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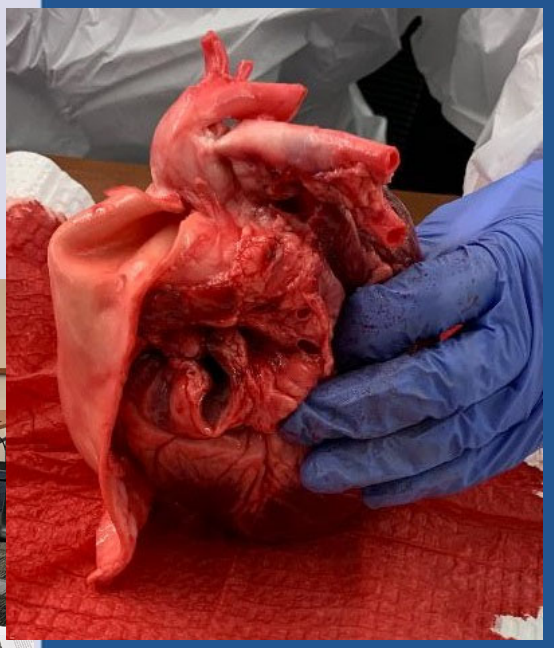
TOPICS IN THIS ISSUE



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Front Cover:
The front cover depicts doctoral students enrolled in the Duke University Nurse Anesthesia Program enthusiastically engaging in dissection of porcine hearts. Pictured from left to right are Christine Parrilli BSN, RN, CCRN, Winifred Hwang, BSN, RN, and Zachary Smith, BSN, RN, CCRN-CSC. The heart dissection lab is part of the program's advanced pathophysiology course in year 1 and enables graduates to visualize how pathophysiological changes impact the flow of blood through the heart.

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For additional information, please contact:

Vicki Callan, PhD, CRNA, CHSE, FAANA
Webster University Department of Nurse Anesthesia
Browning Hall, ISB 107
8274 Big Bend Blvd.
St. Louis, MO 63119
314-246-5928; Intsjna@aol.com

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Thoracoscopy in a Patient with Alpha-1 Antitrypsin Deficiency

Megan Amis, DNAP, BSN
Missouri State University

Key Words: anesthesia, thoracoscopy, pleurodesis, bleb resection, tension pneumothorax, alpha-1 antitrypsin deficiency, one-lung ventilation

Alpha-1 antitrypsin deficiency (AATD) is a genetic disease that destroys elastic lung tissue.[1] Formation of air-filled spaces within the lung parenchyma called bullae increases the risk of spontaneous pneumothorax in these patients.[2] Thoracoscopy with pleurodesis, which is the surgical fusion of the visceral and parietal pleura, is often required to remove damaged lung tissue and prevent recurrence of a pneumothorax. The purpose of this case report is to discuss the anesthetic goals and management of a patient with AATD undergoing thoracoscopy.

Case Report

A 58-year-old male (86.2 kg, 175 cm, BMI 28 kg/m^2) presented to the emergency department with complaints of chest pain and shortness of breath. A chest x-ray revealed a spontaneous left pneumothorax with evidence of chronic hyperinflation. Other significant past medical history included arthritis, systemic lupus erythematosus, and seasonal allergies. The patient was a non-smoker without a previous history of lung disease or pneumothorax. Although genotyping results were not available preoperatively, strong clinical evidence combined with the patient's low alpha-1 antitrypsin (ATT) serum level suggested ATTD. A chest tube was inserted and temporary resolution of the pneumothorax was achieved. The patient was admitted to the Intensive Care Unit (ICU) for observation. However, 2 days after the surgery, the pneumothorax reoccurred and a second chest tube was placed. After discussing his options, the patient consented to surgical treatment of the reoccurring pneumothorax through thoracoscopy with pleurodesis and bleb resection.

The patient presented to the operating room agitated and in moderate pain. He was tachycardic (110/min), normotensive, and his SpO_2 was maintained at 97% on O_2 4 L/min via nasal cannula. All preoperative laboratory values were within normal limits. Standard noninvasive monitors were applied and the patient was pre-oxygenated with O_2 10 L/min via face mask for 5 minutes. General anesthesia was induced with midazolam 2 mg, fentanyl 100 mcg, lidocaine 100 mg, propofol 180 mg, and rocuronium 100 mg. Bag mask ventilation was not attempted. Endotracheal intubation was performed by direct laryngoscopy with a 39 F double-lumen endotracheal tube (DLT). Proper placement of the tube was verified with a fiberoptic bronchoscope and the bronchial cuff was visualized in the left main bronchus. Once intubated, general anesthesia was maintained using sevoflurane 3% inspired concentration in a mixture of O_2 1 L/min and air 1 L/min. The patient was initially ventilated with low tidal volumes (V_T) of 4 mL/kg ideal body weight with peak inspiratory pressures (PIP) maintained below 10 mmHg.

An additional large-bore IV was inserted and the patient was placed in the right lateral decubitus position. Placement of the DLT was verified again with the fiberoptic bronchoscope and the left lung was isolated. Once the left lung was isolated, both chest tubes were removed and V_T was

increased to 8 mL/kg ideal body weight. At this time, the patient experienced sudden, severe hypotension (64/42 mmHg). The surgeon was notified of a suspected tension pneumothorax and quickly began incision. Over the next 20 minutes, 5% albumin 500 mL, lactated ringers 1 L, several epinephrine boluses (10 mcg), and a phenylephrine infusion at 100 mcg/min was initiated to maintain cardiovascular stability. The patient's SpO_2 and $EtCO_2$ were maintained at 90-94% and 40-45 mm Hg respectively throughout this period of the case. Once the bullae were resected, the tension pneumothorax resolved and hemodynamic stability returned.

The remainder of the case proceeded without further incident. Manual and apneic ventilation were utilized periodically to facilitate surgical exposure. Suture lines were visualized, and the absence of an air leak was confirmed using a Valsalva maneuver. At the end of the case, a new chest tube was inserted and sutured in place. Neuromuscular blockade was reversed using sugammadex 200 mg. The patient was extubated fully awake and transferred on standard noninvasive transport monitors and O_2 10 L via simple face mask to the ICU for further observation. Of note, the patient experienced significant post-operative pain and required additional opioid administration upon awakening.

Discussion

Although considered rare, AATD is the most common hereditary disorder in adults.[1] ATT is a protease inhibitor synthesized primarily by hepatocytes in the liver.[1] Its main function is to inhibit neutrophil elastase, the enzyme responsible for degrading elastin and other types of connective tissue in the lungs.[1] Several different types of mutations in the *SERPINA1* gene can lead to misfolding or reduced synthesis of ATT, resulting in inflammation and destruction of lung tissue and emphysema.[1] Furthermore, intrahepatic accumulation of ineffective AAT can result in liver disease.[3] Treatment for AATD focuses on early diagnosis and implementation of preventative measures, such as avoidance of smoking, pollutants, and alcohol.[3]

While damage to lung tissue begins at an early age, AATD often goes unrecognized and is not diagnosed until late signs of irreversible lung disease are evident.[3] End-stage emphysematous destruction of an area of lung tissue is known as a bulla.[2] Positive pressure ventilation can cause expansion or rupture of bullae, resulting in a pneumothorax. Thus, positive pressure ventilation should be avoided in favor of spontaneous ventilation whenever possible. If positive pressure ventilation must be used in patients with severe emphysema, peak inspiratory pressure (PIP) should be limited to < 10 cm H_2O until isolation of the affected lung is achieved.[2] Once the affected lung has been isolated, proper management of one-lung ventilation is critical for preventing severe hypercapnia, hypoxemia, and acute lung injury (ALI). Protective one-lung ventilation strategies include ventilation with V_T of 6-8 mL/kg with positive end-expiratory pressure (PEEP) 5 cm H_2O, respiratory rate to maintain $PaCO_2$ between 35 and 40 mmHg, frequent alveolar recruitment maneuvers, and avoidance of fluid overload.[2]

Although the PIP was maintained at <10 cm H_2O prior to lung isolation in this case, the patient did develop a tension pneumothorax. Once the chest is open (or the chest tube has been removed), bulla compliance is no longer limited by chest wall integrity. This can lead to further expansion and rupture of the bulla.[2] In this case, the decision was made to administer a neuromuscular blocker to prevent spontaneous respirations and facilitate the placement of the

DLT. In hindsight, maintenance of spontaneous ventilation may have been safer for this patient and may have helped to avoid the occurrence of the tension pneumothorax.

As anesthesia practitioners, it is imperative to recognize the signs of a tension pneumothorax. Failure to do so quickly could result in sudden respiratory or cardiac arrest.[4] While symptoms may vary greatly among individuals, those most commonly reported include progressive tachycardia, severe hypotension, hypoxia, respiratory distress, decreased or absent unilateral breath sounds, and mediastinal shift.[4] Treatment includes immediate needle decompression or chest tube insertion.[4] When rapid decompression is not possible, hemodynamic stability should be achieved by fluid resuscitation and the use of vasopressors.[4] Because the surgeon was in the room and ready to begin immediately, the decision was made in this case to maintain hemodynamic stability with fluids and vasopressors instead of needle decompression.

Despite receiving fentanyl 300 mcg during this procedure, the patient reported significant pain upon waking up from surgery. Pleurodesis, which is the surgical fusion of the visceral and parietal pleura, causes severe inflammation and pain within the pleural cavity. Insufficient pain management after thoracic surgery can prolong recovery and result in increased postoperative complications,[5] thus, adequate pain management is essential for recovery. Thoracic epidurals have traditionally been used as the gold standard for pain relief for post-thoracotomy pain.[5] However, several disadvantages to thoracic epidurals including hypotension, pruritus, urinary retention, accidental intrathecal injection, and high failure rates limit their use.[5] Instead, opioids and multimodal analgesia techniques including nonsteroidal anti-inflammatory drugs and acetaminophen were utilized during this case. Recently, the thoracic erector spinae plane (ESP) block has been utilized as an alternative to the thoracic epidural due to its similar analgesic efficacy and fewer adverse effects. Going forward, anesthesia practitioners at this facility should consider the possibility of better pain control utilizing the ESP block.

After reviewing the existing medical literature, it is clear that AATD is a rare but serious condition that often results in the formation of reoccurring spontaneous pneumothoraxes. While chest tube insertion can be effective, surgical intervention is often required. Patients with AATD are at an increased risk of pulmonary complications in the perioperative period. There should be a high suspicion of tension pneumothorax when clinical manifestations are present, and prompt action should be taken to ensure hemodynamic stability of the patient. To limit the risk of pulmonary complications, it is imperative for anesthesia practitioners to use best practices when managing patients with AATD. These measures include limiting the use of positive pressure ventilation until lung isolation is achieved, as well as proper DLT placement and the use of protective one-lung ventilation strategies.

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Mentor: Jill Layman, DNAP, MSNA, CRNA

Anesthetic Management of a Patient with Noonan Syndrome

Danielle Van Eron, DNP, BSN
Northeastern University

Keywords: Noonan syndrome, congenital heart defect, pulmonary valve stenosis, non-operating room anesthesia

Noonan syndrome (NS) is an autosomal-dominant disorder with an estimated prevalence of 1 in 1000 to 2500.[1-3] Features most consistent with NS include widely set eyes, low-set ears, short stature, and pulmonary valve stenosis.[1-4] Other conditions associated with NS include hypertrophic cardiomyopathy (HCM), atrial septal defect (ASD), varying degrees of developmental delay, bleeding diatheses, and malignancy.[2-5] A thorough preoperative airway assessment is prudent as patients with NS may be a difficult tracheal intubation due to anatomical abnormalities.[5,6] This case study describes the use of general anesthesia in a pediatric patient with NS undergoing magnetic resonance imaging (MRI).

Case Report

A 2-year-old, 8.5 kg female patient with NS presented for MRI of the brain and spine under general anesthesia to evaluate a known neuronal migration disorder, dysplastic left frontal lobe, and paraspinal lesion. Other comorbidities included gastrointestinal dysmotility, vesicoureteral reflux, HCM, status post pulmonary valve stenosis, ASD, obstructive sleep apnea, hypernatremia, venous thromboembolism, acquired von Willebrand disease, and developmental delay. The patient had multiple previous cardiac catheterizations as well as echocardiograms to evaluate her heart function. The patient had a preexisting gastrostomy tube for medication administration as well as an ileostomy. Her medication regime included apixaban, atenolol,

cyproheptadine, esomeprazole magnesium, famotidine, ipratropium 0.02% nebulizer, levalbuterol nebulizer, montelukast, and verapamil.

An airway assessment was unattainable due to the child's age, however past anesthetic records revealed the ability to manage her airway with both a laryngeal mask airway (LMA) and an endotracheal tube. She tolerated multiple general anesthetics well. She previously underwent bronchoscopy and fiberoptic laryngoscopy, which were normal, as well as an MRI which revealed normal neck and airway anatomy. The patient's physical exam revealed small stature, micrognathia, hypertelorism, and no audible murmur.

Prior to induction, albuterol 2.5 mg was administered via nebulizer. A pulse oximeter and a 3-lead electrocardiogram (ECG) were applied for induction. General anesthesia was achieved via mask induction with sevoflurane 8% inspired concentration in O_2 4 L/min. The patient was spontaneously ventilating throughout induction. After induction, sevoflurane was decreased to 5% inspired concentration in O_2 2 L/min until intravenous access was obtained. A buretrol was used to administer dextrose 5% and sodium chloride 0.2% with an intravenous filter. An intravenous propofol infusion was initiated at 300 mcg/kg/min distal to the intravenous filter. A size 1.5 LMA was successfully placed. The patient was placed on transport monitors, spontaneous ventilation was maintained with Mapleson C breathing system with O_2 10 L/min, and the patient was transferred to the MRI suite. General anesthesia was maintained with sevoflurane 1.3-1.5% expired concentration in O_2 2 L/min and a propofol infusion at 200 mcg/kg/min.

Anesthesia for the 154-minute MRI was uneventful. To treat episodes of patient movement, two separate propofol 10 mg boluses were administered. A propofol infusion was titrated accordingly at 200-275 mcg/kg/min. Upon completion of the scan, anesthetic gases were discontinued, and the patient was transported back to the pediatric induction area with Mapleson C breathing system with O_2 10 L/min. Standard noninvasive monitors were applied and the propofol infusion was discontinued. When the patient was awake and making purposeful movements, the LMA was removed. A face mask was applied with continuous positive airway pressure of 5 cmH_2O. Once adequate ventilation and oxygenation was confirmed without airway intervention, a face mask was applied with O_2 6 L/min and the patient was transferred to the post anesthesia care unit.

Discussion

Noonan syndrome is an autosomal dominant disorder but sporadic cases have been reported.[1-3,7] A diagnosis of NS can be made on clinical features alone, however genetic testing is ideal to determine a definitive diagnosis.[1-2,4] A mutation of the PTPN11 gene on chromosome 12 accounts for nearly 50% of cases.[2,5] The patient in this case study had a mutation in SHOC2 (S2G) with NS phenotype, which is better described as "Noonan syndrome-like disorder with loose anagen hair".[1] Pulmonary valve stenosis is the most common congenital cardiac defect associated with NS followed by HCM and ASD.[1-5] These patients should have serial echocardiograms and lifelong cardiology evaluation.[1,5]

Phenotypic characteristics may change with age and patient presentations range from mild to severe.[1] Treatment for Noonan syndrome is aimed at symptomatic improvement and supportive care as there is no cure.[2,4] Treatment is multidisciplinary and may include both invasive and non-invasive interventions for cardiac lesions, medications to treat heart failure such as beta blockers and diuretics, growth hormone replacement therapy, treatment of hematologic disorders as well as supportive care for neurodevelopmental delays, hearing deficits, ophthalmic defects, and dental/mouth abnormalities.[1,7] The prognosis of patients with NS is contingent on the severity of their phenotype.[1] While many NS patients have an average lifespan, the involvement of a cardiac lesion and the severity of that lesion is linked to an increase in morbidity and mortality.[1,4]

Several factors should be considered when providing anesthesia for a non-operating room procedure. These factors include the length of the procedure, limited access to the patient, distance from the operating room, the skill and comfort level of the anesthesia practitioner, and the availability of emergency response systems.[8] Diagnostic radiology procedures such as MRI are often long and require patient immobility to facilitate imaging.[8] The addition of a propofol infusion for this patient's MRI allowed for rapid titration to ensure the patient remained motionless. Patient monitoring is more likely to be remote in a non-operating room location, which could result in a delay in recognition of and intervention for adverse events.[8] Clear and open communication with the procedural team is imperative to ensure patient safety.[8] It is a challenge to monitor a patient from afar, especially one with cardiac comorbidities. During this case, a safe time to enter the MRI room was established with the procedural team to physically assess the patient, her intravenous access, and the LMA.

The focus of care for this patient was maintaining adequate oxygenation and diligent cardiovascular monitoring. Airway management of a NS patient may be challenging as they can be a difficult laryngoscopy due to a short, webbed neck, micrognathia, and/or dental/jaw abnormalities.[1,5-7] It is vital to have backup airway equipment available such as video laryngoscopy or a pediatric flexible fiberoptic bronchoscope.[6,7] Hypoxia should be avoided as it can cause right ventricular (RV) strain from increased pulmonary vascular resistance (PVR) which can be detrimental in patients with pulmonary valve stenosis.[7] Other causes of increased PVR should be avoided if possible, such as hypercarbia, increased intrathoracic pressure, sympathetic nervous system stimulation, pain, hypothermia, and the use of N_2O.[4,6] An LMA was used for this patient to facilitate spontaneous ventilation and to decrease the stress response and pain from airway manipulation.[6] The administration of O_2 100% was a deliberate decision to limit the risk of hypoxemia if the patient experienced any respiratory difficulties as well as the avoidance of N_2O to minimize RV strain.

Euvolemia was achieved using a buretrol for strict intravenous fluid administration and to maintain adequate preload and prevent hypervolemia.[7] Afterload was maintained, and the patient required no hemodynamic intervention.[7] Tachycardia was avoided in this patient with a plan to administer diluted esmolol if warranted due to her history of HCM.[5,7] The choice of dextrose 5% and sodium chloride 0.2% was recommended by the patient's urologist due to a recent hospitalization for hypernatremia. While Trisomy 21 is the leading cause of syndromic congenital heart defects, NS is the second most common cause.[3] If caring for a patient with features analogous to NS, a simple non-invasive test such as an ECG can be ordered. Most NS

patients with cardiac involvement often will have abnormal ECG findings such as wide QRS complexes, left axis deviation and/or giant Q waves.[2]

Noonan syndrome poses many anesthetic risks and concerns. While this case study did not involve surgical intervention in the operating room with general anesthesia, it is important to understand the pathophysiology and subsequent implications of NS. This general anesthetic was performed in a non-operating room setting which poses its own unique set of challenges and considerations. Communication with ancillary staff is of upmost importance as well as the preparation and immediate intervention should an emergency arise.

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Mentor: Connie Lorette, PhD, CRNA, APRN

Anesthetic Management of a Patient with Kennedy's Disease

Magdalena Gregorczyk, DNAP
Yale New Haven Hospital School of Nurse Anesthesia

Keywords: Kennedy's syndrome, Kennedy's disease, spinal bulbar muscular atrophy, lower motor neuron disease

Kennedy's disease, a rare x-linked disorder, has unique perioperative anesthetic considerations due to progressive spinal and lower motor degeneration. Bulbar involvement can lead to

spontaneous laryngospasm, aspiration, and inadequate ventilation requiring postoperative respiratory support.[1] Spinal motor involvement causing muscle wasting requires careful titration of nondepolarizing neuromuscular blockers and avoidance of depolarizing neuromuscular blockers.[1] Although Kennedy's disease is uncommon, a combination of a high frequency of misdiagnoses and a slowly progressing disease course makes these individuals likely candidates for requiring anesthetic care.[2] Currently, case studies in the literature are limited, with few recommendations regarding anesthetic care.

Case Report

A 58-year-old male was scheduled for an upper gastrointestinal endoscopy with CRE balloon (Boston Scientific) dilation due to dysphagia and esophageal stricture. The patient presented with a BMI of 20 kg/m^2 and no known allergies. He had a known history of Kennedy's disease, labile hypertension with autonomic instability, chronic pain, hyperlipidemia, hyperthyroidism, colon polyp, non-alcoholic fatty liver disease, and spontaneous laryngospasm. Past surgeries included hernia repair and arthroscopic knee surgery. He had no recorded past anesthetic complications.

Preoperative cardiac clearance was obtained. A recent echocardiogram showed mild concentric left ventricular hypertrophy with an ejection fraction of 65%, left atrial enlargement, ventricular hypertrophy, and sinus bradycardia. A comprehensive metabolic panel was within normal range with the exception of a high creatine kinase of 302 U/L (nl 44-196), a common finding in patients with Kennedy's disease.

The preoperative anesthesia exam revealed a Mallampati score of 2, a thyromental distance greater than three finger breadths, and clear lungs on auscultation. The patient reported difficulty walking up two flights of stairs due to neuromuscular weakness. The anesthetic chosen for this procedure was deep sedation. Viscous oral lidocaine was ordered as a premedication to facilitate smooth insertion of the endoscope.

The patient was attached to standard monitors on arrival to the surgical suite, and O_2 3 L/min was delivered via nasal cannula. A bite block was inserted in his mouth. The patient was placed into a high Fowler's position. On induction, the patient received midazolam 2 mg, glycopyrrolate 0.2 mg, lidocaine 60 mg, ketamine 30 mg, and fentanyl 25 mcg IV. The endoscope was inserted through the oropharynx and into the esophagus while the anesthetist supported the patient's jaw and head. The patient started coughing and received an additional 25 mcg of fentanyl and 40 mg of lidocaine IV. The coughing then resolved. Maintenance medication throughout the procedure included alternating IV boluses of ketamine, propofol, and fentanyl. In total, the patient received an additional 30 mg of ketamine given in 10 mg increments, 40 mg of propofol in 10 mg increments, and an extra dose of fentanyl 25 mcg. The patient also received lactated Ringer's 500 mL.

Hemodynamically the patient was hypertensive throughout the procedure but within range of his normal blood pressure. There were no significant changes in his heart rate or rhythm. He maintained spontaneous respiration at a rate of 6-10, SpO_2 in the 90s-100%, and adequate end-tidal CO_2.

The procedure lasted for a total of 45 minutes and was uneventful. The patient had an uncomplicated postoperative recovery and was discharged home that same day in stable condition.

Discussion

A basic understanding of Kennedy's disease is necessary when performing a preoperative anesthetic assessment. The pathophysiology results from a dysfunctional and toxic androgen receptor.[1,2] Normal cell function is impaired in tissues that hold this receptor. Androgen receptors are primarily found in the lower motor neurons of the nervous system.[2] While the exact mechanism is unknown, neuronal destruction leads to bulbar dysfunction and muscle weakness.[1] Androgen receptors are also found in other body systems, including cardiovascular, immune, and hematopoietic.[3] Non-neurologic conditions in Kennedy's disease also occur, including osteopenia, metabolic syndrome, hyperlipidemia, diabetes, and non-alcoholic fatty liver disease.[3]

The typical onset of Kennedy's disease is in the fourth decade of life and its progression is slow.[2] Initial symptoms include tremors and muscle weakness of the proximal muscle groups.[2] Facial weakness is noted by an asymmetry of the face. A nasal voice signifies palatal weakness.[3] Scalloping and atrophy of the tongue are suggestive of bulbar involvement.[3] In addition, patients may complain of dysphagia and exhibit dysarthria.[2] The symptoms of bulbar dysfunction progress with the disease course. Advanced Kennedy's disease can lead to silent aspiration pneumonia and respiratory failure.[2] The lifespan is usually normal, and most patients do not typically succumb to disease complications.[2]

The choice of anesthesia should be guided by individual symptoms, the complexity of the procedure being performed, and risk factors. Risks of anesthesia vary based on the progression and presentation of the disease course. There are no definitive recommendations in the literature; however, airway manipulation should be avoided when patients present with bulbar involvement and respiratory impairment.[1] Manipulation of the airway places the patient at risk for laryngospasm, aspiration, and postoperative respiratory failure.[1] Ma and associates reported the administration of a successful general anesthetic for bariatric surgery in a patient with Kennedy's disease.[4] In this procedure, a normal pulmonary function test (PFT) was used as a deciding factor to proceed with the case using general anesthesia.[4] It was predicted that in the presence of normal respiratory muscle function preoperatively, the patient would tolerate general anesthesia and recover without postoperative respiratory complications.[4] Other resources suggest that general anesthesia is safe in the early disease course but should be avoided later as the disease advances.[1]

Rapid sequence endotracheal intubation or awake intubation is a safe choice if the patient is at risk for aspiration.[1] Laryngospasm and airway obstruction, however, can occur without tracheal intubation. Passing the endoscope into the esophagus is highly stimulating, so enough sedation must be provided to prevent coughing, gagging, laryngospasm, and vomiting while also keeping the airway safe.

This was a successful case where a patient with Kennedy's disease tolerated an upper endoscopy well. The patient presented with bulbar symptoms that included dysphagia and spontaneous laryngospasm. The risks and benefits of airway manipulation with and without tracheal intubation were deliberated. It was decided that spontaneous ventilation and light to moderate sedation would be the safest option. The patient was at low risk for and had no history of aspiration. All rescue equipment was readily available if airway resuscitation was required. The anesthetic plan included a multimodal approach focusing on ketamine. Ketamine provides analgesia and amnesia, while sparing upper airway muscle tone and laryngeal reflexes and provides sedation without respiratory depression.[6] Glycopyrrolate 0.2 mg was administered IV to counteract increased salivary secretions from ketamine. The use of glycopyrrolate was an important step because patients with Kennedy's disease may have a decreased ability to mobilize secretions.

Since patients with Kennedy's disease may be more sensitive to respiratory depression, only small doses of propofol (10 mg) were used incrementally. Minimal fentanyl in 25 mcg increments was used to depress the cough reflex. In conjunction with intravenous sedation, the use of viscous lidocaine facilitated blunting of airway reflexes from endoscope stimulation but was used sparingly enough to prevent obstruction and aspiration. Sitting the patient upright also decreased the risk of aspiration. Although there was concern that midazolam could add to the depressant effects of other anesthetics, it was used in this case to decrease the amount of propofol administered.

Preoperative PFTs were not available to determine lung function of this patient. Since there were no plans to mechanically ventilate the patient and he did not complain of shortness of breath, they were not warranted. If intubation had been necessary, PFTs would have been useful and awake fiberoptic intubation or RSI would have been the best route.[1]

It is hoped that due to the limited amount of case studies in the literature and the rarity of Kennedy's disease, this case report makes a significant contribution to the literature.

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Mentor: Marianne S. Cosgrove, PhD, DNAP, CRNA, APRN, FAANA

Anesthetic Management for a Patient with Brugada Syndrome

Michael Davidson, DNP
Uniformed Services University of the Health Sciences

Keywords: Brugada syndrome, anesthetic management

Brugada syndrome is an arrhythmic disorder that is characterized by a right ventricular conduction delay that presents on an electrocardiogram (EKG) as ST segment elevation in leads V1-V2.[1,2] It is categorized into three patterns based on the differences in T wave and ST segments.[2] Its prevalence is approximately 1-4 people in every 2000 globally,[3] it commonly presents in middle-aged males, and it is often diagnosed incidentally through EKG.[2] These patients are at risk for sudden cardiac death (SCD) due to abnormal ventricular conduction.[2] This case report describes the anesthetic management for a patient with Brugada Syndrome undergoing general anesthesia.

Case Report

A 31-year-old female (58 kg, 162 cm, BMI 22 kg/m^2) presented for a Lefort I and Bilateral Sagittal Split Osteotomy for treatment of mandibular hyperplasia and dental malocclusion. Her past medical history was significant for Brugada Syndrome status post internal cardiac defibrillator (ICD) placement, asthma, post-traumatic stress disorder, anxiety, depression, and alcohol abuse. Her current medications included citalopram 40 mg every day and buspirone 10mg three times every day. A preoperative EKG revealed sinus rhythm, incomplete right bundle branch block, and Type 3 Brugada pattern, a positive T wave and saddleback ST segment,[4] in leads V1-V2. A physical cardiac exam was performed and a basic metabolic panel (BMP) was drawn; all findings were unremarkable. The surgical team requested permissive hypotension, systolic blood pressure (SBP) of 90 mm Hg or less, due to risk for bleeding during the procedure.

Preoperatively, the patient was given midazolam 2 mg intravenously (IV) and oxymetazoline one spray in bilateral nares. After arriving in the operating room, standard non-invasive anesthesia monitors were applied including a 5-lead EKG and axillary temperature probe. Initial EKG tracing showed sinus rhythm with a rate between 80-95/min with no ectopy noted. Defibrillator pads were applied and were connected to an external defibrillator. The patient was pre-oxygenated at 10 L/min for 3 minutes utilizing a standard anesthesia mask. Intravenous induction medications administered were fentanyl 100 mcg, lidocaine 20 mg, propofol 150 mg and rocuronium 30 mg. The trachea was intubated with a cuffed nasal Right Angle Endotracheal

(RAE) tube, size 6.5, through the right nostril utilizing video laryngoscopy and Magill forceps. Mechanical ventilation was initiated with a respiratory rate of 12 breaths/min, tidal volume (TV) at 8 mL/kg and $EtCO_2$ was maintained between 39 and 42 mm Hg. The patient was given dexamethasone 10 mg and ampicillin and sulbactam 3 g IV. A magnet was placed over the patient's ICD, no changes in EKG were noted. A urinary catheter was inserted and an upper body forced air warmer was applied.

General anesthesia was maintained with isoflurane 1.2% in a mixture of O_2 0.8 L/min and air 0.8 L/min. A remifentanil infusion was started at 0.05 mcg/kg/min and a 20 gauge arterial line was placed in the patient's right radial artery. Neuromuscular monitoring was performed with a peripheral nerve stimulator using the tibial nerve. Additional boluses of rocuronium (10 mg to 50 mg) were given as needed to maintain muscle relaxation. A phenylephrine infusion of 10 mcg/min, intermittent ephedrine boluses of 2.5 mg to 7.5 mg, nitroglycerin boluses of 40 mcg, and an esmolol bolus of 5 mg were given IV to maintain targeted hemodynamic goals. A total of 2000 mL of plasmalyte and 850 mL of hetastarch were infused and the estimated blood loss was 500 mL. The total urine output for the case was 1100 mL. The total surgical time for this case was 4 hours and 47 minutes.

Prior to emergence, the magnet was removed, ondansetron 4 mg IV and acetaminophen 1000 mg IV were administered, and the remifentanil and phenylephrine infusions were stopped. Albuterol 10 puffs (90 mcg/puff) was administered via the nasal RAE due to a slight expiratory wheeze. The neuromuscular blockade was antagonized with sugammadex (2mg/kg). The patient opened her eyes, followed verbal commands while maintaining regular, spontaneous respirations, and the nasal RAE tube was removed. The patient was transported to the Post Anesthesia Care Unit while maintaining spontaneous respirations and an SpO_2 saturation greater than 96%. A post-operative EKG showed no changes from her pre-operative EKG. The patient was admitted to the telemetry unit and discharged 2 days later with no untoward events.

Discussion

Brugada syndrome is an autosomal dominant disorder in which mutations are found mainly in cardiac sodium channels, but also potassium and calcium channels.[4] Patients with this syndrome may experience ventricular arrhythmias, atrial arrhythmias, and even sudden cardiac arrest.[4] Brugada syndrome is diagnosed through EKG findings, typically ST elevation in leads V1-V2.[2,4] Additionally, a right bundle branch block may be present.[4] Even when ST elevation is present, the timing of the EKG must be precise as the ST elevation has the potential to normalize and return to baseline periodically, making it difficult to detect.[4] When a patient is diagnosed with Brugada syndrome, the only definitive treatment is the placement of an ICD in order to correct future ventricular arrhythmias and prevent SCD.[4]

Careful preparation is necessary when crafting an anesthetic plan for a patient with Brugada syndrome. An in-depth pre-operative evaluation, to include a 12-lead EKG and BMP, should be obtained.[2] This patient had recently undergone an interrogation of her ICD, her pre-operative EKG was unchanged from initial diagnosis, and BMP was unremarkable. If a patient's BMP is altered, specific attention should be given to potassium, calcium, and magnesium levels as alterations can precipitate a Brugada EKG pattern.[2] In addition, a post-operative plan needs to be

in place as these patients should be monitored for 24 to 36 hours; it is during this period that arrhythmias are most likely to occur.[2,3]

It is recommended to have the ability to monitor the right precordial leads for ST elevation changes.[2] This patient's heart rhythm was continuously monitored by a 5-lead EKG, with the V lead placed in the fourth intercostal space, right of the sternal border for continuous monitoring of V1. Temperature monitors should be in place and any signs of hyperthermia should be managed promptly as increases in temperature have been shown to induce ST elevation.[2,6] Current literature recommends placement of an arterial line for continuous monitoring of blood pressure,[3] and because this patient had the potential for a large amount of blood loss and the need for vasoactive infusions to maintain desired hemodynamics, an arterial line was placed. ICDs should be disabled to avoid any inappropriate shock.[2] It was for this reason that a magnet was placed over the patient's ICD. Additionally, defibrillator pads should be available and, if feasible, they should be placed on the patient prior to induction.[2] The pads were placed on the patient to allow for prompt external defibrillation since the intrinsic function of the ICD was blocked by the magnet.

Caution should be used when choosing specific anesthetic medications as there have been several linked to increased incidences of ST segment elevation and fatal arrhythmias. Induction boluses of propofol do not need to be avoided, however, long term maintenance anesthetic use, greater than 4 mg/kg/hr, has been associated with propofol infusion syndrome and ST elevation.[2,3] Inhalational agents are safe to use as maintenance anesthesia, although suggestions have been made to utilize sevoflurane as it does not affect QT length.[3] Literature suggests that all opioids are safe to use and are not associated with adverse effects in patients with Brugada syndrome.[2,3] Neuromuscular relaxation with steroidal non-depolarizing medications is safe, but should be reversed with sugammadex.[3] Neostigmine can increase parasympathetic activity causing increased potential for lethal arrhythmias and should be avoided.[2,3] If the need arises to utilize vasoactive medications to adjust the patient's hemodynamics, phenylephrine and ephedrine have been used with no reported complications.[2]

Overall, the anesthetic care given to this patient followed the current recommendations, with one exception. This patient underwent a surgery that required her jaw to be wired shut post-operatively. Ideally, a total intravenous anesthetic with a propofol infusion would have been used because prevention of postoperative nausea and vomiting was a priority. However, due to the recommendations against propofol's long term maintenance use in patients with Brugada Syndrome, isoflurane was used instead. While the use of isoflurane was not outside the standard of care, sevoflurane would have been a better choice for this patient. The literature suggests there is no QT segment alteration with sevoflurane and its potent bronchodilation effects would have been beneficial for potential complications due to the patient's history of asthma.

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Mentor: LCDR Justin Hefley, DNP, CRNA

Anesthetic Management of Syndrome of the Trephined

Daniel Calma, DNP, BSN, LT, NC, USN
Uniformed Services University of the Health Sciences

Keywords: syndrome of the trephined, sunken skin flap, paradoxical herniation

Syndrome of the Trephined (ST) is a rare yet major complication that can occur after a craniectomy. ST consists of neurological symptoms and sunken skin above the skull defect. Neurological symptoms include headaches, alterations in mental status, seizures, and motor deficits.[1] ST may progress to a paradoxical herniation of the brain leading to death.[2] The treatment of ST is by the closure of the cranial defect by cranioplasty.[3] This case report discusses the clinical presentation, planning, and perioperative implementation of an anesthetic plan for ST.

Case Report

A 53-year-old female presented to the emergency department (ED) with worsening lethargy and headache; anisocoria was found with the left eye larger than right, sunken skin over her previous craniectomy site, and a Glasgow Coma Score (GCS) of 12. She had left upper extremity weakness and baseline full strength to her right upper extremity and bilateral lower extremities. The patient did not report any residual deficits from a hemorrhagic stroke 4 months earlier, which was treated with craniectomy and coiling embolization of the right posterior communicating artery. Other medical history included seizures, hypertension, anxiety, and gastroesophageal reflux disease. The patient's routine medications were taken the day of surgery and included alprazolam, sertraline, levetiracetam, atenolol, and pantoprazole. A cranial computed tomography scan was obtained in the ED, revealing a worsening right-hemispheric

paradoxical herniation after craniectomy. The patient's pre-anesthetic neurological exam was unchanged from the ED, and she was arousable to speech and able to follow commands.

Once the patient was taken to the operating room, standard noninvasive monitors were applied, and the patient was pre-oxygenated at 10 L/min. General anesthesia was induced with fentanyl 100 mcg, lidocaine 50 mg, propofol 130 mg, and rocuronium 50 mg. A 7.0 mm oral endotracheal tube was placed in the trachea using video laryngoscopy. The patient was repositioned with the head of the bed raised 15-30 degrees as directed by the surgeon. The OR table was then positioned 180 degrees away from the anesthesia machine.

General anesthesia was maintained with sevoflurane 1.8-2.2% inspired concentration with a mixture of O_2 0.8 L/min and air 1.2 L/min. Fentanyl was administered in divided doses during periods of increased stimulus, totaling 375 mcg. Ventilator settings were set to a tidal volume of 350 mL/breath, respiratory rate of 12/min, and positive end-expiratory pressure (PEEP) of 5 cm H_2O. Mean arterial pressures (MAPs) were maintained between 60-80 mm Hg with a phenylephrine infusion at 50 mcg/kg/min and boluses of ephedrine.

In preparation for emergence and tracheal extubation, ondansetron 4 mg was administered, and neuromuscular relaxation was antagonized with sugammadex 100 mg. The patient was then placed on pressure support ventilation and subsequently transitioned to spontaneous ventilation while maintaining adequate oxygenation and ventilation with an $EtCO_2$ of 38-42 mm Hg. The phenylephrine infusion was titrated off, then propofol 20 mg and fentanyl 25 mcg were given for the patient's comfort during emergence. After the patient opened her eyes and followed commands, the trachea was extubated uneventfully. Intraoperative intravenous fluids totaled 700 mL of 0.9% normal saline and 200 mL of lactated ringers, with an estimated blood loss of 150 mL. The neurosurgical team performed a neurological assessment in the recovery room, showing improved anisocoria and mental status.

Discussion

Syndrome of the Trephined is defined as the neurological or behavioral decline after craniectomy with the improvement of symptoms following reconstructive cranioplasty.[3] The symptoms of ST include weakness, paralysis, headaches, sensory changes, and impaired mentation.[1] Patients can present with an acute neurologic decline or chronic neurologic impairment.[3] The anesthetic management of patients requiring neurosurgery begins with the timely pre-anesthetic evaluation focusing on the patient's preoperative neurological baseline and deficits. The neurologic manifestations may be difficult to recognize in patients already experiencing neurologic deficits, and the importance of a detailed exam and documentation of the neurological baseline for comparison is vital.

Anesthetic management goals included maintaining hemodynamic stability, oxygenation, ventilation, and prevention of neurological complications. Premedication may be omitted as it may exacerbate unwanted focal neurological deficits.[4] Anesthetic goals should be to minimize major stimuli without compromising the postoperative neurological exam. Avoidance of hypertension during laryngoscopy, surgical stimulation, and emergence can be achieved with careful titration of analgesics, but hypotension should also be avoided.[5]

Hemodynamic and monitoring goals should include maintaining blood pressure and heart rate within 20% of the patient's baseline.[5] Intracranial pressure monitoring (ICP) was not a concern since the cranial vault was open at the start of the case and neither trauma nor edema were suspected. Ventilatory and fluid management are also major considerations, and in this case, tidal volumes were maintained at 6 to 8 mL/kg and PEEP was set to 5 cm H_2O to minimize potential inflammatory injury to the lungs[5] Euvolemia should be maintained, and overhydration should be avoided. A 0.9% saline solution was chosen since large volumes of hypotonic solutions such as lactated ringers can contribute to cerebral edema.[5]

To ensure a prompt postoperative neurological assessment, emergence and extubation must be well-timed, including administration of postoperative nausea and vomiting prophylaxis. Although not utilized in the case described, a low-dose remifentanil or lidocaine infusion may be helpful with preventing straining, coughing, and agitation from the endotracheal tube.[5] Intratracheal lidocaine may also be considered.[5]

While ST is associated with craniectomy, literature is limited to case reports, with less than 100 cases reported, and clinical characteristics and presentations often poorly described.[1] Although no adverse events occurred in this case, anesthesia professionals should be aware of this rare complication after a craniectomy. They must also be prepared to maintain hemodynamic stability and adequate oxygenation and ventilation during all phases of their anesthetic plan.

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Mentor: Chad Moore, DNP, CRNA, CHSE

The Postpartum Patient on Veno-Venous Extracorporeal Membrane Oxygenation

Lauren Gilmore, BSN
Duke University

Keywords: veno-venous extracorporeal membrane oxygenation, V-V ECMO, anesthetic management, Acute Respiratory Distress Syndrome, ARDS

A retrospective study of 563 patients requiring veno-venous extracorporeal membrane oxygenation (V-V ECMO) found that 47.8% of these patients also required a noncardiac surgical procedure.[1] Given favorable data to support V-V ECMO as salvage therapy for severe acute respiratory distress syndrome (ARDS)[2], a fast-growing subset of patients has emerged, including patients who develop ARDS in response to hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome. Vigilant attention to episodes of hypoxemia, hypercarbia, systemic anticoagulation, and fluid shifts are critical to the anesthetic management of patients on V-V ECMO presenting for noncardiac surgery.

Case Report

A 36-year-old, 113 kg, 163 cm, female with no previous medical or surgical history was 29 weeks pregnant and developed HELLP syndrome, for which an emergent Cesarean section (C-section) was performed. During the C-section, the patient developed hemorrhagic shock, and an exploratory laparotomy revealed a rupture of a subcapsular hepatic hematoma. The patient's ventilatory status significantly worsened intraoperatively, and the case was aborted due to impaired ventilation. During her post-operative intensive care unit (ICU) stay, she was diagnosed with ARDS and was cannulated for V-V ECMO therapy. When her respiratory status stabilized, she was scheduled to return to the operating room (OR) for a reopening of abdominal laparotomy and hysterectomy.

The patient had been on V-V ECMO for 3 days, and her oxygenation status had improved. On preoperative exam, the ECMO sweep was 0, indicating that the patient's lungs were fully oxygenating the blood. The patient had an endotracheal tube in situ; ICU ventilator settings included positive end-expiratory pressure (PEEP) of 14 cm H_20 and FiO_2 40%. Her preoperative arterial blood gas (ABG) revealed PaO_2 79 mm Hg. Other pertinent labs include hemoglobin 10.5 g/dL, hematocrit 28%, platelets 37 x 10^9 L, fibrinogen 168 mg/dL, PTT 45 seconds, and INR 2.2. The patient was minimally responsive and not on continuous sedation in the ICU. The patient was placed on a travel ventilator and carefully transported to the OR with the nurse anesthetist, student nurse anesthetist, anesthesiologist, perfusionist, and respiratory therapist.

Once in the OR, the patient was connected to the anesthesia machine and the previous ICU ventilator settings were reinstituted. Standard non-invasive monitors were reapplied and an anesthesia depth monitor was placed. The pre-existing arterial line and central venous pressures were also monitored. General anesthesia was induced with inspired isoflurane 1% in a mixture of O_2 1 L/min and air 1 L/min and titrated to achieve an anesthesia depth index between 40-60. Cisatracurium 6 mg was intravenously administered for muscle paralysis. Upon incision, fentanyl 50 mcg was also administered.

When surgical manipulation of the abdominal cavity commenced, the patient became difficult to ventilate. The patient's SpO_2 decreased to 85%, and an ABG showed PaO_2 of 70 mm Hg. The FiO_2 was increased to 80%, and the perfusionist was notified of the hypoxemia. The perfusionist then resumed ECMO sweep. Within a few minutes SpO_2 improved to 98%. The sweep was continued, and SpO_2 remained above 93% for the rest of the case. Within minutes of resuming the ECMO sweep, the expired inhalational agent decreased, so the isoflurane was increased to 1.2%, and subsequent titrations were guided by the anesthesia depth monitor. The patient remained on ECMO sweep for the remainder of the case and throughout the transport to ICU.

Intraoperatively, the patient became hypotensive. A vasopressin infusion was started at 0.02 U/min to maintain mean arterial pressure above 65 mm Hg. Lactated ringer's solution, 800 mL, and 5% albumin, 1250 mL, were administered throughout the case. The patient's baseline coagulopathy and significant surgical blood loss required substantial transfusion effort. There was 500 mL of documented blood loss, with probable larger evaporative fluid losses. Intraoperative laboratory results showed fibrinogen of 150 mg/dL, hemoglobin 8 g/dL, and platelets of 26 x 10^9 L. The surgical team also reported the patient seemed "oozy." Based on laboratory and rotational thromboelastometry (ROTEM) guidance, a total of 2 units of cryoprecipitate, 1 unit of fresh frozen plasma (FFP), 3 units of packed red blood cells (PRBCs), and 2 units of platelets were administered. The surgical team reported anecdotal improvement in the coagulopathy post transfusions. After the procedure, the patient remained intubated and sedated, and was transported back to the ICU with support of the same travel ventilation and team.

Discussion

The use of V-V ECMO is a common supportive therapy for ARDS.[2,3] The V-V ECMO circuit drains deoxygenated blood via an "outflow" cannula into a membrane oxygenator and returns oxygenated blood to the patient's right atrium via the "inflow" cannula. A flowmeter adjusts gas flow into the oxygenator, referred to as the "sweep," and a blender controls FiO_2.[4] Providing anesthesia for a patient on V-V ECMO during noncardiac surgery is becoming more common and can be anticipated for laparotomy, vascular, and thoracic procedures.[1]

Providing anesthesia for the patient on V-V ECMO requires effective collaboration, beginning with patient transport. A minimum of an anesthesia practitioner, perfusionist, and respiratory therapist should be present for the transport of patients on ECMO.[5] The ECMO circuit should allow at least 1 to 2 feet of excess tubing length to avoid pulling the cannula. Transport monitors should have appropriate alarms with sufficient battery supply, and transport oxygen cylinders for the ventilator and ECMO circuit should be full. The transport team should also review the management of unintended pump failure. Moreover, emergency medications should be readily available should the anesthesia practitioner need to support the patient's hemodynamic status.[5]

The ECMO circuit affects anesthetic pharmacokinetics and pharmacodynamics; the risk of underdose or toxicity is amplified in this population.[6] Volume of distribution and medication sequestration are impacted by the ECMO circuit, which typically adds between 800-1500 mL of blood volume.[5] Drugs with higher lipophilicity and protein binding have greater sequestration and degradation within the circuit.[6] For this reason, higher doses of propofol, opioids,

benzodiazepines, ketamine, dexmedetomidine, and inhalational agents are often required.[6] Cephalosporin antibiotics do not require dose adjustment.[5] Regardless of anesthetic type, an anesthetic depth monitor is strongly recommended due to the unpredictability of anesthetic pharmacology and increased sensitization to the hemodynamic effects of anesthetic medications.[1] With increased elimination of volatile anesthetics occurring in the ECMO oxygenator proportional to the sweep flow rate[5], there was significant concern for intraoperative awareness in this case. Administration of intravenous midazolam was discussed, but ultimately forsaken considering appropriate anesthesia depth monitor values.

The ideal anesthetic agent for patients on V-V ECMO is unknown. Because these patients often have low minute ventilation, anesthetic gas delivery and speed of inhalation induction can be impaired. Therefore, a total intravenous anesthetic is generally preferred.[5] However, a recent study purports that accurate administration of anesthetic gas concentrations makes inhalational agents a reasonable anesthetic technique for these patients.[1] Intravenous bolusing of amnestic agents, such as propofol, is not recommended due to the unpredictable nature of drug delivery and risk of hemodynamic compromise.[1] The use of isoflurane was acceptable for this patient since she was on minimal sedation preoperatively and induction of intravenous anesthesia would likely have resulted in hemodynamic instability.

Lung protective ventilation (LPV) strategies should be employed to prevent ventilator-induced lung injury (VILI).[6] Tidal volumes should be < 6 ml/kg and PEEP $\leq$10 cm H_20 to minimize VILI.[5] This patient required a titrated PEEP of 14 cm H_20 per this institution's ICU ARDS protocol and therefore was continued intraoperatively. A travel ventilator was used to prevent transfer-induced loss of PEEP and to maintain alveolar recruitment. In a retrospective study of patients on V-V ECMO, intraoperative hypercarbia was frequently treated by adjusting ventilator settings in lieu of increasing ECMO sweep. However, this is contrary to the current recommendation of adjusting the ECMO sweep first.[1] This underscores the importance of effective communication between the anesthesia professional and the perfusionist during the anesthetic management of the patient on ECMO. In this case report, initial desaturation was treated by increasing FiO_2 concentration with little improvement. However, the resumption of ECMO sweep was able to correct the hypoxemia. Ideally, LPV should have been initiated as soon as oxygenation improved.

Patients on ECMO often prompt challenging management of bleeding and coagulation. An extensive review showed that patients who underwent noncardiac surgery on ECMO had higher rates of bleeding complications.[7] This patient's heparin infusion was stopped 6 hours prior to surgery, consistent with current recommendations.[5] Several units of PRBCs and FFP were available in anticipation of significant blood loss. Baseline laboratory values were drawn at the start of surgery and routinely throughout the case. The use of ROTEM, specifically the FIBTEM assay, showed a low amplitude of 7 mm, which led to early administration of cryoprecipitate. After the cryoprecipitate transfusions, the FIBTEM amplitude increased to 11 mm. The decision for additional blood product administration was made in conjunction with these laboratory values, patient's hemodynamics, and observations from the surgical team.

The anesthetic considerations of patients on V-V ECMO will evolve, and practitioners must remain adaptable in response to hemodynamic and oxygenation changes, as well as the

management of fluid shifts, hemostasis, anesthetic delivery, and monitoring. Currently, the literature provides generalized guidance; however, careful attention must be given to each patient's underlying critical illness and the impact of V-V ECMO on these different comorbidities. Communication and preparation are the most critical interventions. In this case report, optimal patient care was achieved because all team members knew their role, were prepared for an emergency and engaged in open communication.

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Mentor: Emily McClanahan Funk, DNP, CRNA

Craniotomy with Multiple Venous Air Embolisms

Trevor Bloxham, DNP, BSN
Westminster College

Keywords: Craniotomy, air embolism, dead-space ventilation, decreased end-tidal CO_2 ($ETCO_2$), hypercarbia

The true incidence of venous air embolisms (VAE) is unknown because symptoms vary widely and mild events often go unreported.[1] Nevertheless, a VAE is a potentially fatal complication that is generally preventable.[2] This case study presents three separate VAE events during craniotomy, the associated manifestations, and how they were managed. Current VAE management recommendations and how they relate to the care provided will be discussed.

Case Report

A 46-year-old male patient presented to the hospital for a scheduled craniotomy with excision of a right lateral intraventricular meningioma. The patient's past medical history included hypertension and cervical stenosis. He had no surgical history and his only prescribed medication was lisinopril 10 mg once daily. The meningioma was discovered incidentally with magnetic resonance imaging while examining his cervical spine. He had no symptoms related to the meningioma. On the day of surgery, all preoperative blood chemistry values, vital signs, and assessment findings were unremarkable.

In the operating room, standard noninvasive monitors were applied, followed by induction and intubation of the trachea with a 7.5 mm endotracheal tube. Correct tube placement was confirmed, the tube was secured, and mechanical ventilation initiated. General anesthesia was maintained with a continuous intravenous infusion of remifentanil at 0.125-0.2 mcg/kg/min and an expired concentration of desflurane of 3.6 - 4.4%. Fresh gas flows of O_2 and air were each set to 1 L/min. Continuous blood pressure monitoring was then established through a left radial intra-arterial catheter and an intravenous infusion of phenylephrine was initiated to maintain a MAP > 65 mm Hg. The patient was positioned with the head of bed (HOB) elevated to 15 degrees. Per the surgeon's request, end-tidal CO_2 ($ETCO_2$) was to be maintained between 28-30 mm Hg throughout the procedure to decrease blood loss and optimize visualization of the surgical field by vasoconstricting cerebral vessels.

Prior to surgical start, vital signs were HR 60/min, BP 118/50 mm Hg, MAP 70 mm Hg, SpO_2 97%, and temperature 36.4ºC. The $ETCO_2$ was 28 mm Hg and peak inspiratory pressure (PIP) was 17 cm H_2O. Approximately 90 minutes after surgical start, the $ETCO_2$ began decreasing. All vital signs were normal which prompted an initial adjustment of the RR from 18/min to 16/min. The $ETCO_2$ continued to decline despite this adjustment and the surgeon was notified of a suspected VAE, HOB was lowered, surgical field was irrigated with normal saline, bone wax applied to the surgical area, air was turned off, and O_2 flow was set to 2 L/min. Over the next six minutes the $ETCO_2$ decreased from 29 mmHg to 16 mm Hg before beginning to increase back to baseline. During this time, no adjustments were made to continuous infusions or inspired concentration of Desflurane. Vital signs and PIP remained stable, bilateral breath sounds and

heart tones were auscultated and found unremarkable. An arterial blood gas (ABG) resulted with a pH of 7.35, $PaCO_2$ 49 mm Hg, PaO_2 269 mm Hg, and HCO_3 25 mEq/L. Fourteen minutes after the initial decline, $ETCO_2$ was reestablished at 29 mm Hg, the HOB was returned to 15 degrees, and air and O_2 flow settings were reset to 1 L/min.

Approximately 90 minutes after the first event, the $ETCO_2$ began to decrease again. The surgeon was again notified and all of the previous interventions and assessments were implemented. Within four minutes the $ETCO_2$ decreased from 28 mm Hg to 14 mm Hg. Vital signs, PIP, and all assessment findings remained normal during this time and there were no adjustments made to infusion rates or the inspired concentration of Desflurane. An ABG was drawn which resulted with the following: pH 7.32, $PaCO_2$ 54 mm Hg, PaO_2 453 mm Hg, and HCO_3 26 mEq/L. The $ETCO_2$ returned to baseline 17 minutes after the first mark of decline and all interventions were reversed. For the third time, an hour later the same sequence of events unfolded. Over 10 minutes the $ETCO_2$ decreased from 30 mm Hg to 18 mm Hg and back to 30 mm Hg. All previous interventions and assessments were re-implemented, and again all patient findings remained stable.

At the end of the surgery the patient remained hemodynamically stable and was extubated without incident. His postoperative neurological assessment was unremarkable and he was transferred to the intensive care unit per standard procedure. The patient was discharged from the hospital two days later.

Discussion

A VAE can occur anytime the venous circulation is directly exposed to air and the venous pressure in that moment is below atmospheric pressure.[1] These conditions create a pressure gradient between venous circulation and atmospheric air that favors the entrance of air into the circulation.[1] During craniotomy, an elevated HOB can increase this pressure gradient and further optimize the conditions needed for a VAE to occur.[2] The degree of insult and its accompanying signs and symptoms vary greatly depending on the volume and rate of air accumulation, and the patient's position when the air enters venous circulation.[2,3] Signs and symptoms range widely from asymptomatic to sudden cardiac death.[1,3] A definitive recognition of the associated signs and symptoms may be further complicated by general anesthesia that blunts or eliminates them.[3] Under general anesthesia, a decrease in $ETCO_2$ is one of the earliest indicators, while a decrease in SpO_2 is considered a late indicator of VAE.[1,3] Once in the venous circulation the air returns to the heart where it may accumulate and cause an airlock in the right ventricular outflow tract (RVOT) or be ejected into the pulmonary circulation.[4]

The most sensitive monitoring method for VAE is transesophageal echocardiography (TEE), followed by precordial doppler, pulmonary artery catheter measurements, and $ETCO_2$.[2,4] A TEE is an invasive approach to monitoring and in this scenario wasn't practical due to the extended length of the procedure. In this case, the decline in $ETCO_2$ was the only manifestation of a VAE.

Based on symptomology, this decrease in $ETCO_2$ represented the result of air traveling to the heart, entering the pulmonary circulation, and becoming lodged in an alveolar capillary membrane. The air emboli obstructed blood flow which increased dead-space ventilation while

decreasing gas exchange resulting in a worsening $ETCO_2$ gradient. Over the course of several minutes it's suspected that the air diffused across the alveolar membrane to be exhaled as expired gas, which then restored alveolar capillary blood flow, resulting in the $ETCO_2$ returning to baseline. Had the air emboli been larger it may have obstructed a larger percentage of pulmonary circulation or could have lodged itself in the RVOT which could have led to pulmonary hypertension, severe hemodynamic instability related to right heart strain and decreased cardiac output, EKG morphology, or total circulatory collapse.[1,4]

When a VAE is suspected the first priority is to prevent further air entrainment.[1] The surgeon should be immediately notified to flood the surgical field with saline and when necessary apply bone wax.[3,4] The patient should be placed in Trendelenburg and left lateral decubitus position which facilitates the air emboli leaving the RVOT and decreases the risk of cardiovascular instability or collapse.[4,5] It's recommended that that high flow 100 percent O_2 be administered to possibly facilitate nitrogen reabsorption from the air which would decrease the size of the air embolism.[3,5] Although this patient did not have central venous access, it is also recommended to aspirate from a central line if possible. In this scenario, communication with the surgeon was prompt, as was her action. Lowering the HOB decreased the pressure gradient between air and venous circulation, which decreased the risk of further air entrainment. With each event the patient showed no signs of instability so turning him in a left lateral decubitus position was deemed unnecessary. The fresh gas flow was adjusted to administer 100 percent O_2, however flow rate was maintained at 2 L/min. Increasing the O2 to a higher flow rate might have been advantageous to expedite the patient's recovery to his $ETCO_2$ baseline.

Three VAEs during one surgery is a rare event. Early detection and prompt communication with the surgical team may have been a key factor that minimized insult and prevented further complications. Additionally, intervention was according to current recommendations and guided by the patient's symptoms and hemodynamic stability. In hindsight, the option to maintain the HOB in a flat position instead of elevated to 15 degrees was never discussed and in this specific scenario may have been an option that could have decreased the risk of VAE. Also, as mentioned previously the adjustment to a higher O_2 flow rate may have accelerated the recovery of each event. Regardless, in the face of a potentially perilous complication the multidisciplinary actions taken were evidence based and proved effective by resulting in a positive patient outcome.

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Mentor: James Stimpson, DNP, CRNA

Cardiovascular Effects of Intraoperative Hyperoxia in Adult Surgical Patients

C. Michael Hatch, DNAP, BSN
Bryan College of Health Sciences

Keywords: Intraoperative hyperoxia, hyperoxemia, high inspired oxygen, cardiovascular effects

Introduction

The adverse effects of hypoxia are universally accepted by anesthesia providers. Alternatively, the effects of too much oxygen are not nearly as understood. Hyperoxia is defined physiologically as any inspired oxygen fraction (FiO_2) > 21%; however, a consensus of a clinical definition of hyperoxia has not been reached with many variations quoted.[1] Recently the negative impact of hyperoxia on cardiovascular function in some patient populations has been shown. A 2020 study found that patients with coronary artery disease and preexisting myocardial injury are vulnerable to a decline in myocardial function.[2] A 2018 meta-analysis found that hyperoxia may significantly reduce cardiac output and increase vascular resistance.[3] The impact significantly differed between patient populations, with heart failure patients being most sensitive to the negative effects.[3] These studies did not include the operative period.

Perioperative hyperoxia is a common occurrence. A 2020 study of 373 patients undergoing major surgery found that a PaO_2 >150 mm Hg occurred intraoperatively in 82% of patients, and postoperatively in 54%.[4] Another study involving cardiopulmonary bypass (CPB) surgeries found that over 8 years there was no change in practice, and the overall mean PaO_2 was 255 (+/- 48) mm Hg.[5] These studies demonstrate that perioperative hyperoxia is a common occurrence and the potential for adverse intraoperative effects in adult surgical patients should be assessed.

Methods

A PICO question guided the literature search: “In adult surgical patients (P) does hyperoxia (I) compared to normoxia (C) increase cardiovascular adverse effects (O) during the perioperative period?”

Databases searched between March 10 and November 30, 2021 included Scopus, CINAHL, PubMed, and Google Scholar. The search was limited to peer reviewed publications written in English with publication dates between 2013 and 2021. The search terms utilized separately or in combination with Boolean operators were: hyperoxia, high inspired oxygen concentration,

oxygen adverse effects, cardiovascular, cardiac, anesthesia, intraoperative. This search yielded approximately 3,845 studies which were reviewed. Eight met the inclusion criteria of adult surgical patients, a hyperoxia intervention group compared to a group with lower levels of oxygenation as measured by either FiO_2 or PaO_2, and cardiovascular outcomes measured in the intraoperative and/or postoperative period. Included are one meta-analysis, six randomized controlled trials (RCTs), and one unplanned sub-analysis of a RCT; all Level 1 on the Joanna Briggs Institute Levels of Evidence.

Literature Analysis

Several themes were noted in the methods of the eight included studies. First, many of the studies excluded high-risk patients. This varied but several cardiac conditions excluded were presence of atrial fibrillation, pacemaker, hemodynamic instability, preoperative inotrope administration, preoperative intra-aortic balloon pump use (IABP), severe heart failure, and recent acute coronary syndrome (ACS). Non-cardiac exclusions were renal failure, hepatic dysfunction, and chronic obstructive pulmonary disease. Second, anesthetic techniques including medications, hemodynamic goals, and fluid administration were standardized in most studies. Finally, in applicable studies, CPB was standardized for target blood flows, mean arterial pressures (MAPs), patient temperature, cardioplegia administration, aortic clamp time, CPB time, and hemoglobin/hematocrit levels.

A variety of cardiac outcomes were measured. Abou-Arab et al.[1] compared the occurrence of postoperative dysrhythmias, major adverse cardiac and cerebrovascular events (MACCE), and vasopressor use over 15 postoperative days. An FiO_2 of 1.0 versus a PaO_2 of < 150 mm Hg during CPB was compared. Hyperoxia did not increase or decrease postoperative dysrhythmias, postoperative inotrope use, cardiac arrest, MACCE occurrence, or troponin levels in patients undergoing cardiac surgery with CPB.

Myocardial injury was assessed via biomarkers in cardioversion patients who became hyperoxic compared to those who did not.[6] Biomarkers utilized included high-sensitivity troponin I (hs-cTnI) and T (hs-cTnT) as well as an N terminal pro-brain natriuretic peptide (NT-pro-BNP). Levels before the procedure and 4 hours after the cardioversion were compared. No increase in myocardial injury or stress was found in patients treated with oxygen versus room air.
The occurrence of ACS and myocardial infarction (MI) associated with hyperoxia was assessed in a systematic review and meta-analysis.[7] Studies included had an intervention group with a perioperative FiO_2 of 0.8 versus a control group with a FiO_2 of 0.3-0.35. Three studies reported on a total of 3,449 patients. The high FiO_2 arm had an incidence of 25/1705 ACS/MI events and the low FiO_2 arm had 25/1744 events ($p=0.85$). No associations between hyperoxia and ACS/MI events were found.

McGuinness et al.[8] conducted a secondary outcomes analysis evaluating the impact of hyperoxia on cardiac surgery-associated multiorgan dysfunction (CSA-MOD) biomarkers. The control group had a mean PaO_2 of 178 mm Hg during CPB while the intervention group maintained a PaO_2 of 75-90 mm Hg from induction through emergence. No differences in hs-cTnI at baseline (13 vs 13, $p=0.61$), at 6 hours post CPB (641 vs 535, $p=0.23$), or 24 hours post CPB (379 vs 336, $p=0.53$) were found.

Patients at risk for cardiovascular complications and scheduled for moderate to high-risk abdominal surgery anticipated to last 2 or more hours were compared.[9] High risk surgeries included hepatobiliary, colorectal, pancreatic, kidney, prostate, cystectomy, and gynecologic surgeries. Hyperoxia was defined as an FiO_2 of 0.8 and normoxia as a FiO_2 0.3. The NT-proBNP and hs-cTnI were drawn before surgery, at 2 hours postoperatively, and on postoperative days 1 and 3. No differences were found in the biomarkers, occurrence of myocardial injury after noncardiac surgery (MINS), cardiac arrest, new arrhythmias, or intraoperative hemodynamic parameters.

Myocardial injury and cardiac arrest occurrence were assessed in colorectal surgical patients in an unplanned sub-analysis of a trial assessing surgical site infections.[10] The composite outcomes were MINS occurrence as seen via elevated troponin T levels, as well as cardiac arrest occurrence. Hyperoxia compared to FiO_2 0.3 did not significantly impact the composite outcome with an incidence of 26/820 versus 34/827 (p=0.17).

Myocardial damage and hemodynamic parameters were assessed in patients undergoing coronary artery bypass grafting (CABG) with CPB.[11] The hyperoxia PaO_2 target was 200-220 mm Hg during aortic cross-clamping and 130-150 mm Hg in the ICU. The normoxia targets were 130-150 mm Hg and 80-100 mm Hg. Ck-MB, CK, and troponin T were measured before induction, at ICU admission, and 2, 6, and 12 hours after admission. Cardia index (CI) and systemic vascular resistance index (SVRI) were measured before thoracotomy, at chest closure, at ICU admission, and at 2, 6, and 12 hours after admission. No differences were found in enzyme or troponin T values. No differences in CI, SVRI changes, or dopamine use (22/25 versus 20/25) were found.

Myocardial oxidative stress, total antioxidant status, inotropic support, IABP use, postoperative atrial fibrillation, and low cardiac output syndrome occurrence were assessed in CABG surgical patients.[12] Myocardial oxidant status was evaluated via Trolox levels and antioxidant status via hydrogen peroxide levels in arterial blood gases. The FiO_2 of the hyperoxia group was 0.7 after induction, reduced to 0.5 during CPB, and increased to 0.7 during rewarming. The normoxia group had an FiO_2 of 0.35 following induction, maintained during CPB, and 0.45 during rewarming. Myocardial total oxidant status before CBP was compared to 4 minutes after aortic cross-clamp removal and was found to be significantly different (p=0.03). All other endpoints did not significantly differ including myocardial antioxidant status, postoperative inotropic support (8/26 versus 3/22, p=0.15), postoperative IABP use (2/26 versus 0/22, p=0.49), postoperative atrial fibrillation (8/26 versus 5/22, p=0.53), and low cardiac output syndrome (2/26 vs 0/22, p=0.49).

Author, Year	Design, Sample	Intervention, Timing	Outcomes	Conclusion
Abou-Arab et al., 2019[1]	RCT N=330 Adult elective cardiac surgery	FiO_2 of 1.0 during CPB vs PaO_2 of <150mm Hg Timing: During CPB	Postoperative dysrhythmia occurrence Secondary outcome= MACCE Vasopressor use	Dysrhythmias did not differ in occurrence 15 days postoperatively. MACCE was comparable. Troponin levels did not show a significant difference. Vasopressor use did not differ

Lauridsen et al., 2018[6]	RCT N=125 Adult elective cardioversion for atrial fibrillation or atrial flutter	100% O_2 via ventilation mask (10-15 L/min) Timing: O_2 vs RA for 3 minutes pre-cardioversion and continued until patient breathing adequately. Then NC at 3 L/min for 30 minutes.	Myocardial injury measured by: Changes in post-procedure hs-cTnI and hs-cTnT Secondary outcome= Changes in post-procedure NT-pro-BNP levels	No difference between groups in biomarkers of myocardial injury
Mattishent et al., 2019[7]	Meta-analysis 27 studies, 3 reported on cardiovascular adverse events	FiO_2 of 0.8 vs 0.3-0.35 Timing: Perioperative	ACS and MI	High FiO_2 was not linked with cardiovascular adverse events
McGuinness et al., 2016[8]	RCT N= 298 Adult cardiac surgery using CPB	Avoidance of hyperoxia (PaO_2 75-90 mm Hg and SpO_2 of 92-95%) vs usual care (FiO_2 >/= to 99%) Timing: During CPB	Secondary outcome= Serum biomarkers for CSA-MOD	No significant difference in hs-cTnT any measurement period
Reiterer et al., 2021[9]	RCT N=258 Adults >45 years, at risk for cardiovascular complications, moderate to high-risk abdominal surgery	FiO_2 of 0.8 vs 0.3 Timing: Intraoperative and 2 hours postoperative	Postoperative max NT-proBNP Secondary outcomes: MINS, cardiac failure, MI, and arrhythmias	No significant difference between groups in NT-proBNP or troponin concentrations No difference in MINS (p= 0.703) No difference in MI, arrhythmias, cardiac failure occurrence Significant increase in postoperative median MAP
Ruetzler et al., 2020[10]	Unplanned sub-analysis, alternating intervention trial N=1,647 Adult, colorectal surgery	0.8 vs 0.3 FiO_2 Timing: Intraoperatively	MINS and cardiac arrest occurrence	No significant difference in myocardial injury or cardiac arrest

Smit et al., 2016[11]	RCT N=50 Adult, elective CABG with CPB	PaO_2 target 200-220 mm Hg during CPB and 130-150 mm Hg during ICU admission vs PaO_2 target 130-150 mm Hg during CPB and 80-100 mm Hg during ICU admission Timing: CPB and postoperatively	Myocardial injury Secondary outcomes= Changes in hemodynamics, and tissue perfusion	No significant difference in CK-MB and Troponin-T CI, SVRI, and vasopressor use no significant difference
Topcu et al., 2021[12]	RCT N= 48 Adult elective on-pump CABG	0.7 FiO_2 following induction, 0.5 during CPB, and 0.7 during rewarming vs 0.35 FiO_2 following induction and CPB, and 0.45 during rewarming Timing: Intraoperatively	Myocardial TOS before initiation of CPB (T2) compared to 4 minutes after removal of aortic cross-clamp (T4)	Normoxia group experienced reduced myocardial oxidative stress No significant difference in inotropic support, IABP use, POAF, or low CO syndrome occurrence

Abbreviations: CI= cardiac index; CO= cardiac output; CVP= central venous pressure; HR= heart rate; NC= nasal cannula; O_2= oxygen; PAOF= postoperative atrial fibrillation; RA=room air; SV= stoke volume; TOS= total oxidant status; VT/VF= ventricular tachycardia/ventricular fibrillation

Conclusions

Oxygen administration has become a mainstay during the perioperative period due to the known adverse effects of hypoxia. Studies conducted outside of the perioperative area have suggested adverse cardiovascular alterations can occur with hyperoxia.[2] It is unclear if this applies to patients in the perioperative setting and if those effects translate to adverse patient outcomes. In this analysis hyperoxia was not found to translate to adverse patient outcomes. One meta-analysis, four RCTs, and one unplanned sub-analysis demonstrated no significant differences in any cardiovascular outcomes.[1,6-8,10,11] Two RCTs did report a significant difference in an isolated outcome. A higher median postoperative MAP in the hyperoxia group was seen in one, and higher myocardial total oxidant status in another. In both studies, no other outcome differed.[9,12] This evidence could indicate that the potential intraoperative cardiovascular effects of hyperoxia are transient and do not impact clinical outcomes. Intraoperative hyperoxia is typically a short-term occurrence and may not be long enough to impact clinical outcomes as seen in critical care where hyperoxia occurs over days.

The potential adverse impact of hyperoxia along with the lack of cardiovascular benefits should be understood when making clinical decisions. Hyperoxia was not demonstrated to be beneficial in any of the studies included in this analysis. Hyperoxia was not shown to reduce MI, arrhythmias, cardiac failure occurrence, inotrope use, or impact CI.[1,7,9-12] Hyperoxia was also not shown to reduce myocardial injury as indicated by CK-MB, Troponin-T, or NT-proBNP

concentrations.[1,6,8-11] Normoxia was shown to reduce myocardial oxidative stress in patients undergoing CPB for CABG surgery.[12]

While hyperoxia was shown to have limited cardiovascular impact intraoperatively, anesthesia professionals must consider the impact hyperoxia may have on other body systems. Oxygen is a drug and just like all drugs, optimal dosing is required. Currently, an optimal perioperative O_2 level is not clear. With no evidence of harm with normoxia and some indication of a negative impact the longer hyperoxia occurs,[11] the anesthesia practitioner might consider reducing oxygen administration until optimal intraoperative O_2 levels are determined.

This evidence-based practice analysis has several limitations. First, in many of the studies the population was low-risk cardiovascular surgical patients. Research in nonsurgical patients has found that selected at-risk populations are the most susceptible to adverse cardiovascular effects.[3] However, one included RCT focused on at risk patients and found no difference in myocardial injury, MI, arrhythmias, or cardiac failure.[9] Second, the lack of consensus on a definition of hyperoxia makes comparisons difficult. Several studies used PaO_2 levels and others used FiO_2 levels to differentiate the normoxia and hyperoxia groups. In all the normoxia groups, some PaO_2 and FiO_2 levels were supraphysiological and would be deemed by some to represent hyperoxia. Often the differences between the normoxia and hyperoxia groups were relatively small, which may have prevented differences in outcomes from reaching statistical significance. In nine older studies more liberal O_2 levels were used with a greater difference between the groups and more dramatic effects seen.[11] The negative effects of reactive oxygen species are now known to cause cellular damage and can lead to multiple pathologies and thus patients cannot ethically be exposed to those levels.[12] Third, cardiovascular adverse effects were not the primary focus of the meta-analysis and the unplanned sub-analysis. These are the studies with the largest sample size, and the risk of bias is greater. Despite these limitations, utilization of a meta-analysis and primarily RCTs (6/7) published in the most recent five years is a strength. More research is needed in at-risk patient populations and non-cardiac surgeries to allow greater generalization and to identify optimal perioperative O_2 levels.

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Mentor: Sharon Hadenfeldt, PhD, CRNA

Neuroprotective Properties of Dexmedetomidine

Matthew A. Dawson, BSN
Midwestern University

Keywords: dexmedetomidine, perioperative neurocognitive disorder, neuroprotection, postoperative neurocognitive disorder

Introduction

Dexmedetomidine is a highly selective alpha-2 (α2) adrenergic receptor (AR) agonist exhibiting sedative, anxiolytic, and analgesic properties with minimal respiratory effects, making it advantageous for anesthesia professionals.[1] Dexmedetomidine was initially approved by the Food and Drug Administration two decades ago as a sedative for mechanically ventilated patients in intensive care units and as a medication for procedural sedation. However, only recently have there been advances in research and clinical practice regarding its off-label use.

Perioperative neurocognitive disorder (PND) is an anesthetic complication with clinical presentations of delirium, delayed cognitive recovery, mild cognitive impairment, or dementia in the post-operative period or within one year of discharge from a surgical procedure. A retrospective cohort study of Medicare patients between 2013-2016 found that patients with PND had mean increases of more than $17,000 in post-acute healthcare cost within one year of the indexed surgery.[2] The study examined 2.4 million patients and found a diagnosis of PND in nearly 2% of the cohort. In addition, PND prolonged hospital stays and increased mortality within the same period. Patients were less likely to be discharged home, and utilization of long-term care or skilled nursing facilities increased. The increase in healthcare costs was due to readmissions, home health or office visits, radiology, and laboratory tests. However, the development of PND may be a modifiable risk, making it a reasonable goal for mitigation and improvement of value-based healthcare.[2] The risk factors for developing PND are dependent on age; the mean age of patients developing PND in this cohort was 80 years old. The majority were women, Caucasian, and had comorbidities. The type of surgery also plays a factor in developing PND. The most common were cardiac, general, and surgeries; 64% of the cases were orthopedic surgery. Additional risk factors for developing PND are pre-existing cerebral, cardiac, or vascular disease, substance abuse, and low levels of education.[2]

Methodology

Following PICO (population, intervention, comparison, outcome) guidelines for this review of evidence-based practice, the question proposed is as follows: "For inpatient adults requiring general anesthesia for scheduled, non-cardiac major surgery (P), will the use of dexmedetomidine as an adjuvant to postoperative analgesia (I), result in decreased incidences of perioperative neurocognitive disorder in the seven days after the indexed surgery (C, O) in comparison to a normal saline control?"

PubMed, an online research database, was utilized for this literature review. Keywords used were anesthesia, dexmedetomidine, neuroprotection, patient-controlled analgesia, postoperative neurocognitive disorder, and surgery. Filters included full text, peer-reviewed, and English language. Articles selected based on applicability to the PICO question. Excluded articles were those published prior to 2005. Articles were then narrowed down to those published between 2016-2021, except for two seminal works essential to the review published in 2006 and 2008. The level of evidence will be assessed according to the conventional Evidence Pyramid, with level 1 being the highest and level 5 the lowest. Additionally, animal studies are listed below level 5 since they do not involve human subjects. [3] This evidence-based practice analysis report was guided by a more extensive literature review previously conducted by the author.

Literature Analysis

Multiple literature sources support the idea that neuroinflammation is a key aggravating factor in PND development and that dexmedetomidine can reduce inflammation related to this pathologic state.[4,5] Surgical stress can trigger the proliferation of activated microglial cells in the hippocampus leading to inflammation of neural tissues and the formation of reactive oxygen species. This process leads to mitochondrial damage and dysfunction, further inducing tissue damage and hippocampal neuronal loss, contributing to cognitive dysfunction.[5-8] The

hippocampus is considered the memory and learning center of the brain. In addition, mitochondrial dysfunction causes elevated levels of cytochrome c expression, which leaks into the cytosol to trigger apoptosis and autophagy.[5]

Dexmedetomidine has demonstrated the ability to downregulate the expression of a protein known as surfeit locus protein 1 (SURF1). SURF1 aids in the assembly of cytochrome c oxidase. Cytochrome c oxidase is the terminal enzyme of the electron transport chain: Complex IV. Additionally, dexmedetomidine downregulates the expression of cytochrome c, an electron carrier between Complex III and IV.[5] A reduction in cytochrome c levels lowers the likelihood of apoptosis.[9] Thus, it appears that dexmedetomidine prevents PND by reducing the expression of proteins that accumulate during mitochondrial dysfunction resulting in the protection of neural tissue.

Randomized control trial supporting neuroprotective effects. A single-center, prospective, randomized controlled, and double-blinded trial analyzed the effect and optimal dosage of dexmedetomidine used in conjunction with sufentanil for post-operative analgesia in 416 patients over the age of 65 undergoing scheduled, non-cardiac major surgery.[10] The study consisted of four different inpatient groups correlating to the amount of dexmedetomidine administered, including a control group. The control group received no dexmedetomidine. The interventional groups received a loading dose of dexmedetomidine 1 mcg/kg over 10 minutes prior to induction with general anesthesia. In the post-operative period all patients received patient-controlled analgesia (PCA) pumps for up to 72 hours. The PCA pump was set to a continuous infusion of 4 ml/hr, a bolus dose of 3 ml if needed, and a lockout interval of 15 minutes.[10]

All groups had 150 mcg of sufentanil added to 300 ml of 0.9% saline in the PCA pumps. In the intervention groups, dexmedetomidine 100 mcg, 200 mcg, or 400 mcg was also added to the PCA infusion. This study found that the groups receiving PCA pumps with dexmedetomidine 200 mcg and 400 mcg had significantly decreased incidences of PND in the first seven days post-operative. Furthermore, the dexmedetomidine 400 mcg group did not encounter any increases in side effects, making it the superior dose for adjuvant use with PCA pump after open surgery. In this study, PND was effectively reduced by incorporating low doses of dexmedetomidine during the post-operative period. The doses were generally, below conventional doses used in both the intensive care unit and anesthesia. A loading dose of dexmedetomidine 1 mcg/kg over 10 minutes prior to induction and intravenous doses of dexmedetomidine between 3 mcg/hr and 16 mcg/hr in the post-operative period significantly reduced incidents of PND for inpatient populations.[10]

Key points supporting the use of dexmedetomidine for PND preservation of cerebral coupling. The brain requires a large amount of glucose and continuous oxygen supply to function appropriately. Depending on age, co-morbidities, or physiological parameters, approximately 12-20% of cardiac output is directed towards brain perfusion, which facilitates the delivery of glucose and oxygen.[11-12] In addition, the body has several mechanisms that defend cerebral perfusion, one of which is cerebral autoregulation, allowing for consistent and continuous cerebral blood flow (CBF). The cerebral coupling of CBF to cerebral metabolic rate (CMR) is how the brain responds to neuronal activity. When there is an increase in neuronal metabolic demands, the brain will increase CBF. An example of a deficit in this mechanism is

the sudden decreases in CBF in ischemic stroke without a decrease in CMR lead to neurological deficit.[13]

Some reference books note that dexmedetomidine reduces CBF due to vasoconstriction but does not reduce CMR, therefore not preserving cerebral coupling. Initial research on canines regarding dexmedetomidine showed no changes in CMR. However, these findings might be species- or study-specific. [14]

Conversely, more recent trials with human volunteers support claims that dexmedetomidine preserves cerebral coupling by simultaneously lowering CBF and CMR. Investigators measured cerebral blood flow velocity, oxygen content in the artery, the content of oxygen in the jugular vein, and bi-spectral index (BIS). These measurements were recorded during both normocapnia and hypocapnia. The findings are consistent with parameters representing an absence of physiological threats to the cerebral tissues. [14] Notably, α2-ARs are numerous in the cerebral vasculature, particularly in smaller cerebral pial arteries distal to the Circle of Willis. Dexmedetomidine's vasoconstrictive properties and reduction in CBF have previously concerned researchers during hyperventilation, a technique often used in neurosurgery, as it was theorized that it could cause cerebral ischemia. However, this is not the case as dexmedetomidine also reduces cerebral metabolism. Finally, BIS is not an accurate surrogate for CMR during infusions of dexmedetomidine as when aroused to command, BIS reverts to pre-sedation levels while CMR remains reduced. [14]

Table. Summary of Literature Regarding Neuroprotective Effects of Dexmedetomidine

Author Year	**Level of Evidence**	**Population**	**Purpose**	**Findings**	**Limitations**
Zhao et al. 2020	RCT, Prospective Double-Blinded, Level I	Patients >65 yrs undergoing non-cardiac surgery, n=416 Randomized to groups with PCA pumps with 150 µg sufentanil + 300 ml 0.9% NS and: DEX 0 µg group; DEX 100 µg group; DEX 200 µg group; DEX 400 µg group DEX 100, 200, 400 groups received DEX 1 mcg/kg bolus, preinduction	Investigate the effects & optimal dosage of DEX for PCA to prevent POD & early POCD after major surgery in elderly patients	POD & POCD in DEX 200 µg & DEX 400 µg groups < DEX 0 µg & DEX 100 µg groups in all 7 days after surgery ($P < 0.05$)	No determination if reduction of POD & POCD was from pre-operative or post-operative administration

Drummond et al. 2008	Clinical Trial, Level II	6 male volunteers for clinical trial, administration of dexmedetomidine & invasive monitors and hyperventilation	Determine if dexmedetomidine reduces CBF without a change in CMR	Dexmedetomidine reduced both CBF and CMR in a dose-dependent manner which preserves cerebral coupling	Conducted in healthy volunteers who were receiving no other sedative, analgesic, or hypnotic medications
Castillo et al. 2020	Narrative Review, Level V	N/A	Review of pharmacokinetic and pharmacodynamic properties, adverse effects, effects on CV & vent physiology, & applications	May inhibit inflammatory processes, enhance immune system activity by reducing systemic reactions and cytokine levels. Alleviates heart injury during sepsis and demonstrates neuroprotective role	Low level narrative review
Niu et al. 2021	Animal research, RCT Foundational Evidence	66 male Sprague-Dawley rats randomly Assigned to: Control group (n = 15), Anesthesia group (n = 15), Model group (n = 18), Model + Dex group (n = 18)	To determine if dexmedetomidine prevents memory deficits after surgery by suppressing Surf1 and Cytochrome c expression.	In the rat model, dexmedetomidine -Improved spatial memory deficit induced by surgery -Had no effect on pyramidal neurons of the hippocampus - Decreased the levels of Iba-1 in the hippocampus, decreasing overexpression of Iba-1 and GFAP & impaired hippocampal-dependent memory -Mitigated higher density of Iba-1 and GFAP and suppressed the expression of Surf1 and Cytochrome c protein in the hippocampus	Animal research, while this is core foundational evidence extrapolation of data for humans may be difficult
Zhou et al. 2020	Animal research, placebo-controlled, In-Vitro Study Foundational Evidence	60 male, 15 month-old mice under a PND model, BV2 Microglial cells	Explore effects of dexmedetomidine and PND on microglial cells	Dexmedetomidine is an effective inhibitor of the surgical inflammation	Animal research, while this is core foundational evidence extrapolation of data for humans may be difficult

Limitations. Research in animal models shows a benefit to the use of dexmedetomidine in the perioperative period, a reduction in PND, and downregulation of proteins associated with apoptosis of neural tissue resulting in neuroprotective effects. Comprehensive neuroprotection research in humans is limited to observational studies, randomized control trials, and retrospective analysis. Additionally, there is no determination of the optimal timing in this review. Whether or not dexmedetomidine given as a loading dose, intravenous infusion post-operative, or a combination of these is not conclusive on which imparts the neuroprotective effects. Additionally, the researchers did not specify during which post-operative phase the PCA pump was initiated. Therefore, more research is needed to determine the best practices.

Practice Recommendations. Analysis of the evidence shows that a loading dose of dexmedetomidine 1 mcg/kg over 10 minutes prior to induction in addition to intravenous doses of dexmedetomidine between 3 mcg/hr and 16 mcg/hr in the post-operative period significantly reduce the risk of developing PND in geriatric inpatient populations while serving as an effective adjuvant for post-operative pain. This study recommends that infusions of dexmedetomidine should not last longer than 72 hours, and reduction of PND was achieved with doses of dexmedetomidine that average approximately 6 mcg/hr. [10]

Conclusion

Dexmedetomidine has been gaining popularity as a valuable adjuvant to anesthesia in the perioperative period. Thus, anesthesia professionals should assess if their patients benefit from dexmedetomidine. In addition, anesthesia professionals should incorporate dexmedetomidine into their future practice and contribute helpful anesthesia case studies to the scientific community. With the reduction in cost associated with the current generic status of dexmedetomidine and the adaptation of value-based health care, exploration of the clinical implications of dexmedetomidine is imperative. Dexmedetomidine has many benefits beyond procedural sedation and is readily available in the perioperative period. Evidence shows that dexmedetomidine reduces the need for IV anesthetics, opioids and increases patient satisfaction score.[15]

As described in this review, PND is associated with increased healthcare costs and detrimental patient outcomes. Dexmedetomidine can significantly reduce PND because it offers neuroprotective properties and preserves cerebral coupling. In conclusion, dexmedetomidine's ability to attenuate the sympathetic response to surgical stress, reduce oxidative damage, and its powerful neuroprotective properties will prove an asset for the anesthesia professional and may result in safer outcomes for patients.

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Mentor: Morgan Morrow, DNAP, CRNA

Point-of-care Gastric Ultrasound

Tanya Turk, BSN
Midwestern University

Keywords: point-of-care-ultrasound, ultrasound assessment, preoperative assessment

Introduction

Advancements provide the availability of technology for new and creative opportunities. Ultrasound is one of those technologies that has become a readily available tool in the medical field and has the benefit of an excellent safety record.[1] Using ultrasound to aid anesthesia with point of care (POC) gastric ultrasound is an accurate, noninvasive, and effective way to assess gastric contents. POC gastric ultrasound takes minutes to perform, is relatively easy to learn, and allows the clinician to determine if the patient has an empty stomach. It is essential for the stomach to be empty in order to minimize poor outcomes that may be caused by aspirating gastric contents. Identification of these contents via POC gastric ultrasound can be a useful metric. Gastric content assessment is both invasive and time-consuming. Current assessment methods, such as paracetamol absorption, electrical impedance tomography, radiolabeled diet, polyethylene glycol dilution studies, or suctioning via gastric tubes, are not practical in perioperative practice.[2] POC gastric ultrasounds are valuable and practical for perioperative use but are not currently standard practice. Understanding and implementing new procedures must be carefully considered to ensure the change will provide a benefit.

Safe airway management during anesthesia care is essential for a positive patient outcome. A critical consideration of safe airway management is aspiration risk. Significant issues can occur from pulmonary aspiration of gastric content: pneumonia, acute respiratory distress syndrome, multiple organ dysfunction, brain damage, and death.[3] For scheduled surgery, fasting ensures the patient has an empty stomach to avoid or minimize perioperative complications from pulmonary aspiration during sedation. Standardized nil per os (NPO) times given by the American Society of Anesthesiologists[4] provide the patient guidelines. Anesthesia professionals also deal with situations where fasting guidelines are not introduced, such as acute surgical conditions.[5] An empty stomach is determined primarily by patient history; a provider utilizes this assessment to determine the risk of pulmonary aspiration. When the patient is considered an aspiration risk due to gastric content, the anesthesia professional will change the anesthetic induction technique for the surgery to continue. An alternative to the standard induction technique for patients at aspiration risk is rapid sequence induction (RSI), where a patient is not manually ventilated and the esophagus is occluded with cricoid pressure. However, RSI carries additional risks and complications over regular intubation: failed intubation, hypoxia, hypotension, bradycardia, esophageal trauma, awareness, the sensation of pain, and potential aspiration.[5] Using gastric ultrasound may provide additional information for assessing aspiration risk. An accurate assessment of the patient's risk allows the anesthesia professional to provide the care plan for the best possible outcome.

Methodology

Utilizing the PICO (population, intervention, comparison, outcome) guidelines for a review of evidence-based practice guidelines, the proposed research question is: In patients undergoing general anesthesia, does the addition of POC gastric ultrasound to the preoperative assessment change the anesthetic plan to proceed, cancel, modify, or delay the case?

Literature analysis

In practice, there are a variety of situations where relying on patient history and reported fasting is not adequate information to confirm the gastric contents for correctly identifying the aspiration risk. Medical conditions, medications, comorbidities, communication difficulties, and adherence to the guidelines may influence gastric emptying or the stomach not being empty as expected.[6] Haskins et al.[6] noted that despite following NPO guidelines and in the absence of known risk factors regarding gastric emptying, up to 2% of patients may still have gastric contents that could lead to anesthetic complications. Patients recognized as high risk are not always labeled correctly. Holtan-Hartwig et al.[5] performed preoperative gastric ultrasound on patients designated to undergo RSI after being deemed high risk for aspiration by an anesthesiologist. In this study, ultrasound findings were not shared with the anesthesiologists during data collection to not influence any airway management decisions. The results showed 32 of the 63 patients would have been designated low risk by the gastric ultrasound, and the confirmation for the ultrasound results was performed by gastric suction. The gastric ultrasound would have suggested for over half of the patients that an optional airway management strategy may have been possible instead of RSI. Clinical expertise was not shown to improve the ability to predict high-risk aspiration accurately. This study demonstrates that uncertainty exists in determining pulmonary aspiration risk for the anesthesia care plan and demonstrates the role gastric ultrasound can play in assessing gastric contents.

Implications for the obese patient. Obese patients have an increased risk for delayed gastric emptying despite fasting that follows the NPO guidelines. Severe obesity causes the antrum of the stomach to be deeper in the abdominal cavity and larger than in non-severely obese patients.[6] With a larger antrum, these patients have a significantly greater amount of gastric fluid in the cross-sectional antral area (CSA), leading to an increased risk of aspiration.

Pediatric implications. With pediatric patients, it is challenging to determine patient factors or the last time the patient ingested something to comply with fasting guidelines. Factors that delayed pediatric gastric emptying were genetic, comorbid conditions, acute processes, and taking opioid analgesics even with appropriate NPO times.[7] Case reports in pediatrics show that POC gastric ultrasound is a helpful tool to determine an anesthesia care plan by evaluating the potential for pulmonary aspiration and identifying if there is a need to delay or cancel the procedure. Parekh et al.[8] evaluated cases where gastric ultrasound was used to determine the status of the stomach contents. A 3-year-old child was reported drinking clear fruit punch 90 minutes prior to surgery. By performing the gastric ultrasound, it was found that the patient had an empty stomach, and the procedure did not need to be delayed. Another case report found that a 3-year-old child was scheduled for a hernia repair and ate potato chips approximately 6 hours before surgery. Since this time frame is considered on the border of NPO guidelines, a gastric

ultrasound was performed, and solid gastric content was found, thus causing the elective surgery to be canceled and rescheduled for another day. Munlemvo et al.[7] reviewed a case where a 2-hour postponement changed the gastric ultrasound assessment of a 4-year-old from having gastric contents and a high-risk classification, even with 8-hour fasting, to the later low-risk classification on repeat ultrasound, showing an empty stomach. Gastric ultrasound was used to confirm pediatric stomach contents objectively. The range of cases reflects the many factors that can influence the optimal plan for the pediatric procedure. Gastric ultrasound helped ensure the proper measures were taken to help prevent adverse outcomes.

Provider implications. POC gastric ultrasounds aid in achieving positive patient outcomes, and the study by Holtan-Hartwig et al.[5] shows the procedure is easy, fast, and feasible without causing a delay. The learning curve for bedside ultrasound assessment of gastric content by anesthesiologists without prior gastric ultrasound training to achieve a 90% success rate is 24 examinations, and a 95% success rate is 33 examinations.[9] Support for this learning curve is seen in studies by Kruisselbrink et al.[3] and Holtan-Hartwig et al.[5] The mean examination time was found to be 2 minutes 50 seconds by Holtan-Hartwig et al.[5] Haskins et al.[6] noted that gastric ultrasound is less complex than other ultrasounds, such as cardiac; the 2-dimensional mode for gastric content assessment is more straightforward to use than the M mode or Doppler. The technique utilized for gastric ultrasound is found to be reliably and consistently performed to obtain a proper ultrasound image.[1] The appropriate probe for the patient's weight is used, and the upper abdomen needs to be fully exposed. Positioning the patient supine and viewing the gastric antrum will indicate large quantities in the stomach. The patient is placed in the right lateral decubitus (RLD) position to visualize gastric content further and encourage gravitational drainage. The supine position alone cannot rule out an empty stomach, whereas the RLD position helps confirm antral content. The sonographic appearance will differ with the contents; an empty stomach may resemble a "bulls-eye" shape, carbonated or clear liquids just ingested may have a "starry night" appearance, and solid food may appear as "frosted glass." These images are formed by the variable contents of air, fluids, or solid matter and the gastric walls, layers, or folds. Volume is derived by taking measurements and then performing a mathematical calculation. A quantification of gastric content or a grading system, Grade 0, Grade 1, and Grade 2, conveys the low to high risk of aspiration. When performing a POC gastric scan, a provider needs to recognize that patients may have liquid in the stomach within a normal finding regardless of NPO status; any fluid greater than 1.5 ml/kg, however, is considered abnormal or full stomach.[5] Any solid, particulate matter, or thick fluid present likely indicates a higher risk, regardless of the quantity.[2]

Reliability of findings. A gastric ultrasound's objective information is quantity and quality, as in the volume and the type of gastric content: nothing, clear fluid, thick fluid, or solid particulate matter.[3] A trained health care provider can distinguish the gastric content based on the sonographic appearance in the ultrasound.[7] This supplemental information can be used to guide anesthesia care plans. Gastric ultrasound may be performed for all ages, is noninvasive, and does not expose the patient to ionizing radiation.[8] Information to aid in establishing care plans must be reliable and reproducible to be of significant value. The accuracy of POC gastric ultrasound was shown to be highly sensitive and specific.[3] In the controlled study, 40 healthy volunteers with minimum 8-hour fasting were confirmed to have an empty stomach and then were evenly assigned to either remain fasted or ingest a set quantity of fluids and solids. A gastric ultrasound

was performed with results of having a positive or a negative for a full stomach being noted. All full stomachs were correctly identified with no false negatives. However, there was one false positive. The results indicate that POC gastric ultrasound is valuable and reliable for identifying gastric contents in the stomach.

Limitations. Gastric ultrasound is a beneficial tool for an anesthesia professional when implemented appropriately. Recognizing that incorrect results can have fatal implications means appropriate training is necessary to ensure that POC gastric ultrasound is conducted and interpreted correctly. Following the established procedure will give the most accurate information. Additionally, the patient must be positioned appropriately in order to complete an accurate gastric ultrasound scan. The RLD is the ideal patient position; however, the RLD positioning is impractical in certain patients.[2] The semi-recumbent position is a reasonable alternative but is less accurate. Establishing an optimal view can be hindered by some conditions. Obese and pregnant patients may require alterations. Obesity causes the antrum of the stomach to be deeper in the abdominal cavity. An obstetric patient may have mechanical compression or displacement of the stomach by the gravid uterus, tachypnea, or hyperdynamic circulation, which may pose a challenge in performing a gastric ultrasound.[6] Inaccurate or unreliable findings may occur in patients with a large hiatus hernia or previous gastric surgery.[2] In addition to these noted limitations, it needs to be recognized that there is an inconclusive rate of 2% to 3% for gastric ultrasounds due to various issues: anatomical variation, misinterpretation of other structures, or presence of air in other structures.[2] Recognizing limitations should not diminish the value of the POC gastric ultrasound. Instead, it should reinforce the benefit of having additional resources available to identify possible issues so the optimum patient care plan is determined. When combined with clinical judgment, POC gastric ultrasound is a helpful tool to help guide decisions for safe airway management.

Table. Summary of Literature regarding POC Gastric Ultrasound

Author, Year	Study Design, Purpose	Population	Results	Limitations
Arzola et al., 2013	Cohort Study Determine how long it takes for anesthesiologist to become competent at gastric ultrasound	6 advanced level trainee anesthesiologists without gastric ultrasound experience	Estimates it takes 33 gastric ultrasound cases to achieve 95% success rate identifying gastric content	Did not do a volume assessment, limited number of healthy young males with normal body mass index utilized for volunteer participants
El-Boghdadly et al., 2019	Scholarly Article Provide understanding to the purpose, procedure, and use of gastric ultrasound to determine gastric contents	Patients that need to have gastric contents determined prior to anesthesia	Gastric ultrasound is a technique that has the ability to determine gastric contents	Inconclusive results may happen in limited populations
Haskins et al., 2018	Scholarly Article Provide the methodology of gastric ultrasound in the perioperative setting to determine gastric contents	Patients in the perioperative setting needing gastric contents determined	Point of care gastric ultrasound accomplishes the visualization of gastric contents	Additional research is needed to validate use of gastric ultrasound for preoperative evaluation of gastric contents

Holtan-Hartwig et al., 2021	Prospective Observational Study Preoperative evaluation of aspiration risk in patients requiring rapid sequence intubation and feasibility of point-of-care gastric ultrasound in the clinical setting	72 adult surgical patients needing rapid sequence induction intubation	Found over half of the patients undergoing rapid sequence intubation were not at elevated risk of aspiration according to gastric ultrasound with an mean exam time of 2 minutes and 50 seconds	Limited gastric ultrasound experience that can be overcome with proper education, limited participant population
Kruisselbrink et al., 2019	Prospective Randomized Observer-Blinded Design Determine the accuracy of point-of-care gastric ultrasound in detecting a "full stomach"	40 healthy volunteers	Bedside gastric ultrasound is highly sensitive and specific in identifying a full stomach when the ultrasound is performed per guidelines	Controlled circumstances with healthy with normal body habitus volunteers, volunteers scanned multiple times but considered independent, specific food quantities and type
Munlemvo et al., 2021	Case Report Utilization of point-of-care gastric ultrasound to evaluate gastric contents in pediatrics	4 yo female	With point-of-care gastric ultrasound determining a positive full stomach implementing a 2-hour delay resulted in an empty stomach point-of-care gastric ultrasound allowing for a low aspiration risk surgery to take place	Anecdotal evidence
Parekh et al., 2018	Case Report Benefit of gastric ultrasound in determining gastric content in pediatric patients with uncertain duration or adequacy of fasting prior to procedures	6 mo male, 3 yo male, 3 yo female	Improved decision-making based on gastric ultrasound findings	Anecdotal evidence

Practice Recommendations. Implementing POC gastric ultrasound as a preoperative assessment would give the anesthesia professional additional information regarding gastric contents and allow that information to aid in determining the surgical plan.[6] The methodology must be performed and documented as established by standard guidelines to ensure consistency and safety.[3] POC gastric ultrasound is a non-invasive method of assessment that upholds the principle of beneficence as it poses no threat of harm to the patient while improving the method for the anesthesia professional to determine aspiration risk status.[2] Performing POC gastric ultrasound is feasible, practical, and has the ability to impact patient outcomes positively.

Conclusion

A preoperative evaluation is essential to establish aspiration risk and achieve a safe airway management plan.[5] Currently, aspiration risk assessment is primarily determined by clinical judgment based on patient history. An important component in the personal history is adherence to the NPO fasting guidelines. Fasting is the most commonly used measure to attain an empty stomach; however, there are limitations to solely relying on NPO status to risk-stratify patients for anesthesia.[2] POC gastric ultrasound is a powerful tool that allows real-time visualization to quantify gastric contents to determine aspiration risk before anesthesia. This additional information can provide valuable insight to guide decisions to proceed with the surgery or delay, induction techniques for the circumstances, and airway management strategy.[7] POC gastric ultrasound is a potentially valuable tool and should be considered an emerging priority in the preoperative assessment phase for surgical patients.

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Mentor: Morgan Morrow, DNAP, CRNA

Editorial

Having recently returned from the AANA Annual Congress in Chicago, I am reminded of how truly amazing our profession is. I am grateful to be a part of this accomplished, committed, motivated group, where everyone is generous with their knowledge and experience, and also eager to learn and improve as clinicians, educators, and leaders. We all benefit from this mindset, and it is what allows the International Student Journal of Nurse Anesthesia to exist. While I am always sad to announce departures from the editorial board, I do so with immense gratitude for their service, those who currently serve, and our new board members. I would like to acknowledge the following individuals for their years of time and talent who are now stepping down from the board:

Carrie C. Bowman Dalley, PhD, CRNA; Georgetown University
Marjorie A. Everson, PhD, CRNA; Johns Hopkins University
CDR Chad Moore, DNP, CRNA, CHSE, NC; Uniformed Services University

I am excited to announce our newest members of the editorial board:

Jeanne M. Antolchick, PhD, APRN, CRNA; Barry University
Susan Hall, DNP, CRNA; Northeastern University
Susan Krawczyk, DNP, CRNA; NorthShore University Health System
Crystal O'Guin, DNP, CRNA; Georgetown University

Please join me in welcoming Drs. Antolchick, Hall, Krawczyk, and O'Guin to our student journal family, and wishing Drs. Bowman, Everson, and Moore the best in their future pursuits!

Sincerely,

Vicki Callan, PhD, CRNA, CHSE, FAANA
Editor

INTERNATIONAL STUDENT JOURNAL OF NURSE ANESTHESIA
GUIDE FOR AUTHORS

MISSION STATEMENT

The International Student Journal of Nurse Anesthesia (ISJNA) is produced exclusively for publishing the work of nurse anesthesia students. It is intended to be basic and introductory in its content. Its goal is to introduce the student to the world of writing for publication; to improve the practice of nurse anesthesia and the safety of the patients entrusted to our care.

ITEM PREPARATION & SUBMISSION

Case reports, research abstracts, evidence-based practice (EBP) analysis reports, evidence-based practice project abstracts, and letters to the editor may be submitted. These items must be authored by a student under the guidance of an anesthesia practitioner mentor (CRNA or physician). Case reports must be single-authored, while EBP analysis reports and abstracts may have multiple authors. Submissions may list only one mentor. **Mentors should take an active role** in reviewing the item to ensure appropriate content, writing style, and format prior to submission. The mentor must submit the item for the student and serve as the contact person during the review process. Items submitted to this journal should not be under consideration with another journal. Authors and mentors should critically evaluate the topic and quality of the writing – multiple reviews of the item by the mentor, faculty, and peers (fellow graduate students) prior to submission is recommended. If the topic and written presentation are beyond the introductory publication level we strongly suggest that the article be submitted to a more prestigious publication such as the *AANA Journal.*

The journal is committed to publishing the work of nurse anesthesia students. The review process is always initiated with the following rare exceptions. We are conservative in accepting reports where the patient has expired, realizing that you can do everything right and still have a negative outcome. Submissions that report a case demonstrating failure to meet the standard of care (by any practitioner involved in the case) will not be accepted. Unfortunately, while the experiences in these cases can offer valuable insight, these submissions will not be accepted for review due to potential legal risks to the author, journal, and anyone else involved in evaluating the report.
It is the intent of this journal to publish items while the author is still a student. In order to consistently meet this goal, all submissions must be received by the editor at least **3 months prior** (4-6 months recommended) to the author's date of graduation. Manuscripts must be submitted by the mentor of the student author via e-mail to **INTSJNA@aol.com** as an attachment. The subject line of the e-mail should use the following format: ISJNA Submission_submission type_author last name_mentor last name. The item should be saved in the following format – two-three word descriptor of the article_author's last name_school abbreviation_mentor's last name_date (e.g. PedsPain_Smyth_GU_Pearson_5.19.09)

REVIEW PROCESS

Items submitted for publication are initially reviewed by the chief editor. If the chief editor does not acknowledge receipt of the item within two weeks, please inquire to ensure receipt. Upon receipt, the chief editor will review the submission for compliance with the Guide to Authors. If proper format has not been followed, the item will be returned to the mentor for correction. This is very important as all reviewers serve on a volunteer basis. Their time should be spent ensuring appropriate content, not making format corrections. It is the mentor and author's responsibility to ensure formatting guidelines have been followed prior to submission.

All accepted submissions undergo a formal process of blind review by at least two reviewers. After review, items may be accepted without revision, accepted with revision, or rejected with comments. Once the item has been accepted for review the chief editor will assign a submission number and send a blinded copy to an editor, who will then coordinate a blinded review by two reviewers who are not affiliated with the originating program. Submissions are reviewed using the Track Changes function of Word. The editor will return the item to the chief editor, who will return it to the mentor for appropriate action. **The mentor should guide the author through the revision process. The revised copy must be returned clean (no comments or Track Changes) with the original submission number in the filename and subject line of the email.** Every effort is made to complete the process in an efficient, timely matter. Again, the goal is for all articles submitted by students to be published while the author is still a student. If an item is not ready for publication within 6 months after the student author has graduated it will no longer be eligible for publication. Mentors will be listed as contributing editors for the issue in which the item is published.

PHOTOS

Photos of students for the front cover of the Journal are welcome. Please contact the chief editor at intsjna@aol.com to submit photos for consideration. Only digital photos of high quality will be accepted. If the photo is accepted, consent forms must be completed and returned by all identifiable individuals in the photo, and the individual who took the photo.

ACADEMIC INTEGRITY

Issues of academic integrity are the responsibility of the author and mentor. Accurate and appropriate acknowledgement of sources is expected. The two most common breaches of academic integrity that have been identified in submissions to this journal are (AMA 11th ed., 5.4.2):

1. Direct plagiarism: verbatim lifting of passages without enclosing the borrowed material in quotation marks and crediting the original author.
2. Paraphrase: restating a phrase or passage, providing the same meaning but in a different form without attribution to the original author.

Please note that changing one or two words in a reference source passage (e.g. 'of' for 'in', or 'classified' for 'categorized') and then citing it as a paraphrase or summary is also not appropriate, and still falls within the definition of direct plagiarism. If plagiarism in any form is identified, review of the item will be suspended and it will be returned to the mentor. Repeated instances of plagiarism will result in rejection of the item.
Plagiarism detection software (Scribbr, TurnItIn, PlagScan, SafeAssign, etc . . .) can be used to analyze the document prior to submission to ensure proper citation and referencing, but is not required.
"Plagiarism is the presentation of someone else's ideas, writings, or statements as one's own. Plagiarism is a serious breach of academic integrity, and anyone who is found to have committed plagiarism will be subject to disciplinary action.

Paraphrase is the act of putting someone else's ideas into one's own words. The use of paraphrase can be an acceptable practice under some circumstances if it is used sparingly and if the original text is properly acknowledged. Unacknowledged paraphrase, like plagiarism, is a serious breach of academic integrity. Any improper use of sources may constitute plagiarism. Every quotation from another source, whether written, spoken, or electronic, must be bound by quotation marks and be properly cited. Mere citation alone is not sufficient when a scholar has used another person's words. Similarly, every paraphrase or summary (a more concise restatement of another's ideas) must be properly cited."
https://sites.google.com/a/georgetown.edu/gsas-graduate-bulletin/vi-academic-integrity-policies-procedures

GENERAL GUIDELINES

Items for publication **must adhere to the *American Medical Association Manual of Style*** (AMA 11th ed., the same guide utilized by the *AANA Journal* and such prominent textbooks as *Nurse Anesthesia* by Nagelhout and Elisha). Section numbers from the online version are provided for easy reference in the AMA Manual of Style throughout this document. The review process will not be initiated on items submitted with incorrect formatting and will be returned to the mentor for revision.

Reference: Christiansen S, Iverson C, Flanagin A, et al. *AMA Manual of Style: A Guide for Authors and Editors*. 11th ed. Oxford University Press; 2020.

Please note the following:

1. Use complete sentences.
2. Acronyms/Initialisms (2.1.5, 10.6, 13.9) - spell out with first use, do not capitalize the words from which the acronym/initialism is derived unless it is a proper noun or official name. If you are using the phrase only once, do not list the acronym/initialism at all. Avoid beginning sentences with acronym/initialisms.
3. Abbreviations (13.0)
4. Use *Index Medicus* journal title abbreviations (3.11.2, http://www.ncbi.nlm.nih.gov/nlmcatalog/journals)
5. Always provide units of measure (17.0). In most cases The International System of Units (SI) is used. Abbreviations for units of measure do not need to be spelled out with first use. Report height in cm, weight in kg, temperature in °C, pressure in mm Hg or cm H_2O. Report heart and respiratory rate as X/min (e.g. the patient's heart rate increased to 145/min). The manual includes a complete list of SI units (17.1 – 17.5).

6. In general, first use of pulmonary/respiratory abbreviations should be expanded, with the following exceptions: O_2, CO_2, PCO_2, $PaCO_2$, PO_2, PaO_2, $EtCO_2$, N_2O. Please use SpO_2 for oxygen saturation as measured by pulse oximetry.
7. Use the nonproprietary (generic) name of drugs (2.1.3, 10.3.5) - avoid proprietary (brand) names. Type generic names in lowercase. When discussing dosages state the name of the drug, *then* the dosage (midazolam 2 mg).
8. Use of descriptive terms for equipment and devices is preferred. If the use of a proprietary name is necessary (for clarity, or if more than one type is being discussed), give the name followed by the manufacturer in parenthesis (e.g. a GlideScope (Verathon Inc.) was used) (14.5.1). Please note, TM and ® symbols are not used per the AMA manual.
9. Infusion rates and gas flow rates:
    a. Use mcg/kg/min or mg/kg/min for infusion rates. In some cases it may be appropriate to report dose or quantity/hr (i.e. insulin, hyperalimentation). If a mixture of drugs is being infused give the concentration of each drug and report the infusion rate in mL/min.
    b. Report gas flow of O_2, N_2O and Air in L/min (not %) and volatile agents in % as inspired or expired concentration (e.g. General anesthesia was maintained with sevoflurane 3% inspired concentration in a mixture of O_2 1 L/min and air 1 L/min.)
10. Only Microsoft Word file formats will be accepted with the following criteria:
    a. Font - 12 point, Times New Roman
    b. Single-spacing (except where indicated), paragraphs separated with a double space (do not indent)
    c. One-inch margins
    d. End the sentence with the period before placing the superscript number for the reference.
    e. Do not use columns, bolds (except where indicated), or unconventional lettering styles or fonts.
    f. Do not use endnote/footnote formats.
11. If referencing software is used (Endnote, Zotero, etc.), any embedded <u>formatting must be removed</u> prior to submission.
12. Remove all hyperlinks within the text.
13. Avoid jargon and slang terms. Use professional, scholarly, scientific language.
    a. *'The patient was reversed'* - Did you physically turn the patient around and point him in the opposite direction? "Neuromuscular blockade was antagonized."
    b. *The patient was put on oxygen.* "Oxygen 2 L/min was administered via face mask."
    c. *The <u>patient</u> was intubated and put on a ventilator*. "The trachea was intubated and mechanical ventilation was initiated.
    d. *An IV drip was started.* "An intravenous infusion was initiated."
    e. Avoid the term "MAC" when referring to a sedation technique - the term sedation (light, moderate, heavy, unconscious) may be used. Since all anesthesia administration is monitored, pharmacologic, rather than reimbursement, terminology should be used.
14. Direct quotes are discouraged for reports of this length – please express in your own words.
15. Use the words "anesthesia professionals" or "anesthesia practitioners" when discussing all persons who administer anesthesia (avoid the reimbursement term "anesthesia providers").
16. Do not include ASA Physical Status unless it is germane to the report.
17. Do not use the phrase "ASA standard monitors were applied". Instead, "standard noninvasive monitors" is acceptable – additional monitoring can be detailed as needed.
18. References
    a. The **<u>AMA Manual of Style must be adhered to</u>** for reference formatting.
    b. All sources should be published within the past 8 years. Seminal works essential to the topic being presented will be considered.
    c. Primary sources are preferred.
    d. **A maximum of one textbook (must be most recent edition available) may be used as reference for case report submissions only**.
    e. All items cited must be from peer-reviewed sources – use of sources found on the internet must be carefully considered in this regard. URLs must be current and take the reader directly to the referenced source.

<u>Heading</u> – for all submission types (Case Report, Abstract, EBPA Report) use the following format.

1. **Title** is bolded, centered, 70 characters (including spaces) or less
2. Author name (academic credentials only) and NAP are centered, normal font
3. *Graduation date and email address* are centered, italicized, and will be removed prior to publication)
4. **Keywords** is left-justified, bolded – list keywords that can be used to identify the report in an internet search

Title

Author Name
Name of Nurse Anesthesia Program
Anticipated date of graduation
E-mail address

Keywords: keyword one, keyword two, etc.

Case Reports - The student author must have had a significant role in the conduct of the case. The total word count should be between 1200 – 1400 words (references not counted). Case reports with greater than 1400 words will be returned to the mentor for revision prior to initiation of the review process. The following template demonstrates the required format for case report submission.

Heading (see above)

A brief introductory paragraph of less than 100 words to focus the reader's attention and interest them to continue reading. This may include historical background, demographics or epidemiology (with appropriate references) of the problem about to be discussed. It is written in the *present tense*. Although it is introductory, the heading word '***Introduction'*** is not used. Be certain to cite references in this section, especially statistics and demographics pertaining to your topic.

Case Report (400-600 words)

This portion discusses the case performed and is written in the *past tense*. Do not justify actions or behaviors in this section; simply report the events as they unfolded. Present the case in an orderly sequence. Some aspects need considerable elaboration and others only a cursory mention. Under most circumstances if findings/actions are normal or not contributory to the case then they should not be described. Events significant to the focus of the report should be discussed in greater detail. The purpose of the case report is to set the stage (and 'hook' the reader) for the heart of your paper which is the discussion and teaching/learning derived from the case.

- Give dosage and schedule only if that information is pertinent to the consequences of the case.
- **Significant** laboratory values, x-rays or other diagnostic testing pertinent to the case. Give the units of measure after the values (eg. Mmol/L or mg/dL).
- Physical examination/pre-anesthesia evaluation - **significant** findings only.
- Anesthetic management (patient preparation, induction, maintenance, emergence, post-operative recovery).

Discussion (600-800 words)

Describe the ***anesthesia*** implications of the focus of the case report citing current literature. Describe the rationale for your actions and risk/benefits of any options you may have had. This section is not merely a pathophysiology review that can be found in textbooks. *Relate the anesthesia literature with the conduct of your case noting how and why your case was the same or different from what is known in the literature.* Photographs are discouraged unless they are essential to the article. Photos with identifiable persons must have a signed consent by the person photographed forwarded to the editor via first class mail. Diagrams must have permission from original author. This is the most important part of the article. In terms of space and word count this should be longer than the case presentation. End the discussion with a summary lesson you learned from the case, perhaps what you would do differently if you had it to do over again.

References

A minimum of 5 references is recommended, with a maximum of 8 allowed. One textbook may be used as a reference – it must be the most recent edition. All references should be no older than 8 years, except for seminal works essential to the topic. This is also an exercise in searching for and evaluating current literature.

Mentor: mentor name, credentials

E-mail address: *(*will be removed prior to publication)

EBP Analysis Reports - Evidence-based practice analysis reports are limited to 3000 words. Please do not include an abstract. The report should provide a critical evaluation of a practice pattern in the form of a clinical question about a specific intervention, population, and outcome. The manuscript should:

1. Articulate the practice issue and generate a concise question for evidence-based analysis. A focused foreground question following either the PICO or SPICE format should be used.
2. Describe the methods of inquiry used in compiling the data.
3. Critically analyze the quality of research reviewed and applicability to different practice settings.
4. Draw logical conclusions regarding appropriate translation of research into practice.

The same general format guidelines apply with the exception of the section headings as below. Textbooks and non-peer reviewed internet sources may not be used, and sources of reference should be less than 8 years old unless they are seminal works specifically related to your topic of inquiry. A maximum of 16 references is allowed.

Heading

Introduction (bold)
Briefly introduce the reader to the practice issue or controversy, describe the scope or significance or problem, and identify the purpose of your analysis. Describe the theoretical, conceptual, or scientific framework that supports your inquiry.
Methods (bold)
Include the format used for formulating the specific question you seek to answer, search terms and methods used, and levels of evidence.
Literature Analysis (bold)
Analyze and critique the literature relevant to your question, determining scientific credibility and limitations of studies reviewed. Your synthesis table is included in this section. Please follow AMA formatting guidelines for your table (4.1.2, 10.2.3). Your review and discussion of the literature should logically lead to support a practice recommendation. Subheadings may be used if desired.
Conclusions (bold)
Summarize the salient points that support the practice recommendation and make research-supported recommendations that should improve the practice issue, while also acknowledging any limitations or weaknesses
[space]
References (bold, 16 maximum)
Mentor: (bold, followed by mentor name and credentials in normal text)
E-mail address: (normal text, will be removed prior to publication)

Evidence Based Practice Project Abstracts - Evidence-based practice project abstracts are limited to 600 words. References do not impact the word count - a maximum of 5 are allowed. Note that the abstract is different from a project proposal. The following format should be used:

Heading

Introduction (bold)
A brief introductory paragraph including purpose (what change is intended) and rationale (why change is needed/evidence to support the change) here.
Design and Methods (bold)
Include population, intervention, and measures
Outcome (bold)
Present results from statistical analysis – do not justify or discuss here.
Conclusion (bold)
Discuss results (implications). Optionally include limitations, suggestions for future projects/research.
References (bold, 5 maximum)
Mentor: (bold, followed by mentor name and credentials in normal text)
E-mail address: (normal text, will be removed prior to publication)

Research Abstracts - Research abstracts are limited to 600 words. References do not impact the word count - a maximum of 5 are allowed. Note that the abstract is different from a research proposal. The following format should be used:

Heading

Introduction (bold)
A brief introductory paragraph including purpose and hypotheses.
Methods (bold)
Include sample and research design
Results (bold)
Present results from statistical analysis – do not justify or discuss here.
Discussion (bold)
Discuss results (implications, limitations, suggestions for future research)
References (bold, 5 maximum)
Mentor: (bold, followed by mentor name and credentials in normal text)
E-mail address: (normal text, will be removed prior to publication)

Letters to the Editor - Students may write letters to the editor topics of interest to other students. Topics may include comments on previously published articles in this journal. Personally offensive, degrading or insulting letters will not be accepted. Suggested alternative approaches to anesthesia management and constructive criticisms are welcome. The length of the letters should not exceed 100 words and must identify the student author and anesthesia program.

AMA MANUAL OF STYLE

The following is brief introduction to the *AMA Manual of Style* reference format along with some links to basic, helpful guides on the internet. The website for the text is http://www.amamanualofstyle.com/oso/public/index.html. It is likely your institution's library has a copy on reserve. Journal names should be in italics and abbreviated according to the listing in the PubMed Journals Database. PubMed can also be used to perform a search: http://www.ncbi.nlm.nih.gov/pubmed. The International Student Journal of Nurse Anesthesia (ISJNA) is not listed in the PubMed Database. For the purpose of citing the ISJNA *in this Journal* use "**Int Student J Nurse Anesth**" as the abbreviation.

Journals (3.11) - A comma is placed after the first initials until the last author, which has a period. If there are six or less authors **cite all six**. If there are more than six authors **cite only the first three** followed by "et al." Only the first word of the title of the article is capitalized. The first letters of the major words of the journal title are capitalized. There is no space between the year, volume number, issue number, and page numbers. If there is no volume or issue number, use the month. If there is an issue number but no volume number use only the issue number (in parentheses). Page numbers are inclusive - **do not omit digits** (note - some online journals do not use page numbers). Some journals may be available both as hard copies and online. When referencing a journal that has been accessed online, the DOI (digital object identifier) or PMID (PubMed identification number, 3.15.2) should be included (see examples below).

Journal, 6 or fewer authors:

Han B, Liu Y, Zhang X, Wang J. Three-dimensional printing as an aid to airway evaluation after tracheotomy in a patient with laryngeal carcinoma. *BMC Anesthesiol*. 2016;16(6). doi:10.1186/s12871-015-0170-1

Journal, more than 6 authors:

Chen C, Nguyen MD, Bar-Meir E, et al. Effects of vasopressor administration on the outcomes of microsurgical breast reconstruction. *Ann Plast Surg*. 2010;65(1):28-31. PMID: 20548236

Elayi CS, Biasse L, Bai R, et al. Administration of isoproterenol and adenosine to guide supplemental ablation after pulmonary vein antrum isolation. *J Cardiovasc Electrophysiol*. 2013;24(11):1199-1206. doi: 10.1111/jce.12252

Electronic references (3.15) - Only established, peer-reviewed sources may be referenced. Please do not reference brochures, fact sheets, or informational websites where a peer-review process cannot be confirmed. The accessed date may be the only date available. The URL must be functional and take the reader directly to the source of the information cited.

Author (or if no author, the name of the organization responsible for the site). Title. *Name of Website*. Year;vol(issue no.):inclusive pages. Published [date]. Updated [date]. Accessed [date]. URL (with no period following).

Examples:

Kamangar N, McDonnell MS. Pulmonary embolism. *eMedicine*. Updated August 25, 2009. Accessed September 9, 2009. http://www.emedicine.com/med/topic1958.htm

Howlader N, Noone AM, Krapcho M, Garshell J, Miller D, et al. SEER Cancer statistics review, 1975-2012. National Cancer Institute. Published April 2015. Updated November 18, 2015. Accessed February 29, 2016. http://seer.cancer.gov/csr/1975_2012

Textbooks (3.12) - There are two types of books – 1) those that are fully authored by one or more individuals, and 2) those that are edited by one or more individuals, with chapters authored by different individuals. Edited textbooks give primary credit to the chapter authors, who are listed first, and the inclusive page numbers of the entire chapter are provided at the end. Textbooks that are authored do not have different chapter authors and the chapter titles are

not listed, but the inclusive page numbers where the information was found are provided, unless the entire book is cited.

Authored text:
Shubert D, Leyba J, Niemann S. *Chemistry and Physics for Nurse Anesthesia*. 3rd ed. Springer; 2017:405-430.

Chapter from an edited text (3.12.4)**:**
Pellegrini JE. Regional anesthesia. In Nagelhout JJ, Elisha S, eds. *Nurse Anesthesia*. 6th ed. Elsevier; 2017:1015-1041.

SUBMISSION CHECK LIST

Adheres to AMA Manual of Style and all other format instructions
___ Total word count not exceeded (1400 for case report, 600 for abstracts, 3000 for EBPA report)
___ The item is one continuous Word document without artificially created page breaks
___ All matters that are not common knowledge to the author are referenced appropriately
___ Generic names for drugs and products are used throughout and spelled correctly in lower-case
___ Units are designated for all dosages, physical findings, and laboratory results
___ Endnotes, footnotes not used
___ Jargon/slang is absent

Heading
___ Concise title less than 70 characters long (including spaces)
___ Author name, credentials, nurse anesthesia program, graduation date and email are included
___ Three to five **Keywords** are provided

Case Report
___ Introduction is less than 100 words.
___ Case Report section states only those facts vital to the account (no opinions or rationale)
___ Case report section is 400-600 words and not longer than the discussion
___ Discussion section is 600-800 words
___ Discussion of the case management is based on a review of current literature
___ Discussion concludes with lessons learned and how the case might be better managed in the future

Abstracts
___ The 600 word count maximum is not exceeded
___ Appropriate format used depending on type of abstract (research vs. EBP project)

EBPA Report
___ The 3000 word count maximum is not exceeded
___ A critical evaluation of a practice pattern in the form of a precise clinical question about a specific intervention, population, and outcome is presented
___ A focused foreground question following either the PICO or SPICE format is used
___ Includes Introduction, Methodology, Literature Analysis (with synthesis table), and Conclusion sections

References
___ Adheres to AMA Style format
___ Reference numbers are sequenced beginning with 1 and superscripted
___ References are from anesthesia and other current (within past 8 years) primary source literature
___ Journal titles are abbreviated as they appear in the PubMed Journals Database
___ Number of references adheres to specific item guidelines (1 textbook allowed for case reports only)
___ Internet sources are currently accessible, reputable, and peer reviewed

Transmission
___ The article is sent as a Word document attachment to **INTSJNA@AOL.COM**
___ The file name is correctly formatted (e.g. PedsPain_Smyth_GU_Pearson_5.19.09)
___ Item is submitted by the mentor
___ Subject heading format - ISJNA Submission_submission type_author last name_mentor last name