficacy and safety of regional anesthesia and an increased variety of peripheral nerve and infiltration techniques that give a "dizzying" array of possibilities for use in practice. Traditional methods such as the supraclavicular brachial plexus block have seen a resurgence in popularity thanks to the use of ultrasound and newer infiltration methods such as the tranversalis plane (TAP) block and PEC techniques are in high demand in many regional anesthesia workshops across the world.

At the same time justification for the use of regional techniques is becoming increasingly demanding. Minimally invasive surgical techniques and local infiltration methods have vastly improved pain control and early mobility without the need for separate regional anesthesia methods. In addition, public and private health care systems are carefully refining techniques to justify the value of existing and new interventions.

The Institute for Healthcare Improvement (IHI) introduced their Triple Aim of improved population health, patient experience and lower per capita cost in 2008 and since that time this framework has been used as an integral component in a number of health systems around the world including systems in the United States, United Kingdom and Canada to guide advances in care[4]. Surgical populations are a major target for improving value in healthcare because surgically treatable diseases are responsible for approximately 33% of deaths, 28% of disability-adjusted loss in life-years and 23% of years lived with disability[5]. Regional anesthesia techniques have major potential for having a positive impact on triple aim outcomes and this paper (and associated lecture) will summarize the following:

1. Why regional anesthesia has positive benefits on triple aim outcomes?
2. Identify those populations who have most to benefit from regional anesthesia according to the triple aim.
3. Draw conclusions to guide current practice and future research regarding best practice.

Why regional anesthesia has positive benefits on triple aim outcomes?

Regional anesthesia has always demonstrated profound benefits both on pain relief and reduction in need for other systemic analgesic drugs. Patients greatly value good postoperative pain control[6] but the reduction in other systemic drugs also reduces nausea, bowel ileus and dizziness. This in turn can improve postoperative mobility and improve sleep. Although better pain control and reduced side effects would seem to be of sufficient benefit in isolation improved early pain control has been shown in selected populations to also reduce length of stay and chronic pain after surgery[7,8]. Recent data from large patient populations indicates that regional anesthesia can also reduce major morbidity and mortality compared to those patients who have general anesthesia[9]. Patients value good quality pain control and reduce of associated adverse effects and this impact on patient experience should not be undervalued[10].

Mechanisms of improvement in patient outcomes remain unclear but several physiological mechanisms may explain why regional anesthesia has these effects. Reductions in sympathetic drive, decreased surgical stress response and improved cardiovascular responses including reduced myocardial afterload reduce risk of adverse cardiovascular events. Greater pain control facilitates ability to breathe and cough and reduces incidence of respiratory complications. Better pain control may improve sleep and facilitate early rehabilitation.

Table:
Potential Impact of Regional Anesthesia Techniques on the IHI Triple Aim

Early Outcomes	Intermediate Outcomes	Triple Aim Outcomes
Decreased Pain	Decreased LOS	Improved Population Health
Decreased PONV	Decreased readmission	Better Patient Experience
Improved Mobility	Decreased complications	Lower Cost
Improved Organ Function		

Who are the populations with most to benefit from regional anesthesia?

Many proponents could make an argument for the use of local anesthetic techniques in all surgical procedures. However rational use of regional anesthesia is important to balance the cost and time that these procedures necessitate to provide high quality care. Surgical infiltration should be used in even the most minor of surgical cases and regional anesthesia has demonstrated benefits on early pain control, avoidance of side effects and discharge in many ambulatory surgical procedures[11]. Recent evidence from large databases indicate that patients having major orthopedic surgery have significantly reduced incidence of major morbidity and mortality with the use of neuraxial techniques and peripheral

nerve blocks[9,12]. Use of peripheral nerve blocks can also have major impact on morbidity. Perhaps the most surprising aspect is that the use of neuraxial techniques remains disappointingly low in many areas of the world including the United States[13].

Conversely, the use of regional anesthesia techniques in major thoracic and abdominal surgery lacks high quality evidence with regard to triple aim outcomes[14]. In particular, emergency surgery has not been well examined. Further evidence identifying the benefit of regional anesthesia on the triple aim in these populations is necessary before further guidance can be given. The use of newer infiltration methods such as the transversalis plane block and PECS methods require further evaluation before they can replace existing methods such as epidural and paravertebral techniques.

CONCLUSIONS AND FUTURE DIRECTIONS

Regional anesthesia remains a powerful technique for improving early pain control and reducing adverse effects after many types of ambulatory and inpatient surgery. Rational use of regional techniques is important to justify the extra time and expense that is often necessary to provide high quality care. However, for many types of orthopedic and general/pelvic surgery these improvements can be provided in an organized environment. Recent evidence indicates that use of neuraxial techniques and peripheral nerve blocks can have more profound effects on population health after orthopedic surgery especially in older populations. The use of regional anesthesia should be carefully organized to facilitate use in these populations.

In the future, pragmatic randomized trials examining large numbers of patients will provide further data to examine recent evidence from large databases[15]. Patients should have more input on the types of questions being asked in order to provide answers to questions relevant to patient concerns. Finally, the use of qualitative methods to further examine important areas of the triple aim especially around patient experience may be of benefit.

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RCL-06
U.S. Anesthesia Workforce and Group Practice Trends: Data Sources and Research Questions

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BACKGROUND AND OBJECTIVES

At the end of 1966, more than 50 years ago, there were 7,011 physician anesthesiologists in practice in the United States (U.S.); just over half (52.6%) were board certified.1 In 1969, there were an estimated 10,500 professionally active nurse anesthetists and expectations of a long-term severe shortage of anesthesiologists.[1-2] However, some experts questioned how real the shortage might be and whether it could be avoided if current (in 1969) anesthesia professionals were better organized and more effective in meeting their productivity potential.[3] One of the first articles focusing on the U.S. anesthesia workforce was published in 1970 – a time when there were 200 residencies with 1500 residents, with half of the anesthesiology residents from non-US medical schools.[4]

Over the past 50 years, the growth and changes in the medical workforce have been substantial and often surprising to the "experts" who have attempted to predict future workforce needs, expected supply and the implications for education and practice. Predictions of shortages and surpluses have come and gone over time, focusing on both primary care and specialists.[5] In its February 2017 update, the Association of American Colleges (AAMC) projected a total physician shortfall of between 40,800 and 104,900 physicians by 2030; the shortfall for non-primary care specialties is projected to be between 33,500 and 61,800, and AAMC projected a shortfall of surgeons of between 19,800 and 29,000.[6] The majority of the AAMC report text described the complexities of physician supply and demand projections; it is a valuable reference for those researchers interested in studying workforce projections.

There are several data sources and supporting resources available for researchers interested in better understanding the medical workforce, and specifically interested in the demand for, and supply of, physician anesthesiologists, nurse anesthetists and anesthesiologist assistants. However, given the inherent differences among the data sources and the continuing changes in physician practice settings, care delivery models and organizational relationships, there is probably only one statement we can make with confidence: "Every number reported is, in some way, incorrect!"

There have been many assessments of the adequacy of the number of anesthesiologists and predictions for the specialty have varied in recent years.[7-13] The topic of workforce supply and demand is no doubt critical to any specialty; however, it is just one area of important research within the anesthesia workforce space; this Review Course Lecture discusses several other related research topics.

The learning objectives of this Review Course Lecture include to: (1) Identify sources for U.S. anesthesia workforce data and highlight their potential and limitations; (2) Separate popular declarations and myths from evidence-based trends concerning the anesthesia workforce, including group practice characteristics and geographic distribution of anesthesia professionals; and (3) Develop a short list of anesthesia workforce-related research questions to review or undertake.

Workforce Data Resources

There are several sources for workforce-related information, including:

- Accreditation Council for Graduate Medical Education (ACGME) Data Resource Book http://bit.ly/2oPl5AP
- American Medical Association (AMA) http://bit.ly/2oVbpDe, http://bit.ly/2ovzpuY
- Association of American Medical Colleges (AAMC), http://bit.ly/2oV56jd
- Centers for Medicare and Medicaid Services http://go.cms.gov/2p0fkRp, http://bit.ly/2p0hyjw
- Marketing firms and other vendors
  For example, SK&A http://bit.ly/2p0hznJ
- National Plan & Provider Enumeration System/ National Provider Identifier (NPPES/NPI) http://go.cms.gov/2pWJiCX
- National Resident Matching Program (NRMP) Match Data http://bit.ly/2pIbkFT
- Physician Compare National Downloadable File http://bit.ly/2pWWVCf
- U.S. Bureau of Labor Statistics http://bit.ly/2ora3PQ

In addition to the above organizations that provide relevant workforce data, there are several health workforce centers located in universities across the US. These centers provide data and additional workforce research support services. Selected centers include:

- Center for Health Workforce Studies at the State University of New York at Albany (SUNY), School of Public Health
- Center of Excellence in Public Health Workforce Studies at the University of Michigan
- George Washington University Health Workforce Institute
- Health Research, Inc. at Center for Health Workforce Studies at the State University of New York at Albany
- Midwest Center for Health Workforce Studies at UIC Institute for Health Research and Policy
- Program on Health Workforce Research and Policy at University of North Carolina at Chapel Hill

Table 1. Number of U.S. anesthesia professionals reported from various data sources

Data Source	Physicial Anesthesiologists	Nurse Anesthetists	Anesthesiologist Assistants
NPPES National NPI Dataset[1]	49,745	52,350	2197
AMA Master File[2]	46,253	n/a	n/a
AMA Master File[3]	52,545	n/a	n/a
Physician Compare National File[4]	37,661	39,186	1727
Physician Compare National File[5]	39,832	41,930	1843
Bureau of Labor Statistics[6]	29,220	39,410	n/a

[1]Based on listed primary specialty in the mid-month March 2017 National NPI Dataset.
[2]Physicians with a primary specialty of anesthesiology. The file contains another 10,494 physicians missing NPIs.
[3]Includes anesthesiology subspecialties (e.g., pediatrics, pain medicine, critical care, obstetrics). The file contains another 10,950 physicians missing NPIs.
[4]Physician Compare National Downloadable File, March 16, 2017.
[5]Combined Physician Compare files for March 16, 2017 and March 17, 2016.
[6]Estimates do NOT include self-employed workers. http://www.bls.gov/oes

NOTE: Calculations by the ASA Center for Anesthesia Workforce Studies based on the above data sources.

- Regional Center for Health Workforce Studies at UT Health Science Center at San Antonio
- University of California at San Francisco Health Workforce Research center on Long-term Care
- University of Washington Center for Health Workforce Studies

How Many Anesthesia Professionals Are There?

Given the plethora of workforce data sources and resource centers, it seems it should be relatively easy to estimate the number of anesthesia professionals in the U.S. However, differences in the sources of the raw data, the definitions used, and the amount of primary data collection and data "cleaning" conducted all result in substantial differences in the estimates of anesthesia workforce supply.

Table 1 presents anesthesia workforce estimates from four sources; the variation in reported workforce size is substantial. Researchers should understand several key aspects of the workforce data to be used in any analysis:

- What is the specific origin of the data; (e.g., claims data, self-reported, or another source)?
- What are the available data items (variables) and their definitions (e.g., age, specialty, address)?
- Is level/type of activity included (e.g., research, teaching, patient care; full-time or part-time; retired or inactive)?
- Are residents and medical students included?
- What geographic data are included (e.g., U.S. territories)?
- How are the specialties defined? How many specialties can be listed for each physician?

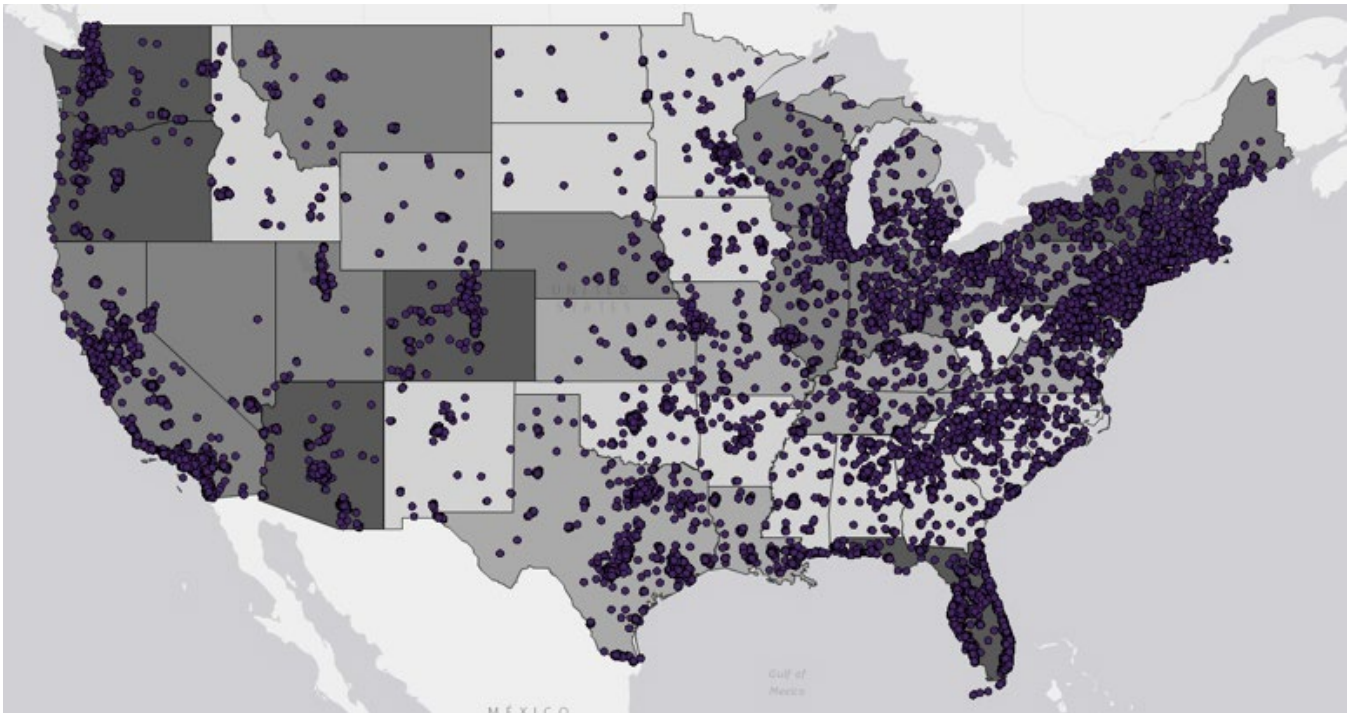

Figure 1. Geographic distribution of physician anesthesiologists in the continental U.S. Source notes: From the AMA Health Workforce Mapper based on the AMA Physician Masterfile 2013; Centers for Medicare and Medicaid Services' National Plan and Provider Enumeration System 2013; and U.S. Census county and states shapefiles 2010. Created by The Robert Graham Center for the ©American Medical Association. (https://www.ama-assn.org/about-us/health-workforce-mapper)

For the data sources reported in Table 1, there are several important differences. Information in the national NPI dataset it typically input and updated by the provider. There is no indication as to the date of the most recent update for the provider's information. The provider's type and level of activity (e.g., research, teaching, patient care, full-time or part-time) are not provided. These data are commonly used in research.[14]

The AMA Master File data exclude non-physicians. The specialty and subspecialty designations are based on self-report. The total count of physician anesthesiologists in the AMA Master File, including those without NPIs, exceeds 63,000. It is likely that this estimate substantially overstates the actual number of physician anesthesiologists for several reasons.

The Physician Compare files include only those providers that have submitted a Medicare claim in the previous 12 months or have recently joined the Medicare roll as a provider. Pediatric anesthesiologists and other anesthesia professionals that do not accept Medicare are probably understated in these data.[15]

Finally, the Bureau of Labor Statistics (BLS) estimates do not include "self-employed workers." Therefore, the number of physician anesthesiologists reported by the BLS is substantially understated.

The above examples illustrate some of the more important differences; there are several others of which researchers should be aware.

In addition to the number of anesthesia professionals, their geographic distribution is of research interest and of interest to policy makers. Figure 1 presents the distribution of physician anesthesiologists in the U.S. In general, the distribution reflects the U.S. population distribution. Other important workforce data include compensation, productivity, organizational relationships and employment models..

Anesthesia-Related Group Practice Trends

Most physician anesthesiologists have seen the headlines or know first-hand about the acquisitions and growth in the physician group practice market; anesthesiology is one of the most active specialties in this arena. Haverford Healthcare Advisors identified 37 anesthesia-related group practice acquisitions in 2016.[16] The number of anesthesia practice acquisitions has increased each year since 2009, and the most acquisitions occurred in Florida, New Jersey, Texas and New York. The largest of the anesthesia-related group practice companies has more than 3,000 anesthesia providers.

Even a topic as seemingly well-defined as "anesthesia-related physician group practices" engenders complexities for the researcher. What minimum number of members constitutes a "group"? Is the measure based on all physicians,

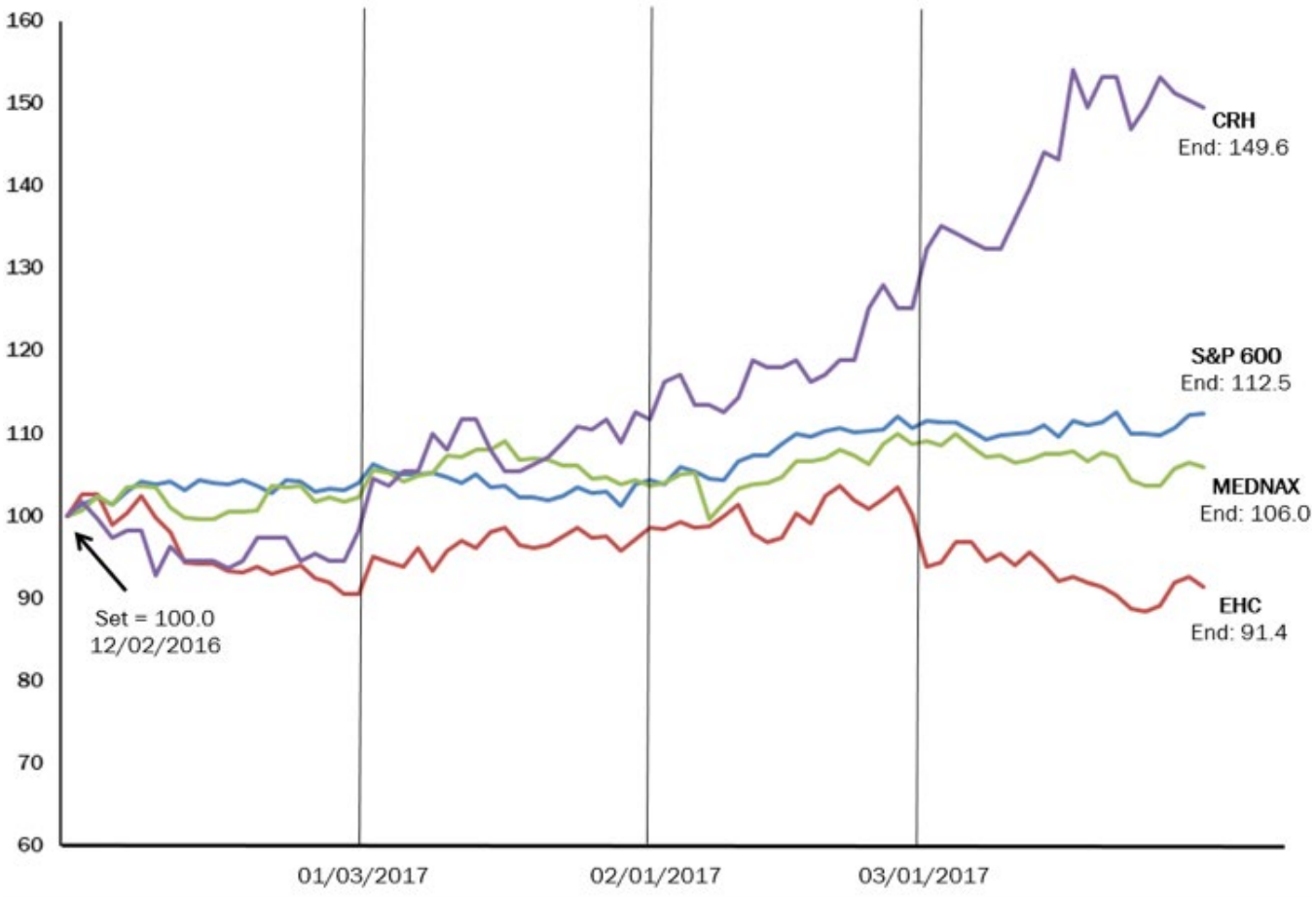

Figure 3. Relative changes in stock prices, 12/2/2016 – 3/28/2017 for Envision Healthcare, Inc. (EHC), MEDNAX Health Solutions Partner (MEDNAX), CRH Anesthesia (CRH), and the S&P 600 Health Care Index Sector (S&P 600). Calculations and graph by ASA's Center for Anesthesia Workforce Studies based on data from Yahoo Finance (https://finance.yahoo.com).

physician anesthesiologists, or all anesthesia professionals? What makes a large group practice large? Is it the total number of employed physicians, the number of all anesthesia professionals, the practice setting, the number of anesthetizing facilities served, the number of different states in which it operates? Should academic-based groups be considered differently from private or publicly-traded groups?

As of March 2017, only three publicly-traded group practice companies, in which anesthesia represents a substantial portion of the business, remain. Figure 3 presents the relative changes in the stock prices of these corporations along with the change in the S&P 600 Health Care Index Sector (S&P 600) between December 2, 2016 and March 28, 2017. EHC represents Envision Healthcare, Inc. and is the combined entities of AmSurg, Sheridan, and EmCare. MEDNAX includes Peidatrix Medical Group, American Anesthesiology, MedData, Surgical Directions, and VRad. CRH is a Canadian-based company focused on providing physicians with products and services for the treatment of gastrointestinal (GI) diseases, primarily in the U.S. CRH's first anesthesia acquisition was in the fourth quarter of 2014. By the end of 2016, CRH Anesthesia Management provided anesthesia services in 18 GI-focused ASCs, using a team of more than 50 nurse anesthetists under the supervision of an anesthesiologist medical director.

Potential Research Questions

There are numerous opportunities for workforce-related research, fueled by anesthesia group practice trends, scope of practice regulations, and the evolution of payment and patient care delivery models. Potential research questions relevant to anesthesiologists and policymakers include:

- How many physician anesthesiologists, nurse anesthetists and anesthesiologist assistants are there in the U.S.? How has the changed over time?
- What is the geographic distribution of the anesthesia workforce and how has it changed over time? What are the implications for health policy?[17]
- What is the demographic profile of the anesthesia workforce and how has it changed over time? What are the implications of an aging workforce[18] and of a more diverse workforce?
- What are the trends in organizational and employment models among anesthesia professionals?
- What will be the demand for anesthesia services and professionals over the next 10 years? What are the implications of a shortage or surplus on educational need? What are the economic implications?
- What impact does the continued growth in anesthesia-related group practices have on the groups negotiating positions vis-à-vis payers and hospitals?[19]
- How much do changes in the supply of surgical and other specialties requiring anesthesia services have on the demand for anesthesia professionals?
- What impact do size and composition of anesthesia-related group practices have on quality of care?
- What are the future educational capacity needs for anesthesia and the implications for financing training programs?[20]

CONCLUSION

Anesthesia workforce data, projections of supply and demand, and related research are important to the specialty of anesthesiology. An understanding of anesthesia workforce trends and complexities is essential to inform health policy at the local, state and national levels. Workforce data are imperfect but improving; understanding the differences and definitions among the various information sources is a critical first step in any workforce-related research. Research gaps are substantial and more research efforts are needed to help define and describe the various characteristics of the workforce and to address critical health policy questions.

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RCL-07
Extubation of Patients Outside of the Operating Room

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Many studies focus on risk factors for respiratory failure and intubation during the post-operative period,[1,2] but few provide information on the frequency of continued mechanical ventilation following surgery,[3] or the location (i.e. post-anesthesia care unit (PACU) versus an intensive care unit (ICU)). For patients admitted to US ICUs, approximately 20% are surgical and are admitted from operating rooms or PACUs, although many of these patients may be admitted without the need for mechanical ventilation.[4] One study of Medicare patients found that approximately 4% of patients undergoing high risk surgical procedures required mechanical ventilation for >96 hours,[3] but the overall rates of post-operative mechanical ventilation are unknown.

Whether care for these patients is provided solely in a PACU or in an ICU, patients requiring postoperative mechanical ventilation are routinely assessed for readiness for extubation. A spontaneous breathing trial is advocated as an appropriate test prior to extubation for all patients to ensure adequate respiratory function.[5,6] There is debate in clinical practice and the literature regarding the "best" way to assess patients.[7] Standard approaches to assessment for readiness for extubation include a trial of pressure support ventilation, with a range of pressure support (0-10 cm H_20) and a range of positive end expiratory pressure (PEEP) of 0-5 cm H_20, or a T-piece trial. Within the category of pressure support ventilation trials, the exact settings are debated, with some advocating for zero peep and zero pressure support (as an approximation of a T-piece trial) while others feel that a slightly higher level of both is appropriate and provides support to "overcome" the resistance of the endotracheal tube.[8]

Martin Tobin in an editorial in 2012 advocated for a T-piece trial for all intubated patients to ensure the lowest likelihood of failure of extubation.[9] However, few studies have focused attention on the post-surgical population and it is important to note that the attitude and approach of different intensivists may be colored by the case-mix of the patients they care for; for example, short-term ventilation of the post-operative surgical patient is associated with a lower risk of reintubation than medical ICU patients.10 In particular, in recent work we assessed the rates of reintubation in 185 US ICUs. We found that the cumulative probability for reintubation for elective surgical patients was 5.9% versus 10.1% in emergency surgery patients and 10.7% in medical patients.10 Admission to ICU from the OR/PACU was associated with a lower rate of reintubation (odds ratio 0.82, 95% CI 0.73-0.92) versus admission from the emergency room, and trauma patients had a higher rate of reintubation (odds ratio 1.59, 95% CI 1.46-1.74) versus patients with a respiratory or thoracic diagnosis. The different risk for elective surgical patients is an important distinction that is often lost in these discussions.

One of the biggest challenges of determining when to extubate a patient who has required mechanical ventilation and appears ready is whether to extubate overnight or wait until the morning. Two studies have addressed this topic to date. The first by Tischenkel et al was a retrospective cohort study using data from 2 hospitals within a single tertiary academic medical center.[11] Of 2,240 patients extubated, 30.6% were extubated at night. They found a lower rate of reintubation within 24 hours for patients extubated at night and a shorter ICU length of stay. However, it is notable that 81.8% of patients extubated at night were cardiac surgery patients. Thus, it is difficult to draw any conclusions regarding care of other critically ill patient populations.

In a more recent study, we examined patients in 165 US ICUs in the Project IMPACT database.[12] Using a definition of overnight extubation of 7 p.m. to 7 a.m. we determined that 20.1% of patients were extubated overnight. We also found that there were very different patterns of extubation timing for patients intubated for <12 hours. Therefore, we split the cohort into patients intubated for greater than, or less than 12 hours. We created a propensity score for the likelihood of overnight extubation and matched individual patients who did or did not get extubated overnight. We found that patients intubated for <12 hours had reintubation rates that were similar to patients extubated in the daytime, but mortality was slightly increased (5.6% at night versus 4.6% during the day; P=0.03), while patients intubated >12 hours had an increase in reintubation rate in the ICU (14.6% versus 12.4%, P<0.001) and substantially higher hospital mortality (16.0% versus 11.1%, P<0.001). The cohort excluded patients who had a tracheostomy or had changes in goals of care (such as a do-not-resuscitate order placed) prior to extubation, but could not account for the possibility of unplanned extubations. It is notable that elective and emergent surgical patients had a similar increased mortality as medical patients if mechanically ventilated for >12 hours.

In summary, extubation of patients during the post-operative period is an everyday occurrence, both in PACUs and ICUs worldwide. Few studies specifically focus on this population, with limited information regarding approaches to extubation. Recent data suggest a lower risk of reintubation among elective surgical patients; therefore, less stringent criteria for spontaneous breathing trials for extubation may be appropriate. For patients requiring mechanical ventilation for longer than 12 hours, it may be prudent to plan for extubation during daytime hours, although more studies are needed to assess risk across the different surgical populations.

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RCL-08
Therapeutic Hypothermia and Neuroprotection

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Hypothermia therapy is mentioned 5000 years ago in ancient Egyptian writings and Hippocrates advised the use of snow and packed ice to reduce hemorrhage in the wounded. Russians have applied hypothermia therapeutically since 1803 by covering the individuals with snow in an attempt to resuscitate them. Baron Dominique Jean Larrey, Napoleon's chief surgeon during the 1812 campaign, packed limbs in ice prior to amputations to induce analgesia. In 1940, Temple Fay, MD, described the successful recovery of a patient with metastatic disease who underwent hypothermia (32.20 C) for 18 hours by surface cooling under anesthesia.[1-3] Therapeutic hypothermia can be defined as mild (330 C -360 C), modest (320C -340C), and moderate (280C -320C) hypothermia.

Therapeutic hypothermia is different from accidental hypothermia. Therapeutic hypothermia preserves adenosine triphosphate stores and induction of poikilothermia. By contrast, accidental hypothermia induces a stress response, shivering, and depletion of energy stores.[4]

The aim of this review is to present the most recent evidence-based advances in the use of therapeutic hypothermia as a neuroprotective agent.

Mechanisms of Neuroprotection by Hypothermia

Improvements in Metabolism

Hypothermia reduces the cerebral metabolic rate of oxygen (CMRO2) by approximately 5% per degree Celsius. Thus, in severe traumatic brain injury (TBI) patients, a one–degree reduction in temperature leads to a 5.9% reduction in energy.[5] Hypothermia also preserves high–energy phosphate compounds like adenosine triphosphate (ATP) and maintains tissue pH. Therefore, hypothermia preserves the brain's metabolic stores and prevents development of metabolic acidosis and accumulation of lactic acid. During ischemia, blood flow is reduced; however, during the reperfusion period there is an overflow of blood (hyperemia), which is followed by a gradual decline over a period of time. Hypothermia blunts the immediate hyperemia and prevents the gradual reduction in cerebral blood flow that follows.[6]

Hypothermia and Cell Survival

The effect of hypothermia on the production of heat shock protein (HSP70) during ischemia is controversial. Hypothermia may increase HSP70 and therefore would contribute to its neuroprotection. However, other studies have shown no effect, and some have shown a reduction in HSP70 levels during ischemic periods.[7-10]

MicroRNAs (miRNAs), a subset of non-coding RNAs, were first described in 1993. They play a very important role in silencing messenger RNAs (mRNAs), and so are considered one of the main regulators for the mRNA coding process. The use of hypothermia (330 C) in the model of TBI was found to affect the levels of miRNAs, which increased after injury. Importantly, hypothermia reduced the levels of miRNA-874 when compared to normothermia. The upregulation of miRNA-874 is responsible for decreased production of several key proteins involved in normal cellular function and

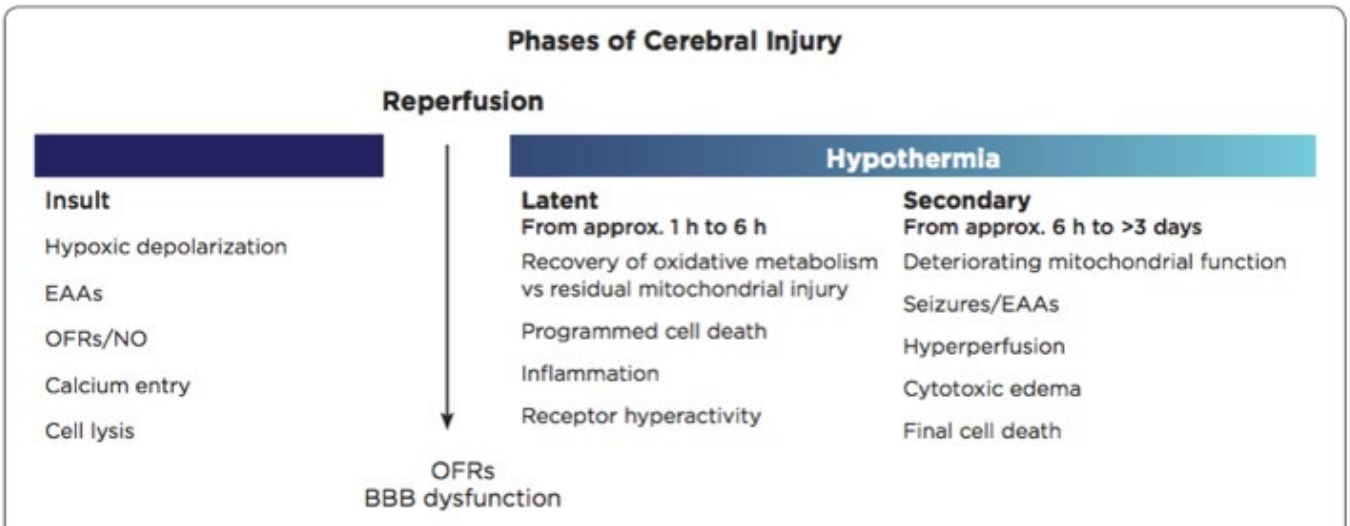

Figure 1. Schematic diagram illustrating the different pathological phases of cerebral injury after severe hypoxic-ischemia.

BBB, blood-brain barrier; **EAAs**, excitatory amino acids; **NO**, nitric oxide; **OFRs**, oxygen-free radicals

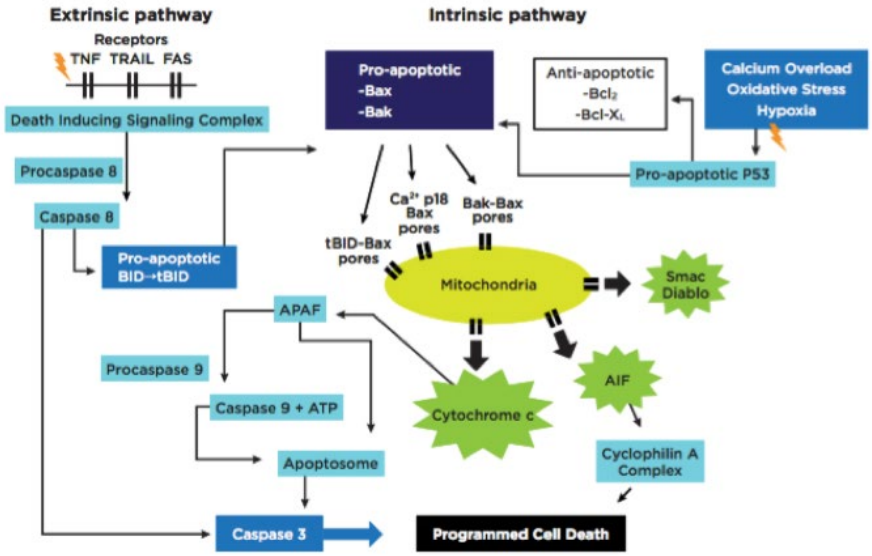

Figure 2. Flow chart depicting several intracellular mechanisms associated with permeabilization of the mitochondrial membranes, leading to progressive failure of mitochondrial oxidative phosphorylation and ultimately delayed programmed cell death.

Upstream triggers such as inflammation and trophic withdrawal activate cell surface death receptors initiating the "extrinsic" pathway to programmed cell death. Conversely, calcium overload and oxygen-free radicals appear to exert their effect predominantly at the mitochondrial level via the "intrinsic" pathway. In addition, crossover activation between the "extrinsic" and "intrinsic" pathway may take place through pro-apoptotic intermediates such as the BID protein.

AIF, apoptosis inducing factor; **Apaf-1**, apoptotic protease-activating factor-1; **ATP**, adenosine triphosphate; **BAK**, Bcl_2-antagonist/killer 1; **BAX,** Bcl_2-associated X protein; **Bcl_2**, B-cell lymphoma 2 protein family; **Bcl-X_L**, B-cell lymphoma-extra-large; **BID**, BH3 interacting-domain death agonist; **Diablo**, direct inhibitor of apoptosis binding protein with low Pi; **P53**, p53 tumor suppressor protein; **Smac**, Second mitochondria-derived activator of caspase; **tBID**, truncated BH3 interacting-domain death agonist; **TNF**, tumor necrosis factor receptor; **TRAIL**, TNF-related apoptosis-inducing ligand receptor

(Based on Wassink et al. *Frontiers in Neuroscience*. 2014;8:40.)

enhances vulnerability to TBI. Therefore, hypothermia might exert a neuroprotective effect by reducing the level of this miRNA.[11]

Hypothermia affects the intrinsic and external pathways of apoptotic cell death. The intrinsic pathway is originated mainly at the mitochondria, while the extrinsic one is triggered at the level of cell surface receptors. Ischemia activates the intrinsic pathway by translocating cytosolic pro-apoptotic Bcl-2 family members, such as Bcl-2 associated X (BAX) protein, to the mitochondria, where it oligomerizes with Bcl-2 to create non-specific protein pores in the outer mitochondria membrane, thereby leaking the pro-apoptotic proteins and cytochrome c into the cytosol. The loss of cytochrome c reduces the mitochondrial coupling of oxidative phosphorylation.

Moreover, the increased permeability of the mitochondrial membrane causes the release of apoptogenic factors including second mitochondria–derived activator of caspase (Smac). The direct inhibition of apoptosis-binding protein with low Pi (Diablo) and apoptosis-inducing factor (AIF) from the mitochondrial intermembrane space could induce irreversible cell death (Figure 1-2).[12-14]

After the release, cytosolic cytochrome c binds to apoptotic protease–activating factor-1 (Apaf-1) and activates caspase-9 to stimulate the final executioner caspase-3, which leads to DNA fragmentation and apoptosis. Hypothermia reduces caspase-3 activation, cytochrome-c release and BAX, whereas it increases the anti-apoptotic member Bcl-2. Hypothermia was shown to reduce the mitochondrial membrane permeability in a swine model of cardiac arrest, which might provide neuroprotection against cerebral injury.[15] Moreover, hypothermia blocks the translocation of the pro-apoptotic protein kinase C δ (PKCδ) to the mitochondria and the nucleus, and stimulates the action of anti-apoptotic factor protein kinase C ε (PKCε).6,14 The extrinsic pathway is mainly activated by the tumor necrosis factor (TNF) superfamily of cytokines, such as TNF-α, Fas ligand (FasL) and the Fas receptor system. The stimulation of this system induces apoptosis by activating caspase-8. Hypothermia reduces the availability of FasL levels and thereby the activation of caspase-8, which occurs downstream of the extrinsic pathway.[16] Phosphatase and tensin homologue (PTEN) is a tumor suppressor molecule with pro-apoptotic functions. Hypothermia deactivates PTEN and induces neuroprotection.[6]

Hypothermia and Survival Pathways

Hypothermia increases the levels of brain-derived neurotrophic factor (BDNF), glial–derived neurotrophic factor (GDNF) and neurotrophin in the brain. Moreover, hypothermia increases extracellular signal–regulated kinase (ERK) phosphorylation, a downstream element of BDNF signaling. However, the pharmacologic inhibition of ERK by U0126, a highly selective inhibitor of the kinase enzyme MEK, failed to prevent the benefit of hypothermia.[6,17] Hypothermia promotes the activation of AKT, a serine/threonine protein kinase that inactivates pro-apoptotic proteins such as glycogen synthase 3β (GSK 3β) and the Bcl-2 antagonist of cell death (BAD).

Hypothermia and Inflammation

Brain injury leads to induction of the inflammatory process with increased release of cytokines and interleukins (IL). The increased inflammatory process enhances microglia activation, leukocyte diapedesis into the ischemic brain, and the production of reactive oxygen species (ROS). The increase in cytokine-mediated inducible nitric oxide synthetase (iNOS) expression and NO levels, which compete with O_2 at its binding site on cytochrome oxidase, result in reduction of ATP levels.

Hypothermia reduces IL-1 β, TNF-α, and IL-6. However, hypothermia reduces anti-inflammatory agents, such as IL-10 and transforming growth factor-β (TGF β). Therefore, hypothermia does not have a solely anti-inflammatory effect.

Hypothermia also affects the mitogen–activated protein kinase (MAPK) pathway, an important pathway that stimulates inflammation in a cell-mediated manner. Hypothermia inhibits the p38 pathway (one of the MAPK family), which is responsible for apoptosis and endothelial dysfunction.[18]

Hypothermia suppresses the activation of nuclear factor-κβ (NF-κβ), the major transcription factor for activating inflammatory–related genes. Hypothermia prevents nuclear NF-κβ translocation and DNA binding by inhibiting the activity of inhibitor of NF-κβ kinase (IKK). IKK is responsible for the phosphorylation and degradation of NF-κβ inhibitor (Iκβ). Of note, NF-κβ also regulates genes involved in cell survival and growth. Therefore, inhibition of NF-κβ by hypothermia might have contradictory effects.

Hypothermia and Excitotoxicity

Excitotoxicity is an important contributor to cell damage during ischemia. Excitatory amino acids (EAA), such as glutamate and aspartate, are significantly elevated in different types of brain injuries and are associated with secondary brain injuries.

The accumulation of glutamate enhances the calcium influx through α-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) and glutamate receptor-2 (GluR2), a sub-unit of the AMPA receptor that limits calcium influx. The increased intracellular calcium concentration activates calcium-dependent protease calpain, which further enhances the apoptotic process. Hypothermia limits calcium influx through AMPA and preserves GluR2 mRNA expression.[19] Mild hypothermia inhibits the activity of calpain II and thereby reduces its degenerative effect on the cytoskeleton.[5]

Moreover, mild hypothermia can reduce the level of glutamate by enhancing its uptake.[20] Mild hypothermia increases the level of inhibitory amino acid gamma-aminobutyric acid (GABA), thereby counteracting the injurious effects by EAA.[21] In addition, hypothermia enhances the restoration of Ca2+/calmodulin–dependent protein kinase II-mediated cell signaling.[21]

Hypothermia and Nitric Oxide

Nitric oxide (NO) plays a role in the development of post-ischemic cerebral edema. Mild hypothermia reduces the activity of neuronal nitric oxide synthetase (nNOS) and the NO level, thereby reducing cerebral edema and secondary brain injury.[22] During cerebral ischemia, elevated levels of glutamate increases NO and its metabolites (nitrite and nitrate). Mild hypothermia not only inhibits this process but also inhibits iNOS as well. The inhibition of iNOS by hypothermia probably results in part from its inhibitory effect on NF-κβ.[5]

Hypothermia and Blood–Brain Barrier Integrity

The blood–brain barrier (BBB) is the target of damaging effects of several agents such as ROS, cytokines, and proteases, especially matrix metalloproteinases (MMPs), during ischemia. Hypothermia reduces MMP activity and increases the expression of endogenous MMP inhibitors, such as tissue inhibitor of metalloproteinase 2 (TIMP2). Mild hypothermia reduces brain edema formation by suppressing aquaporin-4 expressions in models of intracerebral hemorrhage and cardiac arrest. Of note, aquaporin-4 is the main water channel protein in the CNS microvasculature, and its expression is increased in cerebral ischemic lesions.[23,24]

Hypothermia and its Effects on Gliogenesis and Angiogenesis

Mild hypothermia promotes progenitor cell differentiation towards neurogenesis over gliogenesis and protects against progenitor cell death. However, hypothermia of less than 300 C suppresses cell proliferation. Therefore, mild hypothermia has a protective effect on progenitor cell differentiation and prevents their apoptosis, while deep hypothermia has deleterious effects on them.

The effect of mild hypothermia on angiogenesis and neurologic outcomes is very controversial. Mild hypothermia has been shown to enhance angiogenesis. However, some studies have shown enhanced angiogenesis has a harmful effect on brain repair. This fact might explain unfavorable outcomes in recent trials following the use of mild hypothermia for TBI.

Physiological Effects of Hypothermia

Cardiovascular Effects

Hypothermia is associated with an average reduced heart rate of 40-45 beats/min at 320 C. Reduced heart rate with hypothermia enhances left ventricular filling, and thereby compensates for hypothermia-associated reduction of cardiac contractility and cardiac output. Cardiac output decreases by ~7% for every 10 C drop in core temperature.[25] Therefore, augmentation of heart rate during hypothermia is not recommended, as it will increase the cardiac oxygen consumption and arrhythmia as well as impair contractility. Adults may experience atrial fibrillation at temperatures < 320 C and ventricular fibrillation at temperatures <300 C. However, such arrhythmias have not been described in neonates who have been transiently overcooled to <300 C.

Mean arterial pressure (MAP) is increased during hypothermia due to increased peripheral vascular resistance from hypothermia-induced peripheral vasoconstriction. The increase in venous return from peripheral vasoconstriction leads to atrial natriuretic peptide (ANP) activation and reduces the secretion of antidiuretic hormone and, therefore, cold diuresis. With prolonged hypothermia, a decrease in intravascular volume may occur from cold diuresis and the fluid shifts resulting from the shedding effect of ANP on endothelial glycocalyx. This may result in hypotension and hemoconcentration.[3,26]

Pulmonary Effects and Infectious Complications

The incidence of adult respiratory distress syndrome (ARDS) is nearly 50% in intubated patients with neurological injuries treated with hypothermia compared to normothermic patients.[27] The reduced incidence of ARDS in hypothermic patients most probably results from the reduction in metabolic rate, oxygen consumption, and CO_2 during hypothermia. Moreover, the reduction in $PaCO_2$ (the partial pressure of carbon dioxide in arterial blood) is still present following rewarming, as is an increase in the PaO_2-FiO_2 (fraction of inspired oxygen) ratio.[28]

Hypothermia may increase pulmonary vascular resistance and therefore may worsen oxygenation in newborn infants with perinatal asphyxia who are at high risk for persistent pulmonary hypertension.

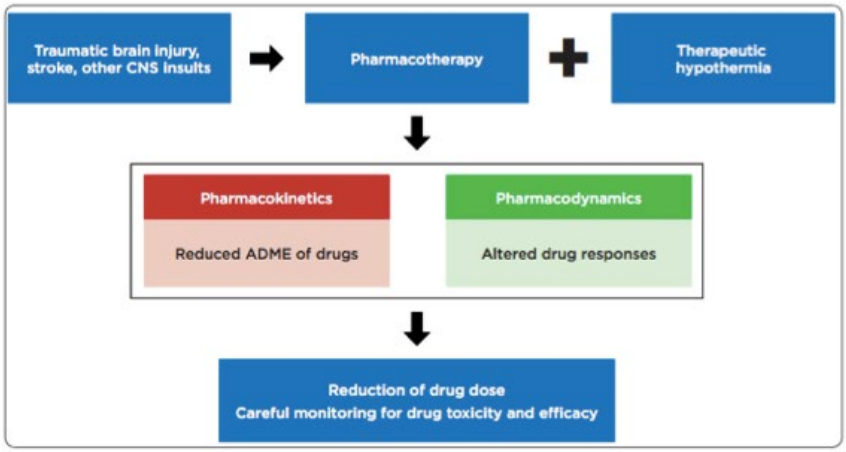

Figure 3. Effects of therapeutic hypothermia on pharmacokinetic and pharmacodynamic parameters.

Upon traumatic brain injury, stroke, and other brain insults, patients may receive pharmacotherapy as well as hypothermic treatment, which may influence the kinetic as well as dynamic parameters of pharmacotherapy. Patients should be carefully monitored to avoid drug toxicity and treatment failure. (Based on Han et al. *Current Neuropharmacology*. 2012;10[1]:80-87.)
ADME, absorption, distribution, metabolism and elimination

Hypothermia does not increase the incidence of pneumonia. However, it may increase the risk for wound infections.[3]

Coagulation System Effects

Hypothermia can induce mild coagulopathy. At 330 C the platelet function and number as well as the synthesis and kinetics of clotting enzymes are reduced. In addition, there is significant prolongation of activated thromboplastin time (aPTT) at lower temperatures. Hypothermia is associated with a reduction in fibrinolytic system activity, which could increase the risk for thrombus formation.

Renal, Endocrine and Gastrointestinal Effects and Drug Metabolism

Hypothermia induces hypomagnesemia and hypokalemia. The magnesium depletion in particular can worsen neurologic injury. Hypothermia induces hyperglycemia via increasing insulin resistance, gluconeogenesis and glycogenolysis. Of note, hyperglycemia has been associated with worse neurologic outcomes, increased infectious rates and higher incidence of renal failure. Therefore, it is very important to monitor and correct hyperglycemia while avoiding hypoglycemia, which also has serious adverse effects on the injured brain.

Hypothermia may induce ileus and delayed gastric emptying. Moreover, hypothermia reduces drug clearance in commonly used medications such as opiates, sedatives, volatile anesthetics, vasopressors and neuromuscular agents. Care should therefore be taken in dosing these medications in patients treated with hypothermia.[3,29,30] (Figure-3)

Hypothermia as Neuroprotective Agent in Clinical Practice

Ischemic Stroke

Hypothermia was shown to be a very effective neuroprotective agent in animal studies of ischemic stroke, with a 44% reduction in infarct size and a robust improvement in functional outcome.[31] The problem in translating those animal studies to clinical practice was that the hypothermia was induced very early, either prior to the stroke or within less than 3 hours after the stroke, which may not be feasible in clinical practice.

The first Cooling for Acute Ischemic Brain Damage (COOLAID) study was a controlled study of 19 patients with middle cerebral artery occlusion; ten were cooled to target moderate hypothermia (320 C) with a surface-cooling blanket in combination with intravenous or intra-arterial thrombolysis. All patients were intubated and mechanically ventilated, and shivering was controlled with neuromuscular blockade.[32] No statistical difference in mortality or complications were observed between hypothermic and non-hypothermic patients. However, neurologic outcomes were only slightly better in the hypothermic group. The extended time to induce hypothermia from stroke onset (6.2 hours) and to reach the target temperature (3.5 hours) could explain the lack of therapeutic effect from hypothermia in this trial.[32]

The COOL AID II study randomized 40 acute stroke patients to either standard therapy or hypothermia to a target temperature of 330 C, and used an endovascular heat-exchange catheter through the inferior vena cava for 24 h.[33] This study achieved faster target temperatures (an average of just 77 minutes) than the previous one. Moreover, no mechanical intubation or neuromuscular blockade was used in this trial. Complications from the endovascular cooling device included deep venous thrombosis and a case of retroperitoneal hematoma. Clinical outcomes measured by the National Institutes of Health Stroke Scale (NIHSS) score showed no difference in both groups. Nevertheless, the infarct volume measured by diffusion-weighted imaging (DWI) was lower in the hypothermic group (73%) versus the non-hypothermic group (124%).[33]

ICTuS-L (Intravenous Thrombolysis Plus Hypothermia for Acute Treatment of Ischemic Stroke) was a randomized feasibility study of endovascular cooling and intravenous tissue plasminogen activator in awake patients treated within 6 hours of ischemic stroke. Eighteen patients were treated at a target temperature of 330 C for either 12 h or 24 h with an endovascular heat exchange catheter. The anti-shivering regimen used in this trial was either a conservative regimen involving surface warming and low-dose meperidine or a proactive regimen that added prophylactic buspirone and meperidine. NIHSS clinical outcomes were similar in both groups at 30 days and 3 months. Of note, more effective cooling was achieved using the proactive anti-shivering regimen.[34]

Selective antegrade cerebral perfusion (ACP) is employed via the right axillary artery, which allows for hypothermic cooling of the brain while avoiding such hypothermic side

effects as shivering. Moderate hypothermia induced by ACP during aortic arch surgery was associated with lower mortality and fewer neurologic complications than deep hypothermia.[35]

The combination of caffeine and ethanol infusion (caffeinol) has been shown to be neuroprotective. Caffeinol combined with hypothermia was therefore tried on stroke patients.[35]

Those trials highlighted important clinical insights into the use of hypothermia in ischemic stroke. Patients can tolerate temperatures up to 330 C without neuromuscular blockade and mechanical ventilation. Endovascular cooling techniques are faster than surface cooling to reach targeted temperatures, but represent more technical challenges. Hypothermia is usually tolerated for 12 h to 24 h, but longer periods of hypothermia are associated with more adverse events.[23,36]

Neonatal Hypoxic–Ischemic Brain Injury and Hypoxic–Ischemic Encephalopathy

Perinatal hypoxic ischemic brain injury (HIBI) stems from a variety of etiologies that include acute perinatal asphyxia, brain hemorrhage, stroke, birth trauma and congenital brain abnormalities. HIBI produces hypoxic–ischemic encephalopathy (HIE) in neonates and preterm infants. HIE is a major cause of global child mortality and morbidity (e.g., cerebral palsy, mental retardation, epilepsy) occurring in an estimated 2.5 of every 1000 term births in developed countries, with a ten-fold higher incidence of 26 per 1000 term births in the developing world.[37,38] Brain injury following hypoxic ischemia (HI) has provided the opportunity to use hypothermia to reduce or even arrest secondary brain injury.

The Cool-Cap trial used selective head cooling with mild systemic hypothermia for treatment of perinatal asphyxia. The trial enrolled 234 infants with moderate to severe neonatal encephalopathy and abnormal amplitude integrated electroencephalography; 116 patients were cooled to a rectal temperature of 340 -350 C for 72 h within 5.5 h of birth versus 118 infants treated with conventional care.[39] The neurological outcomes were not different between the two groups at 18-months follow-up. Nonetheless, the post-hoc analysis after controlling for baseline clinical severity has shown improvement in outcomes.

In a multicenter trial of 208 infants with perinatal asphyxia, which used cooling blankets to reach a target temperature, 102 infants were assigned to be cooled to esophageal temperature of 33.50 C within 6 h of birth for 72 h, with slow rewarming, and 106 infants were assigned to a control group.[40] Follow–up assessment occurred between 18 and 22 months of age, and revealed adverse outcomes (i.e., death or disability) that were significantly reduced in the hypothermic group of patients rather than the control group (44% vs. 62%; risk ratio, 0.72; 95% CI, 0.54 to 0.95; P=0.01).

Moreover, those patients were evaluated up at 6-7 years of age. Of the 208 trial participants, primary outcomes were available for 190 participants. Of the 97 children in the hypothermic group and 93 children in the control group, death or IQ score below 70 occurred in 46 (47%) and 58 (62%) of children, respectively (P=0.06); death occurred in 27 (28%) and 41 (44%; P=0.04); death or severe disability occurred in 38 (41%) and 53 (60%) (P=0.03).[41] Thus the rate of the combined end point of death or IQ score of less than 70 at 6-7 years of age was lower among children undergoing whole-body hypothermia than those undergoing conventional care, but the differences were not found to be significant.

The Whole Body Hypothermia for the Treatment of Perinatal Asphyxial Encephalopathy (TOBY) trial enrolled 325 infants with moderate to severe asphyxia. The target temperature was 330-340 C for 72 h using gel packs in 163 patients versus 162 in the control group. The infants in the cooled group had increased rates of survival without neurologic sequelae at 18-month follow up (relative risk, 1.57: 95% CI, 1.16 - 2.12; P=0.03).[42] In addition, the incidence of cerebral palsy was less among survivors in the hypothermic group.

Shah et al have shown in their meta-analysis a significant reduction in the risk for death or moderate to severe neurodevelopmental disability in a hypothermic (n=249) infant group compared to a control (n=284) group (relative risk, 0.76; 95% CI, 0.65-0.88).[43] Cardiac arrhythmias and thrombocytopenia were common with hypothermia; however, they were clinically benign.

Hypothermia and Traumatic Brain Injury

Hypothermia has been used very successfully in the preclinical setting for TBI models in both animals and humans in isolated trials.[44-46] However, the outcome from using hypothermia for TBI over multicenter trials has been either negative or even harmful. Hutchison et al studied the effect of hypothermia in pediatric patients after TBI.[47] The study randomized 108 patients to the hypothermia (330 C) group and 117 to the normothermia group. The use of hypothermia proved to be harmful, as the mortality rate was 21% in the hypothermic group and 12% in the normothermia group (P=0.06). However, the study was criticized for its short cooling period of only 24 hours and fairly rapid rewarming.[48]

In the Cool Kids trial the patients (younger than 18 years) were randomized to either hypothermia (rapidly cooled to 32-330 C for 48-72 h, then rewarmed by 0.5-1.00 C every 12-24 h) or normothermia (maintained at 36.5-37.50 C). The Cool Kids trial was stopped early for futility as there was no difference between the two groups in either mortality at 3 months, secondary global function outcomes using Glasgow outcome scale (GOS), the pediatrics version of the GOS-extended revision, or the occurrence of serious adverse events.[47] A recent meta-analysis of the efficacy of using therapeutic hypothermia in children with TBI showed no benefit. However, the authors concluded that further large-scale, well-designed, randomized controlled trials on this topic are needed.

There have been three noteworthy multicenter studies of therapeutic hypothermia in adults with TBI: the National Acute Brain Injury Study: Hypothermia I (NABIS:H-I), the NABIS:H-II, and the Japanese Brain Hypothermia (B-HYPO) trial.[44-51] These studies either found no difference or worse mortality rates in the hypothermia group compared to the normothermia group.[49-51]

The European Study of Therapeutic Hypothermia study, an international, multicenter, randomized controlled trial, examined the effect of titrated therapeutic hypothermia (32-350 C) on ICP and neurologic outcome. The study, which enrolled 387 patients at 47 centers in 18 countries, failed to

prove any benefit for using hypothermia in TBI patients, and indeed outcomes may be worsened.[52] However, patients in the hypothermia group had better control of ICP since they required fewer stage-three interventions (e.g., barbiturates, decompressive craniotomy). There were some limitations to the study. First, the assessment of complications during the trial might have been biased, since the investigators were not blinded. Second, the rate of adherence, defined as more than 80% of core temperature measurements within range in four days was lower in both groups (64.8% in the hypothermia group vs 68.8% in the control group). Third, the enrollment included patients with TBI resulting from a variety of causes and there was no subgroup analysis, such as patients with subdural hematomas.

NABISH-II has shown the benefit of therapeutic hypothermia in a selective group of patients. For instance, early hypothermia improved outcomes in patients undergoing surgical decompression surgery for focal insults, but early cooling did not improve outcomes in patients with diffuse brain injury.[1,4] Moreover, the combined vasoconstrictive effects of barbiturates and hypothermia resulted in reduced cerebral blood flow. The subsequent reduction in cerebral blood flow might have worsened cerebral ischemia. Thus, although these measures could reduce ICP, they did not result in beneficial outcomes.[48]

Maintenance of normocapnia is important since excessive hypocapnia can increase ischemia in injured brain tissue, and excessive hypercapnia can increase brain edema.[53] In addition, a slow rewarming rate should be guided not only by the ICP but also by brain injury biomarkers and brain chemistry.[54] Two ongoing studies—the Prophylactic Hypothermia Trial to Lessen Brain Injury (POLAR-RCT) and the Long-Term Mild Hypothermia For Severe Traumatic Brain Injury (LTH-1) trial—may provide valuable data for the use of therapeutic hypothermia in TBI patients.[55,56]

Until the results of ongoing trials are published, maintaining normothermia and avoiding hyperthermia should be advised in managing patients with TBI. However, therapeutic hypothermia can be reserved as a final option in patients with refractory increased ICP.[57]

Hypothermia and Cardiac Arrest

In 2002, two landmark randomized controlled trials showed that induction of mild hypothermia for 12 or 24 hours increased survival and improved neurologic outcomes for a select group of patients who had experienced out-of-hospital cardiac arrest (OHCA).[57,58] Subsequently, therapeutic hypothermia after cardiac arrest was implemented as standard care for unconscious survivors of OHCA by international guidelines.[59] However, the two trials were criticized for including patients with only shockable rhythms.

A recently published targeted temperature management (TTM) trial questioned whether induced hypothermia or avoidance of hyperthermia actually benefitted patients after cardiac arrest.[60] The TTM trial found that cooling to 330 C after witnessed cardiac arrest conferred no benefits compared with maintaining a temperature of 360 C. The TTM authors concluded that benefits of temperature management result mainly from fever control and that further lowering of core temperature provides no benefit.60 However, the study had some limitations, such as late-start cooling (up to 4 hours after the return of spontaneous circulation), slow cooling rates (up to 10 hours to target temperature), and rapid rewarming rates.[61] Recent meta-analysis confirmed the TTM results that support avoiding hyperthermia rather than inducing hypothermia following OHCA.[62] Rittenberger and Clifton, in their editorial, rightly insist that "we should not regress to a pre-2002 style of care that does not manage temperature at all".[63]

Hypothermia and Spinal Cord Injury

Spinal cord injury (SCI) is a catastrophic health problem around the world. In the United States, it is estimated that 12,000 to 20,000 new SCIs occur each year, and currently over 200,000 Americans are living with disability due to SCI.[64]

Therapeutic hypothermia is the only available method for preventing secondary neural damage combined with surgery after SCI. Therapeutic hypothermia applied either locally via epidural catheter or systemically in animal models of SCI reduced neural cell apoptosis as measured by transferase-mediated deoxyuridine triphosphate nick-end labeling (TUNEL), lipid oxidation measured by malone dialdehyde (MDA) and reduced monomeric glutathione-peroxidase (GSH-peroxidase), spinal cord edema and motor function recovery.[65-67]

Moreover, therapeutic hypothermia enhances the neural stem cell (NSC) differentiation into a glial lineage after SCI by attenuating secondary mechanisms and thereby improving the microenvironment for NSC differentiation and functional recovery.[2,68] The clinical experience in humans for use of hypothermia in SCI management dates back to the 1970s and 1980s. The therapeutic hypothermia was mainly applied locally by irrigating the exposed spinal cord or dura with ice-cold (4-50C) saline after laminectomy.

These early studies had small sample numbers, lacked randomization and control groups, and did not reach sufficient statistical power to justify widespread use of hypothermia. Recently, the use of endovascular cooling for inducing modest hypothermia (330 C) after SCI has been shown to be potentially therapeutic. In 2007, modest hypothermia using endovascular cooling to 33.50 C gained public attention after its use in a professional case with cervical SCI. The patient exhibited significant neurologic recovery within two hours of endovascular cooling and additional improvement over the weeks following his injury.[69]

This case was followed by a randomized trial through the Miami Project to Cure Paralysis (University of Miami). The trial employed modest hypothermia (330 C) with endovascular cooling within 8 hours of SCI, which was continued for 48 hours, with a slow rewarming rate of 0.10 C/h. In total, 6 of 14 patients (42.8%) demonstrated some improvement from American Spinal Injury Association (ASIA) grade A (complete motor and complete sensory impairment) to another grade at 12-months follow-up. Three patients improved to grade B (complete motor and incomplete sensory impairment), 2 to grade C (some muscle movement below level of injury), and 1 to grade D (incomplete motor impairment with intact sensation), exceeding the baseline expectations of spontaneous recovery after complete cervical

SCI, as reported elsewhere.[2,70] The American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS) joint section on disorders of the spine and peripheral nerve in November 2013 considered systemic modest hypothermia to be a grade C therapy (with level IV evidence) and might be applied safely in SCI victims.[4]

In conclusion, the use of therapeutic hypothermia is considered to be a promising neuroprotective agent in several clinical settings. However, there is still a need for large, randomized, well-powered trials to prove the usefulness of hypothermia as a neuroprotective agent.

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RCL-09
The Anesthesiologist's Role in Preventing Postoperative Infections

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Surveys from the end of the 20th century and the beginning of the 21st century showed that anesthesia providers often do not follow infection prevention guidelines, including those developed by anesthesia societies[1-11] as closely as recommended. A number of more recent landmark studies by Loftus and Koff increased the awareness of anesthesiology staff and the anesthesia workplace as a potential source of infection[12-14]. National societies have followed suit and released updated national guidelines in the past few years[15-17].

In a recent international focus group survey we asked for compliance with and implementation of anesthesia-related infection control guidelines throughout the world[18]:

The key results were the almost 100% compliance with maximal barrier precautions (sterile gloves, sterile gown, sterile field) for central line placement and a large variability for other procedures such as neuraxial blocks and peripheral nerve catheter placement. Alcohol plus Chlorhexidine or Octenidine is the skin disinfectant of choice for the large majority of participants for central lines as well as for neuraxial blocks, independent of experience, size of hospital or geographical area of practice. Only in North America was there a difference noted in the use of iodine for central lines (only 7%) and neuraxial blocks (21%). Alcohol/Octenidine instead of Alcohol/Chlorhexidine exclusively is the disinfectant of choice in German speaking countries and is not available in several other parts of the world.

Most participants use sterile gel for ultrasound-guided line placement or nerve blocks. Interestingly a number of anesthesiologists reported using sterile dressings to cover the ultrasound probe or using skin disinfectant as contact medium. 14% of respondents use regular gel for ultrasound-assisted procedures.

91% use bacterial filters for all epidural catheters, while only 49% of participants use them for all peripheral nerve catheters. Their use is subject to strong continental preference, ranging from 13% in Africa and 29% in North America to 91% in Oceania.

Procedure packs for central lines are available to 84% of the interviewed anesthesiologists. Alcohol based hand disinfection is provided in 96% of operating rooms. 72% of participants differentiate between clean and dirty area in their workspace and in 77% of their institutions surface disinfection of their workplace is performed after every case.

Needle free connectors are used by 74% of the anesthesiologists but only 60% of the users always perform the mandatory disinfection of those devices.

Disinfection of regular stopcocks before injection is performed by only 39% of all anesthesiologists.

The question about hand disinfection with alcohol based gel asked about several tasks repeatedly performed by anesthesiologists throughout a working day. Participants almost universally disinfected their hands after exposure to bodily fluid (95%) but only 23% do so before handling a stopcock and 30% before drawing up medication although both activities are considered indications for hand disinfection before performing an aseptic task.

63% disinfect their hands between 2-5 times per hour and only 7% more than 10 times per hour.

The breathing circuits on anesthesia delivery units (ADUs) are nowadays mostly single use items and 79% of North American respondents change them after every case, while only 35% of overall responders do so. If the manufacturer allows use for several patients or a reprocessible system is used (together with an adequate filter system) 49% of all responders exchange the breathing circuits after 24 hours and 19% use them for up to a week with a fresh bacterial filter system for each patient. Of those using the same breathing circuit for several cases only 46% disinfect the outer surface after each patient[18].

While almost all anesthesiologists use maximal barrier precautions for the placement of central lines, their use for the insertion of epidural catheters, peripheral nerve catheters and femoral or axillary arterial lines, is very variable, despite being recommended for these indications[19].

One reason might be that infection control campaigns and bundle implementation projects almost exclusively focus on central line placements in the critical care setting and not necessarily include the operating room environment or other indwelling catheters that can potentially become vectors for infection.

While skin disinfection for line and block placement is almost universally performed according to infection control guidelines (with alcohol/octenidine 20 used instead of alcohol/chlorhexidine in German speaking European countries) and most anesthesiologists use sterile barriers for ultrasound guidance, the use of regular ultrasound gel by 9% for central lines and 14% for peripheral nerve catheters is concerning because of potential contamination.

Iodine is still used by some anesthesiologists for disinfections prior to placing neuraxial blocks, especially in North America (21%)[18].These findings might reflect the fear of the potential neurotoxicity of alcohol/chlorhexidine despite its inclusion in current guidelines[15,17] and sound evidence that it is safe to use. Potential neurotoxicity is a risk with every agent if introduced directly into nervous tissue[21,22].

The lack of disinfection of needle free connector devices with every use remains a major concern. Disinfection of the device is mandatory before every injection according to the manufacturer and is recommended by the CDC HICPAC[23].

Disinfection of ports of three way taps, stopcocks or catheter hubs before injecting is not an established practice as of now, although the hub has been identified as an area of concern for the introduction of microorganisms and disinfection procedures are recommended[23].

A recent study by Fernandez et al. assessed the knowledge of anesthesiology practitioners regarding hand hygiene by asking about awareness of the WHO five moments of hand hygiene ("Do you know the five moments of hand hygiene?"). Only 25% had a positive perception of hand hygiene; only one-third of anesthesia providers estimated their hand decontamination events at >3/h 24.

The need for hand disinfection after glove use is equally poorly appreciated 24, indicating perhaps a false sense of safety.

One way to tackle the potential for infections caused by this under-appreciation is to reduce the number of necessary hand disinfections by creating of an efficient workflow throughout induction, maintenance and emergence[19, 26,27,28]. This should include the implementation of the recommended concept of separating clean and dirty areas within the anesthesia workplace[16,19]. Although this is not a new idea, it is only practiced by 72% of anesthesiologists with particularly low values amongst African (50%) and European (63%) respondents[18]. Comprehensive infection control strategies 33 should include the anesthesia team as part of the change effort.

The outer surface of the anesthesia delivery units breathing circuit seems to be an underappreciated area of potential contamination. Despite being in close proximity to the patient's airway and saliva and being frequently handled by the anesthesia provider (especially during induction and emergence) it is only infrequently disinfected after every use (46%) when left in place for more than one case, ranging from 24 hours up to one week[18]. While the multiple use of a breathing circuit is allowed by some manufactures and covered by some guidelines if bacterial filters are used and changed after every patient, outer surface disinfection should be performed as routine after every case[29-31].

In a study related to the cleaning and disinfection of the anesthesia workplace a total of 200 decontamination (cleaning and disinfection) procedures of the anesthesia workplace either by anesthesia nurses or specially trained housekeeping staff were monitored. Time used by housekeeping staff was shorter (1.2 ± 0.1 min vs. 2.6 ± 0.2 min. on average, p <0.001) with less visible marker spots (14.4 ([55%] vs. 17.3 [66.7%] on average, p <0.001) and the bacterial load showed a 67% reduction (p<0.001) compared to anesthesia nurses[32]. Specially trained housekeeping staff outperformed anesthesia nurses in cleaning the anesthesia workplace indicating the need for trained and motivated staff and the support of leadership for their task which is also corroborated by general findings of the systematic review and evidence-based guidance on organization of hospital infection control programs (SIGHT) study group[33].

In conclusion, awareness of and knowledge about infection control has increased in recent years but that there is still need for improvement because of numerous knowledge gaps and the fact that self-reported real life performance of hand disinfection as well as observed compliance[34] is low despite increasing evidence of clinically relevant transmission events[35-38]. Knowledge of real life performance of hygiene standards is also important for the redesign of operating room processes[39] and might assist national and international efforts to tailor educational infection control and prevention programs to the individual needs of anesthesia providers in the developed world with its increasingly economically driven healthcare systems as well as for health care systems in resource-limited areas, keeping in mind that the human being consists of more microorganisms than human cells and we need to live in a balance with our microbiome which can be severely disturbed in case of critical illness and by antibiotic use40. We have to maintain the "good bugs" in and around us but prevent their translocation in "unhealthy territory" by invasive procedures and disturbed mucosa and skin-barriers and limit the impact and transmission of primarily "bad bugs".

Like in other areas related to patient safety, anesthesiologists should take the lead and work together with infection control specialists in order to make infection control measures an automatic behavior, like placing a pulse oximeter probe on the patient's fingertip.

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RCL-10
Health Economics 101: "Value" Rather Than Price Tags

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LEARNER OBJECTIVES

After participating in this activity, the learner will be able to:
(1) Contrast "health economics" with "cost-cutting;"
(2) Define and recognize five common myths about economics in health care; and
(3) Compare the implications of decision making, with and without economics and value in health care, using examples from anesthesia, surgery, and perioperative medicine.

Scarcity, Costs, Price-Tags:

Regardless of whether we are willing to acknowledge it, resources are scarce. This is true, regardless of which sector of society we consider, but is most difficult to discuss in the area of health and healthcare. Even if increasingly more resources could be redirected toward healthcare, those additional resources, too, would be depleted before we deliver upon all needs for healthcare.

This is no less true even if we perceive that the value of health and life should be "infinite" (or, that we should never place a price-tag on health and life) since at some point the resources inevitably run out, and we are forced to accept that our perception of unlimited value of life is at odds with the realities of how much we can pay, or how much resource we can redirect toward health.

As a result of this scarcity, decisions must be made about what will be achieved within our available resources. By default, such decisions also automatically involve tradeoffs about what will not be achieved (opportunity costs). In healthcare, such tradeoffs should be seriously considered. Yet, often they are not. Or, worse, sometimes the price-tag is considered alone, as if "price" or "cost" tells the whole story.

Decisions and Opportunity Costs:

Typically, decisions are made as if opportunity costs did not exist, and as if there is an unending bank of resources available to provide utmost care to each and every patient. However, ignoring opportunity costs does not make them disappear. Rather, such ignorance worsens the very core of our ability to maximize health provided to the patients we intend to serve - and ensures that, in fact, we will achieve less health per resource expended.

Ironically, this inferior approach to decision-making, in disregard for opportunity costs, plays out every day in our healthcare system, in which decision-makers generally remain convinced they are doing the 'best possible' for each patient in isolation, one patient at a time. Yet, in aggregate, without acknowledgement of opportunity cost through economic evaluation, we continually shortchange our patient population of the maximal amount of health that could have been delivered from our given set of resources. Similarly, considering costs alone, divorced from the 'net value' will not allow for improved value for money.

Role of Economics in Determining 'Value':

Economics has been called the science of scarcity. Using economics to inform decisions in healthcare ensures improved value for money, and maximizes benefits to patients served from within our given set of resources. All economic evaluations have a common structure which involves explicit measurement of inputs ('costs') and outcomes ('benefits'), and can be distilled to simple principles for those who wish to use the results (ie, the 'users'), as well as for those who wish to contribute to conducting high-quality economic evaluations (ie, the 'doers').

Economic evaluations that help (rather than hinder) decision-making:

This presentation will provide an clinician-relevant, researcher-relevant, and decisionmaker-relevant overview of various approaches to economic evaluation, including cost-benefit analysis (CBA), cost-minimization (CMA), cost-effectiveness analysis (CEA), cost-consequences analysis (CCA), each of which are designed to compare alternative courses of action in terms of costs and outcomes. The choice of technique depends on the decision they intend to influence.

Demonstrating Value for Money in Anesthesia & Perioperative Medicine

Using examples from anesthesia (Depth of Anesthesia Monitoring; Sugammadex), surgery (Off-Pump versus On-Pump CABG) and perioperative medicine (Hydroxyethyl-starches vs Crystalloids), we will explore learn tips and tricks for conducting, interpreting, and applying the results of cost-effectiveness analyses in order to improve value for money related to decisions about which drugs, technologies, and techniques to implement into your practice, and which to forgo. Economic evaluation issues that are unique to anesthesia and surgery will be addressed.

Navigating Myths and Misconceptions

A number of myths, misconceptions, and prevailing controversies about the role of economic analysis in healthcare will be discussed:

- Does 'cost-effective' mean 'affordable'?
- Does 'cost-effective' mean 'cheaper'?
- Does 'cost-effective' infer it should be implemented into practice?
- Does economic evaluation encourage rationing?
- What is the magic threshold that defines cost-effectiveness?
- Are economic evaluations generalizable across settings?

- How can I ferret out the limitations and 'slippery slope' techniques investigators may use in economic evaluations?

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RCL-11
Ultrasound Findings in Intraoperative Anesthetic Emergencies

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INTRODUCTION

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 anesthetic[s11] 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 monitored 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. This section will focus on malpositioned endotracheal tube (ETT), as unrecognized esophageal intubation is a known cause of intraoperative cardiac arrest.[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 equipment36 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.

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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-12
Surgical Enhanced Recovery: Past, Present and Future

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LEARNER OBJECTIVES

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

(1) Discuss the physiological basis of enhanced recovery strategy
(2) Outline the elements of the enhanced recovery pathway
(3) Discuss the evidence and outcome of the enhanced recovery recommendations
(4) Appraise the future model of surgical patient care

ABSTRACT

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 elements of the enhanced recovery pathway, discusses the evidence and outcome of the enhanced recovery recommendations.

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RCL-13
TAVR : A Transformative Treatment for Patients with Severe Aortic Stenosis: Past, Present and Future Directions

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LEARNER OBJECTIVES

After participating in this activity, the learner will be able to:
(1) Describe the TAVR (transcatheter aortic valve replacement) procedure;
(2) Outline the selection process for patients undergoing the TAVR procedure;
(3) Summarize TAVR outcomes studies;
(4) Describe the current, state-of-the-art anesthetic management for patients undergoing TAVR procedures; and
(5) Estimate future trends regarding TAVR procedures.

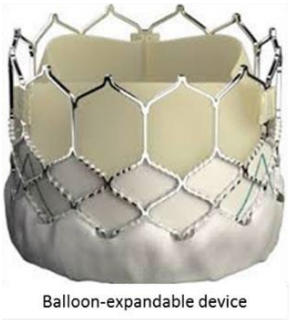
INTRODUCTION

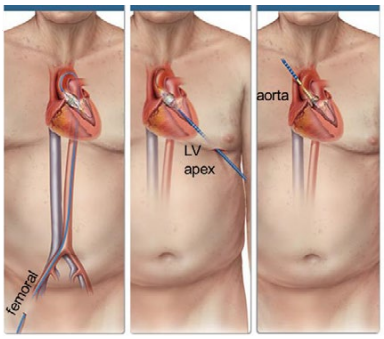
Valvular heart disease is common and its incidence increases with age. In developed countries, aortic stenosis (AS) is the most common valvular heart disease requiring therapy.[1] A recent meta-analysis of 7 studies found that the pooled prevalence of all AS in the elderly (>75 years) was 12.4% and the prevalence of severe AS in the elderly was 3.4%. Of note, 40.5% of elderly with severe, symptomatic AS were not treated surgically. This same analysis concluded that roughly 290,000 elderly patients in Europe and North America could potentially be treated with TAVR and that approximately 27,000 new TAVR candidates present each year.[2] Importantly, the prognosis of untreated or medically treated symptomatic AS is somber with 5 year survival rates of 15-50%.[3] Severe AS also comprises a significant health care resource burden, resulting in nearly 2 hospitalizations and 11.5 hospital days per patient per year alive at a cost of over $29,000 over the same period of time.[4]

TAVR Procedure

Currently, there are 2 TAVR devices approved by the Food and Drug Administration: the balloon-expandable SAPIEN® device (Edwards Lifesciences, Irvine, CA) and the self-expanding CoreValve Evolut R® device (Medtronic, Minneapolis, Minnesota).

The balloon-expandable SAPIEN® device consists of a cobalt chromium alloy frame, three bovine pericardial tissue leaflets, and a polyethylene terephthalate outer skirt to minimize paravalular leaks. The options for access sites are (1) femoral artery, (2) left ventricular apex, and (3) direct aortic approach. Deployment is achieved via balloon valvuloplasty in conjunction with rapid ventricular pacing to prevent


Balloon-expandable device



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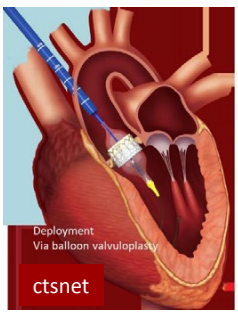

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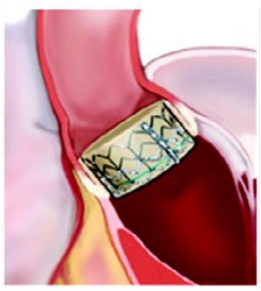
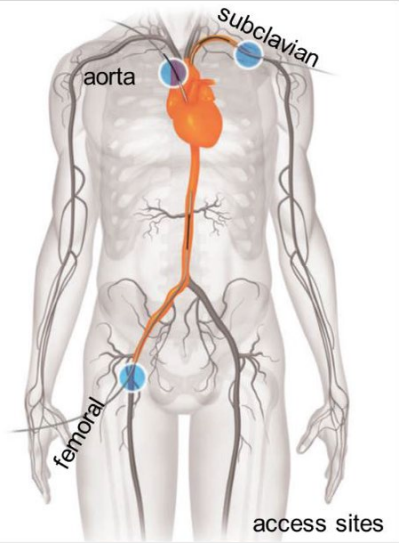

Positioned in AV annulus

Piazza et al, Anatomy of the Aortic Valvar Complex and Its Implications for Transcatheter Implantation of the Aortic Valve.

movement or embolism of the device. The deployed valve is positioned within the native AV at the site of the AV annulus. (see 4 Figures below)

Self-expanding CoreValve Evolut R® device

The self-expanding CoreValve Evolut R® device consists of nitinol frame and three porcine tissue leaflets. Nitinol is shaped at high temperatures but can be deformed (crimped) at cold temperatures for percutaneous delivery. Nitinol has shape memory and as the device delivery sheath is withdrawn, the valve frame expands to its original shape. The options for access sites are (1) femoral artery, (2) subclavian artery, and (3) direct aortic approach. Deployment is achieved via slow withdrawal of the delivery sheath, thus allowing expansion of the crimped frame. Rapid ventricular pacing is typically not needed for deployment of this self-expanding device. The leaflets of the deployed valve are positioned in a supravalvular position, with the frame extending from the left ventricular outflow tract to the proximal ascending aorta. (see 4 Figures below)



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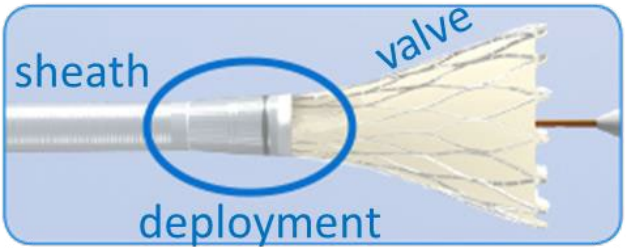
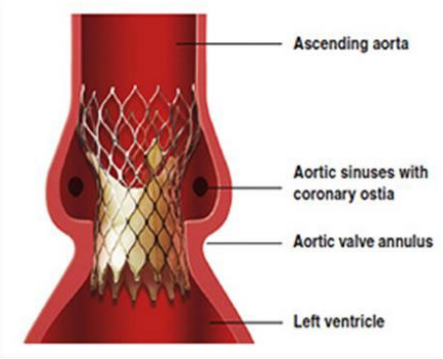


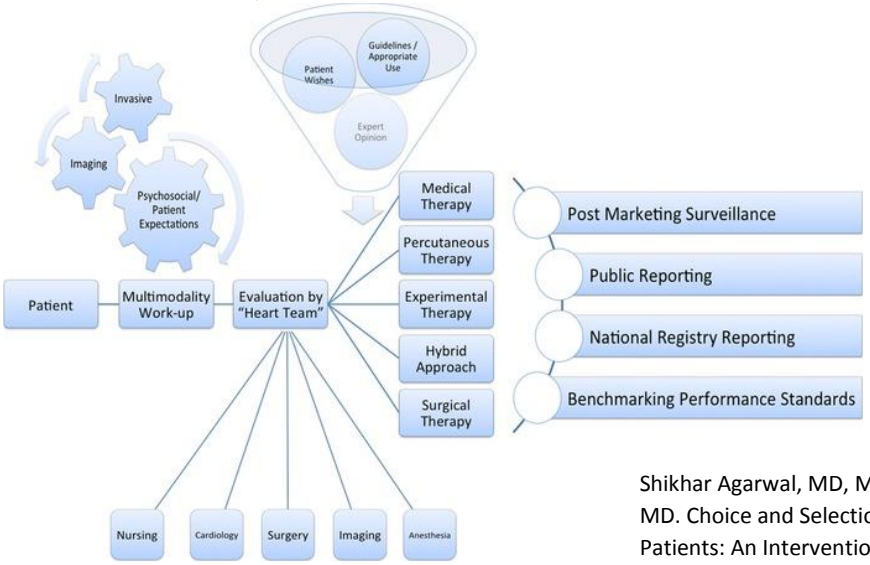


Supravalvular positioning

Piazza et al, Anatomy of the Aortic Valvar Complex and Its Implications for Transcatheter Implantation of the Aortic Valve.

Selection Process

Patients with severe AS who may be TAVR candidates are referred for multidisciplinary evaluation by a "Heart Team" comprised of a interventional cardiologists, cardiac surgeons, and often other specialists including anesthesiologists, radiologists, non-invasive cardiologists, and geriatricians. These consultations are intended to determine the patient severity of disease, symptomatology, prognosis with valve therapy, and surgical risk status. In addition to consultations, patient undergo multimodality testing including CT angiography from the chest through the pelvis to determine aortic dimensions and assess the peripheral vasculature for technical feasibility of the TAVR procedure and to guide device selection and delivery route. Invasive coronary angiography, carotid ultrasonography, and pulmonary function testing are also performed. Patients who are deemed at least intermediate risk for surgical aortic valve replacement (SAVR) and are expected to have a sufficient prognosis following valve therapy (at least one year) may be considered for TAVR if they have suitable anatomy based on CT imaging. TAVR is the preferred therapy in such cases where the surgical risk is high or prohibitive.



Shikhar Agarwal, MD, MPH; E. Murat Tuzcu, MD; Samir R. Kapadia, MD. Choice and Selection of Treatment Modalities for Cardiac Patients: An Interventional Cardiology Perspective. J Am Heart Assoc. 2015;4

Key elements of decision-making in interventional cardiology on complex patients.

Outcomes Studies

Extensive review of the TAVR outcome studies is beyond the scope of this document; the following summarizes the highlights of the major TAVR trials. The initial US studies compared ~800 "extreme risk" patients (those deemed too sick for SAVR) managed medically to those receiving a TAVR. The TAVR cohort had a reduction in all-cause death and CV death (20% vs 50%) and in hospitalization, with an improvement in heart failure symptoms and quality of life. TAVR patients had an increased rate of stroke (5% vs 1%), of vascular complications and of permanent pacemaker requirements.[5,6]

Randomized trials of ~ 1500 "high risk" patients compared patients undergoing AV replacement by TAVR vs replacement by conventional surgery (SAVR). These studies found that TAVR patients had a reduction in all-cause death (22% vs 27%) and similar improvement in heart failure symptoms, quality of life and length of hospitalization. TAVR patients had an increased rate of stroke and transient ischemic attacks (10% vs 5%), of vascular complications, of paravalvular leaks and of permanant pacemaker requirements. TAVR patients were found to suffer less bleeding and less perioperative atrial fibrillation.[7,8]

Randomized trials comparing > 3000 "intermediate risk" patients undergoing AV replacement by TAVR vs SAVR concluded that TAVR was a non-inferior alternative to surgical replacement, with a benefit of TAVR over SAVR observed among patients undergoing tranfemoral TAVR. Of note, the pattern of adverse events varied in regards to method of replacement. Higher rates of acute kidney injury, atrial fibrillation and transfusion requirements were associated with SAVR. Although TAVR patients were found to have higher rates of post procedure aortic regurgitation and of permanent pacemaker requirements, the TAVR valves had lower mean gradients and larger aortic-valve areas.[9,10]

Anesthetic Management

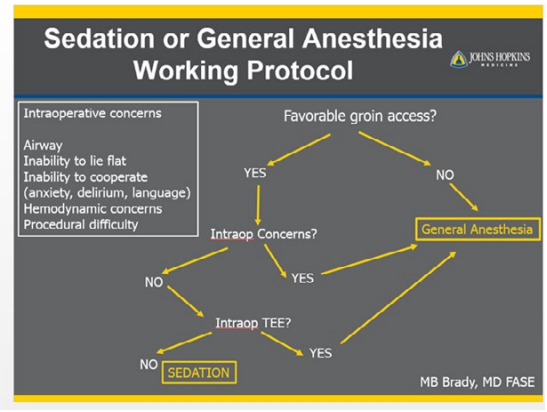
From patient selection to device improvements, everything about the TAVR procedure is evolving. Certainly, this is the case for anesthetic management for these procedures. Traditionally, all TAVR procedures were anesthetized with general anesthesia and extensive invasive monitoring. As procedural experience increases and sheath sizes decrease, more and more centers are performing transfemoral approach TAVRs with conscious sedation, with transthoracic imaging utilized during the procedure.[11] There are no large randomized, prospective studies comparing the 2 anesthetic techniques, but retrospective and observational studies indicate that conscious sedation, compared with general anesthesia, is associated with shorter lengths of stay, shorter procedural times, lower cost, less administration of vasoactive medications, and a decrease in 30-day mortality.[11,12,13] With

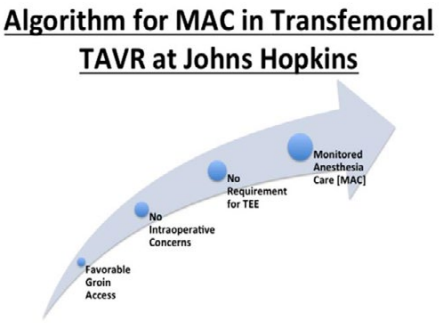
that said, many centers still utilize general anesthesia for these cases with one argument being that the need for TEE is invaluable. Of note, one large study from the Brazilian Registry noted that the use of TEE during TAVR was a protective factor against overall and late mortality.[14] Other reasons favoring TEE utilization include 1) decrease exposure to radiocontrast, 2) assessment and treatment of paravalvular leaks and 3) diagnosis and treatment of life-threatening procedural complications.[15]

No matter the choice of sedation or general anesthesia, one fundamental principle should be followed regarding these patients. It is important to remember that many of these patients are elderly, as well as frail, with multiple co-morbidities and that the procedure is not extremely painful, especially if the transfemoral approach is utilized. As such, low dose administration of short acting medications is recommended.

Regarding the choice of general anesthesia or sedation, there are a few fundamental principles. First, sedation is only an option for transfemoral access TAVRs. If other access sites are utilized, the anesthetic technique should be general anesthesia with an endotracheal tube. Second, sedation should only be offered in experienced centers, not during the initial phase of a TAVR program. Third, the airway exam is of critical importance. It is crucial to evaluate the potential ease or difficulty of establishing an airway in an emergency situation. No matter the patient, the providers, or the experience of the center, cardiovascular emergencies are a noted complication of this procedure. If the ability to secure an airway during an intraprocedural emergency is deemed difficult by an experienced anesthesiologist, it is best to secure the airway from the case start. Of particular note, procedural equipment, such as the C-arm, may interfere with the usual ability to secure a patient's airway. Fourth, other concerns which lead our institution toward general anesthesia over sedation include the patient's inability to lie flat for any reason or the patient's inability to cooperate. This inability may be a result of anxiety, language barrier, or delirium. Often these concerns can be investigated by reviewing the patient's ability or inability to tolerate the pre-procedural cardiac catherization. Finally, if members of the "Heart Team", for any reason, are concerned about potential hemodynamic compromise or sudden change in ventricular function, general anesthesia is utilized. Johns Hopkins TAVR team, utilizes a working protocol addressing the choice of anesthetic technique.16

Historically, early TAVR experience utilized significant invasive monitoring including the use of a pulmonary artery catheter, arterial line, intraoperative TEE and access for temporary transvenous pacemakers.13 Currently, the choice of invasive monitoring rests with the individual institution and should be individualized to each patient. Most centers use a radial arterial line for intraprocedural monitoring, but a femoral arterial catheter may be placed by the interventional cardiologist or surgeon if the radial artery is difficult to access. For those with a permanent pacemaker, experienced





See reference 16

centers may chose not to place a central line, while others place a central line for all TAVR patients. For those without a permanent pacemaker, a temporary transvenous pacemaker may be placed via the internal jugular or via the femoral vein. High volume, experienced centers sometimes chose to remove this line post deployment in the procedural room if the case was deemed "uneventful" and no rhythm disturbances are noted. The post procedure destination varies from center to center: some recover in an intensive care unit, while others do so in a monitored, but not an intensive care, bed.[16]

Anticipate Future Trends

Over the coming years, we expect TAVR volumes to continue to grow as this technology expands to large populations and indications for the procedure increase. This includes patients at lower surgical risk, and TAVR treatment with bicuspid aortic valve disease or aortic insufficiency (as opposed to AS.) Further technological innovation will likely continue to improve both the safety and efficacy of the procedure, from lower sheath sizes and embolic protection devices to retrievable and repositionable valves to enhanced imaging guidance. TAVR likely represents the vanguard of a new field of catheter-based interventions for valvular heart disease that will likely evolve in the coming years.

CONCLUSION

TAVR is a transformative technology that has dramatically altered the landscape of treatment for severe AS. Current data support the use of TAVR over medical therapy and SAVR in patients at high or prohibitive surgical risk, while TAVR is an acceptable alternative to SAVR in patients at intermediate risk. TAVR may be performed safely using conscious sedation in carefully selected patients after considering both patient and procedural factors, with the caveat the both operators

and anesthesiologists must be vigilant for procedural complications and act quickly to mitigate them when they do occur. Further data on outcomes following TAVR relative to anesthetic strategy will be important in guiding procedural planning as this field continues to grow and evolve.

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RCL-16
Predicting and Managing "MODA": The Morbid Obesity Difficult Airway

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INTRODUCTION

In the general population, morbid obesity (MO) has been frequently identified as a risk factor for challenges in airway management. The increasing prevalence of obesity globally coupled with the widespread use of weight loss (bariatric) surgery as a treatment option has given investigators the opportunity to study large cohorts of patients with MO undergoing elective surgery. These and other studies have begun to identify clinical features related to MO that would more accurately predict difficult airways (DA) and develop appropriate management strategies.

In this review, we will use our previously described schema of '7Ps'- Predicting (difficulty), Planning, Positioning and Preoxygenating (the patient), Preparing (equipment), Pharmacology (appropriate choice) and Postoperative (care). While the circumstances and needs of airway management will vary widely and depending on the patient, practitioner and procedure, this review will focus mainly on tracheal intubation as the primary goal of airway management of patients with MO.

Predicting Difficult Airways in Morbid Obesity

Age, Sex, BMI Distribution and OSA: It is well known that though body mass index (BMI) is a good screening tool for obesity per se, amongst patients with morbid obesity (MO), its use alone cannot predict difficult airways (DA). Clearly, other MO related factors should be sought.

Experience from bariatric anesthesia practices has emphasized the importance of distribution of the excessive body mass as a better predictor of DA. When the waist circumference exceeds half the height, the distribution is more 'central' or 'android' and is associated with DA, ventilation, metabolic syndrome, OSA and increased perioperative morbidity. The 'peripheral' or 'gynecoid' pattern of MO is when the WC is less than half the height and is much less likely to be associated with DA. As patients with MO get older, apart from age related changes to their airway anatomy, their comorbidity burden increases and their cardiorespiratory reserve diminishes. There has been an observation of significant difference in the age of patients with MO having uneventful intubation, difficult intubation and those planned for fiberoptic intubation. Other studies have also confirmed that with increasing age both difficulty with face mask ventilation and worse direct laryngoscopy views will be encountered. Indeed, as described elsewhere, age and BMI (either or both >50) are the major diagnostic criteria for Obstructive Sleep Apnea (OSA) and other perioperative MO risk scores. In our opinion, when the numerical sum of the Age and BMI exceeds 100, difficulty in airway management and other perioperative risk increases considerably. In MO, the patient's gender may also increase the incidence of DA. The central distribution of excessive body mass in male patients has been implicated as an independent predictor of difficult face mask ventilation. OSA is also more prevalent with central obesity and has also been previously identified as a risk factor for both difficult face mask ventilation and difficult intubation. In our opinion and experience, difficulties in face mask ventilation frequently observed in patients with OSA who have higher positive pressure (CPAP or BiPAP) settings.

Airway Examination: Amongst the specific airway examination findings, the Mallampati score is a well-established measure of available space in the upper airway relative to the MO related oro-pharyngeal soft tissue mass. This explains why this is probably the most consistent DA test reported in multiple studies of patients with MO. Mallampati scores >2 have been identified as an independent predictors of difficult face mask ventilation and intubation. Increasing neck circumference (NC>40cm) has been described as a significant predictor of difficult face mask ventilation. Neck circumference (NC) has also been proposed as a predictor of difficult tracheal intubation due to increased anterior neck soft tissue. It is also probably worthwhile to remember that increased NC is also one of the diagnostic criteria for OSA. Patients with MO presenting with this finding are likely to have OSA and should be evaluated further for it. Finally, the upper lip bite test (ULBT) is a simple test that provides an objective assessment of the anatomy and proportion of the

Predictors of Difficult Airways in Morbid Obesity

	0	1	2
Age	<40	40-60	>60
Sex		Women	Men
Habitus		Waist< 1/2Height	Waist>1/2Height
OSA	Absent	CPAP 5-15 cmH20	CPAP>15 cmH20
BMI	<40	40-60	>60
Neck Circumference (cm)	<40	40-60	>60
Mallampati Score		≤II	>II
Upper Lip Bite Test (ULBT)		≤II	>II

Table 1: List of Predictors of Difficult Airway (DA) in patients with Morbid Obesity (MO):
The scores (0-2) from each predictor suggested here are additive can produce total scores which predict increasing difficult airways (DA). Total scores with <5 suggest low probability of DA, 5 to 10= moderate to serious difficulty and >10= considerably serious DA. While goals may vary for each patient and procedure, for the provider DA management depends on the available equipment, expertise and experience.

lower jaw, its mobility and protrusion and also assesses the submandibular space. In patients with MO, this test may offer important information with regards to space available for the caudad displacement of the tongue, which improves laryngeal visualization on direct laryngoscopy.

The predictors of DA in patients with MO discussed above are summarized in Table1. Taking into consideration the multifactorial etiology of predicting DA in patients with MO, further investigation and validation will be required.

Managing the Morbid Obesity -Difficult Airway (MODA):

Following an appropriately detailed DA assessment of a patient with MO, a management plan needs to be formulated. Individual components of the above mentioned predictors may influence specific aspects of the DA management. As a 'gestalt'; the first four DA predictors- Age, Sex, BMI and Distribution may influence the decision whether the airway may be safely secured after the induction of anesthesia or if the patient needs to have an awake intubation. Similarly, when difficult face mask ventilation is predicted, amongst others, by increasing neck circumference and higher CPAP settings in patients with OSA, profound and/or prolonged neuromuscular blockade may be avoided. Finally, when the airway evaluation suggests difficult direct laryngoscopy (Mallampati scores and Upper Lip Bite Tests etc.), videolaryngoscopy should be considered as the primary option. It is however essential to appreciate that while some of these predictors may each individually predict some difficulty; they need to be all considered together in any plan, where alternative techniques and rescue methods are also clearly identified.

Another aspect worth emphasizing is the seeking of expert help and adequate assistance when any difficulty in airway management is anticipated. In our experience, this is probably more important in patients with MO than elsewhere. The ultimate choice of airway management will also depend on the locally available equipment, expertise and experience.

Patient Positioning in Morbid Obesity

Irrespective of the plan, appropriate positioning in patients with MO is probably the most important aspect of airway management in these patients. Patients with MO should be positioned in the Head Up or Head Elevated Laryngoscopy Position (HELP), before and during induction of anesthesia. The HELP position is different from the standard 'sniffing' position. In addition to flexion of the lower cervical spine and extension at the sub-occipital joint, the HELP position is achieved when the patient's sternum and ear are aligned in a horizontal line parallel to the ground. This position facilitates intubation by improving the laryngoscopy view and is of vital importance for both spontaneous and assisted ventilation. The HELP position can be achieved by either tilting the table, stretcher or bed into a reverse trendelenburg position or using a propriety positioning device. Newer inflatable devices allow for some degree of customization to the degree of elevation and can be considered.

Preoxygenation in Morbid Obesity and Difficult Airways:

In patients with MO, the importance of adequate preoxygenation cannot be over-emphasized. Indeed in MO, anesthetic induction and neuromuscular blockade coupled with poor positioning and inadequate preoxygenation can lead to rapid oxyhemoglobin desaturation and profound hypoxemia. On the contrary, as evident from busy bariatric anesthesia practices, even in patients with MO who have an anticipated DA, with meticulous attention to both positioning and preoxygenation, the incidence of hypoxia can be greatly minimized.

Preoxygenation can be simply initiated well before anesthetic induction, outside the operating rooms with nasal prongs applied to the patient in a sitting position. This approach has been shown to significantly increase the subsequent safe apnea time during airway manipulation, presumably by maximizing both the FRC and oxygen reserves. Additional evidence for the continuation of passive flow of oxygen during the period of apnea (apneic oxygenation) suggests that this can delay hypoxia by continual replenishment of the alveolar oxygen content by passive uptake. Studies have confirmed benefit from this simple maneuver and other more sophisticated delivery systems are being developed.

Another popular technique that is often considered an extension of preoxygenation is the application of positive pressure mechanical ventilation with a tight fitting face mask in the awake patient for a few minutes. This can be then continued uninterrupted through the anesthetic induction and immediately after tracheal intubation replaced with recruitment and PEEP. A word of caution- patients at risk for regurgitation and aspiration (emergency, inadequately fasted, symptomatic GERD, pregnancy etc.) may not be ideal candidates for this CPAP technique but would still benefit from the previously mentioned passive oxygen flow with nasal prongs.

Planning the Tracheal Intubation:

Direct laryngoscopy (DL) has remained a common and remarkably successful technique for intubation in patients with MO. Widespread availability and familiarity with this highly efficient and economical technique coupled with simplicity in use of adjuncts such as tracheal tube stylet or flexible bougies ensure its continued use in patients with MO who have fewer predictors of DA. Preloading bougies combined with McCoy type DL blades offer fairly effective options when more difficulty is anticipated.

In the last decade, with the introduction and widespread use of videolaryngoscopy (VL), in patients with anticipated DA, both DL and awake fiberoptic intubation (FOI) has been reduced. The benefits of VL are most obvious in patients with MO who have predictors of difficult laryngoscopy (MP, ULBT etc.). In patients with MO, studies comparing VL to DL demonstrate improved laryngeal views, decreased time to tracheal intubation and fewer situations with oxyhemoglobin desaturation.

Another advantage of VL is that if the DA prediction suggests both difficult face mask ventilation and challenging DL, VL can afford an invaluable addition to the management paradigm- the ability to perform an "awake look" laryngoscopy. This may provide a more detailed evaluation of the airway and allow for practical decision making in further management of the patient. Further experience and research with this technique will no doubt impact the future of DA management in patients with MO.

Other Airway Options:

While supraglottic airway devices (SAD) are part of conventional DA algorithms, these have not always been considered ideal rescue devices in patients with MO. The well-known NAP4 report also highlighted multiple complications with SAD use in patients with anticipated DA; a major proportion of whom were patients with MO .

Quite the contrary to this rather unsatisfactory experience, multiple other studies reported the safe and successful use of SADs in patients with MO, either as the primary airway device or as a tool for ventilation prior to tracheal intubation. Newer SADs with gastric ports may provide higher sealing pressures and result in effective positive pressure ventilation while reducing gastric insufflation. It is therefore reasonable to recommend that in patients with MO if SADs are either used electively or needed in a rescue situation, devices with gastric ports should be used. Once again, it is important to emphasize in patients with MO, SAD use in this patient population does not preclude or circumvent the need for attention to the previously mentioned importance of positioning and preoxygenation.

Fiberoptic Intubation (FOI) is a well described technique in all DA algorithms. This is often considered a 'gold standard' and the technical advantage, the safety of FOI lies both in keeping the patient awake and breathing spontaneously. In patients with MO, FOI can be challenging due to the distortion of the upper airway and other problems with sedation and topicalization. For further guidance on advanced FOI techniques that would be useful in patients with MO, the reader is referred to other excellent resources on this subject.

As expected, there is limited evidence in patients with MO for elective or rescue surgical airways or Front of Neck Access (FONA). Studies of tracheostomies, including percutaneous tracheostomies, do however suggest that when compared to lean patients these FONA techniques are more difficult, may take longer and are associated with more post-operative complications in patients with MO. The use of ultrasound to identify landmarks and guide needle based techniques is promising and will undoubtedly increase the safety of FONA in patients with MO.

Overall DA management in patients with MO has to be tempered with the acknowledgement that all the three well-known DA 'rescue techniques'- SADs, FOIs and FONA are known to be themselves difficult with increased failures in MO. It is therefore imperative that the assessment and management of any potential DA in patients with MO be systematic and meticulous, as their limited cardiorespiratory reserve can contribute to additional and often serious morbidity and mortality.

Pharmacology of Airway Management in Morbid Obesity:

The appropriate dose of pharmacological agents needs to be carefully chosen in patients with MO for the induction, maintenance and reversal of anesthesia. These have been described in detail elsewhere. In patients with MO, where no difficulty in either face mask ventilation or laryngoscopy and intubation are anticipated, the standard balanced anesthetic induction with non-depolarising neuromuscular blockade can be used. When difficult face mask ventilation is anticipated, it may be appropriate to consider anesthetic induction followed by tracheal intubation but avoiding neuromuscular blockade. This has been described using short acting agents such as a combination of remifentanil and propofol. Remifentanil delivered as an infusion that can be titrated to effect with ideal intubating conditions that avoids chest wall rigidity and safe return of adequate ventilation almost immediately on discontinuation. For anticipated difficult laryngoscopy, the "awake look" approach previously mentioned may be appropriately combined with topical local anesthetic or remifentanil. More recently, the increasing experience with infusions of dexmedetomidine, providing sedation without respiratory depression for VL assessment and attenuation of hemodynamic responses to intubation, appears a promising addition to the available DA management strategies in patients with MO. These pharmacological approaches can also be applied to Fiberoptic Intubation (FOI) techniques.

Neuromuscular Blockade in MODA:

The risks and benefits of using neuromuscular blockers in MO have been discussed elsewhere. There is a growing debate in this patient population that challenges the routine use of succinylcholine in elective, fasted patients who have low regurgitation- aspiration risk. On one hand, the long standing and well established use of succinylcholine (with or without RSI) in patients with MO was aimed at using deep and profound neuromuscular blockade to achieving excellent intubating conditions and being able to rapidly secure the airway while reducing the risk of oxyhemoglobin desaturation. This dogmatic approach has also touted the rapid onset and short duration of neuromuscular blockade as a 'safety net' for its use and promoted its use to avoid the dreaded cannot intubate- cannot oxygentate (CICO) situation.

Contrary to this view are the multiple serious concerns with the routine use of succinylcholine in patients with MO. Succinylcholine (recommended dose 1-2mg/kg total body weight) can lead to significantly higher desaturation and bradycardia when compared to rocuronium (recommended dose 0.6mg/kg ideal body weight) in patients with MO. The hypoxemia due to succinylcholine may be partially due to the increased oxygen consumption by skeletal muscle fasciculations. More likely and with serious risk of morbidity (and potential mortality) is the profound oxyhemoglobin desaturation attributed to the loss of functional residual capacity (FRC) secondary to the deep and profound neuromuscular blockade. This hypoxemia becomes even more clinically relevant when the return of spontaneous respiration is unpredictably delayed, leading to serious complications from the CICO scenario. Even when the airway is secured quickly and successfully, the desaturation due to succinylcholine continues and possibly explained by extensive basal atelectasis secondary to diaphragmatic paralysis. Till further and more definitive evidence becomes available, it may be prudent to avoid succinylcholine in elective, fasted patients. It is also advisable to limit the use of succinylcholine in patients with MO to rapid sequence inductions and intubations (RSII) where the benefits of preventing regurgitation and aspiration outweigh the risks from potential hypoxemia.

Postoperative Airway Management in Morbid Obesity:

The postoperative airway is the last and final piece of the '7Ps' puzzle for DA management in patients with MO. Once again careful attention should be paid to this phase as was highlighted in the NAP4 report. Other reports also suggest that major adverse airway related events in patients with MO occur after emergence from anesthesia (ASA Closed Claims Database). In a rather indirect way, successful airway management in patients with MO require adequate emergence from anesthetic, reversal of neuromuscular blockade and appropriate analgesia. Extreme caution and care should be exercised during emergence in patients with MO especially those with anticipated (or unanticipated) difficulty in airway management. Use of reversal agents such as suggamadex and naloxone have been described elsewhere and should be considered as indicated. Adequate and appropriate monitoring should be continued as appropriate. Meticulous attention should be paid to keeping the patient with MO in the HELP position and supplementing oxygen with nasal prongs or face mask while in the early phases of recovery. A very useful strategy in these patients is the insertion of a modified nasal trumpet (MNT) airway. Patients with severe OSA and or those with high CPAP settings may require immediate post-extubation resumption of their respiratory support therapy. Monitoring expired CO_2 levels in these patients will aid the early detection of airway obstruction, hypoventilation and/ or impending respiratory failure.

CONCLUSIONS

As obesity continues to increase globally, patients with morbid obesity (MO) will continue to frequently present for elective and emergency procedures where they require airway management. We need to carefully predict difficult airways (DA) in these patients and manage them appropriately as described in this chapter. To improve patient safety and outcomes from airway management, accumulating evidence and vast experience from bariatric anesthesia also needs to be continually incorporated into Morbid Obesity specific Difficult Airway algorithms.

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RCL-17
Organization Fear: The Silent Killer

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January 28, 1986 was a bright and cold morning at Cape Kennedy, Florida. The spectators in the Grand Stands, mostly family and friends, since shuttle launches had become somewhat routine (which itself is a recipe for trouble), bundled in jackets and coats. Christa McAuliffe's parents shaded their eyes against the bright Florida morning sun. As the Challenger lifted off and cleared the gantry, no one was more relieved than, Roger Boisjoly.

Boisjoly, a mechanical engineer, had moved to Utah to take a job with Morton Thiokol and be closer to his Mormon faith. Over the past 18 months, he and fellow engineers Allan McDonald and Bob Ebeling had become concerned about the integrity of the" O-rings in extreme temperatures, most notably cold. They had repeatedly noticed "burn-through" in the rings on previous launches and tests. In July of 1985 he wrote a memo to his superiors alerting then to his concerns that the design of the solid rocket boosters had a fault that he believed could lead to a catastrophic failure. The temperatures this morning were outside of the "test parameters". In fact, that morning they suggested a "No Go"- only to be met with ridicule, humiliation and intimidation. Morton Thiokol immediately reversed that opinion and gave the go ahead for the launch. "Failure Is Not an Option"

On February 1, 2003, we lost another space shuttle, Columbia, when it incinerated on re-entry to the atmosphere due to damage caused foam insulation that had broken off the vehicle (as had happened on every space shuttle since the inception of the program). After months of investigation, a special commission concluded that a key-contributing factor to both disasters was the **"culture that prevented effective communication of critical safety information and stifled professional differences of opinion".**

How could this happen in an industry and organization staffed by some of the most brilliant, talented and dedicated people in the world? Unfortunately, we need look no further than ourselves.

Each year, one in five of your patients will receive the wrong medication; 3.5 million individuals will get a hospital acquired infection (probably from someone who didn't was their hands); 49 times this week we will inadvertently leave something behind in a patient having surgery

and sadly, almost 250,000 people in our care will die from a medical mistake while they are in the hospital. Preventable errors are now the 3rd leading cause of death in the United States. Multiple studies and many of your own root "cause" analyses have shown that most of untoward outcomes are caused by failures in interpersonal communication.

So, one must ask the question again. Are we not smart enough? Do we not work hard enough? Do we not care enough? Why are we so bad at this? Why don't we speak up? Sadly, the answer is - Our people are afraid! They are afraid to speak up. They are afraid to discuss the "un-discussables." They are afraid to hold others accountable. They are afraid to have difficult conversations. They are afraid to deliver uncomfortable messages.

Understanding Fear

We need to understand, what we believe we see, is actually a reflection of what we believe. Business guru Peter Senge talks about the "Ladder of Inference" which is a concept based on the work of psychologist Chris Argyris We select from the reality of observable data and make assumptions based on our experiences and beliefs – we see what we believe! Stephen Covey, in "7 Habits of Highly Effective People", demonstrates how preconditioning influences our interpretations of "what we see".

In the cycle of mistrust, a basic assumption is that supervisors and employees (or in fact anyone with perceived differences in power/influence) cannot trust one another. Each assumes that the other operates from a philosophy of self-interest and each side is expected to try to achieve its self-interest at the expense of the other party – The classic "win-lose" scenario. These behaviors can feed into the "Cycle of Fear" which can become self-sustaining. Fear is a very powerful emotion that leads to a very narrowed focus on perceived threats (dangers) and tends to lead towards a pessimistic view of risk and outcome.

Hospitals are very tight communities – to be excluded, shunned or thought less of can be very fear provoking. **Hospitals are very complex and problem-rich environment.** Lots of things can go wrong and do go wrong in hospitals. Problems are frequent, unpredictable (although my colleagues would argue more are predictable than not) and often severe. **Everyone is guilty of something. People have multiple "bosses" or supervisors who catch their errors.** We have developed systems and structures to make us aware of problems no matter how small. Because all of us fall prey to the Fundamental Attribution Error, **mistakes are seen as a personal reflection of the individual rather than a process. As a result, behaviors become defensive and self-protective.**

From an organization perspective: **1. Fear has a significant impact on staff morale and retention. 2. Fear shifts energy and focus.** According to a Delloitte research study 1/3 of employees are disengaged from the organization and 1/3 are actively "working against you" for a total cost annually of 350 Billion dollars. **3. Fear inhibits creativity and innovation.** An environment of psychological safety is essential for "risk taking" which is necessary for innovation. All new ideas/practices begin with a deviation from the established! **4. "Fear Kills People".** In 2005, American Association of Critical Care Nurses in conjunction with the authors of "Crucial Conversations" published "Silence Kills" and identified 7 conversations that

rarely go addressed in the Hospital (Broken Rules, Mistakes, Lack of Support, Incompetence, Poor Teamwork, Disrespect, and Micromanagement.

Manifestations of Fear

1. *Elephants in the room.* This is the concept of *"undiscussables"* – problem(s) or issue(s) that someone hesitates to talk about with those who are essential to its resolution. These are the secrets that everyone knows yet are not discussed in forums where they can be explored and resolved. The more we refuse to address, the more they contribute to fear in the organization – and the harder it becomes to talk about them. You need to structure the conversation to ensure "psychological safety": 1. Introduce the concept and share why it is important (Purpose). 2. Describe the process and set the ground rules (Structure). 3. "Identify the elephant" –introduce the undiscussable with Leaders going first (Transparency). 4. Talk about the elephant (Mutual Trust and Understanding).
2. *Fear of Speaking Up* (Shooting the Messenger). Because of the "Fundamental Attribution Error" we ascribe poor or "bad" motivations that bring us news we "don't want to hear" which triggers the Cycle of Mistrust. As leaders, we need to "Master or Stories" (remember we don't see reality but rather what we believe). Organizations need to "Embrace the Messenger" – people that don't care won't bring you "bad news".

Leading the Organization out of Fear

Trust is must be established in an organization and become a priority. In the absence of trust, there is no ability to engage in conflict. Conflict (meaningful and passionate conflict) is absolutely essential to a healthy organization. In the absence of conflict there is not ability to reach Consensus and Commitment which leads to being unable to hold others Accountable. Results (Engagement, Service, Quality, Growth, and Finance) are not achievable when people cannot hold each other accountable.

There must be absolute clarity on the organizations core values and "intolerance" for behaviors (from anyone in the organization) who doesn't embody those core values. Violation of core values leads to a loss of identity and provoke fear.

In summary, organizations must spend time, energy and resources in developing skills to engage in meaningful constructive conflict. They must embrace differences of opinion and create safe environments where such differences can be explored. Specific training can be used to guide conversations to promote safety and encourage contributions into the shared knowledge pool. Trust is essential. No one will follow a leader unless they believe that the leader cares about them.

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RCL-18
What Every Anesthesiologist Should Know About Patient Safety

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Patient safety is not a fad. It is not a preoccupation of the past. It is an on going necessity. It must be sustained by research, training and daily application in the workplace. Ellison C. (Jeep) Pierce, Jr., MD, Founding President of the Anesthesia Patient Safety Foundation.

Anesthesiologists have been founders and leaders of the patient safety movement and our specialty has been the poster child for systems-based safety practices. Our specialty has fostered significant improvements in healthcare processes, technology, and training. Our specialty's innovations include the introduction of safety prompted changes in clinical practices, advanced monitoring technologies, simulation-based training, and application of human factors engineering methods, to name but a few. Perioperative care is consequently safer than it was 40 years ago. The Anesthesia Patient Safety Foundation (APSF), an affiliate of the American Society of Anesthesiologists, was the forerunner of the National Patient Safety Foundation and has helped to drive numerous national patient safety initiatives. We have much of which to be proud.

However, our specialty has lost some of our initiative and stature. Part of this is due to a diminished appreciation by the specialty of the importance of safety, the apparent 'safety' of everyday intraoperative practice, an overly narrow view on our role, and increasing production and financial pressures. It is time for a 'call to arms' for anesthesiology to take a broader more active role in patient safety across the full spectrum of perioperative and peri-procedural care.

Unfortunately, too many anesthesiologists and even more of those with whom we work retain the "old view" of safety in which errors by front-line clinicians are considered the cause of events with the corresponding response of individual blame, shame and train. The "New View" of safety (Safety 1.0) focuses on deficiencies in processes, technology, and systems. When events occur, the goal is to consider the entire system, to identify latent failure modes that can be eliminated. The New View asserts that work is process, our processes are complex, and the more complex a process, the higher likelihood of error. Bad outcomes almost always derive from bad processes, not bad people!

The latest thinking about safety (Safety 2.0) accepts that systems can never be 100% safe and thus focuses on how systems succeed rather than retrospectively analyzing failures. Safety is difficult to measure – when we count adverse events it is really a measure of "unsafety." In contrast, productivity and cost-savings are easy to measure. Thus, safety is under constant attack from other organizational objectives. All anesthesiologists should be vigilant for safety encroachment and be actively engaged in helping their facilities/practices enhance safety using systems-based approaches.

In a short article in Anesthesiology that I highly recommend you read, "Human factors engineering in patient safety" (2014 Apr;120(4):801-6), David Gaba and I describe the role of human factors engineering (HFE) in patient safety. Broadly defined, HFE is the study of human interactions with tools, devices, and systems to enhance use safety, efficiency, and satisfaction. Basic knowledge of HFE should be in the armamentarium of all anesthesia providers.

I have created a TOP TEN List of Anesthesia Patient Safety Issues which I present below in reverse order. I only have space to discuss some of these.

10. Errors using advanced medical technology. Due to numerous errors leading to patient harm with the use of complex medical devices (e.g., ventilators, infusion pumps), both the APSF and the Association for the Advancement of Medical Instrumentation (AAMI) have started initiatives to enhance pre-use training of clinicians. The other aspect of this issue is the occurrence of use errors due to inadequate user interface design. In fact, if devices were designed better, less training would be necessary. These issues have become particularly acute for health information technology (HIT) where poor user interface design contributes not only to numerous use errors but undue inefficiency that distracts providers from focusing on much more important patient care tasks. The HFE methods called 'user-centered design' (UCD) are already mandated by the FDA during device development for manufacturers to improve device usability and safety. The rigorous application of UCD is not yet ubiquitous for HIT developers. You can use the same methods to enhance safety and quality improvement interventions in your hospital.

9. Dealing with the 'degraded' provider. Here I am not just talking about the 3-5% of anesthesia providers who have substance abuse problems or to those who work when they are sick or on medications for illness. I am also referring to anesthesiologists who are no longer at the top of their skills. Older age is a predictor of less good patient outcomes in several clinical studies as well as in a recent simulation study of practicing anesthesiologists. Further, older anesthesiologists may have greater performance degradation due to fatigue and sleep deprivation. Having greater experience does not translate directly to having greater expertise. Simulation-based training has an important role in improving and enhancing both technical (i.e., clinical) and behavioral (i.e., teamwork and communication) skills.

8. Patient physical injuries (nerve injury, falls, dislodged catheters). In sum, these account for a significant incidence of preventable patient harm and focused

local continuous quality improvement (QI) initiatives can yield significant safety benefits.

7. Perioperative medication errors. A recent study by Karen Nanji (Anesthesiology. 2016 Jan;124(1):25-34) confirmed that intraoperative drug errors occur in about 4% of cases. The APSF proposed the STPC initiative to reduce the risk of medication errors –Standardization (e.g., of labeling, packaging, processes), Technology (e.g., to double-check high risk medications, to reduce manual pump programming), Pharmacy Practices (e.g., provision of single-use, pre-filled syringes), and Culture of Safety.

6. Failure to follow other best practices (DVT prophylaxis, production pressure, distractions, fire safety, etc.). Again, taken together, these account for a significant incidence of preventable patient harm and some can be readily addressed with local QI initiatives. Production pressure was mentioned previously. The APSF recently held a consensus conference on the adverse effects of distractions, and particularly on the intraoperative use of personal electronic devices (PEDs). A summary of this conference and its summary recommendations will appear soon in Anesthesia and Analgesia. The overall recommendation was to not use PEDs except for urgent matters and then only briefly.

5. Residual neuromuscular blockade. The literature is unequivocal that a failure to use quantitative monitoring and to reverse non-depolarizing neuromuscular blockade are associated with post-operative respiratory depression and pneumonia (Curr Opin Anaesthesiol. 2016 Dec;29(6):662-7). One might hope that the release of sugammadex will mitigate this issue but my suspicion is that it will not as: a) muscle relaxants will consequently be used more widely, especially outside the operating room; and b) there will still not be consistent reversal (e.g. "I just gave a little dose," or "I gave one dose at induction more than an hour ago").

4. Intraoperative hypotension à organ injury. There is increasing evidence that inadequately treated intraoperative hypotension (generally a mean of less than 65 mmHg) is associated with a spectrum of undesirable post-operative outcomes including acute renal failure, myocardial injury, and CNS dysfunction. Not surprisingly, these injuries are most likely in the elderly and infirm.

3. Postoperative opioid-induced respiratory depression. Due to innumerable respiratory arrests and brain injury/death events due to opioid-induced respiratory depression, both the APSF and the AAMI Foundation have strongly advocated for continuous cardiorespiratory monitoring of post-operative patients receiving parenteral opioids. Anesthesiologists should (and increasingly have a legal obligation to) screen patients who are expected to receive post-operative parenteral opioids and, where available, recommend continuous cardiorespiratory monitoring and/or use of multimodal (low to no opioid) therapy. The risk is higher in patients who have obstructive sleep apnea, pre-existing pulmonary or CNS impairment, and are on CNS depressants. After painful surgeries (e.g., orthopedics), these patients should be on continuous postoperative monitoring. However, opioid-induced respiratory depression still occurs in healthy patients and thus a risk-informed selective use strategy will not prevent all events. If possible, it is probably prudent to continuously monitor all post-operative patients. The role of end-tidal capnography and other specific measures of ventilation (in addition to pulse oximetry) is still evolving.

2. Postoperative surgical or catheter-induced infections. There is much that anesthesia providers can do to reduce the incidence of perioperative infections which are the largest single category of preventable events associated with surgery and place a huge burden of harm and cost on each of your facilities. Besides following evidence-based practices for antibiotic selection & dosing and for sterile ultrasound-guided insertion of central lines, I strongly encourage you to become familiar with the seminal work of Randy Loftus who has shown that our everyday medication management practices contribute to perioperative infections (see Curr Opin Anaesthesiol. 2016 Apr;29(2):192-7).

1. Communication & teamwork failures. Failures of communication are the top contributor to patient harm in healthcare today. Recent data document significant performance gaps during simulated emergencies in board-certified anesthesiologists, particularly in terms of teamwork or behavioral performance skills. Other data show that real world non-technical skills can be improved with deliberate multimodal interventions (e.g., in the context of PACU handovers, Weinger et al. Anesth Analg 2015 Oct;121(4):957-71). All anesthesiologists should be experts in crisis resource management with recurrent training in this and related non-technical/teamwork skills.

What are the elements of a safer perioperative care environment? Such a facility should have a robust event reporting system – one that is widely used by physicians and staff alike. When errors and events occur, they should be welcomed by facility leadership as opportunities for improvement, not as situations to be hidden and shunned. Those who are unfortunate enough to be on the 'sharp end' of an event, and those who report such events, should not be punished. HFE processes and tools must be used to develop a detailed understanding of the work processes so as to inform safety interventions. All safety activities, but especially interventions, should be done in a multidisciplinary (including especially surgeons) manner. A primary focus of

all such efforts should be to foster better communication and teamwork to enhance the system overall.

When you have identified a safety problem, the first step should be to understand the problem thoroughly. Then, you need to get broad (both leadership and front line personnel) agreement that this problem must be addressed (and consequently the team should be given the resources to address it). Then, a user-centered design approach allows iterative design and evaluation of solutions in 'pilot' trials.

In summary, healthcare is a complex "sociotechnical system" that is prone to failure. Many factors can degrade system performance, predisposing to adverse events. Creating truly safe systems requires not only a thorough understanding of the system but leadership commitment and a multidisciplinary approach to continuous improvement. To really have an impact on perioperative safety, anesthesiologists must step outside the OR doors (and their comfort zone). All anesthesiologists should be actively involved as leaders in the design of systems-based interventions in their facilities/practices to improve patient safety and perioperative quality.

RCL-19
Improve Sleep After Surgery: What Can We Do As Anesthesiologists

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Sleep Disturbances After Surgery

Patients often develop significant sleep disturbances immediately after surgery, especially major surgery. Polysomnographic manifestations usually include severe sleep deprivation, sleep fragmentation, decrease or loss of SWS and REM sleep during the night after surgery.[1-4] Patients may report decreased sleep time, increased numbers of arousals or awakening, lowered sleep quality, and frequent nightmares.[5] During the subsequent postoperative period, sleep structure gradually returns to normal with a REM rebound within one week.[2]

Factors associated with postoperative sleep disturbance

Preoperative comorbidity

Severe preoperative comorbidity is associated with worse sleep quality after surgery. In a small sample size study of Yilmaz et al.,[6] 52 patients undergoing coronary artery bypass graft surgery were assessed for postoperative sleep quality with Pittsburgh Sleep Quality Index. The results showed that patients with preoperative myocardial infarction had significantly worse sleep quality after surgery, and higher preoperative angina score was an independent predictor of poor sleep quality after surgery.

Type of anesthesia

Regional anesthesia is helpful to relieve sleep disturbances after surgery. In a randomized controlled trial, 162 women scheduled to undergo fast-track abdominal hysterectomy randomly received general or spinal anesthesia; the results showed that patients in the spinal anesthesia group experienced less bad sleep in the night after surgery, which was attributed to lower opioid consumption.[7]

Severity of surgical trauma

Sleep disturbances are more severe after major surgery. For example, in patients after open cholecystectomy under general anesthesia, significant sleep disturbances (manifested as increased N2 sleep, and decreased or lost N3 and REM sleep) occurred during the night of surgery;[2] whereas in patients after laparoscopic cholecystectomy under general anesthesia, sleep disturbances were less severe (manifested as decreased N3 sleep but not REM sleep) during the same night.[3]

Postoperative factors

Many postoperative factors are associated with the development of sleep disturbances. Among them pain is possibly the most important one.[4,8] Environmental factors including noise and lights in the ward, disturbances from healthcare staff, and disturbances from other patients are also important sleep disturbers.[4,8] Furthermore, various kinds of discomforts such as needing to use toilet facilities, nausea, anxiety, fever, etc., leads to sleep disturbances as well.[4]

Harmful effects of sleep disturbances on postoperative outcomes

Sleep disturbances and delirium

Sleep disturbances are considered important risk factors of delirium development. In patients undergoing arthroplasty or non-cardiac surgery, preoperative sleep disruption was associated with an increased risk of postoperative delirium.9, 10 In elderly patients undergoing arthroplasty, preexisting obstructive sleep apnea was a significant predictor of postoperative delirium.11 In Veteran patients enrolled in hospice, poor sleep quality was also associated with a high risk of developing delirium.12

Sleep disturbances and pain

The relationship between sleep and pain is reciprocal; poor sleep also leads to increased sensitivity to pain. Studies of patients hospitalized for burn injury showed that significant temporal relationships exist between sleep, pain and analgesic medication, i.e., a night of poor sleep was followed by a significantly more painful day and higher analgesic intake; further, high levels of pain and analgesic medication during the day were both significant predictors of poor sleep on the following night.[13,14]

Sleep disturbances and cardiovascular events

Sleep disturbances are associated with increased risk of cardiovascular events in high risk patients. In a cross-sectional prospective cohort study, 388 patients after percutaneous coronary intervention were assessed for symptoms of disturbed sleep at 1 month and followed-up for at least 4 years for major cardiac events. The results showed a positive relationship between the number of sleep disturbance symptoms and the occurrence of major cardiac events (including cardiogenic death, myocardial infarction, and repeated revascularization). Each additional sleep symptom was associated with a hazard ratio of 1.2 (P=0.001).[15]

Sleep disturbances and postoperative recovery

Sleep disturbances have significant impacts on the recovery after surgery. In patients after fast-track hysterectomy, poor sleep quality during the first postoperative night was strongly associated longer hospital stay.7 In patients after total knee replacement surgery, sleep disruptions 1 month following surgery was associated with functional limitations 3 months following surgery, indicating the importance of adequate sleep during postsurgical recovery.[16]

Measures to Improve Postoperative Sleep

Non-pharmacological measures

The first thing we can do to improve postoperative sleep is to remove environmental factors. For patients admitted to

the intensive care unit after surgery, managements according to sleep care guidelines, such as maintaining a quiet and dim environment and decreasing interruptions from care activities at night, improve sleep quality and sleep efficiency.[17,18] A meta-analysis showed that the use of ear plugs and eye mask is also helpful in promoting sleep among patients in ICU.[19]

Zolpidem

Zolpidem is a short-acting non-benzodiazepine compound of the imidazopyridine class that increases the activity of GABA, an inhibitory neurotransmitter, by binding to GABAA receptors at the same location as benzodiazepines.[20] In a small sample size study of patients undergoing hip or knee replacement, zolpidem administered 1 night before and on the first night after surgery improved feeling of sleep quality and fatigue but not sleep architecture.[21]

Melatonin

Melatonin is secreted by the pineal gland and its secretion regulates and modifies circadian rhythms and sleep.[22] Plasma melatonin levels are decreased after surgery and in hospitalized patients.[23] In a small sample size study of patients undergoing prostatectomy, preoperative melatonin enhanced sleep quality, decreased pain scores and tramadol consumption, but produced sedation during the postoperative period.[24]

Dexmedetomidine

Dexmedetomidine is a selective α2 adrenoceptor agonist with both sedative and analgesic properties;[25] and exerts sedative effects through an endogenous sleep-promoting pathway and produces a N2 sleep-like state.[26] In mechanically ventilated ICU patients, nighttime infusion of sedative dose of dexmedetomidine preserved the day-night cycle of sleep and improved the sleep architecture by increasing sleep efficiency and stage N2 sleep.[27,28] In non-mechanically ventilated elderly patients who were admitted to the ICU after surgery, low-dose dexmedetomidine (0.1 μg/kg/h) during the night after surgery prolonged total sleep time, increased N2 (and decreased N1) sleep, and improved subjective sleep quality.[27-29]

Effects of Sleep Promotion on Patients' Outcomes After Surgery

Sleep-promotion is helpful for recovery of postoperative patients. In ICU patients, improving sleep with ear plugs and eye mask reduces the incidence of delirium.[19,30] In a recent large sample size study of 700 patients (≥ 65 yr) who were admitted to ICU after surgery, low-dose dexmedetomidine (0.1 μg/kg/h) during the night after surgery decreased the prevalences of delirium on postoperative days 1 to 3, which was in accordance with the improved subjective sleep quality during the 3 nights of the same period. For patients after orthopedic surgery, use of zolpidem reduces postoperative pain, fatigue, and narcotic consumption;[31] and improves quality of life.[32]

SUMMARY

Sleep disturbances frequently occur after surgery, especially major surgery. Factors associated with the occurrence of postoperative sleep disturbances include preoperative comorbidity, type of anesthesia, severity of surgical trauma, postoperative pain, environment stress, as well as other factors leading to discomfort of patients. Development of sleep disturbances produces harmful effects on postoperative patients, i.e., higher risk of delirium, increased sensitivity to pain, more cardiovascular events, and poorer recovery. Both non-pharmacological and pharmacological measures can be used to improve postoperative sleep and may be helpful for postoperative recovery. Long-term effects of sleep promotion therapy deserve further study.

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RCL-20
State-of-the-Art Topics on Malignant Hyperthermia (MH)

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LEARNER OBJECTIVES

After participating in this activity, the learner will be able to:
(1) Identify which patients need a non triggering technique, and understand the phenotypic variability of MH
(2) Recall updates on diagnosis and treatment of MH;
(3) Describe the genetics of MH and related disorders
(4) Evaluate about connection between MH and exertional heat illness (EHI)

INTRODUCTION

This review course lecture will review various aspects of malignant hyperthermia (MH). These include 1) Pathophysiology and epidemiology of MH; 2) Care of MH susceptible patients with updated clinical evidence; 3) Current diagnostic tests available for MH and dilemmas of genetic testing; 4) Various phenotypes associated with MH susceptibility. Evidence to support in each will be presented.

1) Pathophysiology and Epidemiology of MH

Malignant hyperthermia (MH) is a potentially fatal hypermetabolic condition, caused by uncontrolled rise of calcium (Ca^{2+}) in skeletal muscle cells.[1,2] Three genes (RYR1, CACNA1S, and STAC3) have been identified to be associated with MH susceptibility.[1,3] All these genes are involved in Ca^{2+} handling in skeletal muscle cells. The known anesthetic triggers for MH are volatile anesthetics and succinylcholine. MH reaction can present during intraoperative or early postoperative period with hypercarbia, hyperthermia, tachycardia, and rigidity. The hypermetabolism can result in rhabdomyolysis, myoglobinuria, DIC and death.[4]

The incidence of MH reaction under anesthetic is estimated at 1/10,000.[5] The prevalence of MH is predicted to be much higher due to the variable penetrance nature of MH (i.e. MH reaction may not happen in MH susceptible patients with every exposure to triggers). In a recent study the prevalence is estimated to be 1 in 400.[6]

With morbidity of over 35%, and mortality rate of 12-15%, MH is one of the most feared complications of anesthesia.[7,8] In a recent review of North American MH registry data, risk of dying from MH was shown to have increased by 7 fold in 2007-2012, compared to previous cohort.[9]

2) Care of MH susceptible patients with updated clinical evidence

Upon suspicion of an MH reaction, triggers should be stopped and supportive measures such as cooling, hyperventilation and support of hemodynamics should be initiated. The main treatment for an MH reaction is Dantrolene sodium. It is shown that delay in dantrolene administration is associated with increased rate of complications from MH.[4] The dose of Dantrolene suggested by MH association of United States (MHAUS) is 2.5-10 mg/kg. There are two preparations of Dantrolene available, Dantrium® (20 mg vial, requiring 60 mL of sterile water to reconstitute), and Ryanodex®(250 mg ampoules, requiring 5 mL of sterile water to reconstitute).

A patient known to be positive for MH (MH susceptible-MHS) should be given trigger free anesthetic (i.e. anesthetic not containing volatile or succinylcholine). Anesthetic delivery machine should be cleaned according to the manufacturers' guidelines to remove any traces of volatile anesthetic. Activated charcoal filters are suggested for a faster reduction of volatile anesthetic concentration.[10]

Prophylactic administration of Dantrolene sodium is not required. MHS patients can be discharged the same day as the surgery, and there is no requirement for extended stay in MHS patients treated with trigger-free anesthetics.[11]

3) Current Diagnostic tests available for MH and dilemmas of genetic testing

MH susceptibility is diagnosed by abnormal contractions of surgically-cut fresh muscle bundles exposed to halothane and/or caffeine, known as caffeine-halothane contracture test (CHCT) or in vitro contracture test (IVCT). The sensitivity of 97% and specificity of CHCT are estimated at 97% and 78%, respectively.[12] CHCT is performed in 4 centers in US and one in Canada. IVCT is used outside of North America with a sensitivity of 99% and a specificity of 94%.[13]

The alternative is genetic screening of RYR1, CACNA1S, and STAC3 genes with a sensitivity of 60%, collectively.1 There are only 35 variants in RYR1 and two variants in CACNA1S that are listed as causative mutations for MH as per European MH group (www.emhg.org). However, to date there are over 400 variants have been identified in RYR1 and CACNA1S. Association of these variants with MH or causative nature of these is not known. Moreover, there are a few discordant reports of families who have negative contracture test, yet positive genetic results.[14] Therefore, interpretation of genetic results of at risk individuals can be quite complex.

4) Phenotypic variability of MH susceptible patients

MH susceptibility has been classically described as hypermetabolic reaction to triggered anesthetic as described above. However, over the last few decades case reports and case series have described a hypermetabolic reaction in MHS patients triggered by heat, and exercise.[15,16]

There are increasing reports of patients with idiopathic hyperCKemia, viral induced rhabdomyolysis, statin induced rhabdomyolysis who test positive for MH susceptibility with either contracture testing or genetics.[17,18] MH susceptibility is not considered an anesthetic-only condition anymore and many survivors of MH reaction may suffer from excessive myalgia and fatigue later on their lives and may develop rhabdomyolysis from heat and exercise. Despite a connection between exertional heat illnesses (EHI) and MH susceptibility, the extent of overlap of these two disorders is

not very clear. Patients with repeated EHI episodes should be assessed extensively by a neuromuscular specialist and if a clear etiology is not discovered, MH susceptibility should be assessed. [19]

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RCL-21
Flying the Anesthesia Machine: Lessons for Anesthesiology from Aviation

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INTRODUCTION

The evolution of anesthesiology has paralleled that of aviation in many interesting and useful ways. This lecture explores and develops those parallels, with the goal of extracting lessons that are valuable to both fields. Aviation is ahead of anesthesiology in the application of some novel technologies, and we will examine these as a way of predicting and perhaps guiding our own future.

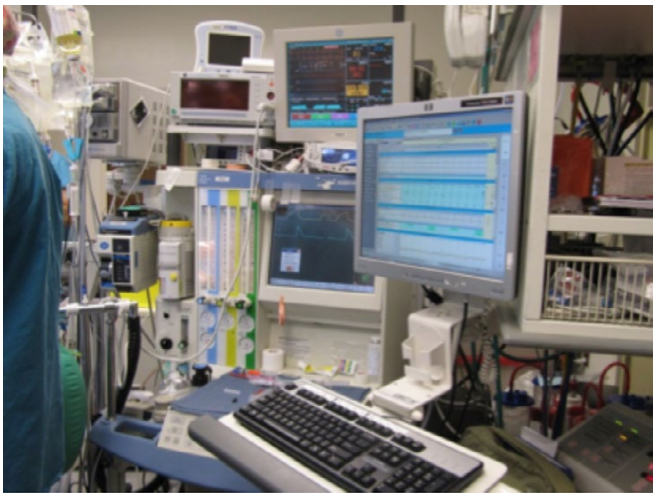
Specific examples of this parallel evolution include cockpit displays, use of checklists, "smart" alarm systems, and simulators. In each of these areas, we will discuss actual accidents, both in aircraft and operating rooms, to see how the lessons from these can guide new applications of technology. Accident analysis in aviation can actually help us prevent "disasters" in the operating room. The lecture contains both audio and video clips to illustrate these key points.

This lecture offers a different perspective of anesthesiology and critical care, from the viewpoint of a former aeronautical engineer and current anesthesiologist. As such, I hope that you will find it to be informative as well as entertaining.

Cockpit Displays

Modern aircraft cockpit displays are masterpieces of human factors analysis, efficiency, and prioritization of vital information. By comparison, our "anesthesia cockpit" displays are primitive, disorganized, and difficult to use. The modern aircraft pilot sees this:

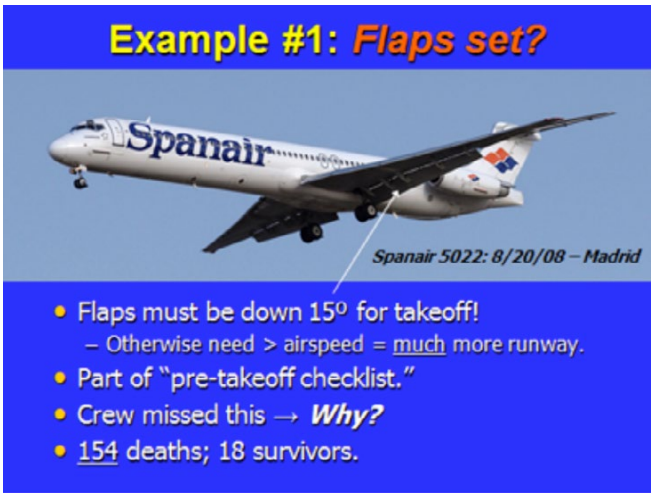
and to look at the "real world" outside of the cockpit, he/she only needs to gaze upwards a few inches. Meanwhile, in the anesthesia world, we see this:



and to look at our "real world" (i.e., at the patient), we must stand up and turn 180 degrees, with our backs turned to our instrument panel. There are several ways to improve this situation, all of which were developed in aviation. These approaches can include "augmented reality" visual aids as well as auditory inputs. We have recently started to modernize our anesthesia cockpit, but we still have far to go, as we shall discuss.

Checklists

The start-up checklist for a Boeing-747 contains 85 items – no pilot could remember all of those every day before starting to taxi to the runway. The aviation solution, of course, is the use of checklists, not only for starting the airplane, but for almost every aspect of both normal and emergency flight procedures. We will discuss examples of the disastrous consequences of failure to follow checklists during flight, and examine how those failures have high similarity to common adverse events in anesthesia. What are the checklist lessons from aviation, and how should these be applied to anesthesia? Here is a tragic aviation example, from which we can learn much:



Of course I am not the only person advocating the use of checklist in medicine – Atul Gawande has accomplished a great deal in the surgery world, starting with his book "The Checklist Manifesto."[1] He has even followed this up with an outcomes study, showing that the use of his intra-operative checklist leads to measurable improvements. If Dr. Gawande can persuade surgeons to use checklists, surely we can do the same in anesthesia.

A vital part of my message on checklists is that these are not "recipes for doing anesthesia." They do not take away our need for creative thinking or replace our skills in making a vital diagnosis in limited time with incomplete information. On the contrary, checklists are simply tools to help prevent us from "forgetting stuff." Like the start-up checklist for the B-747, no one can reliably and consistently remember all of the steps required in our complex procedures. This becomes even truer in the presence of "distractors" – those little unexpected and perhaps unimportant events that distract our attention when we are in the middle of an anesthesia induction, for example. Examples of distractors will also be discussed.

A final important feature of checklist use is knowing when to "leave" the checklist when it has not solved the problem at hand. A good example from aviation is of course the "Miracle on the Hudson," portrayed in the recent movie "Sully." Sullenberger (pilot) and Skiles (copilot) went through their engine-out checklist, but then due to the pressures of limited time and low altitude, they decided correctly that they needed to leave the checklist and improvise. We live in the same world – a good example from the operating room will be described.

Alarms

Frankly, most of our operating room alarms are almost worthless. Today's cockpit alarms actually talk to the pilot, as I will demonstrate: "too low, pull up" or "collision alert." Meanwhile, our alarms go "beep-beep-beep." In the poor acoustic environment of the operating room, we cannot even determine the source of the alarm, much less what it actually means. "Is that the pulse oximeter, or someone's pager beeping?" In 1992, Dr. Butch Loeb played 19 different alarm sounds to 44 anesthesia clinicians in a quiet room (not in a noisy OR). They correctly identified the source of the alarm 34% of the time![2] Our alarm sounds have changed little since that study was done, while aircraft alarms have become "smart" and specific: they tell you what is wrong, and in many cases what to do about it.

Some have objected to the idea of "talking alarms" in the OR because it might create a distraction. But there is no need for these advanced alarms to be heard by everyone in the room. If they are intended for the anesthesia provider, then they should play into our private, Bluetooth-connected earpiece. In fact, this alarm communication system could be two-way: we hear an alarm, and we give "Siri" – our digital anesthesia assistant – verbal instructions on what to do next. Too far-fetched? Why? The technology for it is quite simple today.

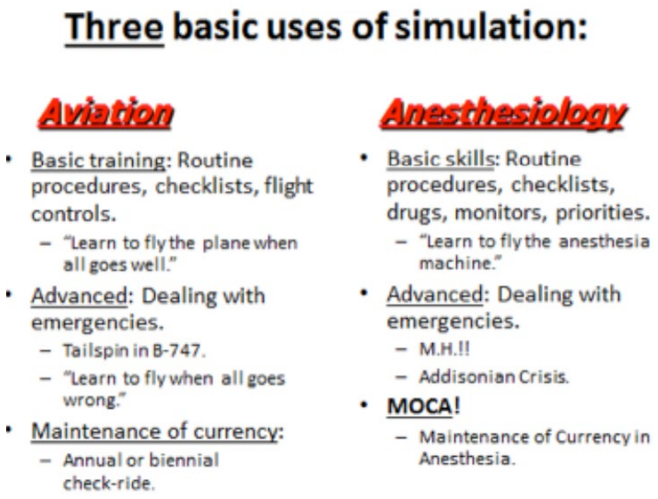
Simulation

Cockpit simulators have been used for training in aviation since 1909, as we can see below. Anesthesia simulators have been on the market for about 20 years, but are still in a fairly early stage of development.[3]

Early aircraft simulator, 1909


Anesthesia "cockpit" simulator, 2000

Aircraft simulators are used in three phases of pilot training (see table below), and anesthesia simulators have analogous applications. The probability that an anesthesia resident will deal with a full-blown episode of malignant hyperthermia during training is very small. Yet that resident must be capable of handling this life-threatening emergency if and when it happens. How do we train for this? The answer is obvious: through simulation. Not only can we simulate rare emergencies such as MH, but we can even allow the "patient" to "die" in the process. Then, by computer magic, we can back up the clock by thirty minutes, and say to our trainee: "OK, what did you learn, and what do you want to do differently this time?" This is exactly what is done in aviation simulation – the pilot can "crash" the airplane, time is reversed, and the pilot learns from his/her mistakes.



Additional uses of simulation include human factors research, such as designing and optimizing the displays and alarms that we discussed earlier.

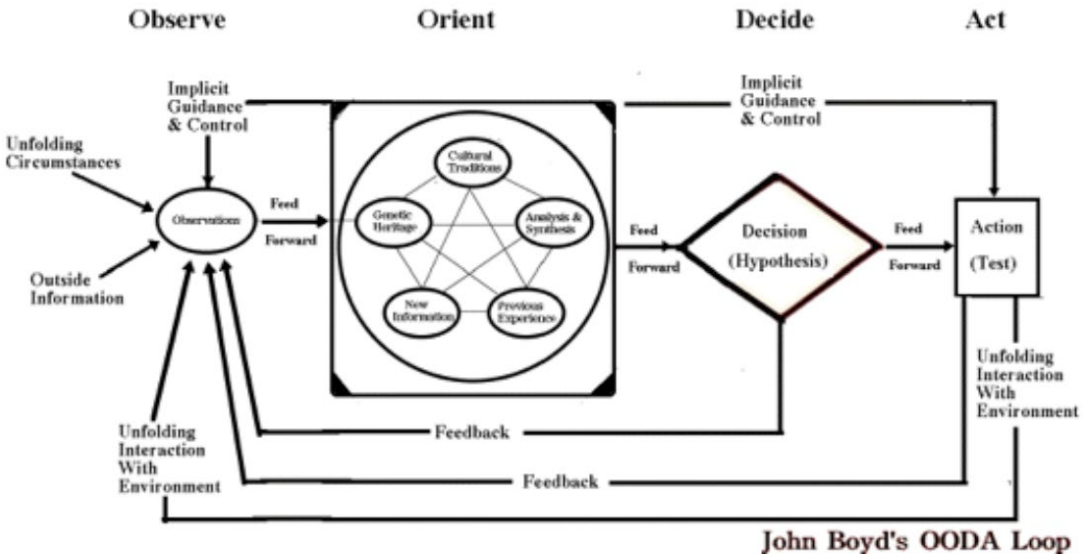
Decision-Making Processes

Anesthesiology, perhaps more than any other specialty, requires that we gather and sort relevant data, interpret it, make a diagnosis, and treat the patient in "real-time." We usually do not have the time to order additional tests or consult with other specialist experts. In many cases, we must literally act within seconds to prevent disaster. In this sense, doing anesthesia care is very similar to air combat. Yes, you heard right – I said AIR COMBAT. Why do I say that?

John Boyd is recognized as a pioneer of the "science" of air-to-air combat.[4] As a fighter pilot in both the Korean and Vietnam wars, he developed a decision-making algorithm for the combat process. This algorithm is called the "OODA Loop", and I have added in italics some key words for translating it into patient care:

- OBSERVE: Carefully watch and remember everything the other pilot (the patient) does.
- ORIENT: Understand their motivations, capabilities, reactions – "be" the other pilot (patient). This includes understanding their genetic and cultural heritage (history).
- DECIDE: Form a hypothesis (diagnosis) on what the other pilot (patient) will do next.
- ACT: Take an action (treatment) based on the above, and immediately go back to "observe" the result. Start the loop again, so that the "action" becomes a "test."

Here is Boyd's original OODA Loop diagram. Lest you think I have gone off the deep end, this algorithm has been applied to several other fields where similar decision processes apply, including business management.[5]



We will discuss an example of using OODA in the diagnosis and management of an anesthesia emergency. This is basically a "checklist" for real-time decision processes, the type that we do multiple times every day in the operating room.

CONCLUSIONS

There are many lessons that anesthesiology can learn from aviation, and we have only discussed a few of them here. The reverse is also true – there are lessons from anesthesiology that can be useful in aviation. The parallels and analogies with aviation are stronger in anesthesiology than any other field of medicine. In both anesthesia and aviation, the required knowledge base, training, and skills have grown rapidly with improved technology. Yet despite this increased complexity (and I will argue because of it), both aviation safety and anesthesia safety have made great strides in the past 30 years. We should continue to learn valuable lessons from aviation wherever possible, and I believe we can teach them a thing or two as well.

As my final thought, some have implied that new technology and better drugs will make anesthesia care so simple that "anyone can do it." That statement is totally false. Which of these two aircraft requires more skill and training to fly, and which provides better performance?

This one?

Or this one?

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RCL-22
Implementing Operating Room Management Improvement

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Disclosure: I am employed by the University of Iowa, in part, to consult and analyze data for hospitals, anesthesia groups, and companies. The Department of Anesthesia bills for my time, and the income is used to fund our research. I receive no funds personally other than my salary and allowable expense reimbursements from the University of Iowa, and have tenure with no incentive program. I own no healthcare stocks, other than indirectly through mutual funds.

My colleague Ruth Wachtel and I previously performed a systematic literature review to understand why it is challenging to find solutions to operating room management problems.1 One of our findings was that most people seeking assistance with medical or computer-related issues relied on colleagues.[1]

What is the best use of technology to improve the process of obtaining information from colleagues?[2] This is a poorly posed (insufficiently worded) question. First, we need to inquire as to the conditions when such communication results, at least on average, in evidence-based management decisions.[2] It does not help if there is communication but the decision made is inconsistent with the available evidence (i.e., science).

The scientific studies are limited to those for which teams make decisions and the quality of those decisions can be evaluated objectively (e.g., mathematics problems).[2] If there are N=30 teams in each of 2 groups, the N=30 is the teams and each of the teams has several study participants.[2] All members of the control group receive the information needed to make the correct decision.[2] The information is provided to all members before decisions are made.[2] In the "real world" groups, information about how to make a correct decision is provided to only one group member.[2] From a managerial perspective, the one person provided the full information is analogous to the one person at a meeting who knows the operations research, informatics, engineering, analytics, etc. Effect size is the odds ratio.[2] For example, a study had an odds ratio of 107, implying that the control group's odds of producing a correct decision were 107 times the odds of the "real world" group.[3] A correct decision was produced by 89% of control groups.[3] A correct decision was achieved by 7% of the "real world" groups.[3] The odds ratio of:

$$107 = (89\% / [100\% - 89\%]) / (7\% / [100\% - 7\%])$$

Among the 8 studies of team decisions for problems with correct answers, the minimum odds ratio was 18.2 The odds ratio of 107 was typical (i.e., median). Thus, for problems with correct answers, and the fact but that there are correct answers cannot be discerned without study, the odds of a group making the correct decision is very low.[2] Likely, when an anesthesiologist is trying to educate an operating room governance committee about science, the odds of success would typically be even worse than this *107 to 1*, because some members benefit from the status quo and/or may stand to gain from poor quality decision-making. Group-wise, consensus-driven, decision-making is not an appropriate leadership style for teams tasked with solving mathematical, operations research, type problems. Hospitals rely heavily on the leadership style of group-wise decision making because it is appropriate for most decisions, including those of an operating room governance committee; it is not an appropriate leadership style for operations type decisions (e.g., those that affect how late anesthesiologists work).[4]

Shared information is information that group members all know before group discussion.[2] An example is that surgeons differ in case durations (operating room times) for the same procedure. Unshared information is known only to one group member before a discussion and becomes known to others during a discussion.[2] The corresponding example, related to surgeons' operating room times, is that the extra time attributable to the primary surgeon when averaged over all cases at a hospital was only approximately 0.4 minutes (SE 0.1).[5]

When comparing shared and unshared information, the effect size is the standardized mean difference.[2] For example, in one study, groups discussed mean 10.72 items of shared information versus 7.05 items of unshared information, with pooled SD of 0.96 items.[6] The standardized mean difference was 3.84 = (10.72 – 7.05) / 0.96.[6]

Among the 12 studies with shared and unshared information, the minimum standardized mean difference (effect size) was 1.25.[6] Thus, shared information is more influential than unshared information during group discussions.[2] Group-wise, consensus-driven, decision making is not an appropriate leadership style for the operations research type problems because the discussion becomes focused on topics other than the mathematics even when the decision to be made is mathematical, and this is under the best possible conditions.[2] Shared information (i.e., not the mathematics related to the decision) is discussed earlier than unshared information ($P < 0.001$).[7,8] Shared information is repeated in discussion more than unshared information ($P < 0.001$).[9] Finally, group members with primarily shared information take more speaking turns than do members with primarily unshared information ($P < 0.005$).[10]

Knowing that meetings are ineffective for operations research type problems when used for group level decision-making (i.e., consensus) or consultative type level 2 decision-making (i.e., peer discussion), the subsequent study of technologies was for those that could help leaders to obtain solutions from outside his/her department.[11] A literature search is one of these technologies (i.e., it lets a leader obtain knowledge from outside his/her department). The scientific question, then, is what makes literature search for operating room management difficult? The answer turns out to be that the searcher needs to know the vocabulary as used in the

operating room management articles.[1] Since the objective of a search is to find articles, this means that the searcher needs to know the vocabulary before searching. Reference (1) is an experimental paper. We tried to find articles that we knew about and that were appropriate for specific managerial decisions.[1] Without knowing the precise scientific vocabulary, even we failed.[1] If the vocabulary is not known ahead, then one either needs to rely on a web site that provides the vocabulary or an advisor who provides initial papers.

An example of a web site with vocabulary is mine: www.FranklinDexter.net/education.htm. The structure of the website was developed based on the scientific results.[1] There are lectures on many topics in operating room management. Once we knew what was needed from the lectures (i.e., vocabulary), I assured that each lecture provided the vocabulary. In addition, each fact includes the corresponding reference. Multiple references assure that people can view the lectures, even without knowing the exact vocabulary, and then have access to at least one related article. A search can begin by using the citations of that article (e.g., using Google Scholar) and the references within that article.

The alternative approach for learning how to make correct problem-solving decisions is to rely on an advisor. Appropriate (best) ways to communicate with an advisor have been examined in many different experimental and some observational studies.[11] Our interest was in determining which communication technology was most suitable for problems with correct mathematical answers: face-to-face meetings, video (web) conferences, animated computer agents (avatars), telephone meetings (audio), live electronic chats, discussion forums (listserv, social media), and e-mail (asynchronous 1:1 written).[11]

There are advantages to using e-mail for communication with an advisor for these types of decisions.[11] E-mail is easy to use across organizational boundaries.[11] It is convertible to tasks (e.g., set follow-up flag), and it is asynchronous: no appointment arranged.[11] There is no expectation of an immediate response but there is an expectation of an eventual response, creating responsibility and reduced social loafing.[11] Training with e-mail programs significantly increases productivity in use (e.g., search rather than folders).[11] The decision-maker can construct (frame) the message carefully to increase the likelihood of receiving a useful response.[11] The decision-maker can read the response when least distracted and reread complicated portions.[11] The decision-maker has reduced cognitive load vs. face-to-face, video conferencing, or avatar; for factual material, written text is consistently easier to understand and as effective, or more effective, at changing behavior as other methods of communication.[11] On the advisor's end, the advisor can control cues to appear credible; titles and degrees in the signature line are expected.[11] The advisor can focus on constructing the content of the message rather than their physical appearance or the color of their slides.[11] By using e-mail, the advisor can include attachments with details.[11] In addition, the advisor can include written expression(s) of confidence in advice. That is the best predictor of usage in experimental studies.[11]

You might be thinking that e-mail is so old fashioned. However, our interests are the use of e-mail for purposes of obtaining advice about decisions with correct, mathematical answers. E-mail is not a good communication method for asking someone out on a day or requesting a pay raise. E-mail is a good choice of communication method for asking: "What formula should I use to quantify each nurse anesthetist's contribution to the department's overall fresh gas flow?"[12]

The next issue, then, for implementation of operating room management improvement, is how best to use e-mail for obtaining answers to questions. E-mail can include attachments, often with the expert as one of the authors.[11] What type of articles should be attached? Would it best be review articles with text and simple figures or primary article including data? Would it be articles with/without appendices with formulas?

The next study that we were able to perform evaluated the relative effectiveness of different articles used in a course. The operating room management course includes approximately 50 hours of material.[13] Reviewing statistics and learning the vocabulary while reading related articles takes 5 to 20 hours depending on the course participant's background.[13] The classroom time is 35 hours over 3.5 days, time spent mostly working in teams to complete cases.[13] Within a few days of finishing the course, N = 17 subjects completed a 36 item survey form, with 9 items about each of 4 articles.[13] Sequences of survey items were fully randomized.[13]

One example of the 4 articles studied was the reading for lecture #5. The article contained formulas, data, and 19 references.[14] A previous study showed that the number of references may be a cue to the quality of the article.[15] A second example of the 4 articles studied was the reading for lecture #4. The article did not contain formulas or data; the article was a traditional narrative review (about measuring adjusted and raw operating room utilization), with many (76) references.[16]

The subjects scored trust in the content using a 9-item assessment of trust, with questions about quality, usefulness, and reliability of each article's content.13 Quality, usefulness, and reliability are attributes of a unidimensional construct: trust in the information in the articles. Each of the 9 items was answered on a response scale from 1 being strongly disagree through 7 for strongly agree.[13] For example, the 3 questions about quality of the reading for lecture #5 were the following: A) In general, the Reading #5 provides me with high quality information; B) Overall, I would give information from Reading #5 high marks. C) Overall, I would give the information provided by Reading #5 a high rating in terms of quality. The 3 questions about the usefulness of the reading were: A) The information in Reading #5

is helpful for my work; B) The information in Reading #5 is valuable for my work; C) The information in Reading #5 is informative for my work.

Trust in an article's content was unaffected by data (P = 0.148).13 In other words, examples from other hospitals did not influence perception of the quality, usefulness, or reliability of the information. Rather, formulas in the articles increased trust (P = 0.0019).[13] Formulas in appendices serve an important role to audiences uninterested in the mathematics. Even if the person receiving the article will not use the formulas, or even understand the formulas, they will see the formulas in the published journal article; they are a significant cue that the article can be trusted.[13]

In summary, group-wide consensus-driven decision-making makes good sense for many, likely most, managerial decisions at hospitals. However, that leadership style appears highly unsuitable for operations research type operating room management decisions. The appropriate leadership style should be applied to each type of decision. For mathematical problems, the odds that a knowledgeable, single decision-maker with information will make correct decisions can literally be greater than 100:1 versus a committee. An individual hospital is rarely the source of answers to operating room management problems. Rather, the data from a hospital characterizes which problems need to be answered. Use a literature search and/or external advisor(s) to identify the few article(s) to read. Then, rely on the committee to assist in the implementation of the solution from the scientific study.

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RCL-23
Lies, Damn Lies and Anesthesia Myths

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INTRODUCTION

Physicians are no different from members of the lay public in preferring a plausible explanation (particularly when accompanied by a molecular mechanism) to an admission of ignorance. As a result, falsehoods, opinions, and guesses are repeated in lectures and textbooks and sometimes become embedded in the liturgies and canon of our specialty.

In this brief presentation we will brush over whether these old chestnuts arise from the scheming of "liars, damned liars, or scientific experts," emphasizing the more important question as to whether they now should be called out as anesthesia myths.[1]

Resuscitation Topics

Is Normal Saline "Normal" or Beneficial?

Intravenous fluid therapy arose in the 1800s to combat dehydration from cholera, then became part of routine care for surgical patients in the 1900s.[2] At present day, the IV fluids of choice for adults in most surgical suites are either 0.9% (Normal) saline or a "balanced" salt solution (Normosol, Plasma-lyte, or lactated Ringer's (Hartmann's) solution). Multiple lines of evidence demonstrate that use of 0.9% saline leads predictably to a greater incidence of hyperchloremia, a condition associated with worse outcomes (including longer lengths of stay and a greater likelihood of death).[3,4] In the absence of hypochloremic metabolic alkalosis there are sparse indications for large volumes of 0.9% saline, and no good reasons to use 0.9% saline as a routine maintenance solution.[5,6] Even in kidney transplantation there appears to be little advantage.[7]

Cricoid pressure improves patient safety during emergency intubations

Cricoid pressure was introduced to medicine by Brian Sellick in 1961.[8] In 26 patients considered at risk for aspiration, no regurgitation occurred during or after application of cricoid pressure in 23. In 3 patients, regurgitation occurred only after cricoid pressure was relieved following tracheal intubation. Sellick surmised that cricoid pressure had prevented regurgitation from occurring prior to and during intubation in these 3 patients. Nevertheless, Sellick provided no details regarding induction drugs, ventilation, patient body habitus, or other relevant factors that might also explain his findings.[9]

Sellick made several key assumptions.

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

Current data using CT and MR imaging techniques show that assumptions 1 & 2 are false.[9] There are no outcome studies supporting assumption 3, but such studies likely would not be feasible given rates of medically consequential aspiration during emergency surgery of ≤1 per 1000. As for assumption 4, multiple studies have shown that cricoid pressure can worsen the clinician's view of the airway during direct laryngoscopy.[10] Recent studies suggest that female patients require less forceful cricoid pressure than male patients.[11] If one were to grade the quality of the evidence supporting the use of cricoid pressure using standards of the Oxford Centre for Evidence Based Medicine, a grade no better than D could be assigned![9] In a recent survey, only 30% of Swiss and 52% of Austrian anesthesiologists use cricoid pressure as part of rapid sequence induction.[12] A Cochrane Collaboration review has concluded that a randomized trial is required.[13] Should we regard cricoid pressure both standard care and/or standard of care?

General Anesthetic Topics

Does invasive monitoring increases hemodynamic stability during induction?

Is there good evidence that having information from a central venous line or a pulmonary artery catheter increases hemodynamic stability during induction of general anesthesia? In a randomized comparison, inductions conducted without benefit of pulmonary artery catheter data required no more interventions to maintain stable hemodynamics than inductions "guided" by data from the pulmonary artery catheter.[14] Moreover, placement of the pulmonary artery catheter after induction of general anesthesia took less time than when performed before induction. Finally, there are no convincing data showing that pulmonary artery catheterization reduces the likelihood of mortality in this or any other circumstance.[15,16]

Does a slow induction increase hemodynamic stability?

Is there evidence that a slow induction results in fewer hemodynamic perturbations than a well-conducted rapid sequence induction? In patients scheduled for coronary artery surgery, rapid sequence induction with sufentanil and succinylcholine produced similar hemodynamics and necessitated no more interventions with vasoactive drugs or intravenous fluid boluses than a slower (2 min) opioid-relaxant induction or a very slow, careful (5-10 min) opioid-relaxant induction.[17-19]

Regional Anesthetic Topics

Methemoglobinemia and prilocaine

Methemoglobinemia has long been associated with prilocaine, the only local anesthetic that is metabolized to o-toluidine. According to many textbooks, prilocaine will reliably produce medically important degrees of methemoglobinemia when doses >600 mg are administered. Vasters and colleagues found that serious degrees of methemoglobinemia can arise after prilocaine doses as small as 400 mg in fit adult patients.[20] Interestingly, in a recent North American study, the local anesthetic most commonly associated with dangerous methemoglobinemia was benzocaine.[21]

Interscalene blocks and general anesthesia

In 2000 a report appeared in Anesthesiology describing four patients who experienced disastrous neurological complications after undergoing interscalene blocks while anesthetized.[22] The author suggested (and the suggestion was repeated in an ASRA guideline) that "Interscalene blocks should not be performed in anesthetized or heavily sedated adult or pediatric patients."[23,24] A more recent version of the ASRA guideline is less specific.[25] But, does the evidence show that anesthetized or heavily sedated patients are more likely to have neurologic damage?

There are case reports of nerve damage after interscalene blocks performed in awake patients.[26] Children routinely undergo nerve blocks (including interscalene blocks) while anesthetized and infrequently experience nerve damage.[27] Moreover, large series of interscalene blocks performed in patients receiving general anesthesia report an incidence of adverse neurologic events no more frequent that that reported after interscalene blocks performed without general anesthesia.[28,29] Is it reasonable to issue a practice guideline based only case reports and opinions that, in effect, labels the use of deep sedation or general anesthesia before interscalene block as malpractice when there are large published series that provide contradictory evidence?[30]

CONCLUSIONS

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

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