Anaesthesia for Uncommon and Emerging Procedures

Basavana G. Goudra
Preet Mohinder Singh
Michael S. Green
Editors

Springer

Anaesthesia for Uncommon and Emerging Procedures

Basavana G. Goudra
Preet Mohinder Singh
Michael S. Green
Editors

Anaesthesia for Uncommon and Emerging Procedures

Springer

Editors
Basavana G. Goudra
Perelman School of Medicine
Hospital of the University of
Pennsylvania
Philadelphia, PA
USA

Michael S. Green
Department of Anesthesiology
Thomas Jefferson University Hospital
Philadelphia, PA
USA

Preet Mohinder Singh
Department of Anesthesiology
Washington University in Saint Louis
St. Louis, MO
USA

ISBN 978-3-030-64738-4 ISBN 978-3-030-64739-1 (eBook)
https://doi.org/10.1007/978-3-030-64739-1

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Foreword

Medicine is ever changing, particularly in the realm of surgical procedures and the development of novel minimally invasive techniques. Anesthesiologists need to understand the surgical procedure in order to develop and implement an anesthetic plan. There are many textbooks which include major procedures and categories of procedures. In *Anaesthesia for Uncommon and Emerging Procedures*, Dr. Basavana Gouda Goudra collected a series of short chapters written by a diverse group of authors. This book fills the niche of practical textbooks which help the reader in providing daily care to their patients by including the details of the procedure, anesthetic care, and potential complications.

Dr. Goudra, a Clinical Associate Professor of Anesthesiology and Critical Care at the Perelman School of Medicine at the University of Pennsylvania, has been a prolific academic and has already published several textbooks. He integrates his academic approach to care with the pragmatism of a practicing clinician. The readers of this text will clearly be enlightened and prepared to care for patients undergoing these newer surgical procedures.

Philadelphia, PA, USA — Lee A. Fleisher

Preface

To a large extent, advances in anesthesiology are dictated by innovations in other branches of medicine. In this age of technology-driven inventions, newer procedures (both surgical and non-surgical) to our enduring problems demand innovative anesthesia approaches. Often, such an approach is a readaptation of existing techniques, drugs, and tools in novel ways to suit the requirements of surgery (or procedure) and the surgeon (or proceduralist). Some of these procedures include peroral endoscopic myotomy and bronchoscopic volume reduction. These require an understanding of unique anesthesia challenges posed by such approaches and post-procedural complications. Similar emerging procedures include brachytherapy, proton beam therapy, and many robotic surgical approaches to rectify both abdominal and genitourinary tract pathologies.

In addition to many emerging procedures, advancements have taken place in the anesthetic management of many uncommon procedures. The majority of anesthesia textbooks either do not mention these procedures or make a cursory reference. An anesthesia provider needs to do research painstakingly to have an understanding of these procedures and their unique anesthesia requirements.

In *Anesthesia for Uncommon and Emerging Procedures*, anesthesiologists with experience and expertise in providing anesthesia for such procedures have spent many months to deliver an excellent and in-depth review. The material presented in these chapters is directly from their extensive experience of taking care of these patients. The contributors are largely from the United States, with some contributions from Europe and India. The chapters cover wide areas and both pediatric and adult practice.

The book is useful for anesthesia providers who are occasionally called upon to provide their services for uncommon procedures such as catecholamine-secreting glomus jugulare tumor resection and paraesophageal hernia repair. In addition, anesthesia providers caring for rare complex procedures such as pediatric heart and lung transplantation, surgical ventricular remodeling, and conjoined twins separation will find the information provided in this book a ready reference. As a result, the book is useful for both regular anesthesia providers and those involved in caring for complex and highly specialized procedures.

We are thankful to many outstanding contributors for their excellent contributions. We hope that *Anesthesia for Uncommon and Emerging Procedures* will be an excellent book to have in the shelf of any practicing anesthesiologist or library. We also thank Mr Prakash Jagannathan and Ms Elizabeth Pope from Springer for their untiring support throughout the preparation of this book.

Philadelphia, PA — Basavana G. Goudra
St. Louis, MO — Preet Mohinder Singh
Philadelphia, PA — Michael S. Green

Contents

1 Anesthesia for Endoscopic Bariatric Surgery

Kathleen Kwiatt, Adib Chaaya, and Angelo Andonakakis

Learning Points

- Obesity and its associated comorbidities can be managed by effective, low-risk, minimally invasive endoscopic bariatric procedures.
- Both MAC and general anesthesia are acceptable and must be tailored to the individual and procedure specific circumstances.
- Understanding how obesity affects pharmacology is critical to prevent over and underdosing, and small, judicious doses of sedating and pain medications are appropriate to prevent respiratory complications.

Introduction

Obesity is a prevalent diagnosis with cardiovascular, pulmonary/respiratory, orthopedic, and metabolic health consequences. Noninvasive medical treatment including lifestyle modifications, diet, physical activity, and pharmacologic treatment is relatively low-risk, but has limited efficacy and long-term durability. Traditional bariatric surgery is effective with significant, sustainable weight loss, reduced obesity-related comorbidities [1], and decreased mortality [2], but also has a higher complication rate compared to noninvasive medical management. Not all patients are able or willing to undergo invasive surgery for a host of reasons: unacceptable perioperative risk due to underlying comorbidities, fear, potential long-term complications, and financial hardship (procedure cost, time lost from work, time unable to function as a primary caregiver) [3]. Endoscopic bariatric surgery has emerged as an intermediate to medical management and traditional surgery, offering an efficacious weight loss alternative that can be performed in the outpatient setting with minimal procedural complications.

Endoscopic bariatric surgery (EBS) consists of multiple endoscopic procedures that manipulate the gastrointestinal tract to promote weight loss. These procedures evolved from traditional bariatric surgery to achieve gastric restriction/manipulation, malabsorption, neuro-hormonal alterations, or a combination of these, facilitating weight loss. EBS can be used in isolation or as a springboard for weight loss in patients needing to decrease their BMI and obesity-related comorbidities to become acceptable candidates for traditional bariatric surgery. EBS is less invasive with fewer major adverse events compared with traditional

K. Kwiatt (✉) · A. Andonakakis
Department of Anesthesiology, Cooper Medical School of Rowan University, Cooper University Hospital, Camden, NJ, USA
e-mail: Kwiatt-kathleen@cooperhealth.edu; andonakakis-angelo@CooperHealth.edu

A. Chaaya
Division of Gastroenterology, Department of Internal Medicine, Cooper Medical School of Rowan University, Cooper University Hospital, Camden, NJ, USA
e-mail: Chaaya-Adib@cooperhealth.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_1

surgery, the procedures can be performed in the outpatient setting, and EBS is potentially reversible and repeatable. EBS procedures are in various phases of development and FDA approval, and both the procedures and their role in the management of weight loss will continue to evolve.

Endoscopic Bariatric Surgery Procedures

Endoscopic bariatric surgical procedures can be classified as restrictive, malabsorbtive, mixed restrictive and malabsorbtive, or aspiration therapies.

Restrictive Procedures

Restrictive procedures facilitate weight loss by decreasing the free gastric volume which promotes satiety and reduced oral intake. Endoscopic restrictive procedures evolved from traditional surgical procedures such as the laparoscopic band and sleeve gastrectomy to achieve similar gastric restriction without the need for surgical incision or port insertion.

Intragastric Balloons

Space-occupying intragastric balloons (IGBs) are inserted perorally with endoscopic assistance and filled with saline to the desired capacity [4]. They are temporary and must be removed after 6 months, but the procedure can be repeated. Patients lose and average of 7–15% of their total body weight, and 30–47% of their excess body weight [5]. Intragastric balloons are used both as stand-alone procedures or to jump-start weight loss before definitive bariatric surgery [5]. Both insertion and removal are routinely performed as outpatient procedures. The mechanism for weight loss is thought to be mechanical restriction, however delayed gastric emptying, hormonal modulation, neuronal effects, and behavior modification may contribute [6]. Compared with other bariatric procedures, the risk is minimal, and the procedure is technically easy to perform. The most common side effects are self-limiting pain (33.7%) and nausea (29%). Severe side effects are rare, including small bowel obstruction (0.3%), perforation (0.1%), and death (0.08%) [5].

The first intragastric balloon was introduced in the United States in 1985, and there are currently three intragastric balloons approved for FDA use. The Orbera IGB (Apollo Endosurgery, Austin, TX, United States), the ReShape Duo (ReShape Medical, San Clemente, CA, United States), and the Obalon IGB (Obalon Therapeutics, Inc., Carlsbad, CA, United States). These have been FDA approved for patients with body mass index (BMI) between 30–40 kg/m^2 for 6 months duration [5].

Endoscopic Sleeve Gastroplasty

Endoscopic sleeve gastroplasty (ESG) is another restrictive endoscopic procedure where endoscopic sutures are placed over the greater curvature of the stomach to decrease the volume by 70%. Refer to Fig. 1.1 for an example of an endoscopic suturing device used for this purpose. This procedure leads to early satiety, improves insulin sensitivity, slows gastric emptying, and alters hormones that contribute to appetite [7]. It is indicated for patients with a BMI between 30–40 kg/m^2, and results in an average of 12–19% total body weight loss at 6–24 months [5]. Most patients report mild, self-limited adverse events including nausea and vomiting. Rarely, patients reported more significant adverse events including gastrointestinal bleeding and perigastric fluid collection, but did not require surgical management [8]. Compared with IGBs, the ESG offers a long-term weight-loss option and results in greater weight loss, but is technically more challenging to perform. Compared with traditional bariatric surgery, the observed weight loss is less, but ESG can be performed in the outpatient setting, is less invasive, and has fewer side effects. ESG has demonstrated safety and short and mid-term efficacy, with centers reporting good outcomes up to 5 years, however data beyond 5 years is not yet available [9].

Malabsorbtive Procedures

Gastrointestinal Bypass Sleeves

The duodenal-jejunal bypass sleeve, EndoBarrier (GI Dynamics Inc., Lexington,

Fig. 1.1 OverStitch™ by Apollo Endosurgery Inc. Images courtesy of Apollo Endosurgery. OverStitch is an endoscopic suturing devise that allows full-thickness flexible suturing for bariatric procedures including gastric bypass and gastric sleeve pouch revision

MA), is a 60 cm impermeable polymer sleeve that is inserted endoscopically and anchored via a nitinol stent to the duodenum. It acts as a barrier, preventing food from contacting the proximal bowel mucosa, and excluding food from mixing with pancreatic enzymes and biliary secretions. This is designed to mimic the effects of roux-en-y gastric bypass with decreased morbidity and mortality. It is removed 12 months after insertion [10].

Gastrointestinal bypass sleeves are not FDA approved. A double-blinded study of first-generation devices, the ENDO Trial, was terminated early in July 2015 due to 3.5% hepatic abscess formation. The etiology is not well understood, but is thought to result from seeding of infection from the foreign device to the liver, or the obstruction of the ampulla of Vater. Second generation devices have evolved with atraumatic anchoring and retrieval systems, and are undergoing clinical human trials [5]. The other reported adverse events are mild and the device is generally well tolerated. In preliminary studies, patients experience weight loss and improved HbA1c levels at 12 months, but gain an average of 3 kg after device removal [10].

Aspiration Therapies

AspireAssist (Aspire Bariatrics, King of Prussia, PA) is a percutaneous gastrostomy tube that is placed via endoscopic guidance. Two weeks after insertion, the external tube is shorted and a skin port with a valve is attached. 20–30 min after consuming a meal, the patient opens the port and aspirates stomach contents, draining approximately 30% of consumed calories. This procedure is approved for patients with a BMI of 35–55 kg/m^2 and is performed in the outpatient setting. It can be used long-term, and has the advantage of reversibility. Patients who were randomized to AspireAssist lost an average of 12.1% of total body weight and 31.5% of their excess body weight, which was statistically significant compared with patients making lifestyle modifications alone. The most common adverse events included short-term pain with resolution within the first week, nausea, peristomal granulation tissue formation, peristomal irritation, and peristomal infection. Less commonly, patients reported peritonitis, pre-pyloric ulcer formation, and the need for device replacement due to malfunction [11].

Pathophysiology of Obesity

Obesity leads to pathologic changes affecting multiple systems. Figure 1.2 highlights major systems that are impacted by obesity with relevance to the anesthesia provider.

Anesthetic Considerations

As with all surgeries involving the obese population, there are significant concerns involving positioning, airway management, establishing intravenous access, and management of associated comorbidities.

Endoscopic bariatric procedures are minimally invasive and generally well tolerated with few operative complications. Procedural length generally ranges between 2–4 h, depending on the difficulty or ease of accessibility and facility of the specific operator. New operators may take up to 4 h to do a procedure, where someone more experienced may be able to do the same procedure in 1–2 h. Longer procedures and increased patient weight are both associated with increased risk for nerve compression injury and rhabdomyolysis.

These procedures can be done in supine or lateral position, based on operator training and preference. Lateral position has the potential of additional compression on the dependent side, putting the patient at greater risk of neuronal injury due to positioning.

The decision to proceed with monitored anesthesia care (MAC) or general anesthesia is highly individualized. It should be a team-based decision, with consideration of the procedure length, procedure steps including the need for muscle relaxation, patient comorbidities, aspiration risk, and institutional resources including staffing.

Monitored Anesthesia Care (MAC)

While MAC anesthesia is commonly used for endoscopy, it presents a number of challenges for EBS. Assisting ventilation is difficult due to patient position, interference with endoscopy equipment, and obese body habitus (large neck, redundant oropharyngeal tissue). Long procedures can lead to an accumulation of carbon dioxide due to hypoventilation. There is an increased risk of aspiration compared to general anesthesia. Advantages include avoidance of neuromuscular blockade and decreased postoperative respiratory complications. Medications that do not suppress ventilation such as dexmedetomidine and ketamine increase the potential for success.

General Anesthesia

General anesthesia offers the advantage of definitive airway control, reduces incidence of hypoxia/hypercapnia, ensures adequate depth to prevent coughing/bucking, and permits use of neuromuscular blockade to facilitate the procedure.

Airway management is of vital importance, as most, if not all of these individuals have significant reduction of functional residual capacity (FRC), reducing the time allotted to secure the airway before hypoxia occurs. Video laryngoscopy or fiber-optic equipment should be readily available as difficult airway is common. If awake fiber-optic technique is opted, good topical anesthesia of the airway is vital to the success of the technique. Aerosolized 4% lidocaine and 4% viscous lidocaine applied onto a gauze secured firmly on a tongue depressor are used to numb the posterior tongue and oropharynx. Laryngeal nerve blocks, while useful, are more challenging to perform due to poorly identifiable landmarks related to obese body habitus. Once the airway is secured, ventilation is made difficult by the increase in dead space and decrease in chest wall and lung compliance due to obesity. The addition of peak end expiratory pressure (PEEP) improves oxygenation.

Monitoring

At a minimum, the standard American Society of Anesthesia monitors are required, including capnography, continuous pulse oximetry, continuous electrocardiography, and noninvasive blood pressure. Temperature is appropriate for cases expected to last greater than 1 h or with significant temperature changes. Urine output measured by Foley catheter is reasonable for cases expected greater than 2 h. Arterial blood pressure monitor-

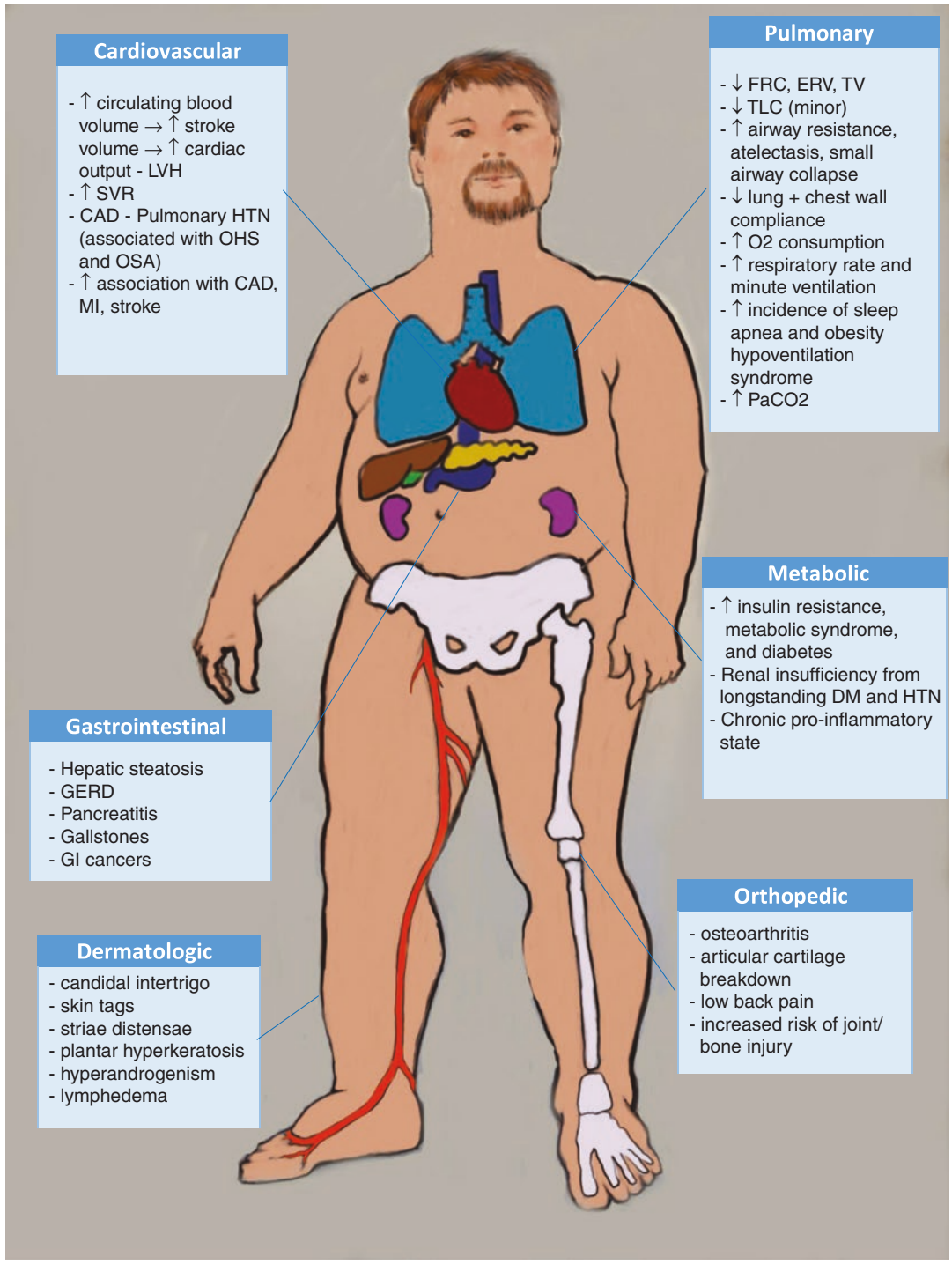


Fig. 1.2 Obesity Pathophysiology. Original artwork by Angelo Andonakakis, DO. Multiple systems are routinely impacted by obesity including: pulmonary [12], cardiovascular [13], metabolic [14, 15], GI [16], dermatologic [17], and orthopedic [18]

ing is not frequently required for endoscopy, but is appropriate for super morbid obese patients in whom a blood pressure cuff does not provide a consistent accurate reading, and for patients with significant cardiovascular morbidity who benefit from beat to beat blood pressure monitoring.

Intra-operative Complications

Bleeding and perforation are common complications during endoscopic procedures. The use of CO_2 insufflation to distend the gastrointestinal tract decreases the risk of embolism compared to air due to its rapid absorption, but its rapid absorption can lead to hypercarbia, even in the setting of controlled mechanical ventilation.

Pharmacology

Obesity impacts the pharmacokinetics and pharmacodynamics of a drug with varying outcomes. In some instances, obesity leads to exaggerated side effects, or narrows the therapeutic window, and must be dosed judiciously to avoid adverse outcomes. For example, obese patients are more susceptible to the respiratory depressive effects of opioids. In other instances, obesity leads to under-dosing because of increased volume of distribution or increased clearance, resulting in decreased efficacy. For example, succinylcholine is dosed by total body weight, rather than adjusted or ideal body weight, and is often inappropriately under-dosed.

Both drug selection and drug dosing require combining knowledge of pharmacokinetics and pharmacodynamics with clinical judgement. Consideration must be given to the patient's medical history, the institution's resources, and the procedural variations including duration of procedure, need for muscle relaxation, and level of stimulation.

Drug dosing is often weight based. Weight is described as total, lean, or ideal body weight. This provides a starting point, from which doses can be adjusted based on clinical factors.

Total body weight (TBW) is the patient's measured weight

Lean body weight (LBW) based on the James Formula* [19]

Men = 1.1 × weight kg – 128 (weight kg/height cm)^2

Women = 1.07 × weight kg – 148 (weight kg/height cm)^2

Ideal body weight (IBW) based on the JD Robinson Formula* [20]

Men = 52 kg + 1.9 kg per inch over 5 feet

Women = 49 kg + 1.7 kg per inch over 5 feet

*Multiple formulas exist for each calculation, though they share relative agreement.

The following charts (?) provide dosing suggestions and clinical considerations for medication administration for obese patients undergoing endoscopic bariatric procedures. This information is not intended to replace clinical judgment, but rather provide a framework to help select and dose medications judiciously.

Opioids

Many endoscopic procedures can be performed with little to no opioid therapy, as the procedures are less stimulating and pain inducing compared to traditional invasive surgical procedures. Opioids are sometimes necessary as an adjunct to anesthesia, to depress respiratory drive or sympathetic tone, and for pain management. Obese patients are exquisitely susceptible to respiratory depression and airway obstruction with opioid medications. Small, incremental doses titrated to effect are preferred over large boluses. Nearly half of the American Society of Anesthesia closed claims reports of adverse respiratory events involved obese patients. Many of these complications could have been mitigated with judicious dosing and improved monitoring via capnography/pulse-oximetry [21]. Table 1.1 summarizes recommendations for commonly used opioids in obese patients.

Nonopioid Analgesics and Anxiolytics

Effective analgesia promotes early ambulation, reduces guarding and hypoventilation, and facilitates discharge. Nonopioid analgesics are effective in reducing pain without causing respiratory depression. Many endoscopic bariatric procedures are performed in the outpatient setting, where early pain control and ambulation are important to allow for patient discharge. Recommendations for commonly used analgesics and anxiolytics are summarized in Table 1.2.

Sedative Hypnotics

Sedative hypnotics facilitate induction and airway management, and can be used for maintenance of anesthesia. A summary of these drugs can be found in Table 1.3.

Table 1.1 Opioids

Drug	Dose	Considerations
Fentanyl	LBW	Highly lipophilic. Titrate incremental bolus doses to effect. Infusion is not popular in bariatric patients due to long, unpredictable context sensitive half-life
Sufentanil	TBW BMI <39.9 kg/m^2 LBW BMI >40 kg/m^2	Highly lipophilic. Dosing recommendations are based on small studies and not validated in patients with a BMI >40, thus close observation and titration to effect are essential [22]
Remifentanil	LBW	Rapid onset (peak 1 min) with elimination via plasma esterases. Short context-sensitive half-life with little accumulation. Long-acting analgesia is needed if post-operative pain is expected
Morphine	IBW	Morphine use in the obese correlates with increased incidence of PACU respiratory events compared to normal weight patients [23]. Titrate small fixed doses to effect

Table 1.2 Nonopioid analgesics and anxiolytics

Drug	Dose	Considerations
Acetaminophen	15 mg/kg IBW	Analgesic without respiratory depression, platelet dysfunction, or GI side effects. Hepatoxicity avoided with IBW dosing, as metabolic enzymes do not increase with obesity [24]
NSAIDs	IBW	Caution if procedure requires anastomosis, as long-term use increases risk of anastomotic ulceration. Short-term use is typically well tolerated without major adverse events
Ketamine	Small doses 0.2 mg/kg are often adequate for analgesia	*N*-Methyl-D-aspartate antagonist and PCP derivate with analgesic properties. It is synergistic with opioids and preserves respiration
Midazolam	1–2 mg	Provides anxiolysis with minimal respiratory depression. Use caution if administering opioids, because respiratory depression can be exaggerated

Table 1.3 Sedative hypnotics

Drug	Dose	Considerations
Propofol	Induction: LBW Maintenance: TBW	Lipophilic with increased volume of distribution, V_d. Rapid onset and rapid redistribution, with a short duration of action. In obese patients, the increased V_d is offset by increased clearance. Maintenance doses, like any anesthetic, should be titrated to clinical effect
Etomidate	LBW	Lipophilic, action is terminated by redistribution. Stable hemodynamic profile
Dexmedetomidine	0.2–0.7 μg/kg/h TBW, titrate infusion to effect	Selective α-2 adrenergic agonist with sedative, analgesic, and sympatholytic properties. Minimal respiratory depression and ideal to facilitate fiberoptic airway management

Inhaled Anesthetics

Inhaled anesthetics are useful for the maintenance of anesthesia, but do not provide any post-operative analgesia (with the exception of nitrous oxide). The dose does not require weight-based adjustment, but accumulation in the adipose tissue can occur with prolonged procedures, and timely emergence requires dose reduction and close coordination with the proceduralist. Considerations for inhaled anesthetics in obese patients are summarized in Table 1.4.

Neuromuscular Blocking Agents

Neuromuscular blocking agents facilitate laryngoscopy, surgical manipulation, and minimize patient movement during critical procedural steps. Recommendations for their use in obese patients are found in Table 1.5.

Reversal Agents

Reversal agents facilitate recovery from anesthesia. Their use is frequently planned to promote emergence from anesthesia and decrease time to recovery. Reversals are also lifesaving drugs in cannot intubate/cannot ventilate scenarios, and in the setting of respiratory distress. Recommendations are summarized in Table 1.6.

Post-operative Management

Hypoventilation is a common post-operative complication. If a patient has diagnosed or sus-

Table 1.4 Inhaled anesthetics

Drug	Clinical consideration
Desflurane	Low blood:gas coefficient makes this an ideal choice for bariatric procedures. It has rapid onset and elimination. Time to emergence, extubation, and orientation after bariatric surgery was shorter with desflurane compared with Propofol or isoflurane. Associated with decreased incidence of hypoxia post-operatively [25]
Sevoflurane	Cost-effective alternative to desflurane with rapid onset and emergence. Faster recovery compared with isoflurane, randomized trials comparing it with desflurane are lacking [26]
Isoflurane	Higher blood: gas coefficient. Small studies show increased time to emergence and extubation with increased oxygen desaturation in the recovery phase, compared with sevoflurane and desflurane. However, isoflurane used judiciously by a skilled anesthetist with judicious titration and good coordination with the surgeon results in acceptable conditions in the obese population [27]
Nitrous oxide	Analgesia and rapid elimination. Use cautiously, as it decreases oxygen availability in patients with increased oxygen consumption. It causes dose dependent bowel distention, and post-operative nausea + vomiting, limiting its use to brief periods of administration in endoscopic bariatric surgery [28]

Table 1.5 Neuromuscular blocking agents

Drug	Dose	Considerations
Succinylcholine	1 mg/kg TBW	Depolarizing muscle relaxant with rapid onset and short duration. Metabolized by pseudocholinesterase. Pseudochlinesterase levels and V_d are both increased in obese patients, often resulting in underdosing. Intubating conditions were improved when TBW was used, compared with LBW or IBW [29]. Post-operative myalgias are rare in obese
Rocuronium	IBW	Highly ionized, weakly lipophilic, aminosteroid nondepolarizing muscle relaxant. Duration of action is prolonged when doses are based on TBW. It is reasonable to use IBW dosing with close monitoring of twitches [30]
Vecuronium	IBW	Aminosteroid nondepolarizing muscle relaxant. Prolonged recovery is observed in the obese due to delayed hepatic clearance and increased time for redistribution [31]
Atracurium	LBW	Benzylisoquinolone muscle relaxant eliminated by Hoffman degradation, independent of hepatic and renal metabolism. Studies report conflicting recommendations regarding LBW vs. TBW dosing, thus it is reasonable to administer LBW doses and titrate to effect with twitch monitoring
Cisatracurium	LBW	Benzylisoquinolone muscle relaxant eliminated by Hoffman degradation [32]

Table 1.6 Reversal agents

Drug	Dose	Considerations
Neostigmine	0.04–0.08 mg/kg up to 5 mg	Recovery is slower in obese patients after vecuronium use but similar to non-obese patients after atracurium. Onset is 1–2 min with peak effect 6–10 min. Reversal is sometimes incomplete with neostigmine in the obese population, necessitating administration of sugammadex or increased duration of respiratory support
Sugammadex	TBW [33] 2 mg/kg: 2/4 twitches 4 mg/kg: 1–2 post-tetanic twitches 16 mg/kg if need urgent reversal after intubating dose of muscle relaxant is administered	Selective aminosteroid non-depolarizing relaxant binding agent that rapidly reverse neuromuscular blockade. Studies have shown TBW dosing to be effective in the obese, but additional studies are necessary to determine if reduced dosing would be efficacious
Naloxone	0.01–0.02 mg every 1–2 min to achieve desired effect	Opioid antagonist. Titrate slowly to avoid precipitating sympathetic overdrive from abrupt opioid reversal
Flumazenil	0.2 mg/dose, repeat at 1 min intervals, max dose 3 mg/h	Benzodiazepine antagonist. Half-life 30–60 min, so patients should be observed for 2 h after administration to ensure re-sedation does not occur

pected obstructive sleep apnea (OSA), it is important to have noninvasive positive pressure ventilation (NIPPV) available in recovery to optimize oxygenation. The efficacy of NIPPV in patients both with and without a diagnosis of OSA is well established. Specifically, patients without an OSA diagnosis who developed hypoxemia after abdominal surgery had decreased incidence of endotracheal intubation, pneumonia, infection, and sepsis when NIPPV was used compared to oxygen alone [34]. Placing the patient in the sitting position with the head up and legs lowered improves ventilation. Most patients can be discharged on the same day.

Conclusion

Endoscopic bariatric surgery offers patients a safe, effective weight-loss option. Consideration of the physiologic and pharmacologic implications of obesity allow the anesthesia provider to facilitate a safe and effective perioperative course.

References

1. Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: a systematic review and meta-analysis. JAMA. 2004;292:1724–37.
2. Sjostrom L, Narbro K, Sjostrom CD, et al. Effects of bariatric surgery on mortality in Swedish obese subjects. N Engl J Med. 2007;357:741–52.
3. Ju T, Rivas L, Arnott SM, Olafson SN, Whitlock A, Sparks AD, Johnstone DA, Lin PP, Vaziri K. Barriers to bariatric surgery: factors influencing progression to bariatric surgery. J Am Coll Surg. 2018;227(4):S15.
4. Imaz I, Martinez-Cervell C, Garcia-Alvarez EE, et al. Safety and effectiveness of the intragastric balloon for obesity: a meta-analysis. Obes Surg. 2008;18:841–6.
5. Glass J, et al. New era: endoscopic treatment options in obesity—a paradigm shift. World J Gastroenterol. 2019;25(32):4567–79. https://doi.org/10.3748/wjg.v25.i32.4567.
6. Konopko-Zubrzycka M, Baniukiewicz A, Wroblewski E, et al. The effect of intragastric balloon on plasma ghrelin, leptin, and adiponectin levels in patients with morbid obesity. J Clin Endocrinol Metab. 2009;94:1644–9.
7. Abu Dayyeh BK, Acosta A, Camilleri M, Mundi MS, Rajan E, Topazian MD, Gostout CJ. Endoscopic sleeve gastroplasty alters gastric physiology and induces loss of body weight in obese individuals. Clin Gastroenterol Hepatol. 2017;15:37.e1–43.e1.
8. Sartoretto A, Sui Z, Hill C, Dunlap M, Rivera AR, Khashab MA, Kalloo AN, Fayad L, Cheskin LJ, Marinos G, Wilson E, Kumbhari V. Endoscopic sleeve gastroplasty (ESG) is a reproducible and effective endoscopic bariatric therapy suitable for widespread clinical adoption: a large, international multicenter study. Obes Surg. 2018;28:1812–21.
9. de Miranda Neto AA, de Moura DTH, Ribeiro IB, Khan A, Signh S, da Ponte Neto AM, Madruga Neto AC, do Monte Junior ES, Tustumi F, Bernardo WM, de Moura EGH. Efficacy and safety of endoscopic sleeve gastroplasty at mid term in the management of overweight and obese patients: a systematic review and meta-analysis. Obes Surg. 2020;30(5):1971–87. https://doi.org/10.1007/s11695-020-04449.9.

10. Patel N, Mohanaruban A, Ashrafian H, et al. EndoBarrier®: a safe and effective novel treatment for obesity and type 2 diabetes? Obes Surg. 2018;28(7):1980–9. https://doi.org/10.1007/s11695-018-3123-1.
11. Thompson CC, Abu Dayyeh BK, Kushner R, Sullivan S, Schorr AB, Amaro A, Apovian CM, Fullum T, Zarrinpar A, Jensen MD, Stein AC, Edmundowicz S, Kahaleh M, Ryou M, Bohning JM, Ginsberg G, Huang C, Tran DD, Glaser JP, Martin JA, Jaffe DL, Farraye FA, Ho SB, Kumar N, Harakal D, Young M, Thomas CE, Shukla AP, Ryan MB, Haas M, Goldsmith H, McCrea J, Aronne LJ. Percutaneous gastrostomy device for the treatment of class II and class III obesity: results of a randomized controlled trial. Am J Gastroenterol. 2017;112:447–57.
12. McClean KM, Kee F, Young IS, et al. Obesity and the lung: 1-epidemiology. Thorax. 2008;63:649–54.
13. Poirier P, Giles T, Bray G, Hong Y, Stern J, Pi-Sunyer F, Eckel R. Obesity and cardiovascular disease: pathophysiology, evaluation, and effect of weight loss. An update of the 1997 American Heart Association scientific statement on obesity and heart disease from the obesity committee of the council on nutrition, physical activity, and metabolism. Circulation. 2006;113:898–918. https://doi.org/10.1161/CIRCULATIONAHA.106.171016.
14. Haffner S, Taegtmeyer H. Epidemic obesity and the metabolic syndrome. Circulation. 2003;108(13):1541–5.
15. Mancuso P. Obesity and lung inflammation. J Appl Physiol. 2010;108(3):722–8. https://doi.org/10.1152/japplphysiol.00781.2009.
16. Nam SY. Obesity-related digestive diseases and their pathophysiology. Gut Liver. 2017;11(3):323–34. https://doi.org/10.5009/gnl15557.
17. García HL. Dermatological complications of obesity. Am J Clin Dermatol. 2002;3(7):497–506. https://doi.org/10.2165/00128071-200203070-00006.
18. American Academy of Orthopedic Surgeons. Position Statement: The Impact of Obesity on Bone and Joint Health. March 2015. https://aaos.org/contentassets/1cd7f41417ec4dd4b5c4c48532183b96/1184-the-impact-of-obesity-on-bone-and-joint-health1.pdf.
19. Absalom AR, Mani V, DeSmet T. Struys. Pharmacokinetic models for propofol-defining and illuminating the devil in the detail. Br J Anaesth. 2009;103:26–37.
20. Robinson JD, Lupkiewicz SM, Palenik L, Lopez LM, Ariet M. Determination of ideal body weight for drug dosage calculations. Am J Hosp Pharm. 1983;40(6):1016–9.
21. Bird M. Acute pain management: a new area of liability for anesthesiologist. ASA Newslett. 2007;71:7–9.
22. Slepchenko G, Simon N, Goubaux B, Levron JC, LeMoing JP, Raucoules-Aime M. Performance of target-controlled sufentanil infusion in obese patients. Anesthesiology. 2003;98:65–73.
23. Patanwala AE, Holmes KL, Erstad BL. Analgesic response to morphine in obese and morbidly obese patients in the emergency department. Emerg Med J. 2014;31(2):139–42.
24. Rumack B. Acetaminophen misconceptions. Hepatology. 2004;40(1):10–5.
25. Golembiewski J. Considerations in selecting an inhaled anesthetic agent: case studies. Am J Health Syst Pharm. 2004;61(20):S10–7.
26. Sollazzi L, Perilli V, Modesti C, Annetta G, Ranieri R, Maria Taccino R, Proietti R. Volatile anesthesia in bariatric surgery. Obes Surg. 2001;11:623–6.
27. Torri G, Casati A, Albertin A, Comotti L, Bignami E, Scarioni M, Paganelli M. Randomized comparison of isoflurane and sevoflurane for laparoscopic gastric banding in morbidly obese patients. J Clin Anesth. 2001;13:565–70.
28. Peyton PJ, Wu CY. Nitrous oxide–related postoperative nausea and vomiting depends on duration of exposure. Anesthesiology. 2014;120(5):1137–45.
29. Lemmens HJ, Brodsky JB. The dose of succinylcholine in morbid obesity. Anesth Analg. 2006;102:438.
30. Leykin Y, Pellis T, Lucca M, Lomangino G, Marzano B, Gullo A. The pharmacodynamic effects of rocuronium when dosed according to real body weight or ideal body weight in morbidly obese patients. Anesth Analg. 2004;99(4):1086–9.
31. Weinstein JA, Matteo RS, Ornstein E, Schwartz AE, Goldstoff M, Thal G. Pharmacodynamics of vecuronium and atracurium in the obese surgical patient. Anesth Analg. 1988;67:1149–53.
32. Leykin Y, Pellis T, Lucca M, Lomangino G, Marzano B, Gullo A. The effects of cisatracurium on morbidly obese women. Anesth Analg. 2004;99(4):1090–4.
33. Monk TG, Rietbergen H, Woo T, Fennema H. Use of sugammadex in patients with obesity: a pooled analysis. Am J Ther. 2017;24(5):e507–16. https://doi.org/10.1097/MJT.0000000000000305.
34. Chung F, Nagappa M, Singh M, Mokhlesi B. CPAP in the perioperative setting: evidence of support. Chest. 2016;149(2):586–97. https://doi.org/10.1378/chest.15-1777.

2 Anesthesia for Peroral Endoscopic Myotomy (POEM)

Basavana G. Goudra and Preet Mohinder Singh

Learning Points

- General anesthesia with endotracheal intubation is regarded as the standard of care for peroral endoscopic myotomy. Rapid sequence induction and intubation is preferred.
- Extended fasting times for solids (up to 3 days) is recommended to minimize the risk of aspiration.
- There is small risk of clinically significant intraoperative complications and these include pneumothorax, capnopericardium, mediastinal emphysema, subcutaneous emphysema, and pneumoperitonium. These complications can also manifest for the first time in the post-procedural period.
- High index of suspicion and aggressive management are necessary to prevent any catastrophic effects resulting from the above complications.

Introduction

Gastric motility disorders could be both hypermotility and hypomotility related. These include gastroparesis, functional dyspepsia, enteric dysmotility, irritable bowel syndrome and constipation. They can occur both in children and adults [1].

Majority of childhood motility disorders are functional and require a standardized diagnostic and if necessary therapeutic approach. Toddlers and preschool age children mainly suffer from functional constipation and the management includes demystification, diet and concomitant laxative treatment. Among the organic motility disorders in childhood, Hirschsprung disease (a hypomotility disorder) is the most relevant one [2].

Hypomotility disorders are caused by smooth muscle dysfunction, such as inherited abnormalities of contractile proteins. Achalasia of the esophagus is one such hypomotility disorder that is commonly misdiagnosed initially as gastroesophageal reflux disease (GERD) [3]. It is a primary esophageal motor disorder of unknown etiology characterized manometrically by insufficient relaxation of the lower esophageal sphincter (LES) and loss of esophageal peristalsis. Achalasia (Latin and Greek origin), literally translates into absence of relaxation, although, the absence of relaxation of the affected esophageal segment is not absolute [4]. High-resolution

B. G. Goudra (✉)
Department of Anesthesiology and Critical Care, Hospital of the University of Pennsylvania, Perleman School of Medicine, Philadelphia, PA, USA
e-mail: goudrab@uphs.upenn.edu

P. M. Singh
Department of Anesthesiology, Washington University in Saint Louis, St. Louis, MO, USA

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_2

esophageal manometry has been very helpful in accurately predicting bolus movement and recognizing clinically relevant esophageal dysfunction.

Historically, surgical treatment was described by Heller and consisted of longitudinal division of the anterior muscle fibers. It is still the standard surgical approach for achalasia [5]. However, the preferred access could be open abdominal and thoracic or as performed over the last two decades, by laparoscopy and thoracoscopy. Even though thoracic and the abdominal open approaches lead to similar symptom improvement, the former is associated with twice more GERD symptoms after surgery. On comparing laparoscopy and thoracoscopy, laparoscopy has shown better symptom improvement rates and lower GERD incidence. Postoperative complications between these surgical options are similar.

Laparoendoscopic single site surgery, robot-assisted myotomy and peroral endoscopic myotomy (POEM) are some of the newer approaches. The purpose of this chapter is to understand the preoperative aspects related to anesthesia, anesthetic management, intraoperative complications and postoperative challenges of POEM.

Paranesthesia Evaluation with Reference to Achalasia

Achalasia is not a single static entity. It is a heterogeneous disease categorized into three distinct types based on manometric patterns: type I (classic) with minimal contractility in the esophageal body, type II with intermittent periods of panesophageal pressurization, and type III (spastic) with premature or spastic distal esophageal contractions [6]. The clinical presentation differs slightly depending on the subtype. Treatment modalities, include pharmacologic, endoscopic, and surgical methods. They depend on the clinical presentation. Progressive dysphagia to solids and liquids is the main presenting symptom. As stated, a significant number of patients complain of heartburn prompting a misdiagnosis of gastroesophageal reflux disease. Consequently, many of these patients are placed on proton pump inhibitor (PPI) therapy. Chest pain, regurgitation, and varying degrees of weight loss or nutritional deficiencies can occur. Failure to effectively treat with medications in the face of ongoing symptoms typically leads to further evaluation and a diagnosis of achalasia. In terms of prevalence of various symptoms, dysphagia ranks number one (82–100%) followed by regurgitation (76–91%), weight loss (35–91%), chest pain (25–64%), nocturnal cough (37%) and aspiration (8%). Although high-resolution manometry is regarded as a confirmatory test, esophagogastroduodenoscopy (EGD) is needed to rule out pseudoachalasia from an obstructing mass [6].

From an anesthetic standpoint, severity of reflux, history of regurgitation and pneumonia and weight loss are important.

Patients with achalasia are known to experience an average weight loss of 28 lbs. on presentation (14–40 lbs). It is observed that some patients lose significantly more weight compared to others. It is also reported that type II achalasia patients are most likely and type III achalasia are least likely to have weight loss compared to type I achalasia. It is possible that type II achalasia might have a different proinflammatory response compared to other subtypes of achalasia that induces a higher catabolic state with alterations in gastrointestinal hormones that mediate energy homeostasis or suppress appetite. If the weight loss is significant enough to cause protein malnutrition, it can have a bearing on the drug binding and the pharmacokinetics. In the event of any post-operative complications or need for emergency surgical intervention, the outcome could be affected.

The respiratory symptoms of achalasia include nocturnal cough, recurrent aspiration, and pneumonia. These patients might have experienced these symptoms in the past or it could be ongoing. In addition to obtaining any relevant history, a review of any investigations including a chest x-ray might be necessary. Depending on the amount and nature of the aspirated material, the frequency of aspiration, and the host's response to the aspirate, the pulmonary manifestations vary. Some of the pulmonary aspiration syndromes are aspiration pneumonitis (acute and

chronic), diffuse aspiration bronchioloitis, isolated bronchospasm and aspiration pneumonia. Chronic interstitial fibrosis is possible in the long term as a result of recurrent aspiration [7].

Diagnostic findings of esophagography are dilatation/tortuosity of the esophagus, retained food in the esophagus and poor emptying of barium, smooth conical narrowing of the esophagogastric junction (bird-beak sign), absence or diminution of gastric air bubbles and abnormal esophageal motility [8]. EGD is always performed before scheduling these patients for POEM. Diagnostic features on upper gastrointestinal endoscopy are dilatation of the esophageal lumen, abnormal retention of food and/or liquid remnants in the esophagus, whitish change and thickening of the esophageal mucosal surface, functional stenosis of the esophagogastric junction (endoscope passes through the stenotic segment although the esophagogastric junction fails to be dilated by insufflation; the procedure may involve winding of tissue around the scope or leafing of tissue on scope rotation) and abnormal contraction waves of the esophagus. Esophageal manometry may provide the following diagnostic features: deglutitive dysrelaxation of the LES, disappearance of primary peristaltic waves, increased esophageal static pressure (higher than the intragastric pressure), increased LES pressure and occurrence of simultaneous contraction waves [8].

A history of medications might include oral calcium channel blockers or nitrates that produce a prompt reduction in LES pressure ranging from 0% to 50%. They can reduce dysphagia symptoms. However, their use has not been shown to halt disease progression [9]. 5′-phosphodiesterase inhibitors such as sildenafil can be beneficial in achalasia and spastic disorders of the esophagus. They lower LES pressure and attenuates distal esophageal contractions by blocking the enzyme that degrades cyclic guanosine monophosphate induced by nitric oxide. Finally, injections of bolutinum toxin into the muscle of the LES is employed as an achalasia treatment on the basis of its ability to block acetylcholine release from nerve endings.

Anesthesia Management

Patients with achalasia require anesthesia for an EGD as part of pre POEM evaluation, for POEM itself and often post procedure EGDs. The anesthesia management depends on the severity of symptoms at presentation and the degree of relief after POEM. The anesthesia aspects include evaluation for suitability for an outpatient endoscopy center and need for endotracheal intubation. Additionally, one should anticipate, prepare and be able to manage both intraoperative and postoperative complications.

Technically, POEM involves making a transverse mucosal incision in the mid-esophagus, entering it, and creating a submucosal tunnel all the way to the gastric cardia by using a forward viewing endoscope with a transparent distal cap and a triangular endoscopic submucosal dissection knife [9]. After the tunnel creation is complete, the endoscope is removed, and its adequacy is assessed by luminal inspection of the esophagogastric junction (EGJ) and proximal stomach (by instilling a dye into the tunnel so that its path is visible intraluminally). The tunnel just created is reentered again and selective myotomy of the circular muscle is accomplished with electrocautery tools for a minimum length of 6 cm up the esophagus and 2 cm distal to the squamocolumnar junction onto the gastric cardia. The endoscope is withdrawn thereby collapsing the tunnel and endoclips are used to seal the entry incision. Some of the anesthesia challenges and their management are discussed below.

Full Stomach and Risk of Aspiration

One of the first issue that needs to be dealt with is the possibility of esophagus filled with undigested food material and likely aspiration. Regurgitation of ingested food into the oral cavity, chest pain, weight loss, and nocturnal cough in the presence of dysphagia suggest food in the esophagus. Based on the endoscopic findings, the following four types are recognized [8]. Review of these endoscopic findings is helpful in prepar-

ing and planning induction, especially in recommending duration of fasting.

- Normal type: there is no obvious retention of ingested food or dilatation of the esophagus.
- Retained type: retention of ingested food or fluid in the esophagus, but no apparent dilatation.
- Dilated type: dilatation of the esophagus is evident, but no retained ingested food is seen in the esophagus.
- Retained-dilated type: the esophagus is dilated with retained ingested food

For POEM, a general anesthesia with endotracheal intubation is preferred. In our own experience, these patients often present with significant esophageal contents [10]. This is in spite of prolonged fasting times much longer than standard ASA recommendations. Suggestions have been made to do a preprocedural suctioning in selected patients who can tolerate it, while still awake [11]. In their series of 28 consecutive procedures, Tanaka et al., who practiced this approach in all of their patients, did not report any aspiration. However, ability to tolerate an awake or sedated esophagoduodenoscopy might depend on the local culture. In an USA center, Yang et al., did not find any merit in performing an awake suctioning and did not experience aspiration related issues [12]. A longer clear fluid regimen is appropriate in patients considered to be at higher risk of aspiration (documented by significant food retention in the esophagus in a preprocedural esophagoduodenoscopy). These authors routinely used rapid sequence induction and intubation irrespective of the length of fasting and had no documented cases of pulmonary aspiration.

On the balance, it is sensible to recommend prolonged fasting times to solids (>24 h) depending on the severity of symptoms, EGD findings and monomeric studies. The question of rapid sequence induction (RSI) is debated [13, 14]. It may not occlude esophagus and prevent aspiration. However, properly applied cricoid pressure can be effective in occluding the esophagus [15]. In addition to RSI, it is beneficial to position these patients slightly head end up (about 30°).

These patients are very rarely prone to sudden airway obstruction that may occur secondary to tracheomalacia with dynamic airway collapse [16]. This is secondary to massive esophageal dilation with resulting posterior tracheal wall compression (from degeneration of the tracheal cartilages). The obstruction could be triggered by strong protective reflexes in sedated patients undergoing EGD prior to general anesthesia with muscle relaxation. In anesthetized and paralyzed patients, reopening of the airway requires positive pressure mask ventilation, which is consistent with dynamic upper or lower airway collapse.

Choice of Muscle Relaxant

If RSI is chosen, the choice of muscle relaxants is between succinylcholine and rocuronium. These procedures last over an hour and as a result, rocuronium is a more sensible choice. One can also avoid muscle facilitations and associated postoperative muscle pain. The gastroenterologists typically do not like any unexpected movements, coughing and bucking. As a result, administration of supplemental relaxant doses at the appearance of third twitch of the train of four is helpful. Availability of sugammedex allows an anesthesia provider to err on the side or caution than inadequate paralysis.

Choice of Endotracheal Tube

Cuffed reinforced endotracheal tubes are preferred to avoid kinking or obstruction of the endotracheal tube during endoscopy. In addition, the endotracheal tube should be positioned in the right lateral angle of the mouth and taped independently from the endoscopy mouthpiece. Endotracheal tubes with subglottic evacuation ports and a suction lumen may also be considered [17]. Efficient submucosal dissection requires

irrigation with significant volumes of fluid which is performed using the water jet channel of the gastroscope. The irrigated fluid can regurgitate toward the pharynx, predisposing to aspiration. A tube designed to provide subglottic secretion drainage is shown to protect against micro-aspiration and ventilator assisted pneumonia [18]. In patients undergoing POEM, prevention of aspiration is important not at the induction of anesthesia but also for the duration of the procedure.

Maintenance of Anesthesia

Both total intravenous anesthesia and inhalational anesthesia are suitable. Some of the complications resulting from surgical intervention include pneumothorax, mediastinal emphysema, subcutaneous emphysema, and pneumoperitonium. Even tension-pneumothorax while undergoing POEM under general anesthesia is reported [19]. As a result, avoidance of nitrous oxide is mandatory. As the procedure does not involve surgical incisions, significant postoperative pain is unlikely and as a result, a short acting opiate such as remifentanil or alfentanil is appropriate. One should be able to visualize abdomen at all times to identify pneumoperitoneum. Pressure control ventilation is better and if the ventilation is ineffective, any contributing factors should be sought.

Monitoring

Pulse oximetry (SpO_2), noninvasive blood pressure, electrocardiography (ECG), capnometry, urine volume, and temperature monitoring are regarded as standard monitors. Additional monitoring is based on merits of each case and anticipated challenges and complications. POEM carries a substantial risk for perforation (5–10%), which may lead to severe pain, subcutaneous emphysema, pneumomediastinum, pneumoperitoneum, or compartment syndrome. CO_2 has been advocated as the insufflation gas of choice for POEM. Monitoring of transcutaneous carbon dioxide is advocated by some [20].

Intraprocedural Complications

Although rare, many serious and life threatening complications are reported in patients undergoing POEM under general anesthesia. Both a high degree of suspicion and a plan of management is essential. Some of the complications are mentioned above and include pneumothorax, capnopericardium, mediastinal emphysema, subcutaneous emphysema, and pneumoperitonium. Other complications are delayed hemorrhage, pleural effusion, minor inflammation or segmental atelectasis of the lungs, and gas under diaphragm or aeroperitoneum [21].

Pneumothorax

The mechanism of pneumothorax in patients undergoing POEM is likely to be gas leakage via surgical tear of mediastinal pleura when dissecting thoracic portion of the esophagus. Use of air as insufflation gas may provide for better distension with better manipulative space, however ill advised. Comparing to carbon dioxide, air is less absorbable in pleural cavity. Moreover, positive pressure ventilation under general anesthesia may facilitate the development of pneumothorax. Use of air is associated with a higher rate of gas-insufflation related complications than the use of carbon dioxide. The esophageal wall is thinly separated from or directly exposed to surrounding structures during the procedure. Asymptomatic pneumothorax is extremely common, reported in 25% of patients undergoing POEM [21]. In this study, Ren et al., used CT scanning for diagnosis and there were no adverse clinical outcomes except the need for chest tube placement in some patients. In contrast, Kurian et al., published their findings which included seven of their patients developing capnoperitonium and another bilateral capnothoraces in a study involving 40 consecutive patients undergoing the POEM procedure. These were associated with hemodynamic instability, but were resolved by Veress needle decompression [22].

As discussed earlier, the occurrence of pneumo/capnomediastinum, pleural effusion, pneumo/capnothorax, and capnopericardium is

related to proximity of the esophagus to the mediastinum and lungs.

Capnopericardium

Capnopericardium can cause cardiac arrest [23]. If the circular and longitudinal muscles are very thick, and fused together, or adherent to the pericardium, the risk of this complication could be higher. Disappearance of pulse and absence of any recordable blood pressure are an indication of capnopericardium. Removal of endoscope and cardiopulmonary resuscitation is essential. A transthoracic echocardiogram will not visualize the heart and a portable roentgenogram will reveal a capnopericardium. Procedure abortment is necessary and any closure of the mucosotomy may exacerbate the capnopericardium. Follow-up x-rays are necessary to track the progress of capnopericardium. Late effects of capnopericardium include atrial fibrillation. Contrast esophagram to assess any extravasation into the mediastinal tunnel or pericardial space [23] is necessary before deciding to discharge home. Overnight intubation and ICU admission are often necessary in these cases.

Subcutaneous Emphysema

Subcutaneous emphysema and pneumomediastinum commonly result from blunt or penetrating trauma, soft-tissue infections, or any condition that creates a gradient between intra-alveolar and perivascular interstitial pressures [24]. This is the result of continuum of fascial planes that connect cervical soft tissues with the mediastinum and retroperitoneum, permitting aberrant CO_2 arising in any one of these areas to spread elsewhere. In patients undergoing POEM, features of subcutaneous emphysema are crepitus, insufflation problems (flow and pressure), hypercarbia (monitor end-tidal CO_2), acidosis, changes in lung compliance, sinus tachycardia, other cardiac arrhythmias, hypertension and intraoperative increase in partial pressure of end-tidal $CO_2 > 50$ mmHg [25]. Ultrasonography-guided needle puncture using a 14- or 16-gauge angiocatheter cannula inserted at the point of the right upper abdominal quadrant at least 5 cm below the rib cage is used for percutaneous abdominal needle decompression.

Pneumomediastinum

During POEM, symptomatic or clinically significant pneumomediastinum is rare and often occurs in association with subcutaneous emphysema. Increasing $EtCO_2$, falling SpO_2 and inability to attain appropriate tidal volume even with aggressive manual ventilation are suggestive of pneumomediastinum. Procedure stoppage and evaluation is necessary. The $EtCO_2$ will continue to raise, to dangerous levels with an inability to wash it out. Malignant hyperthermia is an obvious differential diagnosis, however inability to ventilate and absence of hyperthermia should exclude it. Arterial blood gas is likely to show severe acidosis, inspite of 100% oxygen ventilation. Hemodynamic failure, including arrhythmia or hypotension are possible. Chest radiography will show pneumomediastinum and subcutaneous emphysema, the degree of which depends on the presentation. Abdominal paracentesis at another location is necessary for deaeration. Continuation of positive pressure ventilation with appropriate ventilator settings is necessary [26].

Postoperative Complications

The complications mentioned above such as pneumothorax, pneumoperitonium, mediastinal emphysema, and subcutaneous emphysema, all related to gas insufflation and gas leakage via minor esophageal tear can occur in the post procedural period [19]. Post-operative pleural effusion and focal atelectasis are possible and might require a CT scan for a reliable diagnosis. These are common and non-life threatening complications and patients usually recover with conservative treatment or tube drainage. Atrial fibrillation is reported in the post procedure period and could be related to left atrial compression from esophageal submucosal hematoma [27].

Gastric POEM (G-POEM)

Peroral endoscopic myotomy (POEM) is also employed in the pylorus of the stomach for treatment of gastroparesis (GP) and is known as gas-

tric POEM (G-POEM), also called endoscopic pyloromyotomy, or peroral pyloromyotomy [28]. The principles of G-POEM are similar to POEM and involve submucosal injection, mucosal incision, submucosal tunneling, myotomy, and closure of mucosal entry. Similar to POEM, carbon dioxide (CO_2) gas insufflation is necessary to minimize the risk of tension pneumoperitonium. Late postoperative upper gastrointestinal bleeding (at 2 weeks), swallowing difficulty and hospital-acquired pneumonia are some of the post-operative complications [29].

Follow-Up EGD in Patients Who Underwent POEM

The clinical outcomes of POEM are good. In a mean follow-up of 30 months, mean preoperative and postoperative Eckhart scores decreased from 7.4 to 1.4, respectively, while the mean postoperative lower esophageal sphincter pressure decreased from 32.8 mmHg prior to treatment to 13.7 mmHg. The total success rate was 92.9 ± 6.1% [30]. The Eckardt symptom score is the gold standard self-report assessment tool and is a simple and more commonly used measure to grade symptom severity for achalasia patients in both clinical and research settings. Yet, a careful preprocedural evaluation is necessary and in the presence of significant symptoms, appropriate measures need to be taken to minimize the risk of aspiration.

Conclusions

POEM is a promising endoscopic procedure performed under general anesthesia with unique challenges. It is important that anesthesia providers identify relevant issues and be prepared to address as they arise. While aspiration poses the greatest risk at induction, leakage of carbon dioxide across various facial planes is the major intraprocedural risk. Abortment of the procedure, aggressive treatment including CPR may be necessary.

Funding and Conflicts of Interest None.

References

1. Bielefeldt K, Tuteja A, Nusrat S. Disorders of gastrointestinal hypomotility. F1000Res [Internet]. 2016;5:F1000 Faculty Rev-1897. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4972088/.
2. Gfroerer S, Rolle U. Pediatric intestinal motility disorders. World J Gastroenterol. 2015;21(33):9683–7.
3. Ates F, Vaezi MF. The pathogenesis and management of achalasia: current status and future directions. Gut Liver. 2015;9(4):449–63.
4. Fox M, Hebbard G, Janiak P, Brasseur JG, Ghosh S, Thumshirn M, et al. High-resolution manometry predicts the success of oesophageal bolus transport and identifies clinically important abnormalities not detected by conventional manometry. Neurogastroenterol Motil. 2004;16(5):533–42.
5. Torres-Villalobos G, Martin-del-Campo LA. Surgical treatment for achalasia of the esophagus: laparoscopic heller myotomy. Gastroenterol Res Pract [Internet]. 2013;2013:708327. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3852767/.
6. Patel DA, Lappas BM, Vaezi MF. An overview of achalasia and its subtypes. Gastroenterol Hepatol (N Y). 2017;13(7):411–21.
7. Ali HA, Murali G, Mukhtar B. Respiratory failure due to achalasia cardia. Resp Med CME. 2009;2(1):40–3.
8. Japan Esophageal Society. Descriptive rules for achalasia of the esophagus, June 2012: 4th edition. Esophagus. 2017;14(4):275–89.
9. Pandolfino JE, Kahrilas PJ. Presentation, diagnosis, and management of achalasia. Clin Gastroenterol Hepatol. 2013;11(8):887–97.
10. Goudra B, Singh PM, Gouda G, Sinha AC. Peroral endoscopic myotomy-initial experience with anesthetic management of 24 procedures and systematic review. Anesth Essays Res. 2016;10(2):297–300.
11. Tanaka E, Murata H, Minami H, Sumikawa K. Anesthetic management of peroral endoscopic myotomy for esophageal achalasia: a retrospective case series. J Anesth. 2014;28(3):456–9.
12. Yang D, Pannu D, Zhang Q, White JD, Draganov PV. Evaluation of anesthesia management, feasibility and efficacy of peroral endoscopic myotomy (POEM) for achalasia performed in the endoscopy unit. Endosc Int Open. 2015;3(4):E289–95.
13. Bhatia N, Bhagat H, Sen I. Cricoid pressure: where do we stand? J Anaesthesiol Clin Pharmacol. 2014;30(1):3–6.
14. Brimacombe JR, Berry AM. Cricoid pressure. Can J Anaesth. 1997;44(4):414–25.
15. Hannallah M. Airway protection during anesthesia for esophagogastroduodendoscopy in patients with achalasia. J Anesthe Clinic Res [Internet]. 2013;S3:001. https://www.omicsonline.org/airway-protection-during-anesthesia-for-esophagogastroduodendoscopy-in-patients-with-achalasia-2155-6148.1000307.php?aid=13006.
16. Atkins JH, Mandel JE, Metz DC. Sudden tracheal collapse during EGD and subsequent anesthetic

management with dexmedetomidine-ketamine in a patient with achalasia and tracheomalacia. Case Rep Anesthesiol [Internet]. 2011;2011:281679. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3350073/.
17. Saxena P, Pippenger R, Khashab MA. Preventing aspiration during peroral endoscopic myotomy. J Anesth. 2014;28(6):959.
18. Smulders K, van der Hoeven H, Weers-Pothoff I, Vandenbroucke-Grauls C. A randomized clinical trial of intermittent subglottic secretion drainage in patients receiving mechanical ventilation. Chest. 2002;121(3):858–62.
19. Li T-S, Lee T-Y, Liao KH. Tension pneumothorax during peroral endoscopic myotomy for treatment of esophageal achalasia under general anesthesia. Brazil J Anesthesiol. 2017;67(4):415–7.
20. Lo SK, Fujii-Lau LL, Enestvedt BK, Hwang JH, Konda V, Manfredi MA, et al. The use of carbon dioxide in gastrointestinal endoscopy. Gastrointest Endosc. 2016;83(5):857–65.
21. Ren Z, Zhong Y, Zhou P, Xu M, Cai M, Li L, et al. Perioperative management and treatment for complications during and after peroral endoscopic myotomy (POEM) for esophageal achalasia (EA) (data from 119 cases). Surg Endosc. 2012;26(11):3267–72.
22. Kurian AA, Dunst CM, Sharata A, Bhayani NH, Reavis KM, Swanström LL. Peroral endoscopic esophageal myotomy: defining the learning curve. Gastrointest Endosc. 2013;77(5):719–25.
23. Banks-Venegoni AL, Desilets DJ, Romanelli JR, Earle DB. Tension capnopericardium and cardiac arrest as an unexpected adverse event of peroral endoscopic myotomy (with video). Gastrointest Endosc. 2015;82(6):1137–9.
24. Maunder RJ, Pierson DJ, Hudson LD. Subcutaneous and mediastinal emphysema: pathophysiology, diagnosis, and management. Arch Intern Med. 1984;144(7):1447–53.
25. Bang Y-S, Park C. Anesthetic consideration for peroral endoscopic myotomy. Clin Endosc. 2019;52(6):549–55.
26. Okada T, Izuta S, Mizobuchi S. A case of ventilatory impairment during per-oral endoscopic myotomy under general anesthesia. JA Clin Rep. 2018;4(1):23.
27. Saleem AM, Hennessey H, von Renteln D, Vassiliou MC. Atrial fibrillation as an unexpected complication after peroral endoscopic myotomy (POEM): a case report. Surg Laparosc Endosc Percutan Tech. 2014;24(5):e196–9.
28. Chung H, Khashab MA. Gastric peroral endoscopic myotomy. Clin Endosc. 2018;51(1):28–32.
29. Khashab MA, et al. Gastric per-oral endoscopic myotomy for refractory gastroparesis: results from the first multicenter study on endoscopic pyloromyotomy (with video). Gastrointest Endosc [Internet]. 2017;85(1):123–8. https://www.ncbi.nlm.nih.gov/pubmed/27354102
30. Li H, Peng W, Huang S, Ren Y, Peng Y, Li Q, et al. The 2 years' long-term efficacy and safety of peroral endoscopic myotomy for the treatment of achalasia: a systematic review. J Cardiothorac Surg. 2019;14(1):1.

Anesthesia for Endoscopic Skull Base Surgery

3

Paul B. Audu, Mansour Ousmane Mahamane, Marc D. Fisicaro, and Angelo Andonakakis

Learning Points

- Endoscopic endonasal approach to skull base surgery is a minimally invasive technique used with increasing frequency to resect, debulk or biopsy midline tumors from the *crista galli* to the *foramen magnum.*
- General endotracheal anesthesia is required. An inhaled agent is adequate unless precluded by the use of neurophysiological monitoring. In that case, a propofol based total intravenous anesthetic is administered.
- An arterial line is required for close hemodynamic monitoring. A large bore intravenous access should be placed in the unlikely event of significant hemorrhage.
- Clinically significant venous air embolism rarely occurs with patients in a 30° semi-sitting position.
- Central venous access is only required in select cases.
- Use of neurophysiologic monitoring may require modification of the anesthetic technique.
- A subset of patients with endocrinopathies might have unanticipated challenging airways. Intubation and extubation are critical points of anesthetic care.

Anatomy of the Skull Base

The skull base (Fig. 3.1) is composed of five major bones (frontal, ethmoid, sphenoid, temporal and occipital) that form the resting floor for the brain. It is sub-divided into three sections, each comprising a shallow depression or fossa. The **anterior cranial fossa** houses the frontal lobes, olfactory bulbs and cribriform plate. The *sella turcica*, which protects and supports the pituitary gland (Fig. 3.2), and the squamous and petrous parts of the temporal bone are found in the **middle cranial fossa**. The **posterior cranial fossa** contains the brainstem, cerebellum, clivus, and foramen magnum. The nasal cavity and nasopharynx lie inferior to the anterior cranial vault. With some limitations, all three fossae are accessible by the endoscopic transnasal approach (Table 3.1).

The original version of this chapter was revised: A typo in the second author's name has been corrected. The correction to this chapter is available at https://doi.org/10.1007/978-3-030-64739-1_43

P. B. Audu (✉) · M. D. Fisicaro · A. Andonakakis
Department of Anesthesiology, Cooper Medical School of Rowan University, Cooper University Hospital, Camden, NJ, USA
e-mail: audu-paul@cooperhealth.edu; fisicaro-marc@cooperhealth.edu; andonakakis-angelo@CooperHealth.edu

M. O. Mahamane
Cooper Medical School at Rowan University, Camden, NJ, USA
e-mail: ousman46@rowan.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*, https://doi.org/10.1007/978-3-030-64739-1_3

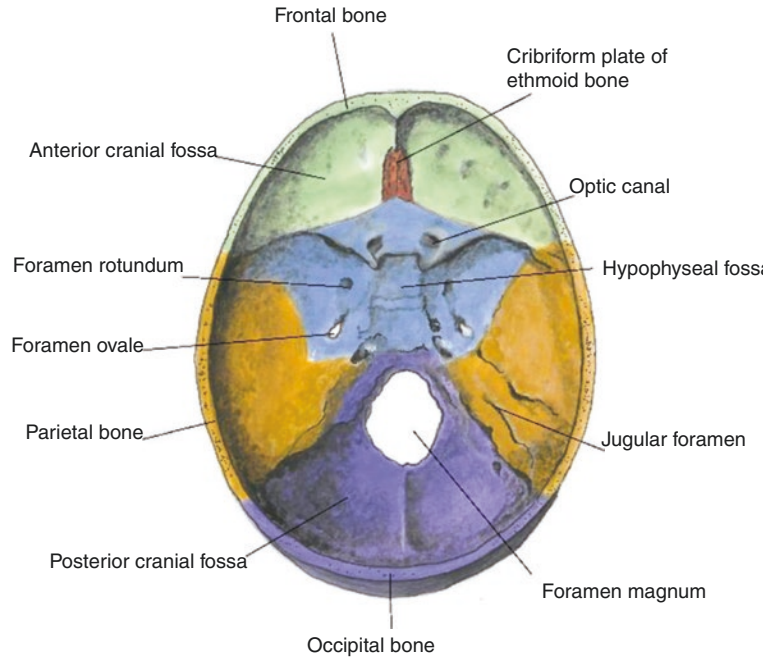


Fig. 3.1 Bones of the skull base

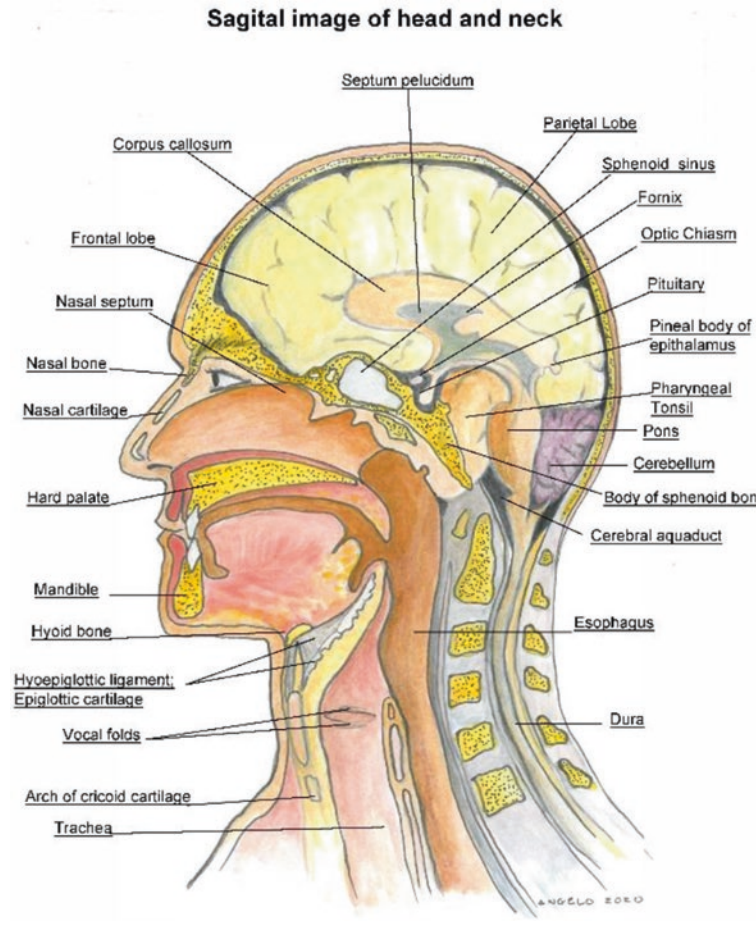


Fig. 3.2 Sagittal view

Table 3.1 Anatomic regions accessible by the endoscopic approach

Anatomic region	Disease
Anterior cranial fossa	
Cribriform	Olfactory groove tumors Esthesioneuroblastomas
Midline anterior cranial fossa	Meningiomas
Middle cranial fossa	
Parasellar region	Pituitary adenomas Meningiomas Craniopharyngiomas Epidermoid cysts Resection of Rathke's Cleft cysts
Pterygopalatine Fossa (Lateral location of the tumor may limit its resectability)	Paragangliomas Schwannomas Sphenoid wing Meningiomas Juvenile nasopharyngeal angiofibromas
Petrous Apex	Cholesterol Granuloma Meningiomas Chordomas, Chondrosarcomas
Posterior cranial fossa	
Spino-medullary junction	Resection of odontoid pannus in patients with rheumatoid arthritis
Clivus	Chordomas Chondrosarcomas

Historical Perspective

The evolution of skull base surgery over the course of the last 100 years illustrates the accomplishments that are possible when technological advances are placed in the hands of skillful pioneering clinicians charged with the task of healing complex human disease. What could only previously be performed through a transfrontal or transtemporal craniotomy (with a mortality as high as 80%) [1] can now be achieved through the endonasal transsphenoidal approach. This technique is associated with fewer complications, a much shorter hospital stay and a mortality of less than 1%. The fascinating history of endoscopic pituitary (and ultimately skull base) surgery is more extensively discussed elsewhere [1]. Briefly, the trajectory of accessing the cranial vault through the nose was used by the Egyptians to drain liquified intracranial contents during the mummification process. Its surgical application was not appreciated for over two millennia when Herman Schloffer, in 1907, performed the first transnasal hypophysectomy. Several technological developments including the introduction of the endoscope by Gerard Guitot in the 1950s and stereotactic navigation guidance systems in the 90s, have contributed to the opening of a new frontier in endoscopic skull base surgery.

Surgical Considerations

Endoscopic transnasal approach offers better visualization compared with the microscopic approach, providing a panoramic view of the operative field. Other advantages include improved cosmesis, reduced morbidity, shorter surgical time and hospital stay as well as greater patient satisfaction. Tumors that are located more laterally or those requiring extensive debulking require alternative approaches.

By far the most common endoscopic skull base procedure performed is transsphenoidal resection of pituitary adenomas. Advances in the field have enabled surgeons to reach beyond the sella and to resect a variety of tumors that reside in all three of the cranial fossae (see Table 3.1).

Many institutions favor the two-specialty team approach [2]. An otorhinolaryngologist performs the intranasal exposure until the dura is reached. The neurosurgeon broaches the dura and resects the tumor. To reduce bleeding during exposure, the nasal passages are first packed with pledgets soaked in cocaine. Then the nasal mucosa is infiltrated with epinephrine containing local anesthetic. Profound hypertension can occur from systemic absorption of epinephrine. Hypertensive patients taking beta-blockers may be more susceptible [3]. A recent prospective study in normotensive patients found that preoperative Lopressor was effective in reducing intraoperative hypertension and reducing blood loss [4]. The anesthesia provider should be aware of other surgical complications (Table 3.2) that might impact anesthetic management.

Anesthetic Considerations

Pre-operative Evaluation and Testing

In addition to a routine history, physical and standard laboratory testing, certain comorbid conditions necessitate special testing and pre-operative preparation (Table 3.3). Patients with acromegaly may develop a cardiomyopathy characterized by cardiomegaly, conduction defects and in later stages, a low cardiac output state [5]. A screening electrocardiogram and 2-D echocardiogram may be indicated. One report describes pre-operative treatment with somatostatin to reverse the cardiac dysfunction prior to successful endonasal surgery, several months later [6].

Table 3.2 Surgical complications

CSF leak	10–20%
Endocrine dysfunction (temporary or permanent) • Diabetes Insipidus • Hypo-pituitarism	20%
Infections • Sinusitis • Meningitis	5% 2%
Vascular complications • Epistaxis • Intracranial bleed • Carotid artery injury	
Rare complications • Cranial nerve palsies • Visual loss • Deep vein thrombosis • Pulmonary embolus • Myocardial infarction	

Airway Management

General endotracheal inhalational anesthesia is the default anesthetic [7]. The airway should be secured using an oral RAE or flexible reinforced endotracheal tube taped to the lower jaw, to provide the surgeons an unobstructed view of the surgical field. Intubation may be challenging in acromegalic patients [8], who may present with facial bone hypertrophy and an enlarged tongue. These characteristics can cause difficult bag-mask ventilation. In addition, overgrowth of pharyngeal soft tissue and cartilaginous hypertrophy of the arytenoids present unique challenges to traditional laryngoscopy, often requiring multiple attempts. It is prudent to have a Video-laryngoscope or fiberoptic scope readily available. Preoperatively, it is reasonable to discuss with patients the risk of a prolonged intubation, possibly overnight, if securing the airway is challenging or surgery is protracted.

There are proponents for using a laryngeal mask airway in patients undergoing endonasal surgery. They argue that coughing at emergence can be avoided and a well seated LMA prevents excessive airway soiling [9–11]. Given the longer duration and the unpredictable nature of the intracranial component of endoscopic skull base surgery, endotracheal intubation is preferable.

Monitoring and Maintenance of Anesthesia

In addition to standard monitors, (EKG, temperature, non-invasive blood pressure, train-of-four),

Table 3.3 Pre-operative considerations

Comorbid condition	Anesthetic issues	Plan
Acromegaly	Increased risk for sleep apnea Potential for difficult ventilation and intubation	Consider a sleep study Have a video-laryngoscope and fiberoptic scope available
Addison's disease	Possible intraoperative hypotension	Consider stress dose steroids
Panhypopituitarism	Patients may already be on hormone replacement therapy (HRT)	Anticipate need for post-op HRT Consider pre-op endocrinology consult
Cushing's Disease	Obesity, hypertension, and insulin resistance are common	Potential for difficult intubation Management of intraoperative hypertension and glucose required
Chordoma	Possible airway impingement	Fiberoptic intubation may be required

an arterial line should be placed to monitor swings in blood pressure that might occur during infiltration with epinephrine and to also guide management of antihypertensive treatment should the surgeon request hypotension. The latter is held by some to reduce bleeding and facilitate exposure, but its effectiveness has been questioned [12]. An arterial line also facilitates blood draws for determining serial hematocrits and serum sodium or glucose concentrations, should the need arise. Two large bore peripheral intravenous catheters should be placed in case significant hemorrhage ensues and a blood transfusion is required. While not routine, a central venous catheter should be considered in tumors investing the carotid artery or infiltrating the cavernous sinus that might carry a significant risk of massive hemorrhage. A urinary catheter should be placed to monitor the urine output and to detect the onset of diabetes insipidus (DI) which complicates as many as one in five transsphenoidal hypophysectomies [1]. DI usually presents post-operatively but may occur during surgery, with patients making as much as a liter of urine an hour for several hours (personal observation). Serum Na concentrations should be measured frequently, and urine volume should be replaced cc for cc with 0.45% NaCl. Hypovolemia and hypotension must be avoided. Excessive polyuria might require a 5–10 units of intramuscular or subcutaneous Vasopressin.

Intracranial hypertension and hydrocephalus rarely complicate large pituitary tumors [13]. Intraoperative management would necessitate avoidance of inhaled anesthetics and the use of total intravenous anesthesia (TIVA) as well as other interventions tailored to reduce intracranial pressure.

Perhaps the most ergonomically comfortable patient position for the surgeon is the semi-sitting "conversation position" [14]. The patient's head is fixed in Mayfield pins, with the neck slightly flexed and rotated in the direction of the surgeon. The torso is flexed 30° at the hip. The head up position reduces surgical bleeding but creates optimal conditions for venous air embolism (VAE). The elevation of the head relative to the heart, generates a pressure gradient that drives air into open venous sinuses. In one mini-series, VAE was detected in 3 of 31 patients undergoing endoscopic transsphenoidal hypophysectomy [15]. For this reason, some centers favor using the supine position [16]. In any case, with current surgical techniques, the incidence of *clinically significant* VAE in the conversational position at 30° of flexion is low [17]. Routine use of the precordial doppler for an uncomplicated pituitary microadenoma may be unnecessary. Monitoring for VAE is typically reserved for patients whose tumors erode or are in close proximity to a venous sinus. Excessive bleeding in this setting might require additional head elevation to reduce bleeding until surgical control is regained. At this point the likelihood of air entrainment is dramatically increased. One should be reminded that selective use of the precordial doppler does not relieve the clinician of her/his obligation for close vigilance. Indeed, a sudden, inexplicable drop in end-tidal carbon dioxide ($ETCO_2$) must be assumed to be secondary to an embolic event until proven otherwise.

Neurophysiological Monitoring

As surgeons become more comfortable with the transnasal endoscopic approach, more extensive and complicated surgeries are being performed. This has heightened the risk of iatrogenic injury to neural structures. Intraoperative neurophysiologic monitoring, which historically was the exclusive adjunct of open skull base procedures, is now used with increasing frequency in selective endoscopic surgeries [18]. Commonly utilized modalities include EEG, somatosensory evoked potentials (SSEPs), Motor evoked potentials (MEPs), Brain Auditory Evoked Potentials and motor cranial nerve electromyography (EMG). Monitoring for endonasal skull base surgery is covered elsewhere in greater detail [18]. The precise modalities employed depend on the brain region at risk and influence the anesthetic choice. Since the amplitude of MEPs and to a lesser degree, SSEPs, can be diminished by volatile anesthetics, TIVA [19] using a combination of propofol and remifentanil with intermittent

boluses of fentanyl is an ideal choice. After an initial intubating dose, neuromuscular blocking drugs (NMBDs) should be avoided since they impair EMG and MEPs. This places an additional burden on the anesthesia team to ensure immobility without the use of paralytics. Fortunately, there is a logical strategy. Movement under anesthesia is a reflex, with an afferent and efferent limb. NMBDs interrupt the efferent limb. An equally effective alternative is to block the afferent limb either with local anesthetic infiltration of the surgical field (provided by the surgeon) or with narcotics that block synaptic transmission at the substantia gelatinosa of the spinal cord. Both these interventions diminish the afferent nociceptive volley that would otherwise generate the reflex movement. Remifentanil is particularly helpful since it provides a potent opiate effect without the risk of delaying emergence. Processed EEG monitoring indicates the degree of anesthetic induced cortical suppression and guides the dosing of sedative-hypnotics. Unfortunately, mutual interference between the navigation system and processed EEG is not uncommon [20]. Valuable data regarding anesthetic depth can be garnished from the neurophysiologist. An increase in EEG frequency and shift in the spectral edge may signal that the patient is light. Increase in spontaneous muscle EMG during SSEP stimulation suggests the need for additional narcotics [18]. Frequent communication with the neurophysiologist can generate additional qualitative data to help guide anesthetic management.

Intraoperative visual evoked potentials for monitoring the visual pathway are labile and their predictive value in preventing visual field loss has been questioned [21].

Tranexamic Acid

Tranexamic acid is an antifibrinolytic that inhibits the activation of plasminogen into plasmin. It has been shown to reduce blood loss and improve visibility in endoscopic sinus surgery [22, 23]. It may confer the same advantage in endoscopic skull base surgery. In adults, the benefit of some reduction in blood loss must be weighed against the rare but real risk of serious thrombotic complications. It may have greater value in pediatric skull base surgery since fibrinolysis may play a greater role in pediatric surgical bleeding [24]. Tranexamic acid is also effective topically [25].

Spinal Drains

A fenestrated subarachnoid catheter (or spinal drain) may be placed before surgery, at the discretion of the surgeon. It can be used to enhance resection of pituitary tumors with extra-sellar extension. Once resection of the intra-sellar portion is complete, 10–20 mL of air is injected slowly (1–2 cm^3/s) into the subarachnoid space. Since the patient is in a 30° head up position, the air tracks cephalad into the suprasellar space and pushes down any residual suprasellar tumor bringing it into the surgeon's endoscopic view, thereby enabling resection of additional tumor [26, 27]. It is important to inject air slowly since injecting too much air too quickly can result in transient intracranial hypertension manifesting as systemic hypertension and severe bradycardia (personal observation). Intrathecal fluorescein (ITF) may also be injected through the catheter into the CSF to assess the integrity of the dural closure. Leakage of dye into the surgical field helps to identify any dural defects that can easily be repaired using fat graft harvested from the anterior abdominal wall. This may obviate a return trip to the operating room. ITF has excellent sensitivity and specificity for the detection of CSF leaks intraoperatively [28]. This benefit is thought to justify the high incidence of postoperative symptomatic postdural puncture headache that frequently requires treatment with an autologous blood patch [29]. Side effects of ITF can be severe and include seizures, flash pulmonary edema and lower extremity weakness [30]. They are dose dependent and are mitigated by using a low dose injectate and pretreatment with diphenhydramine (Benadryl) and steroids [31]. If concerns remain regarding the integrity of the repair, the catheter may be left for a few days, to allow the repair to heal. Catheters are usually removed at the bedside. Use of excessive force may result in fracture of a catheter and retention of a fragment [32].

Intraoperative Valsalva Maneuver

In a patient without a spinal drain, the surgeon may request an intraoperative Valsalva maneuver to an airway pressure of 30–40 cm H_2O, and held for a few seconds. In lieu of ITF, it helps identify a CSF leak. The increase in venous and capillary pressures also reveals sites of inadequate hemostasis that may cause postoperative bleeding, should the patient retch, sneeze or cough. The "toothpaste extrusion technique" describes the use of the Valsalva to squeeze any extra-sellar pituitary tumor into endoscopic view and allows a more complete visualization and resection [33]. It is an alternative to the pneumocisternogram in patients who do not have a spinal drain. It is important to ensure that the patient is deep prior to initiating the Valsalva, to avoid excessive bucking and uncontrolled coughing in a patient in pins.

Pediatric Transnasal Skull Base Surgery

If adult endoscopic endonasal skull base surgery is in its infancy, the pediatric version is a neonate. These procedures were first reported in the literature in the late 1990s and are currently being performed in specialized pediatric institutions worldwide. The smaller size of the nasal passage, the anatomical differences between adults and children and concerns that this approach might interfere with craniofacial development, have all contributed to slowing the adoption of transnasal skull base surgery in the pediatric age group [34]. Surgeon experience has now grown to a point where surgery has been performed in patients 6 years and younger [35]. For a detailed discussion of this burgeoning subspecialty, the interested reader is referred to core pediatric anesthesia textbooks and a recent publication along with its accompanying editorial [34].

Emergence and Extubation

Intraoperative anesthetics should be tailored to ensure a smooth emergence with minimal coughing and as quick a return to a normal sensorium as is possible. Long acting narcotics should be avoided in the last hour of surgery. Any throat packings inserted at the start of surgery, are removed. An orogastric tube placed at the start or conclusion of the anesthetic, is suctioned to empty the stomach prior to extubation, to reduce the risk of emesis and aspiration. Anti-emetics should be administered. An infusion of either Nicardipine or Clevidipine may be required to prevent rebound hypertension that may occur at emergence. Coughing may be minimized by running an infusion of remifentanil at one tenth the normal maintenance dose of 0.1–0.3 μg/kg/min, until extubation [36].

If intubation was difficult, re-intubating the patient with post-extubation respiratory distress may be impossible. The nares are usually packed with nasal packing, making the patient an obligate mouth breather. Despite meticulous hemostasis, some blood invariably dribbles into the posterior pharynx, obscuring visibility. The airway may be edematous. All these factors can make for a near-impossible ventilation and intubation. Equipment and personnel to establish an emergent surgical airway should be at hand. An LMA may be placed as a bridge to intubation.

Conclusion

Minimally invasive procedures are becoming more common as the discovered benefits and indications increase. As with any novel procedures, endoscopic skull base surgery presents distinct challenges and requires the anesthesiologist to adapt techniques to facilitate a safe and successful outcome. Although basic anesthetic fundamentals do not change, anesthesiologists must be able to adapt to rapidly changing technologies.

References

1. Senior BA, et al. Minimally invasive pituitary surgery. Laryngoscope. 2008;118(10):1842–55.
2. Snyderman C, Carrau R, Kassam A. Who is the skull base surgeon of the future? Skull Base. 2007;17(6):353–5.

3. Schechtman SA, et al. Preoperative beta-blockade and hypertension in the first hour of functional endoscopic sinus surgery. Laryngoscope. 2017;127(7):1496–505.
4. Sadek AA, Mostafa M, Abdel-Monem T. Metoprolol significantly improves visual clarity and hemodynamic parameters during functional endoscopic sinus surgery. Biomed Hub. 2019;4(2):1–8.
5. Sharma MD, et al. Cardiovascular disease in acromegaly. Methodist debakey. Cardiovasc J. 2017;13(2):64–7.
6. Hashimoto K, et al. A patient with acromegalic heart disease—a case report. Masui. 1997;46(7):951–4.
7. Gollapudy S, et al. Total intravenous versus inhaled anesthesia in transsphenoidal tumor surgery. Am J Otolaryngol. 2018;39(5):567–9.
8. Friedel ME, et al. Airway management and perioperative concerns in acromegaly patients undergoing endoscopic transsphenoidal surgery for pituitary tumors. Otolaryngol Head Neck Surg. 2013;149(6):840–4.
9. Amorocho MC, Fat I. Anesthetic techniques in endoscopic sinus and skull base surgery. Otolaryngol Clin N Am. 2016;49(3):531–47.
10. Kaplan A, Crosby GJ, Bhattacharyya N. Airway protection and the laryngeal mask airway in sinus and nasal surgery. Laryngoscope. 2004;114(4):652–5.
11. Webster AC, et al. Anesthesia for intranasal surgery: a comparison between tracheal intubation and the flexible reinforced laryngeal mask airway. Anesth Analg. 1999;88(2):421–5.
12. Boonmak S, Boonmak P, Laopaiboon M. Deliberate hypotension with propofol under anaesthesia for functional endoscopic sinus surgery (FESS). Cochrane Database Syst Rev. 2013;6:CD006623.
13. Joshi SM, Chopra IS, Powell M. Hydrocephalus caused by giant pituitary tumors: case series and guidelines for management. Br J Neurosurg. 2009;23(1):30–2.
14. Ekanayake J, et al. The conversational position in endoscopic pituitary surgery. Br J Neurosurg. 2018;32(1):44–6.
15. Newfield P, et al. Air embolism during transsphenoidal pituitary operations. Neurosurgery. 1978;2(1):39–42.
16. Fraioli B, et al. The supine position for transsphenoidal surgery. Neurosurg Rev. 1994;17(4):275–6.
17. Ture H, et al. Effect of the degree of head elevation on the incidence and severity of venous air embolism in cranial neurosurgical procedures with patients in the semisitting position. J Neurosurg. 2018;128(5):1560–9.
18. Singh H, et al. Intraoperative neurophysiological monitoring for endoscopic endonasal approaches to the skull base: a technical guide. Scientifica (Cairo). 2016;2016:1751245.
19. Gunter A, Ruskin KJ. Intraoperative neurophysiologic monitoring: utility and anesthetic implications. Curr Opin Anaesthesiol. 2016;29(5):539–43.
20. Hemmerling TM, Desrosiers M. Interference of electromagnetic operating systems in otorhinolaryngology surgery with bispectral index monitoring. Anesth Analg. 2003;96(6):1698–9, table of contents.
21. Chung SB, et al. Intraoperative visual evoked potential has no association with postoperative visual outcomes in transsphenoidal surgery. Acta Neurochir. 2012;154(8):1505–10.
22. Alimian M, Mohseni M. The effect of intravenous tranexamic acid on blood loss and surgical field quality during endoscopic sinus surgery: a placebo-controlled clinical trial. J Clin Anesth. 2011;23(8):611–5.
23. Ping WD, et al. Role of tranexamic acid in nasal surgery: a systemic review and meta-analysis of randomized control trial. Medicine (Baltimore). 2019;98(16):e15202.
24. Goobie SM, Haas T. Bleeding management for pediatric craniotomies and craniofacial surgery. Paediatr Anaesth. 2014;24(7):678–89.
25. Kang H, Hwang SH. Does topical application of tranexamic acid reduce intraoperative bleeding in sinus surgery during general anesthesia? Braz J Otorhinolaryngol. 2020;86(1):111–8.
26. Spaziante R, de Divitiis E. Forced subarachnoid air in transsphenoidal excision of pituitary tumors (pumping technique). J Neurosurg. 1989;71(6):864–7.
27. Helbig GM, Cohen-Gadol AA. The use of intraoperative suprasellar pneumocisternogram for resection of large pituitary tumors. Clin Neurol Neurosurg. 2010;112(10):897–9.
28. Raza SM, et al. Sensitivity and specificity of intrathecal fluorescein and white light excitation for detecting intraoperative cerebrospinal fluid leak in endoscopic skull base surgery: a prospective study. J Neurosurg. 2016;124(3):621–6.
29. Zhang M, et al. Lumbar puncture for the injection of intrathecal fluorescein: should it be avoided in a subset of patients undergoing endoscopic endonasal resection of sellar and parasellar lesions? J Neurol Surg B Skull Base. 2018;79(6):554–8.
30. Juneja S, Sandhu K. Fluoroscein toxicity—rare but dangerous. Indian J Anaesth. 2019;63(8):674–5.
31. Placantonakis DG, et al. Safety of low-dose intrathecal fluorescein in endoscopic cranial base surgery. Neurosurgery. 2007;61(3 Suppl):161–5; discussion 165–6
32. Guppy KH, Silverthorn JW, Akins PT. Subarachnoid hemorrhage due to retained lumbar drain. J Neurosurg Spine. 2011;15(6):641–4.
33. Baker C, Karsy M, Couldwell WT. Resection of pituitary tumor with lateral extension to the temporal fossa: the toothpaste extrusion technique. Cureus. 2019;11(10):e5953.
34. Azab WA. Pediatric endoscopic endonasal skull base surgery-where do we stand and where are we going? Childs Nerv Syst. 2019;35(11):2079–80.
35. Nation J, et al. Pediatric endoscopic endonasal approaches for skull base lesions in the very young: is it safe and effective? J Neurol Surg B Skull Base. 2018;79(6):574–9.
36. Aouad MT, et al. The effect of low-dose remifentanil on responses to the endotracheal tube during emergence from general anesthesia. Anesth Analg. 2009;108(4):1157–60.

4 Anesthesia for Jugular Foramen Tumors: Paragangliomas and Schwannomas

Alexander Huynh and Adam Thaler

Learning Points

- General anesthesia with endotracheal intubation is the standard of care for surgical management jugular foramen tumors.
- Preoperative evaluation should place special focus on possible endocrine and anatomical involvement, as well as a neurological assessment, as these may have a significant bearing on perioperative and postoperative complications.
- Most common perioperative complications include cranial nerve deficits, significant blood loss, venous air embolism, increased intracranial pressure. The most common complication, cranial nerve deficits increases the risk of postoperative pulonary aspiration or obstruction.
- Management of jugular foramen tumors presenting with signs and symptoms of increased ICP should follow basic principles of other intracranial tumors.

Introduction

The jugular foramen is located at the floor of the posterior fossa, posterolateral to the carotid canal and located between the occipital bone and inferiormedial portions of the temporal bone. This area can be further subdivided in the posterolateral pars venosa and anteromedial pars nervosa which are separated by a fibrous or bony septum. These compartments house important anatomical areas, the pars venosa containing the jugular bulb, posterior meningeal branch of ascending pharyngeal artery, vagus and spinal accessory nerves, while the pars nervosa contains the glossopharyngeal nerve (IX) and the inferior petrosal sinus [1].

Jugular foramen tumors (JFT) are rare skull base lesions. The most common pathologies involving the jugular foramen are paragangliomas also known as glomus jugulare tumors arising from the neural crest cells, schwannomas of the lower cranial nerves, meningiomas, chordomas, chondrosarcomas, and metastatic tumors [2]. Jugular foramen tumors can be classified by the location whether they are intrinsic or extrinsic to the foramen.

The most common tumors, paragangliomas, arise from the paraganglia cells (derived from neural crest) at the following sites including: (1) adventitia of the jugular bulb beneath the middle ear, (2) bony walls of tympanic canals related to tympanic branches of CN IX and X and (3) in the

A. Huynh (✉) · A. Thaler (✉)
Department of Anesthesiology, Thomas Jefferson University Hospital, Philadelphia, PA, USA
e-mail: Alexander.Huynh@jefferson.edu; Adam.Thaler@jefferson.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_4

Table 4.1 Fisch classifications of glomus tumors [5]

A	Tumors limited to middle ear space
B	Tumors limited to middle ear or mastoid w/o involvement of the infralabyrinthine space of the temporal bone
C	Tumors involving infralabytinthine and apical spaces of temporal bone, with extension into the apex
D1	Tumors with intracranial extension <2 cm in diameter
D2	Tumors with intracranial extension >2 cm in diameter

Trombetta M, Silverman M, Colonias A, Lee V, Mohanty A, Parda D. Paraganglioma: A Potentially Challenging Tumor. Cancer Network. 2008;22(3). https://www.cancernetwork.com/oncology-journal/paraganglioma-potentially-challenging-tumor

bone of the promontory, close to the mucosal lining of the middle ear [3]. Paragangliomas can arise sporadically or as part of an inherited syndrome that have predisposition to the development of pheochromocytomas (e.g., Multiple endocrine neoplasia type 2 (MEN2), von Hippel-Lindau disease (vHL) and neurofibromatosis 1 (NF1). The estimated incidence is 1 in 300,000. Paragangliomas outside the head and neck are termed pheochromocytomas due to their secretion of vasoactive peptides [4]. Paragangliomas can be classified based on their location by Fisch (see Table 4.1).

Jugular foramen schwannomas constitute the second most common jugular foramen tumors, making up for approximately 10–30% of all tumors observed in the jugular foramen [6]. JF schwannomas have been categorized into four groups based on their anatomical location: type A, located in the cerebellopontine angle with minimal enlargement; type B, tumors primarily in the JF with intracranial extension; type C, extracranial tumors with extension into the JF (and with clinical signs of XII involvement); and type D, dumbbell-shaped tumors with both intra and extracranial components [7].

The mainstay of treatment of JFT is surgical resection with numerous surgical approaches developed due to the important neurovascular anatomy that must be accounted for. Surgical resection may be total or subtotal, which may be required to preserve important cranial or vascular structure [8]. An infratemporal fossa approach described by Fisch et al. is considered the gold standard for resection of large tumors. With this approach the facial nerve is transpositioned and direct exposure of the jugular bulb is achieved. Facial nerve monitoring is typically performed in these cases [9]. Studies have reported complete elimination of H&N paragangliomas in 83% of patients with preservation of facial nerve function in 65–80% [9]. The size of the lesion directly correlates to the complication rates of surgical removal [10].

Other anatomical considerations play a vital role in the management of these lesions. If there are concerns of carotid artery involvement, a balloon occlusion test is typically performed. In cases where there is involvement, a high-flow shunt is typically reconstructed using a saphenous or radial artery graft. Tumors that are highly vascularized may require preoperative embolization to reduce the bleeding risk and reduce surgical time [11]. Reconstruction of the skull base is typically done with abdominal fat, local and distant muscle flaps and free muscle flaps vascularized with microsurgical anastomosis [12]. Other modalities including radiotherapy and chemotherapy have also been employed in the treatment of JFTs (see Fig. 4.1).

Paranesthesia Evaluation with JFTs

A thorough history and physical is imperative in patients with JFT. Patients typically would have undergone numerous imaging studies such as CT scans, MR imaging and MR angiography for analysis of bone structures, vascularization and relationship to neighboring structures prior. The clinical symptoms that patient's experience vary significantly depending on the tumors growth pattern.

The most common symptoms in patients with JFTs are pulsatile tinnitus and conductive hearing loss in approximately 60–80% of cases [14, 15]. Other symptoms include vertigo, ataxia, headaches, blurry vision, dysphagia and hoarseness. Cranial nerve involvement is common and typically involves the lower cranial nerves. Tumors

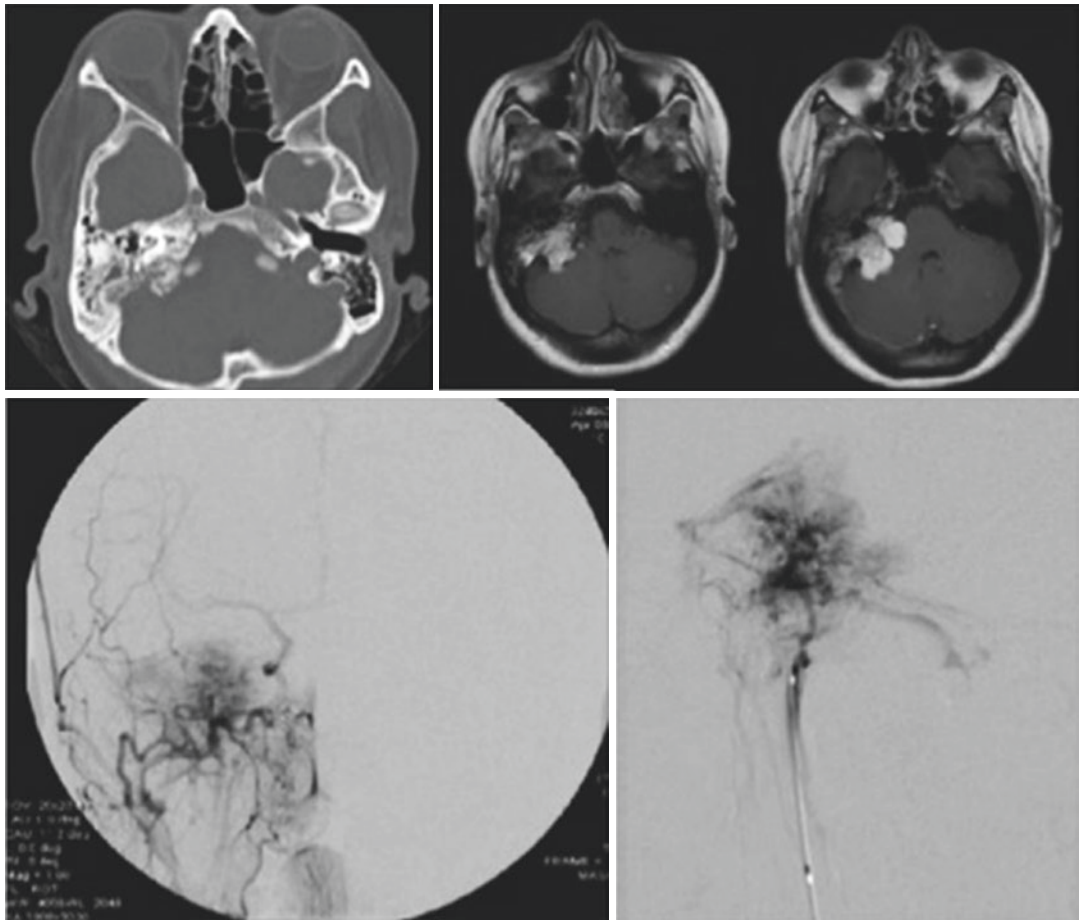


Fig. 4.1 On the superior left, glomus tumor of the right jugular foramen seen on the tomography (moth-eaten pattern); on the superior right, magnetic nuclear resonance with "salt and pepper" appearance; below, angiography evidencing irrigation of a glomus tumor of the head predominantly by the right ascending pharyngeal artery. (Reproduced with permission from Nery, et al.) [13] Breno Nery, Rodrigo Antônio Fernandes Costa, Eduardo Quaggio, Ricardo Lopes Araújo, Bernardo Alves Barbosa, Diogo Fabricio Coelho de Melo, Carolina Salviano de Abreu Nery, Fred Bernardes Filho and George Peter Stevens (March 27th 2019). Jugular Foramen Paragangliomas, Brain and Spinal Tumors—Primary and Secondary, Lee Roy Morgan and Feyzi Birol Sarica, IntechOpen, DOI: 10.5772/intechopen.84232. Available from: https://www.intechopen.com/books/brain-and-spinal-tumors-primary-and-secondary/jugular-foramen-paragangliomas

invading into the ear canal may cause a cranial nerve VII palsy. Skull base invasion may cause CN XII nerve palsy and/or other cranial nerves including IX, X and XI. They may also grow intracranially into the middle or posterior fossa involving CN V and VI [15]. Schwannomas commonly arise from purely motor neurons and it is hypothesized that jugular foramen schwannomas arise from ganglia of the IX and Xth cranial nerves; however, often the exact origin is not discovered until the surgery is performed. In a large surgical series by Baker et al., the majority of schwannomas originated from CN IX and X; however, in 112 of 199 patients, the origin was undetermined [6].

Syndromes have been described based on the variable combination of neurovascular involvements. Vernet syndrome involves CN IX, X and XI and is characterized by loss of taste in the posterior third of the tongue, paralysis of the vocal cords and palate and weakness of the trapezius and SCM muscles. In Avellis syndrome, patients

Table 4.2 Common syndromes and CN involvement

	CN involvement	Clinical symptoms
Vernot syndrome	IX, X, XI	Dysphagia, Dysarthria, Dysphonia, weakness of SCM and trapezius
Collet-sicard syndrome	IX, X, XI, XII	Deviation of tongue, palate palsy, weakness of SCM and trapezius (may also have signs of dysphagia, dysarthria and dysphonia)
Villaret syndrome	IX, X, XI, XII	Signs of both Vernot and Collet-Sicard plus Horners syndrome
Avellis syndrome	X	Paralysis of soft palate and vocal cord typically on one side and loss of pain/temp on other side

experience paralysis of the vocal cords and palate associated with contralateral loss of pain and temperature due to spinothalamic involvement. Collet-Sicard syndrome involves CN IX, X, XI and XII resulting in loss of taste in the posterior third of the tongue, paralysis of the tongue and hemianesthesia of the palate, pharynx and larynx. Villaret manifests similarly but with the addition of Horner's syndrome [16] (see Table 4.2). Numerous other syndromes have been documented and shows the importance in anatomical variation that can present in a wide range of clinical symptoms.

In addition to a routine physical exam, careful emphasis should be placed by the anesthesia provider while performing a neurological exam and assessment of the cranial nerves. Involvement of CN X and IX may impair normal swallowing reflexes and lead to increased risk of aspiration and pulmonary complications. Signs of intracranial hypertension should be evaluated preoperatively as the tumor may have intradural extension. This should be carried out with the neuro exam and supported imaging. Medications should also be reviewed with special emphasis on anticonvulsants, diuretics and corticosteroids as this may change intraoperative management.

Patients with paragangliomas that present with unexplained hypertension may have associated endocrine abnormalities which should be evaluated prior to surgery. Approximately 1–4% of paragangliomas secrete catecholamine which may be subclinical. Suggestive symptoms of endocrine abnormalities include severe hypertension, chest pain, palpitations, diaphoresis or a history of MI and cardiovascular disorder which can be attributed to the catecholamine excess. The signs include excessive wheezing, flushing, diarrhea, valvular murmurs that may suggest excess serotonin causing a carcinoid like syndrome [17].

If the patient is suspected of having catecholamine or serotonin secreting involvement, urinary and plasma catecholamine and 5-HIAA levels should be drawn. Patients who test positive for excess catecholamine may benefit with alpha-beta blockade prior to surgery similarly to a pheochromocytoma [18]. Additionally, 10% of patients with jugular paragangliomas have been found to have additional paraganglioma tumors and should undergo appropriate studies including a thorough family history to rule out genetic causes [19]. With paragangliomas, there is a 10–25% chance of a second craniocervical paragangliomas, usually of carotid body origin [20]. On the other hand, Schwannomas are usually not associated with extra-endocrine function.

Anesthesia Management

The management of patients with JFT varies greatly depending on the extent of the tumor spread and involved structures. Tumors of the jugular foramen may be confined to the jugular foramen or extend into the nasopharynx, middle fossa or posterior fossa through the intracranial opening of the jugular foramen. They can also extend into the neck through the extracranial opening. Numerous approaches have been developed and based on a case by case basis, they can be broken down into anterior lateral approaches which rely on dissection of structures in front and lateral to jugular foramen and posterolateral which gain access to the jugular foramen via structures behind and lateral to it [1].

Surgery begins with proper patient positioning which plays vital importance in anesthetic management. Patients are typically positioned supine

with the head rotated 45° away from the lesion. Excessive flexion at this point can impede jugular venous drainage and increase ICP. It is important to ensure the opposite jugular vein is free of compression. Patients are then positioned with the head of the bed 90°–180° away from the anesthesia workstation. It is critical during this step that all lines and access points are established to be appropriately functioning. General anesthesia with an endotracheal cuffed tube is the standard with these procedures. It is important to ensure positioning and securement of the endotracheal tube is optimal and functioning during this time, as access may be difficult once the patient is turned away and draped.

An important consideration during this process is head positioning during Mayfield clamping which may be necessary. This step has been shown to produce severe painful stimulation resulting in dramatic hemodynamic effects. Healthy patients with minimal comorbidities may be able to tolerate these changes; however, in patients with significant neurological deficits or cardiac comorbidities, the harm could be substantial. Methods such as deepening the level of anesthetic and infiltration of the area with local anesthetics are useful [21]. Other well recognized complications that have been associated with clamps include venous air embolisms due to air entry in the wounds from the pins, epidural hematomas due to the skull clamp and impression fractures [22].

Once positioning is complete, surgery typically begins with a C shaped incision near the temporal region. Neck dissection begins with identification of the major vessels of the neck namely, common carotid artery, internal carotid artery and the internal jugular. Thereafter, a radical mastoidectomy is performed to dissect the temporal bone. Craniectomy and opening of the jugular foramen follows, thereby exposing the posterior fossa dura and a portion of the jugular foramen. Once exposure is complete extra and intradural tumor resection begins. During this time, the lower cranial nerves are typically identified allowing total tumor removal and preservation, however parts of the lower cranial nerve may show infiltration and need resection. Intraoperative monitoring of these caudal cranial nerve may be necessary during this portion of the surgery. After tumor removal, reconstruction begins using a graft to prevent CSF leak complications [1, 14].

Another consideration for anesthetic management of patients with JFT is the possible involvement of carotid artery or jugular vein and highly vascularized nature of these lesions, especially with paragangliomas [22]. It is important to recognize this involvement as to ensure brain protective strategies such as maintenance of appropriate cerebral blood flow and perfusion pressures. Patients may have had an angiography which can reveal adequate collateral circulation. This is of particular importance if carotid clamping is performed and resection begins of the artery. Involvement of the internal jugular vein can contribute to major complications including severe hemorrhage and possible air embolus.

Monitoring

Standard monitoring includes noninvasive blood pressure, pulse oximetry (SpO_2), electrocardiography (ECG), $ETCO_2$, temperature and peripheral neve stimulator. In addition, urine output via a foley catheter should be employed especially in the setting of increased intracranial pressure. Invasive arterial blood pressure is also recommended to accurately assess the patient's hemodynamic status while being able to sample for blood gases or electrolyte abnormalities. Given the highly vascular nature of paragangliomas, arterial blood monitoring plays an important role in monitoring blood loss and to maintain blood pressure should the surgeon encounter significant blood loss. Depending on patient's comorbidities, central venous monitoring may be considered; however, intravascular involvement of the tumor is weighed in choosing the insertion site [15].

Another important aspect in monitoring of these cases involves neurological monitoring to prevent postoperative deficits. Neurophysiological monitoring is patient specific and may include SSEP, EEG, brainstem auditory evoked potential, electromyography monitoring of cra-

nial nerves such as VII and XII [23]. Electrophysiogical monitoring may also be used to assess the depth of anesthesia. Other monitors such as bispectral index and spatial entropy have also been used for neuromonitoring with some success [24].

Choice of Muscle Relaxant

The choice of muscle relaxant does not play a crucial in the decision making of anaesthetizing patients with jugular foramen tumors. If the patient exhibits symptoms of difficulty with swallowing or poses a serious threat for aspiration, an RSI technique should be employed, commonly with succinylcholine or rocuronium. Patients with brain tumors with or without motor response do not appear to have exaggerated hyperkalemic response to succinylcholine [25]. In cases with concern for elevated intracranial pressure, there is some controversy with the use of succinylcholine. In a literature review of RSI using succinylcholine in patients with head injuries, no definitive evidence was found that succiynlcholine caused a rise in ICP in patients with brain tumors. However, the conclusions were based on weak or smaller studies. However, pretreatment with defasciculating doses of neuromuscular blocking agents reduced rises in ICP in patients undergoing elective surgery for removal of brain tumors [26]. Currently there are no absolute contraindications for the use of succinylcholine in these patients.

In cases where neurophysiogical monitoring is employed, muscle paralysis should not be maintained due to interference. If this is the case, one should be vigilant that the patient has achieved deep anesthesia for the case to proceed.

Maintenance of Anesthesia

Both total intravenous and inhalational techniques are suitable for maintenance of anesthesia. The main goals of the anesthesia are provision of a smooth and hemodynamically stable induction and operative course, as well a rapid emergence to adequately assess the level of consciousness and perform a neurological assessment [27]. One of the key considerations must be the ability to not cause further neurological injury by preserving appropriate cerebral perfusion pressure. Choosing suitable anesthetic agents requires an understanding of their effects on cerebral blood (flow), cerebral metabolic rate (CMR) and intracranial pressure (ICP). In cases where there is concern for increase ICP, anesthetic that reduce CBF and ICP are desirable.

One of the major concerns with the use of volatile agents and nitrous oxide is the risk of dose dependent increase in CBF and risk of increase ICP which has caused some to avoid its use. The intravenous agents with the exception of ketamine decrease CBF, CMR and ICP; however, may have undesirable effects such as delayed emergence. Inhalational agents have been investigated for their effects on ICP, in at least five trials. With the exception of one study, all showed minimal increases in ICP, while one showed ICP increasing by 5–13 mmHg in 6 out 14 patients. It should be noted in this study no adverse outcomes were noted and treatment protocol was not changed [28, 29]. Given the numerous modalities that may be used to decrease intracranial pressure such as patient position, spinal drainage, hyperventilation, hyperosmotic and diuretic agents, one may argue for the use of inhalational agents. Todd et al. compared three anesthetic techniques (propofol/fentanyl, isoflurance/nitrous oxide and fentanyl/nitrous oxide) in 121 patients with intracranial masses, and was unable to demonstrate any significant perioperative outcome differences between the groups [27].

For the maintenance of anesthesia with the concomitant use of neuromonitoring in place, jugular foramen tumors are monitored using EMGs, somatosensory evoked potentials, brainstem evoked, motor evoked or visual evoked potentials with special emphasis on the lower cranial nerves. Halogenated inhalational agents dose dependently increase latency and reduce amplitude by inhibiting the pyramidal activation of spinal motor neurons at the level of the anterior grey column or by depressing synaptic trans-

mission in the cerebral cortex. Additionally, they abolish MEPs more easily than SSEPs, and at MAC values more than 0.5, MEPs are unreliable [30].

In contrast, intravenous agents have much less effect on evoked potentials. Opioids cause only slight depression of the amplitude and latency of cortical potentials. Continuous infusions of opioids allow for stable serum concentrations permitting accurate and consistent measurements of potentials [30]. Due to these reasons, synthetic opioids are currently the mainstay in anesthesia with neurophysiological monitoring [31]. Additionally, propofol has shown to provide more reliable SSEP and MEP readings than inhalational agents, while allowing for stable serum concentrations and titration of the anesthesia depth without compromising intraoperative nerve monitoring [32]. The current gold standard for intraoperative nerve monitoring is TIVA without neuromuscular block, using propofol as a hypnotic and remifentanil, sufentanil or ketamine as analgesics [31, 33].

Intraprocedural Complications

Given the slow growing nature of these tumors, symptoms typically do not arise until the tumors have grown to a certain size. It is uncommon for patients with this diagnosis to undergo these procedures in an urgent or emergent settings. Rather, patients typically undergo these surgeries in an elective fashion where they have had a thorough workup beforehand. Nonetheless, there are numerous important anesthetic complications that must be considered in the management of these patients which include endocrine derangements, aspiration risk, airway obstruction, impaired gastric emptying, increased intracranial pressure, venous air embolisms and catastrophic blood loss.

Endocrine Derangements

The endocrine capabilities of jugular paragangliomas are not surprising, as these tumors are of neural crest origin outside the adrenal medulla and are capable of secreting various neurohormones [34]. It was first reported by Duke et al. that glomus tumors can independently secrete large amounts of norepinephrine and can present similarly to a pheochromocytoma [35].

Jugular paragangliomas are also capable of producing 5-hydroxytraptamine (serotonin), kallikrein and histamine producing features similar to carcinoid syndrome. Although they often originate in the small intestine, carcinoid tumors can arise from any organ system. Such a syndrome produced by paragangliomas was first reported by Farrior et al. in 1980 [36, 37]. This can manifest preoperatively with history of wheezing, tricuspid regurgitation, significant diarrhea resulting in electrolyte derangements, cutaneous flushing, headaches and unexplained hypertension. To an anesthesia provider, this can manifest intraoperatively with profound hypotension and shock due to the histamine and bradykinin release from surgical manipulation [38]. Bronchospasm is another concern of histamine and bradykinin release.

Management of these endocrine abnormalities requires vigilance on the part of the anesthesia provider as noted above. The perioperative management of catecholamine secreting tumors is similar to that of pheochromocytomas. The most common treatment relies on both alpha and beta adrenergic blockade prior to surgery. One suggested regiment recommends pheoxybenzamine 1–2 weeks prior to surgery, starting with an initial dose of 10 mg twice a day and gradually increasing it to final doses of 40–100 mg/day. Beta blockade is typically not necessary but if needed it is imperative that it is never started prior to alpha blockade due to possible hypertensive crisis [17]. Other therapeutic interventions have been implemented which include magnesium and nicardipine. Nicardipine can be used orally in the preoperative period (60–120 mg/day) and intravenously perioperatively at a rate of 2.5–7.5 μg/kg/min [39]. Magnesium sulfate (in combination with fentanyl) at doses of 40–60 mg/kg intravenous followed by a continuous infusion of 1–2 g/h has been used [40].

For patient exhibiting carcinoid syndrome features, significant electrolyte derangement and dehydration should be corrected preoperatively.

One of the main concerns is significant bronchospasm due to histamine, serotonin and bradykinin release. Inhaled B-agonists and inhaled anticholinergics are the mainstay of treatment due to the underlying pathophysiology. Recall that these substances work through direct stimulation of the afferent cholinergic pathway resulting in release of acetylcholine causing bronchoconstriction [41]. Octreotide, a long acting somatostatin analog acts by inhibiting serotonin release and decreases storage and release of mediators. A recommended regimen consists of 100 μg subcutaneously, two to three times daily, started 2 weeks before surgery in symptomatic patients [42]. At induction, the main goal is to block the chemical mediators and IV octreotide at dose of 100 μg has been recommended at induction [43]. For hypertensive crisis caused by the carcinoid syndrome, Ketanserin, a selective antagonist at 5-HT2-recepors, a1 and H1 receptors has been suggested at 5 mg/h by intravenous route.

Aspiration Risk and Airway Obstruction

Due to lower cranial involvement (IX, X, XI, XII) which may manifest preoperatively or postoperatively, these patients may be at high risk for aspiration events. This is due to loss of airway tone, swallowing reflex and sensation. The risk with vagus nerve involvement has been found to occur in nearly 25% of patients [40]. The risk of airway obstruction after cranial nerve injury can be further worsened due to the risk of unilateral vocal cord paralysis, in the setting of significant airway edema or upper airway distortion. Signs of stridor or wheezing should be examined frequently during management of these airways [17].

Increased Intracranial Pressure

For the majority of these tumors, concern for acute management of elevated intracranial pressure is rare due to their slow growing nature and propensity to grow extradural. However, it is still prudent to understand that there is always such risk and management should follow the same general principles followed during the management of intracranial mass lesions. The relationship between cerebral perfusion pressure, intracranial pressure and mean arterial pressure should provide the basis for management of these lesions.

Blood Loss

There is a significant risk of intraoperative blood loss, in particular with the highly vascular paragangliomas. The major source of bleeding in these procedures involves sigmoid sinus, inferior petrosal sinus and the tumor itself [44]. Blood loss is of particular concern when there is intracranial extension requiring opening of the sigmoid sinus due to intrajugular extension [17]. Preoperative embolization of these lesions have been employed to mitigate the risk or catastrophic bleeding. It has been shown to diminish blood loss and shorten operative times [45]. Nonetheless, some surgeons may not want to have preoperative embolization performed due to risk of vascular injury, stroke and death [46]. Given such risks, it is clear that in addition to standard monitors, an arterial catheter, foley catheter and possible central venous pressure monitoring may be prudent. Additionally, large bore intravenous access are recommended as rapid transfusion may be necessary.

Postoperative Complications

In addition to the above complications, significant postoperative complications also warrant special consideration. The most common are lower cranial nerve injuries, facial nerve injuriy, CSF leakage, hearing loss, aspiration pneumonia and vocal cord paralysis [6, 8].

Cranial Nerve Injury

The important and common postoperative complications in jugular foramen tumors relate to cranial nerve deficits. In a study by Lustig and

Jackler, preoperative lower cranial nerve deficits were present in nearly 20% of paraganglioma patients and 50% schwannoma patients. They found that new postoperative cranial nerve deficits occurred in approximately 35% of the paraganglioma patients and 15% in the schwannoma patients [47]. In a retrospective review, the prevalence of post-operative cranial nerve injury was greatest with CN IX, followed by XI, X and XII. This study also found a significant relationship between new lower CN deficits, tumor size and tumor classifications suggesting that early tumor diagnosis may be of crucial importance [8].

CSF Leak

Another important postoperative complication to consider are CSF leaks. The reported incidence is 3.9–4.5% [48]. The importance of this is the possible need for reoperation or development of meningitis. Surgical techniques that address this issue use fat and muscle grafts such as abdominal, temporalis or sternocleidomastoid. Patients may also recover with the use of postoperative lumbar drainage and shunts.

Impaired Gastric Emptying

Slow gastrointestinal mobility is observed in these patients due to elevated cholecystokinin (CCK) levels that places them at risk for postoperative ileus. In a study by Jackson et al., it was observed that patients undergoing glomus tumors excision had increased risk of GI complications including postoperative ileus, pancreatitis, and cholecystitis [49]. They hypothesized that was due to a increase in CCK levels resulting in failure of gastric emptying, diminished pancreatic activity and gallbladder contraction [50]. These patients should be seen as having a significant increased aspiration risk especially in the setting of cranial nerve injury. Postoperative care should be tailored to reduce these complications.

Conclusions

Jugular foramen tumors are rare pathologies; however, they present difficult challenges to the anesthesia provides given their unique characteristics. Understanding the anatomical involvement of nearby structures plays an important role in managing these patients. A thorough preoperative evaluation is required given the possible endocrine involvement, risk for intraoperative bleeding, which may have devastating consequences. In addition, a carefully performed neurological evaluation is vital as cranial nerve injury may lead both intraoperative and postoperative complications.

Acknowledgements We thank Dr. Basavana Goudra and Dr. Michael Green for their work on coordinating the formation of this book. We also thank Dr. Breno Nery for allowing us to utilize his research in the formation of this chapter.

Funding and Conflicts of Interest None.

References

1. Griessenauer C, McGrew B, Matusz P, De Caro R, Loukas M, Shane Tubbs R. Surgical approaches to the jugular foramen; a comprehensive review. J Neurol Surg Skull Base. 2016;77(4):260–4.
2. Laigle-Donadey F, Taillibert S, Martin-Duverneuil N, Hildebrand J, Delattre JY. Skull-base metastases. J Neuro-Oncol. 2005;75(1):63–9.
3. Vogl T, Bisdas D. Differential diagnosis of jugular foramen lesions. Skull Base. 2009;19(1):3–16.
4. Gjuric M, Gleeson M. Consensus statement and guidelines on the management of paragangliomas of the head and neck. Skull Base. 2009;19(1):109–16.
5. Trombetta M, Silverman M, Colonias A, Lee V, Mohanty A, Parda D. Paraganglioma: a potentially challenging tumor. Oncology (Williston Park). 2008;22(3):341–3. https://www.cancernetwork.com/oncology-journal/paraganglioma-potentially-challenging-tumor.
6. Baker B. The jugular foramen schwannomas: review of the large surgical series. J Korean Neurosurg Soc. 2008;44(5):285–94.
7. Samii M, Babu RP, Tatagiba M, Sepehrnia A. Surgical treatment of jugular foramen schwannomas. J Neurosurg. 1995;85(6):924–32.
8. Fayad JN, Keles B, Brackmann DE. Jugular foramen tumors: clinical characteristics and treatment outcomes. Otol Neurotol. 2010;31(2):299–305.

9. Briner HR, Linder TE, Pauw B, Fisch U. Long-term results of surgery for temporal bone paragangliomas. Laryngoscope. 1999;109:577–83.
10. Bowdino B, Farrell P, Moore G, et al. Long term surgical results of glomus temporale tumors. Neurosurgery. 2004;14:19–26.
11. Murphy TP, Brackmann DE. Effects of preoperative embolization on glomuss jugulare tumors. Laryngoscope. 1989;99:1244–7.
12. Anand V. Reconstruction in craniel base surgery. In: Al-Mefty O, editor. L surgery of the cranial base. Boston: Kluer Academic Publishers; 1989. p. 297–314.
13. Nery B, Costa RAF, Quaggio E, Araújo RL, Barbosa BA, de Melo DFC, de Abreu Nery CS, Filho FB, Stevens GP. Jugular foramen paragangliomas, brain and spinal tumors—primary and secondary, Lee Roy Morgan and Feyzi Birol Sarica. IntechOpen. 2019; https://doi.org/10.5772/intechopen.84232. https://www.intechopen.com/books/brain-and-spinal-tumors-primary-and-secondary/jugular-foramen-paragangliomas.
14. Ramina R, Maniglia JJ, Fernandes YB, Paschoal JR, Pfeilsticker LN, Coelho NM. Tumors of the Jugular Foramenn: diagnosis and management. Neurosurgery. 2005;57(1):59–68.
15. Ghani G, Sung YF, Per-Lee J. Glomus jugulare tumors-origin, pathology and anesthetic considerations. Anesth Analg. 1983;62:686–91.
16. Svien HJ, Baker HL, Rivers MH. Jugular foramen syndrome and allied syndromes. Neurology. 1963;13:797–809.
17. Jensen NF. Glomus tumors of the head and neck. Anesthetic considerations. Anesth Analg. 1994;78(1):112–9.
18. Jensen NF. Glomus tumors of the head and neck: anesthesic considerations. Anesth Analg. 1994;78:112–9.
19. Lawson W. Glomus bodies and tumors. NY State J Med. 1980;80(10):1567–75.
20. Jackson CG, Cueva RA, Thedinger BA, Glasscock MEI. Conservation surgery for glomus jugular tumors: the value of early diagnosis. Laryngoscope. 1990;100:896–901.
21. Arshad A, Shamim M, Wagas M, Enam H, Enam S. How effective is the local anesthetic infiltation of pin sites prior to application of head clamps: a prospective observational cohort study of hemodynamic response in patients undergoing elective craniotomy. Surg Neurol Int. 2013;4:93.
22. Baerts W, Lange J, Booij L, Broere G. Complications of the mayfield skull clamp. Anesthesiology. 1984;61:460.
23. Press RL, Luders H. Acoustic (loudspeaker) facial electomyographic monitoring: evoked electomyographic activity during acoustic neuroma resection. Neurosurgery. 1986;19:392–400.
24. Dahaba AA. Different conditions that could result in the bispectral index indicating an incorect hypnotic state. Anesth Analg. 2005;101:765–73.
25. Abou-Madi M, Trop D, Kardash K. Succinylcholine, motor deficits, intracranial hypertension and potassium levels in brain tumor patients. Intracranial Pressure. 1993;VIII:668–71.
26. Clancy M, Galford S, Walls R, Murphy M. In patients with head injuries who undergo rapid sequence intubation using succinylcholine, does pretreatment with a competitive neuromuscular blocking agent improve outcome? A literature review. J Emerg Med. 2001;18(5):373–5.
27. Todd MM, Warner DS Sokoll MD, et al. A prospective, comparative trial of three anesthetics for elective supratentorial craniotomy: propofol/fentanyl, isoflurane/nitrous oxide, and fentayl/nitrous oxide. Anesthesiology. 1993;78:1005–20.
28. Weglinski MR, Perkins WJ. Inhalation versus total inhalational anesthesia for neurosurgery: theory guides, outcome decides. J Neurosurg Anesthesiol. 1994;6(4):290–3.
29. Grosslight K, Foster R, Colohan AR, et al. Isoflurane for neuroanesthesia: risk factors for increases in intracranial pressure. Anesthesiology. 1985;63:533–56.
30. Nunes RR, Bersot CDA, Garritano JG. Intraoperative neurophysiological monitoring in neuroanesthesia. Curr Opin Anesthesiol. 2018;31(5):532–8.
31. Laratta JL, Ha A, Shillingford JN, et al. Neuromonitoring in spinal deformity surgey; a multimodality approach. Global Spine J. 2018;8:68–77.
32. Sloan TB, Kohta A, Sloan TB, Toleikis JR. Anesthesia management and intraoperative electrophysiological monitoring. Monitoring the nervous system for anesthesiologist and other healthcare professionals 2nd ed. Cham: Springer; 2017. p. 317–41.
33. Kang H, Gwak HS, Shin SH, et al. Monitoring rate and predictability of intraoperative monitoring in patients in patients with intradural extramudullary and epidura metastatic spinal tumos. Spinal Cord. 2017;55:906–10.
34. Kremer R, Michel RP, Posner B, et al. Catecholamine secreting paraganglioma of glomus jugulare region. Am J Med Sci. 1989;297:46–8.
35. Duke WW, Boshell BR, Soteres P, Carr JH. A norepinephrine-secreting glomus jugulae tumor presenting as a pheochomocytoma. Ann Intern Med. 1964;60:1040–7.
36. Jackson CG, Haris PH, Glasscoc MEI, et al. Diagnosis and management of paragangliomas of the skull base. Am J Surg. 1990;159:389–93.
37. Farrior KB, Hyams VJ, Benje RHm FArior JB. Carcinoid apudoma arising in a glomus jugular tumor: a review of endocrine activity in glomus tumors. Laryngoscope. 1980;90:110–9.
38. Stoelting RK, Diedorf SF, McCammon RL. Anesthesia and co-existing disease. 2nd ed. New York: Churchill Livingstone; 1988. p. 402–4.
39. Proye C, Thevenin D, Cecat P, et al. Exclusive use of calcium channel blockers in the peroperative and intraoperative control of pheochromocytomas: hemo-

dynamic and free catecholamine assays in ten consecutive patients. Surgery. 1989;106:1149–54.
40. James MFM. Use of magnesium sulphate in the anesthetic management of pheochromocytoma: a review of 17 anesthetics. Br J Anaesth. 1989;62:616–23.
41. Cascale TB. Mast cell mediators and their effect on airway smooth muscle. In: Townley A, editor. Inflmmatory cells and mediators in bronchial asthma. Boston: CC Press; 1991. p. 58–69.
42. Hughes EW, Hodkinson BP. Carcinoid syndrome: the combined use of ketanserin and octreotide in the managment of an acute cisis during anaesthesia. Anesth Inten Care. 1989;17:367–70.
43. Roy R, Carter R, Wright P. Somatostatin, anaesthesia and the carcinoid syndrome. Anaesthesia. 1987;42:627–32.
44. Jackson CG, Cueva RA, Thedinger BA, Glasscock MEI. Cranial nerve preservation in lesions of the jugular fossa. Otolaryngol Head Neck Surg. 1991;105:687–93.
45. Murphy TP, Brackmann DE. Effects of preoperative embolization on glomus jugulare tumors. Laryngoscope. 1980;99:1244–7.
46. Valvanis A. Preoperative embolization of the head and neck: indications, patient selection, goals, percaustions. AJNR. 1986;7:927–36.
47. Lustig LR, Jackler RK. The variable relationship between the lower craniel nerves and jugular foramen tumors: impoication for neural preservation. Am J Otolaryngol. 1996;17:6558–68.
48. Jackson CG, McGrew BM, Forest JA, et al. Lateral skull base surgery for glomus tumors: long term control. Otol Neurotol. 2001;22:377–82.
49. Jackson CG, Gulya AF, Knox GW, et al. A paraneoplastic syndrome associated with glomus tumors of the skull base? Early observation. Otolaryngol Head Neck Surg. 1989;100:583–7.
50. Rossenwasser H, Parsier SC. Tumors of the middle ear and mastoid. Otolaryngology. 1981;1:1576–99.

Anesthesia for Robot-Assisted Gynecological Surgery

5

Eilish M. Galvin and Henri J. D. de Graaff

Learning Points

- Patient positioning is a priority for the entire team after the induction of anesthesia.
- In general patients can tolerate the physiological challenges posed by the positioning, length of surgery and capnoperitoneum; however those with severe cardiopulmonary comorbidities require careful evaluation.
- The following intraoperative emergencies should be quickly recognized and treated: massive hemorrhage, venous gas embolism, pneumothorax, venous thromboembolism and robotic malfunction.

Introduction

Robot-assisted gynecological surgery is increasingly commonplace, with well recognized benefits during the intraoperative and post operative phase such as reduced blood loss, less post operative pain, faster recovery time and shorter hospital stays. It's development has been a natural progression from minimally invasive laparoscopic procedures and learning curves are steadily flattening, as it is being used in an expanding variety of surgical specialties [1–3]. All this has happened in a relatively short time period of just 15 years since the US FDA first approved robot-assisted surgical system for gynecological conditions in 2005 and the first robot-assisted radical hysterectomy took place in 2006 [4].

While the quality of the surgical equipment and techniques improve, challenges for anesthesia providers are increasing, as patients previously deemed unsuitable are now scheduled for robot-assisted surgery. As a consequence, careful patient management and optimization from preoperative assessment through to the post operative recovery phase is essential.

Preoperative Assessment

There are considerable challenges during these robot-assisted procedures, including steep Trendelenburg positioning, lithotomy position and prolonged surgical time. All of these should be carefuly considered during preoperative assessment.

Frequently, the referring gynecologist would have applied a first patient selection process, based on comorbidities, before considering patients eligible to undergo a robot-assisted oper-

E. M. Galvin (✉)
Department of Anesthesiology Erasmus Medical Centre, University of Rotterdam the Netherlands, Rotterdam, The Netherlands
e-mail: e.galvin@erasmusmc.nl

H. J. D. de Graaff
Department of Anesthesiology, Maasstad Ziekenhuis, Rotterdam, The Netherlands
e-mail: graaffh@maasstadziekenhuis.nl

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_5

ation. However, in the preoperative anesthetic assessment, a systematic approach to evaluation and possible optimization of the patient's condition is essential.

Cardiovascular

The cardiac status of each patient must be evaluated according to the current ACC/AHA guideline onperioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. Robot-assisted gynecological operations are currently regarded as 'elevated risk' operations (risk of >1% of major adverse cardiac event) [5].

Elderly patients frequently use anticoagulants. In deciding whether to partially withhold anticoagulants, the risk of surgical bleeding should be weighed against the risk of thrombosis.

The lithotomy position and subsequent pneumoperitoneum increase (left and right) ventricular preload [6], which means an increase in ventricular wall stress and therefore myocardial oxygen consumption is increased with potential for ischemia in patients with coronary artery disease.

Alternatively, in patients suffering from heart failure, these changes can lead to acute decompensation. To date, there is no absolute contraindication or lower limit for the left ventricle ejection fraction for determining a patient's eligibility for laparoscopic surgery. On the contrary, a study has concluded that laparoscopy is safe in patients with congestive heart failure undergoing surgery [7].

The management for patients with cardiovascular implantable electronic devices (CIED: ICD/Pacemaker) is similar to non robot-assisted operations. Bipolar electrocautery is advised to decrease the likelihood of interaction with the CIED [5].

Consultation of a cardiologist is recommended when (pharmacological) optimization is necessary (e.g. atrial fibrillation with rapid ventricle response) or further diagnostic evaluation is needed according to the ACC/AHA guideline.

Pulmonary

Pulmonary disease remains a particular challenge to robot-assisted surgery. During laparoscopy, there is an increase in (peak) airway pressure and a decrease in pulmonary compliance secondary to the increased intra-abdominal pressure (IAP) and Trendelenburg positioning exacerbates it [8]. Within minutes after deflation of the pneumoperitoneum, the pressures return to baseline levels. Furthermore, the increased IAP shifts the diaphragm cephalad, resulting in closure of smaller airways leading to atelectasis with a decrease in functional residual capacity. Combined with preferential ventilation of nondependent parts of the lung, this results in ventilation-perfusion (V/Q) mismatch with a higher degree of intrapulmonary shunting [9]. Even in patients without lung disease, the arterial oxygen tension is significantly decreased during pneumoperitoneum [10].

In patients with severe lung disease, these alterations may be poorly tolerated. Therefore, thorough preoperative pulmonary function testing and optimization is important. For patients with obstructive lung disease, such as COPD or asthma, a consultation with the pulmonologist should be considered to ensure optimal medication usage (i.e. corticosteroids and inhaled beta2-sympathomimetic agents) prior to anesthesia and surgery [11].

In 2019, a meta-analysis showed that laparoscopic major gastrointestinal surgery in properly selected COPD patients resulted in less intraoperative blood loss, shorter length of hospital stay, less postoperative pulmonary complications, reduced wound infection rates, and less abdominal abscess rates [12]. This suggests that for selection of patients for robot-assisted surgery, medium and longer term benefits must be weighed against the shorter term challenges of the anesthesia technique.

Intracranial

Both Trendelenburg positioning and pneumoperitoneum increase the intracranial pressure (ICP) [13–15]. However, in patients without intracranial pathology, the cerebral perfusion pressure remains within the limits of cerebral autoregulation and regional cerebral oxygenation is preserved [16]. Park showed in 2009 that the proportionate relation between $PaCO_2$ and cerebral blood flow remains intact during T rendelenburg positioning and capnoperitoneum: this means that normocapnia should be the target intraoperatively [17].

For patients with intracranial pathology who have a functional shunt, there have been serious concerns regarding the risks of creating a pneumoperitoneum and whether shunt patency monitoring should be used intraoperatively. Recent literature shows that these patients can safely undergo laparoscopic operations [18–20]; however, the use of non-invasive shunt monitoring is still a topic of discussion. Transcranial Doppler monitoring of middle cerebral flow velocity monitoring is suggested by some authors [20], while others recommend routine anesthetic monitoring [18, 19].

We recommend that the functionality of the shunt must be assessed preoperatively by neurosurgical/neurology departments and that these patients should undergo robot-assisted surgery in a hospital with neurosurgical facilities.

Intraocular

There are two main concerns with regard to the eyes during Robot-assisted surgery; raised intraocular pressure and corneal abrasions.

The intraocular pressure (IOP) is on an average 13 mmHg higher at the end of an laparoscopic operation with Trendelenburg positioning. Duration of the surgery and end-tidal carbon dioxide ($ETCO_2$) measurements are the predictors of this IOP increase [21]. It is important to be aware that prolonged surgery or pre-existing ocular pathology can lead to dangerous intra ocular pressure increases that risk retinal detachment or periorbital edema [22]. To date, there are no guidelines for monitoring and treating patients with an increased IOP/glaucoma undergoing surgical procedures while in the Trendelenburg position. Consultation with an ophthalmologist is recommended in patients with (suspected) glaucoma as various intraoperative approaches have been described in at-risk patients and these should be discussed in advance of surgery [23, 24]. The anesthesia provider should strive to maintain the $ETCO_2$ within normal range, to prevent further increases in the IOP.

According to a review based on data from the National Inpatient Sample (NIS), the risk of corneal abrasion was increased nearly four-fold with the laparoscopic technique and nearly 6.5 fold with the robotic technique compared to open hysterectomy [23]. Proposed etiologies for perioperative corneal abrasion include exposure, reduced corneal hydration, and chemical or direct mechanical trauma [25]. Corneal or conjunctival edema may also occur from increased central venous pressure and raised intraocular pressure, causing further stress to the eye via direct fluid pressure on the globe or pressure causing the eyes to tend to remain open [25]. Some clinics describe a high incidence of transient postoperative pain in both eyes after robot-assisted operations possibly due to scleral or corneal edema [26]. We recommend careful attention to eye protection during robot-assisted procedures; at our institution we apply a combination of eye ointment and carefully placed tape, however, no standardized regime exists in the literature.

Renal

The renal function should be determined preoperatively by serum creatinine and urea levels, because robot-assisted operations decrease blood flow to the visceral organs. At a pressure of above 10 mmHg, pneumoperitoneum has been shown to produce reduced renal blood flow, renal dysfunction and a transient oliguria [27, 28]. The decrease in renal function is dependent on preoperative renal function, level of hydration, level of pneumoperitoneum, patient positioning (*reverse*

Trendelenburg also worsens renal perfusion), and duration of pneumoperitoneum [29].

Patient Positioning on the Operating Table: 2 Phases

Phase 1: Patient Positioning for Induction of Anesthesia (Table 5.1)

Prior to positioning of the patient on the operating room table, one must ensure that the appropriate pressure mattress is placed on the table. In our hospital, a specialized mattress with a top layer of memory foam (Premium Sof-Care cushion, Maquet GmBH, Rastatt, Germany) is now routine for robot-assisted surgical procedures. Its use has greatly improved the process of patient positioning from both a time saving and safety perspective. In the past, a vacuum mattress was placed on the operating table from the sacrum to just above the shoulders. Following the removal of air from this mattress, it was shaped to prevent the patient from slipping cranially on the table during Trendelenburg positioning. However, there have been reports and personal communications of alopecia due to pressure effects of the vacuum mattress for prolonged periods of time against the head [30, 31]. As a result, it has been replaced with the aforementioned memory foam mattress.

For induction of anesthesia, the patient lies on the operating table, in a standard supine position, with the head resting on a normal hospital pillow or an intubation cushion (Slotted head positioner, Covidien, Mansfield, USA.) which is routinely used in our operating rooms.

Prior to induction of anesthesia, both arms are placed on arm boards placed at angles of <90° from the operating table. Standard monitoring equipment is attached to the patient, according to the American society of anesthesia guidelines, 'Standards for basic anesthetic monitoring' [32]. In the past, an arterial line was routinely placed; but as the duration of surgery is decreasing, arterial line placement is also decreasing.

Table 5.1 Positioning

Positioning/protection	Reasoning
• OR mattrass with memory foam • Disposable surface overlay (foam/paper)	• Excellent pressure distribution, preventing pressure injuries • Surface overlay enhances service life of the memory foam
• Arms: IV lines preferably in the lower arm, not near the wrist or elbow joint • Synthetic cast padding around the arms, extra thick layer around the elbow • Arm guards	• The IV lines cannot be inspected during the operation, therefore a location that is the least vulnerable for any manipulation should be selected. • Special attention for padding of the ulnar groove • To prevent the arm from being compressed by surgical personnel or surgical equipment
• Legs are moved laterally on movable distal sections of the operating table, so called 'table blades' rather than in classic lithotomy position • Fixation with leg straps	• The degree of leg elevation is greatly lessened and so also the risk of compartment syndrome • Lessens chance of leg displacement
• Positioning of the head on a shoulder supporting head rest. • Customized metal fixation device • Plexiglass frame over the head (allowing space between the plexiglass and patient's face)	• This construction prevents the patient from sliding during Trendelenburg position, while providing good support for the shoulders • This prevents surgical equipment/robot arms from compressing the patient's face
• Temperature management – oral or nasal pharyngeal temperature probe – forced-air warming blanket	• Adequately warm or cool the patient
• A urinary collection bag is placed hanging from the proximal end of the table	• Monitor intraoperative urinary output
• Neuromuscular monitoring device: TOF guard either placed at the hand (ulnar nerve) or at the face (facial nerve)	• Monitor the neuromuscular blockade

The fluid administration line is lengthened to ensure ease of drug administration during surgery. A second venous line is inserted following induction of anesthesia. One venous line is used for warm fluid administration using a fluid warming device while the second cannula is used for administration of drug infusions. Commonly used infusions are a vasopressor agent, a neuromuscular blocking agent and an opioid infusion. Any bolus dosing of drugs may be administered via the warmed fluid line to avoid inadvertent bolus administration of infusion drugs.

As with anesthesia for all surgical procedures, a variety of anesthetic drug combinations may be used, influenced by the co-morbidity of the patient undergoing surgery and likelyhood of a difficult intubation. Our preferred technique consists of preoxygenation with 100% oxygen, administration of a small bolus of sufentanil or fentanyl, followed by an infusion of remifentanil throughout the procedure until approximately 30 min before the end of surgery. The advantage of using remifentanil is that patients remain very stable throughout surgery, risk of patient movement is low and requirement for additional muscle relaxant administration is also reduced. An added benefit is the fast onset and offset time of remifentanil, allowing easy titration during surgery. However, this advantage has to be weighed against the suggested possibility of hyperalgesia and potential opioid tolerance at higher doses in excess of 0.2 μg kg^{-1} min^{-1} [33]. To avoid this potential risk, our technique utilizes multimodal analgesia consisting of local anesthetic wound infiltration, NMDA receptor antagonists, acetaminophen, non - steroidal anti-inflammatory drugs as well as longer acting opioids towards the end of surgery. During the procedure or in the recovery room, clonidine (1–2 μg/kg) is administered as necessary.

After anesthesia, a muscle relaxant is administered. Maintenance of anesthesia is provided with either a propofol infusion or an inhalational agent such as Sevoflurane or Isoflurane. To date there is little evidence supporting the use of propofol over inhalational agents for maintenance during robot-assisted surgery, although a study has been published showing less intraocular pressure increase with propofol versus sevoflurane during 30° Trendelenburg position [34]. A recently published retrospective cohort study of 631 patients found that propofol anesthesia was associated with improved overall survival in robot-assisted radical prostatectomy compared with desflurane anesthesia [35]. Clearly, further studies are indicated in this area, before any firm conclusion can be made. Another potential advantage of propofol maintenance during surgery is a lessening of post-operative nausea and vomiting (PONV), a known side effect of laparoscopic surgery [36].

Robot-assissted gynecological surgey is associated with a high rate of post operative nausea and vomiting and all patients should be given prophylactic antiemetics intraoperatively [37]. At our center, patients receive at least two of the following medications; a $5HT_3$ antagonist, a low dose of dexamethasone or a low dose dehydrobenzperidol. When an infusion of a neuromuscular blocking agent is administered during the procedure and muscle relaxation is monitored using a train of four device.

Following intubation of the trachea with a standard cuffed oral endotracheal tube (ETT) and attachment of a cuff manometer, it is important that the ETT is well secured with tape, as the patient is placed in Trendelenburg position during surgery. As a routine, a protective eye gel is placed on both eyes followed by careful taping.

An oral or nasal pharyngeal temperature probe is placed. A gastric tube is passed orally into the stomach to decompress gastric acid and air. As this will be removed at the end of surgery, placement via the nose is not required.

A urinary catheter is placed by the gynecologist under sterile conditions and the urinary collection bag is hung from the cranial end of the table. Due to Trendelenburg positioning, urinary output cannot be reliably measured intraoperatively.

Phase 2: Patient Positioning for Surgery Following Induction of Anesthesia

Once induction of anesthesia is complete, the second phase of patient positioning ahead of the surgical procedure is done. The patient's legs are

moved laterally on movable distal sections of the operating table, to allow surgical access. In the past, the patient's legs were placed in the lithotomy position, raised above the table, however, such a position for several hours with the legs elevated even further during extreme Trendelenburg may contribute to the development of compartment syndrome in the lower limbs [38]. With the described leg positioning technique, the degree of leg elevation is greatly lessened and so also the risk of compartment syndrome.

The arms of the patient are placed along the sides of the thorax and abdomen, wrapped in cotton wool/synthetic cast padding and secured in position, so that they remain immobile during the procedure. Particular care is taken to ensure that the ulnar nerve is protected and that the vascular access (IV and arterial) lines are functioning.

Head and shoulder positioning is very important during robot-assisted gynecological procedures; it is essential that the head is carefully positioned on an appropriate cushion and that a system is employed to ensure that the patient does not move cranially on the operating table. In our hospital, we use a specially designed head, neck and shoulder supporting cushion (Da Vinci Cushion, MediPlac GmbH, Borchen, Germany) which is fixed in place using a metal fixation device (local hospital product) (Photo 5.1). The soft cushion under the patients head lessens the potential risk of developing localized alopecia.

At this point, it is essential that a careful review of patient positioning is performed. All pressure points need to be checked and additional protective padding placed where necessary to ensure adequate protection during surgery. Injury to the nerves of both upper and lower limbs have been reported [39]. Once surgery starts, it is very difficult to gain access to the intravenous cannulas and arterial line due to the degree of surgical equipment around the operating table as well as the Trendelenburg positioning, therefore a thorough final check of correct attachment of anesthesia monitoring equipment and venous/arterial line functioning must be performed before commencing the surgical procedure.

A warming blanket is now placed over the patient extending to the level of the xiphisternum and attached to an air blower. A device designed to protect the face of the patient from inadvertent pressure from the robot arms made of plexiglass (local hospital product) (Photo 5.2) is then placed over the patient's face, checking at regular intervals that the patient's nose is clear of the plexiglass.

Once the anesthesiologist and surgeon are satisfied with patient position, the disinfection and surgery can commence. Local anesthetic is injected at the sites of port insertion (ropivicaine 0.75%, 5 mL to each of 4 ports). Once the first port is inserted, pneumoperitoneum is created by insufflating carbon dioxide. Following the insertion of a further 3 ports, the patient is placed in

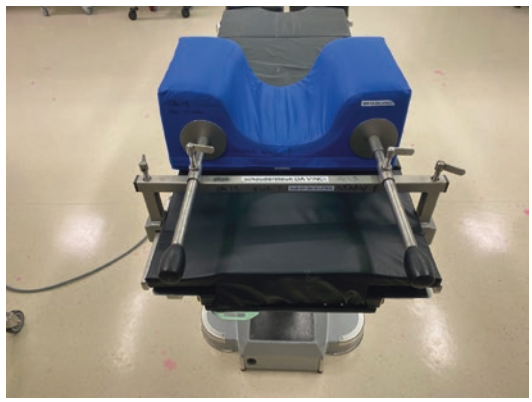


Photo 5.1 Head, neck and shoulder supporting cushion, held in place by a metal fixation device.

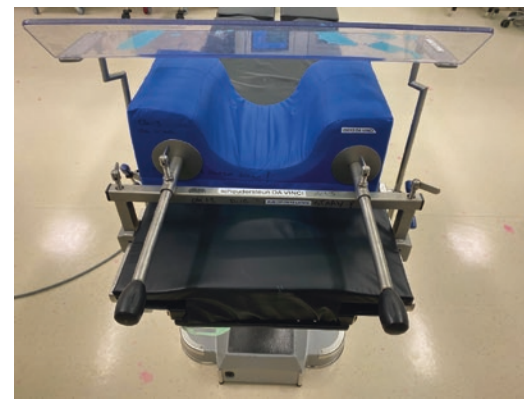


Photo 5.2 Plexiglass placed above head of patient to provide protection against robot arms

Trendelenburg position, with a further check of the head and shoulder position. Unlike during the earlier years of robot-assisted surgery, the amount of Trendelenburg used is no longer extreme; in our hospital a maximum Trendelenburg of 25° is used. Maximum intraperitoneal pressure is limited to 15 mmHg.

Clearly, with the requirement for so much technical equipment within an operating room, spatial restrictions imposed by the robot relative to the conventional anesthetic area need to be taken into account to ensure safe and effective functioning within the operating room. It is essential that the anesthesiologist has a clear plan for the placement of anesthesia equipment to ensure patient safety as well as a comfortable working space.

Intra Operative Changes in Physiology

Hemodynamic

Pneumoperitoneum (IAP limited to 15 mmHg) and steep Trendelenburg position significantly increase mean arterial pressure and systemic vascular resistance (SVR). However, there are no significant changes in cardiac output or stroke volume [40]. At IAP levels greater than 15 mmHg, venous return decreases as the inferior vena cava and the surrounding collateral vessels are compressed, leading to decreased cardiac output and hypotension [41]. A moderate to low IAP (12 mmHg) is recommended, as this limits the decrease in splanchnic perfusion, and consecutive organ dysfunctions will be minimal [27].

Due to the increased SVR, a vasopressor is generally not required, however norepinephrine is preferred over fenylephrine, because norepinephrine is shown to be better at maintaining the cardiac output and splanchnic perfusion [42]. Special attention is warranted in Trendelenburg position when using invasive blood pressure monitoring to ensure that the pressure transducer is positioned at the level of the heart. In patients with a decreased ventricular function, an inotropic agent may be indicated. Both dobutamine and phosphodiesterase type 3 inhibitors (such as enoximone) are possible agents, to date there have not been randomized trials to compare these drugs in patients under general anesthesia.

Maintaining an adequate intravascular volume is important since hypovolemia will exaggerate the decreased venous return during pneumoperitoneum. However, blood loss is significantly lower during robot-assisted gynecological operations as compared to conventional, open procedures [43–45]. Blood loss and urine output should be replaced by crystalloids at first. Furthermore, some authors suggest limiting IV fluids to reduce soft-tissue edema of the head and neck from positioning [26]. Bradyarrhythmias, including significant bradycardia, atrioventricular dissociation, nodal rhythm, and asystole can occur. These are the result of vagal stimulation caused by pneumoperitoneum-induced peritoneal stretch, stimulation of the fallopian tube during electrocauterization, or carbon dioxide embolization [46]. Tachyarrhythmias can occur because of increased concentrations of carbon dioxide and catecholamines [9]. The treatment of these arrhythmias is primarily to remove the stimulus (ie desufflation of the pneumoperitoneum), rather than pharmacological treatment.

Ventilation

Pulmonary compliance is decreased during pneumoperitoneum and Trendelenburg positioning, therefore the ventilation strategy is very important. Recent studies prefer pressure controlled ventilation over volume controlled ventilation, because of a lower peak airway pressure, a greater dynamic compliance and a better-preserved ventilation-perfusion matching for the same levels of minute ventilation [47, 48].

A tidal volume of 6–8 mL/kg and a positive end-expiratory pressure of 4–7 cmH_2O are recommended for the prevention of atelectasis and maximal airway pressure should be kept under 35 cmH_2O [49, 50]. A prolonged inspiratory time has a beneficial effect on both oxygenation and carbon dioxide elimination: instead of the conventional I:E ratio of 1:2, this can be altered to 1:1 or even 2:1 provided there is sufficient time for expiration (to avoid air trapping) [51].

After Trendelenburg positioning and pneumoperitoneum the distance from the vocal cord to the carina is reduced by approximately 1 cm compared to pre-positioning [52]. Therefore, reconfirmation of the tracheal tube position is recommended after positioning.

Emergence from Anesthesia

At the end of surgery, following reversal of pneumoperitoneum and removal of the robotic arms and surgical ports from the patient, the operating table is returned to the neutral position. During the initial years of robot-assisted surgery, it was standard practice to maintain anesthesia for up to 2 h after the end of surgery, with the patient in a head up position to reduce edema. Indication for early reintubation as a result of airway edema has been reported [53]. Various recommendations such as performing a leak test have been suggested, although supporting evidence is weak [54]. Currently, it is no longer standard practice to mandate a period of head elevation for all robot-assisted surgery patients prior to extubation, though it may be indicated for individual patients.

All patients have the level of residual muscle relaxation measured with a train of four device and where indicated an antagonist such as neostigmine (and atropine) or sugammadex is administered. Patients remain in the recovery room according to the same rules as for all general anesthesia patients.

Postoperative Analgesia

A standard protocol for postoperative analgesia includes acetaminophen, NSAID (in the absence of contraindications) and a delayed release oral opioid, in addition to an immediate release oral opioid as escape analgesia. In our experience, such a regime maintains satisfactory levels of pain control. Occasionally, when oral opioids are insufficient, a patient controlled analgesia (PCA) device administering an opioid is used. As for all laparoscopic surgery, additional anti-emetics should be administered intravenously as necessary. Rates of PONV for robot-assisted hysterectomies are reported to be up to 42% [37]. Residual gas can be a prominent cause of post-laparoscopy pain, which is frequently reported in the postoperative period [55].

The role of a transversus abdominis plane (TAP) block after robot-assisted operations remains a subject of discussion: randomized controlled trials show conflicting results [56, 57]. Epidural analgesia is not routinely used for laparoscopic gynecological procedures [58], because of the good alternative analgesics, combined with the reduced length of hospital stay and enhanced recovery programs [59]. Single shot intrathecal bupivacaine/morphine has proven to result in lower pain scores during exertion, although it is associated with an increased incidence of pruritus after robot-assisted radical prostatectomy [60]. Intrathecal analgesia can therefore be considered, however data for robot-assisted gynecological surgery is not currently available.

Intraoperative Emergencies

Intraoperative emergencies are rare during robot-assisted gynecological operations, but when they do happen they represent a major challenge to the anesthesiologist and gynecologist because of the limited access to the patient. These major events lead to the cessation of the surgical procedure and are reason for triggering the ‘emergency undocking procedure’. We describe the most life threatening emergencies, followed by the emergency undocking protocol.

Massive Intraoperative Hemorrhage

Various studies have shown that robot-assisted surgery is associated with less blood loss than either open or traditional laparoscopic techniques [17]. Hemorrhage during robot-assisted surgery is not a common occurrence, however when it does occur there are a number of significant factors which must be taken into account. Due to

both the head down positioning and the pneumoperitoneum, a source of bleeding can be masked until a late stage. This has been highlighted in the literature, where a case of arterial bleeding during robot-assisted surgery was masked until cessation of abdominal insufflation and return of the patient to the neutral position [61]. The Trendelenburg positioning resulted in adequate blood pressure measurements and the increased intra-abdominal pressure likely suppressed the hemorrhage. Massive hemorrhage during robot-assisted surgery triggers the undocking of the robot and usually conversion to an open procedure. Anesthesiologists should be alert to the possibility of operative bleeding right up until the very end of the procedure and any unexpected variations in blood pressure should trigger measurement of a hemoglobin level and clear communication to the operative gynecologist to check for occult bleeding.

Venous Gas Embolism

Venous gas embolism (VGE) can occur during pneumoperitoneum; direct intravascular gas insufflation, a tear in an abdominal wall or a damaged peritoneum vessel can lead to VGE [9]. One study has shown that 100% of the patients undergoing a laparoscopic hysterectomy had intraoperative VGE's (determined by transesophageal echocardiography), although none of these events caused hemodynamic instability or electrocardiogram changes at the time of VAE occurrence [62]. A severe VGE is characterized by a sudden increase of end-tidal CO_2, followed by a rapid decrease due to cardiovascular collapse and reduction of pulmonary blood flow. Other signs include tachycardia, hypotension, diminished breath sounds in a specific lung field on auscultation, cyanosis, and a classic cardiac murmur (mill-wheel murmur) [9, 63].

When a VGE is suspected, insufflation of CO_2 should immediately be stopped and the pneumoperitoneum must be released. Subsequent emergency undocking of the robot must be performed, while the patient is ventilated with 100% oxygen. After undocking, patients should be turned to the left lateral decubitus with a head-down position. Placement of a central venous line to aspirate the VGE should be considered [9, 26].

Pneumothorax

Pneumothorax is a known complication of laparoscopic abdominal surgery [64], which can occur when the CO_2 traverses into the thorax through a tear in the visceral peritoneum or by spontaneous rupture of pre-existing emphysematous bulla. The reported incidence of the occurrence of pneumothorax during laparoscopy is 0.01–0.4% [65], however, frequently a pneumothorax during laparoscopy is asymptomatic [32]. Symptoms include increased peak airway pressures, decreased oxygen saturation and in severe cases, profound hypotension and cardiac arrest. The treatment depends on the severity; from conservative treatment with close observation to chest tube placement [64].

Case reports have been published on the topic of massive subcutaneous emphysema and pneumomediastinum after robotic sacrocolpopexy. Subcutaneous emphysema is recognized by subcutaneous crackles throughout the upper chest and neck, this resolves generally within 1 week of surgery and does not cause airway obstruction [66]. Symptoms of a pneumomediastinum include shortness of breath, tachycardia, tachypnea and increased oxygen requirement. The literature describes such a case managed with supportive therapy with intensive care admission and reports that the pneumomediastinum resolved within 1 day of surgery [67].

Venous Thromboembolism

The risk of developing postoperative venous thromboembolism (VTE) has been shown to be significantly lower compared to open surgery [68, 69]. Prevention strategies vary from mechanical prophylaxis (including sequential compression devices and compression hose) to pharmacological prophylaxis with blood thinners such as heparin and low molecular–weight hepa-

rin [70]. A review published in 2018 showed that the incidence of VTE in patients with endometrial cancer who underwent robotic-assisted surgery was low (1.6%), all patients received thromboprophylaxis with subcutaneous heparin and sequential pneumatic compression devices [71].

Robotic Malfunction

A comprehensive analysis of the adverse events reported to the publicly available MAUDE database (maintained by the U.S. Food and Drug Administration) included data of over 1.75 million robotic procedures performed in the United States across various surgical specialties. During 2007–2013, the estimated rate of deaths was 5.7 per 100,000 procedures in gynecology, urology and general surgeries. The rate of injuries and procedure conversions was 71.5 and 29.2 per 100,000 procedures. A major portion of the abovementioned reports were due to 'device and instrument malfunctions', such as falling of burnt/broken pieces of instruments into the patient, electrical arcing of instruments, unintended operation of instruments, system errors and video/imaging problems [72]. Recent data from the MAUDE database report a peak adverse event rate in robot-assisted urological operations during the years 2013–2014, and a decrease since, as experience and technology improve [73].

From the anesthesiologist's point of view, we recommend active participation in crew resource management training, awareness of the 'emergency undocking' protocol and to report (near) incidents to the appropriate national organization.

Emergency Undocking Protocol for Da Vinci® Robot

It is essential that there is a clear protocol in place in the event of an emergency situation developing which requires the immediate stopping of robot-assisted surgery, removal of the surgical arms/ports and return of the patient to the supine position for further medical management. All operating room staff should be familiar with the details of such a protocol. One possibility is to briefly run through the steps during the 'time out' procedure prior to commencement of surgery, establishing a clear plan of action in the event of an emergency situation. An important part of the undocking procedure is a clear knowledge of individual roles for each member of the operating room team [74].

Conclusions

Robot-assisted gynecological surgery is being increasingly performed with consequent increases in available data on techniques and outcomes. From an anesthesia perspective, it continues to present challenges and the importance of appropriate patient selection and preoperative optimization cannot be understated. Careful intraoperative positioning is crucial as is the awareness of potential intraoperative adverse events and their management.

References

1. Chauvet D, Hans S, Missistrano A, Rebours C, Bakkouri WE, Lot G. Transoral robotic surgery for sellar tumors: first clinical study. J Neurosurg. 2017;127:941–8.
2. Zhao Y, Jiao W, Ren X, et al. Left lower lobe sleeve lobectomy for lung cancer using the Da Vinci surgical system. J Cardiothorac Surg. 2016;11:59.
3. Bellia A, Vitale SG, Lagana AS, et al. Feasibility and surgical outcomes of conventional and robot-assisted laparoscopy for early-stage ovarian cancer: a retrospective, multicenter analysis. Arch Gynecol Obstet. 2016;294:615–22.
4. Krill LS, Bristow RE. Robotic surgery: gynecologic oncology. Cancer J. 2013;19:167–76.
5. Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. J Am Coll Cardiol. 2014;64:e77–137.
6. Rist M, Hemmerling TM, Rauh R, Siebzehnrubl E, Jacobi KE. Influence of pneumoperitoneum and patient positioning on preload and splanchnic blood

volume in laparoscopic surgery of the lower abdomen. J Clin Anesth. 2001;13:244–9.
7. Speicher PJ, Ganapathi AM, Englum BR, Vaslef SN. Laparoscopy is safe among patients with congestive heart failure undergoing general surgery procedures. Surgery. 2014;156:371–8.
8. Rauh R, Hemmerling TM, Rist M, Jacobi KE. Influence of pneumoperitoneum and patient positioning on respiratory system compliance. J Clin Anesth. 2001;13:361–5.
9. Gerges FJ, Kanazi GE, Jabbour-Khoury SI. Anesthesia for laparoscopy: a review. J Clin Anesth. 2006;18:67–78.
10. Salihoglu Z, Demiroluk S, Baca B, Ayan F, Kara H. Effects of pneumoperitoneum and positioning on respiratory mechanics in chronic obstructive pulmonary disease patients during Nissen fundoplication. Surg Laparosc Endosc Percutan Tech. 2008;18:437–40.
11. Silvanus MT, Groeben H, Peters J. Corticosteroids and inhaled salbutamol in patients with reversible airway obstruction markedly decrease the incidence of bronchospasm after tracheal intubation. Anesthesiology. 2004;100:1052–7.
12. Guo Y, Cao F, Ding Y, et al. Laparoscopic major gastrointestinal surgery is safe for properly selected patient with COPD: a meta-analysis. Biomed Res Int. 2019;2019:8280358.
13. Halverson A, Buchanan R, Jacobs L, et al. Evaluation of mechanism of increased intracranial pressure with insufflation. Surg Endosc. 1998;12:266–9.
14. Irgau I, Koyfman Y, Tikellis JI. Elective intraoperative intracranial pressure monitoring during laparoscopic cholecystectomy. Arch Surg. 1995;130:1011–3.
15. Mavrocordatos P, Bissonnette B, Ravussin P. Effects of neck position and head elevation on intracranial pressure in anaesthetized neurosurgical patients: preliminary results. J Neurosurg Anesthesiol. 2000;12:10–4.
16. Kalmar AF, Foubert L, Hendrickx JF, et al. Influence of steep trendelenburg position and CO(2) pneumoperitoneum on cardiovascular, cerebrovascular, and respiratory homeostasis during robotic prostatectomy. Br J Anaesth. 2010;104:433–9.
17. Park EY, Koo BN, Min KT, Nam SH. The effect of pneumoperitoneum in the steep trendelenburg position on cerebral oxygenation. Acta Anaesthesiol Scand. 2009;53:895–9.
18. Jackman SV, Weingart JD, Kinsman SL, Docimo SG. Laparoscopic surgery in patients with ventriculoperitoneal shunts: safety and monitoring. J Urol. 2000;164:1352–4.
19. Sankpal R, Chandavarkar A, Chandavarkar M. Safety of laparoscopy in ventriculoperitoneal shunt patients. J Gynecol Endosc Surg. 2011;2:91–3.
20. Staikou C, Tsaroucha A, Mani A, Fassoulaki A. Transcranial Doppler monitoring of middle cerebral flow velocity in a patient with a ventriculoperitoneal shunt undergoing laparoscopy. J Clin Monit Comput. 2012;26:487–9.
21. Awad H, Santilli S, Ohr M, et al. The effects of steep trendelenburg positioning on intraocular pressure during robotic radical prostatectomy. Anesth Analg. 2009;109:473–8.
22. Berger JS, Taghreed A, Dayo L, Paul D. Anesthetic considerations for robot-assisted gynecologic and urology surgery. J Anesthe Clinic Res. 2013;4:345.
23. Lee M, Dallas R, Daniel C, Cotter F. Intraoperative management of increased intraocular pressure in a patient with glaucoma undergoing robotic prostatectomy in the trendelenburg position. A A Case Rep. 2016;6:19–21.
24. Borahay MA, Patel PR, Walsh TM, et al. Intraocular pressure and steep trendelenburg during minimally invasive gynecologic surgery: is there a risk? J Minim Invasive Gynecol. 2013;20:819–24.
25. Roth S, Thisted RA, Erickson JP, Black S, Schreider BD. Eye injuries after nonocular surgery. A study of 60,965 anesthetics from 1988 to 1992. Anesthesiology. 1996;85:1020–7.
26. Awad H, Walker CM, Shaikh M, Dimitrova GT, Abaza R, O'Hara J. Anesthetic considerations for robotic prostatectomy: a review of the literature. J Clin Anesth. 2012;24:494–504.
27. Gutt CN, Oniu T, Mehrabi A, et al. Circulatory and respiratory complications of carbon dioxide insufflation. Dig Surg. 2004;21:95–105.
28. Wiesenthal JD, Fazio LM, Perks AE, et al. Effect of pneumoperitoneum on renal tissue oxygenation and blood flow in a rat model. Urology. 2011;77:1508.e9–15.e9.
29. Demyttenaere S, Feldman LS, Fried GM. Effect of pneumoperitoneum on renal perfusion and function: a systematic review. Surg Endosc. 2007;21:152–60.
30. Bagaria M, Luck AM. Postoperative (pressure) alopecia following sacrocolpopexy. J Robot Surg. 2015;9:149–51.
31. Gollapalli L, Papapetrou P, Gupta D, Fuleihan SF. Post-operative alopecia after robotic surgery in steep Trendelenburg position: a restated observation of pressure alopecia. Middle East J Anaesthesiol. 2013;22:343–5.
32. Ludemann R, Krysztopik R, Jamieson GG, Watson DI. Pneumothorax during laparoscopy. Surg Endosc. 2003;17:1985–9.
33. Yu EH, Tran DH, Lam SW, Irwin MG. Remifentanil tolerance and hyperalgesia: short-term gain, long-term pain? Anaesthesia. 2016;71:1347–62.
34. Yoo YC, Shin S, Choi EK, Kim CY, Choi YD, Bai SJ. Increase in intraocular pressure is less with propofol than with sevoflurane during laparoscopic surgery in the steep Trendelenburg position. Can J Anaesth. 2014;61:322–9.
35. Lai HC, Lee MS, Lin KT, et al. Propofol-based total intravenous anesthesia is associated with better survival than desflurane anesthesia in robot-assisted radical prostatectomy. PLoS One. 2020;15:e0230290.
36. Yoo YC, Bai SJ, Lee KY, Shin S, Choi EK, Lee JW. Total intravenous anesthesia with propofol

reduces postoperative nausea and vomiting in patients undergoing robot-assisted laparoscopic radical prostatectomy: a prospective randomized trial. Yonsei Med J. 2012;53:1197–202.
37. Turner TB, Habib AS, Broadwater G, et al. Postoperative pain scores and narcotic use in robotic-assisted versus laparoscopic hysterectomy for endometrial cancer staging. J Minim Invasive Gynecol. 2015;22:1004–10.
38. Pridgeon S, Bishop CV, Adshead J. Lower limb compartment syndrome as a complication of robot-assisted radical prostatectomy: the UK experience. BJU Int. 2013;112:485–8.
39. Wen T, Deibert CM, Siringo FS, Spencer BA. Positioning-related complications of minimally invasive radical prostatectomies. J Endourol. 2014;28:660–7.
40. Falabella A, Moore-Jeffries E, Sullivan MJ, Nelson R, Lew M. Cardiac function during steep Trendelenburg position and CO2 pneumoperitoneum for robotic-assisted prostatectomy: a trans-oesophageal Doppler probe study. Int J Med Robot. 2007;3:312–5.
41. Odeberg S, Ljungqvist O, Svenberg T, et al. Haemodynamic effects of pneumoperitoneum and the influence of posture during anaesthesia for laparoscopic surgery. Acta Anaesthesiol Scand. 1994;38:276–83.
42. Mets B. Should norepinephrine, rather than phenylephrine, be considered the primary vasopressor in anesthetic practice? Anesth Analg. 2016;122:1707–14.
43. Ko EM, Muto MG, Berkowitz RS, Feltmate CM. Robotic versus open radical hysterectomy: a comparative study at a single institution. Gynecol Oncol. 2008;111:425–30.
44. Sert BM, Boggess JF, Ahmad S, et al. Robot-assisted versus open radical hysterectomy: a multi-institutional experience for early-stage cervical cancer. Eur J Surg Oncol. 2016;42:513–22.
45. Wallin E, Floter Radestad A, Falconer H. Introduction of robot-assisted radical hysterectomy for early stage cervical cancer: impact on complications, costs and oncologic outcome. Acta Obstet Gynecol Scand. 2017;96:536–42.
46. Sprung J, Abdelmalak B, Schoenwald PK. Recurrent complete heart block in a healthy patient during laparoscopic electrocauterization of the Fallopian tube. Anesthesiology. 1998;88:1401–3.
47. Choi EM, Na S, Choi SH, An J, Rha KH, Oh YJ. Comparison of volume-controlled and pressure-controlled ventilation in steep Trendelenburg position for robot-assisted laparoscopic radical prostatectomy. J Clin Anesth. 2011;23:183–8.
48. Jaju R, Jaju PB, Dubey M, Mohammad S, Bhargava AK. Comparison of volume controlled ventilation and pressure controlled ventilation in patients undergoing robot-assisted pelvic surgeries: An open-label trial. Indian J Anaesth. 2017;61:17–23.
49. Gupta K, Mehta Y, Sarin Jolly A, Khanna S. Anaesthesia for robotic gynaecological surgery. Anaesth Intensive Care. 2012;40:614–21.
50. Lee JR. Anesthetic considerations for robotic surgery. Korean J Anesthesiol. 2014;66:3–11.
51. Kim WH, Hahm TS, Kim JA, et al. Prolonged inspiratory time produces better gas exchange in patients undergoing laparoscopic surgery: a randomised trial. Acta Anaesthesiol Scand. 2013;57:613–22.
52. Chang CH, Lee HK, Nam SH. The displacement of the tracheal tube during robot-assisted radical prostatectomy. Eur J Anaesthesiol. 2010;27:478–80.
53. Phong SV, Koh LK. Anaesthesia for robotic-assisted radical prostatectomy: considerations for laparoscopy in the Trendelenburg position. Anaesth Intensive Care. 2007;35:281–5.
54. Mikaeili H, Yazdchi M, Tarzamni MK, Ansarin K, Ghasemzadeh M. Laryngeal ultrasonography versus cuff leak test in predicting postextubation stridor. J Cardiovasc Thorac Res. 2014;6:25–8.
55. Jackson SA, Laurence AS, Hill JC. Does post-laparoscopy pain relate to residual carbon dioxide? Anaesthesia. 1996;51:485–7.
56. Torup H, Bogeskov M, Hansen EG, et al. Transversus abdominis plane (TAP) block after robot-assisted laparoscopic hysterectomy: a randomised clinical trial. Acta Anaesthesiol Scand. 2015;59:928–35.
57. Hutchins J, Delaney D, Vogel RI, et al. Ultrasound guided subcostal transversus abdominis plane (TAP) infiltration with liposomal bupivacaine for patients undergoing robotic assisted hysterectomy: A prospective randomized controlled study. Gynecol Oncol. 2015;138:609–13.
58. Baker J, Janda M, Belavy D, Obermair A. Differences in epidural and analgesic use in patients with apparent stage i endometrial cancer treated by open versus laparoscopic surgery: results from the randomised LACE trial. Minim Invasive Surg. 2013;2013:764329.
59. Rawal N. Epidural technique for postoperative pain: gold standard no more? Reg Anesth Pain Med. 2012;37:310–7.
60. Koning MV, de Vlieger R, Teunissen AJW, et al. The effect of intrathecal bupivacaine/morphine on quality of recovery in robot-assisted radical prostatectomy: a randomised controlled trial. Anaesthesia. 2020;75(5):599–608.
61. Nakano S, Nakahira J, Sawai T, Kadono N, Minami T. Unexpected hemorrhage during robot-assisted laparoscopic prostatectomy: a case report. J Med Case Rep. 2016;10:240.
62. Kim CS, Kim JY, Kwon JY, et al. Venous air embolism during total laparoscopic hysterectomy: comparison to total abdominal hysterectomy. Anesthesiology. 2009;111:50–4.
63. Kaye AD, Vadivelu N, Ahuja N, Mitra S, Silasi D, Urman RD. Anesthetic considerations in robotic-assisted gynecologic surgery. Ochsner J. 2013;13:517–24.
64. Joshi GP. Complications of laparoscopy. Anesthesiol Clin N Am. 2001;19:89–105.
65. Raveendran R, Prabu HN, Ninan S, Darmalingam S. Fast-track management of pneumothorax in laparoscopic surgery. Indian J Anaesth. 2011;55:91–2.

66. Celik H, Cremins A, Jones KA, Harmanli O. Massive subcutaneous emphysema in robotic sacrocolpopexy. JSLS. 2013;17:245–8.
67. Crawford NM, Pathi SD, Corton MM. Pneumomediastinum after robotic sacrocolpopexy. Female Pelvic Med Reconstr Surg. 2014;20:56–8.
68. Barber EL, Gehrig PA, Clarke-Pearson DL. Venous thromboembolism in minimally invasive compared with open hysterectomy for endometrial cancer. Obstet Gynecol. 2016;128:121–6.
69. Freeman AH, Barrie A, Lyon L, et al. Venous thromboembolism following minimally invasive surgery among women with endometrial cancer. Gynecol Oncol. 2016;142:267–72.
70. Mueller MG, Pilecki MA, Catanzarite T, Jain U, Kim JY, Kenton K. Venous thromboembolism in reconstructive pelvic surgery. Am J Obstet Gynecol. 2014;211:552.e1–6.e1.
71. Laskov I, Kessous R, Abitbol J, et al. Risk of thromboembolic disease with cost estimates in patients undergoing robotic assisted surgery for endometrial cancer and review of the literature. J Obst Gynaecol Canada. 2018;40:1571–9.
72. Alemzadeh H, Raman J, Leveson N, Kalbarczyk Z, Iyer RK. Adverse events in robotic surgery: a retrospective study of 14 years of FDA data. PLoS One. 2016;11:e0151470.
73. Nik-Ahd F, Souders CP, Houman J, Zhao H, Chughtai B, Anger JT. Robotic urologic surgery: trends in food and drug administration-reported adverse events over the last decade. J Endourol. 2019;33:649–54.
74. O'Sullivan OE, O'Sullivan S, Hewitt M, O'Reilly BA. Da Vinci robot emergency undocking protocol. J Robot Surg. 2016;10:251–3.

6 Anesthesia for Proton Beam Therapy

David S. Beebe and Kumar G. Belani

Introduction

Proton beam radiation therapy is being used increasingly to treat malignancies, particularly brain tumors, both in adults and in children. Protons have higher mass than the photons used in standard radiation therapy and thus can be better directed into the tumor and cause less harm to surrounding tissues. Anesthetic management is similar to that for radiation therapy but usually takes a longer, generally 15–20 min for each session. Often they receive four to five sessions a week and may be treated for a month or more. During each treatment period the patient has to hold very still. Often a plastic mask is constructed that is placed over the patient's face to keep them from moving their head during treatment. Adults and often older children can receive proton beam therapy without anesthesia. Smaller children, particularly those less than 3 years of age, require anesthesia to safely receive proton beam therapy [1].

Anesthesia for an infant or child receiving proton beam therapy presents the following challenges to the Anesthesiologist. (1) The Anesthesiologist cannot be present in the treatment room when the actual treatment takes place to avoid radiation exposure. They must therefore be monitored remotely. (2) Often these children must be treated several times a day for several weeks or more. A technique must be chosen that allows early recovery without nausea to ensure the patient takes adequate oral hydration and nutrition. (3) For the same reason a technique that does not require instrumentation of the airway is beneficial to prevent sore throats and airway trauma. (4) The proton beam device is often located in a remote location without facilities for anesthetic gas evacuation, and limited space for anesthetic induction and recovery [1].

Preoperative Evaluation and Preparation

Proton beam therapy requires extensive preparation by the radiation therapist prior to beginning the procedure. Often plastic masks to hold the patient in the proper position must be constructed prior to treatment. The table where the therapy takes place often also must be modified prior to beginning treatment depending upon the patient's weight and body habitus. Infants or small children may require anesthesia prior to beginning proton beam therapy to obtain images to determine where to direct the beam. This often takes much longer (approximately 1 h) than the actual proton beam therapy itself [1].

Prior to beginning proton beam therapy, the patients underlying medical conditions have to be

D. S. Beebe (✉) · K. G. Belani
Department of Anesthesiology, University of Minnesota Medical School, Minneapolis, MN, USA
e-mail: beebe001@umn.edu; belan001@umn.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_6

thoroughly reviewed. Of particular concern are conditions which may affect the airway since many of these patients can be managed during the procedure using spontaneous ventilation without airway instrumentation. Also vascular access is important because the patients require repeated treatments. Often these patients have long term peripheral or central venous catheters placed for this purpose prior to beginning treatment [1].

Patients should also be assessed for the effects of chemotherapy and the proton beam therapy. One of these effects is bone marrow suppression with thrombocytopenia and neutropenia. This can result in mucositis which may complicate airway management and result in bleeding in the mouth from suctioning. Chemotherapy and radiation therapy can also result in chronic nausea, a poor appetite, and poor nutrition. Therefore patients are kept NPO for solid foods 6 h before surgery, but are allowed clear liquids up to 2 h to try to maintain adequate hydration [1, 2].

The facility where the treatment is being performed must also be prepared preoperatively. Often there is no mechanism to exhaust waste anesthetic gases in these facilities [3]. However at a minimum oxygen and suction must be available. Often a portable, stand-alone monitor can be utilized that measures end-tidal carbon dioxide tension, pulse oximetry, blood pressure, and the electrocardiogram. There also has to be a video-camera to watch the patient and the values from the monitor from an outside room because the Anesthesiologist cannot be present in the treatment room during therapy [1].

Finally the maturity of the patient needs to be assessed. Some patients, particularly older children, may not require anesthesia for the procedure. Also one program reports success in reducing the number of children who require anesthesia by having them go through a preoperative preparation program. The aim is to reduce their level of anxiety when undergoing proton beam therapy. After this program many children successfully undergo radiation therapy without anesthesia or sedation [4].

Anesthetic Techniques

Proton beam therapy is not a painful procedure but it does require that the patient lie still so that the beam of radiation is delivered to the proper area. Many anesthetic techniques have been successful utilized for proton beam radiation therapy. They include general inhalational anesthesia with endotracheal intubation or a laryngeal mask airway, and deep sedation with midazolam, ketamine, meperidine, dexmedetomidine or propofol. Currently the most common technique is intravenous propofol by infusion and spontaneous ventilation without endotracheal intubation (Native airway technique). This avoids the trauma of repeat endotracheal intubations or laryngeal mask insertions, and may facilitate immobilization with the thermoplastic masks that are often required. Propofol is also a strong anti-emetic. This is helpful for patients undergoing proton beam therapy can be associated with nausea. Reduction in nausea between treatments may allow for the patients to maintain their nutrition and level of hydration [1, 3].

Most of these patients have central venous port or catheter which is accessed before beginning the procedure, and may remain accessed if they are receiving daily treatments or more throughout the week. If the patient appears dehydrated and has not been eating well, 10–20 mL/kg of balanced salt solution may be administered [2]. Anesthesia using intravenous propofol and the native airway technique is then begun with a bolus dose of propofol (2 mg/kg) followed by a propofol infusion via a syringe pump (250 μg/kg/min). Often glycopyrrolate (10 μg/kg) is administered to reduce oral secretions. More propofol may need to be administered, both by bolus and infusion, in a patient who has developed tolerance to sedative medications. Oxygen at a low flow rate (2–4 L/min) is administered via nasal canula or face mask. Often the canula must be placed through the openings in the face mask used to hold the head in place for the therapy. Often initially the head and shoulders must be adjusted to ensure adequate ventilation, and occasionally an oral airway or laryngeal mask airway must be placed. End-tidal carbon dioxide,

pulse oximetry, blood pressure using an automatic cuff, and electrocardiogram are all measured and transmitted remotely to the viewing room while the proton beam therapy takes place. Also the patient must be viewed remotely via a video camera in the viewing room to be sure the patient remains spontaneously breathing but not moving inappropriately. Following the treatment the propofol infusion can be discontinued and the patient brought to the recovery room. Usually these children awaken quite rapidly, and can resume eating if there are no further treatments that day [1–3].

Since patients receiving proton beam therapy may receive daily or twice daily treatments for several weeks, some, but not all of them may develop tolerance to propofol. One study showed that only approximately thirty percent developed tolerance to propofol when receiving it for proton beam radiation [5]. Patients who develop tolerance may require progressively higher infusion rates. Occasionally ketamine and/or dexmedetomidine may need to be added to the propofol infusion to keep the patients from moving improperly.

Complications using this technique are rare. For example, Owusu-Agyemang and Grosshans et al. reviewed a total of 9328 anesthetics using intravenous propofol and spontaneous ventilation in 340 children were administered to 340 children with a median age of 3.6 years (range, 0.4–14.2) for proton beam therapy at a stand-alone center near the MD Anderson Hospital Campus in Texas. The median daily anesthesia time was 47 min (range, 15–79). The average time between start of anesthesia to the start of radiotherapy was 7.2 min (range, 1–83 min). Most (96.7%) children received supplemental oxygen by non-invasive methods. No patient required daily endotracheal intubation. Two episodes of bradycardia occurred, as well as one episode each of seizure, laryngospasm and bronchospasm. The cumulative incidence of complications in their series was only 0.05%. The authors concluded that in their series of children undergoing proton therapy at a freestanding center, intravenous propofol by infusion without daily endotracheal intubation provided a safe, efficient, and less invasive option of anesthetic care for proton beam therapy [2].

The other anesthetic technique used although less commonly is inhaled anesthesia with sevoflurane using a laryngeal mask airway. The same basic principles and monitoring apply. A similar low complication rate for children who were managed using this technique for proton beam therapy (0.0074%) was reported by Buchsbaum et al. [6]. However an anesthesia machine must be available, with the ability to measure the end-tidal anesthetic gases if this technique is used. Proper scavenging systems must be available as well. In their survey of anesthesia practice for proton beam radiation therapy Owusu-Agyemang and Popovich et al. found that 41% of the facilities surveyed that provided proton beam therapy did not have any means to scavenge waste anesthetic gases [3]. Therefore it is likely that intravenous propofol with spontaneous ventilation will continue to be the most common anesthetic technique used for proton beam therapy.

Conclusion

Proton beam therapy is a new, powerful form of radiation therapy. Although adults and older children may not need anesthesia for this treatment, infants and young children for immobilization. Although many anesthetic techniques have been utilized for proton beam therapy, intravenous propofol by infusion using the native airway technique and spontaneous ventilation has proved to be a valuable technique with few complications.

References

1. McFadyena J, Pellya N, Orra R. Sedation and anesthesia for the pediatric patient undergoing radiation therapy. Curr Opin Anesthesiol. 2011;24:433–8.
2. Owusu-Agyemang P, Grosshans D, Arunkumar R, Rebello E, Popovich S, Zavala A, et al. Non-invasive anesthesia for children undergoing proton radiation therapy. Radiother Oncol. 2014;111:30–4.
3. Owusu-Agyemang P, Popovich S, Zavala A, Grosshans D, Van Meter A, Williams U, et al. A multi-institutional pilot survey of anesthesia practices

during proton radiation therapy. Pract Radiat Oncol. 2016;6:155–9.
4. Mizumoto M, Oshiro Y, Ayuzawa K, Miyamoto T, Okumura T, Fukushima T, et al. Preparation of pediatric patients for treatment with proton beam therapy. Radiother Oncol. 2015;114:245–8.
5. Kang R, Shin B, Shin Y, Gil N, Oh Y, Jeong J, et al. Incidence of tolerance in children undergoing repeated administration of propofol for proton radiation therapy: a retrospective study. BMC Anesthesiol. 2018;18:125.
6. Buchsbaum J, McMullen K, Douglas J, Jackson J, Simoneaux V, Hines M, et al. Repetitive pediatric anesthesia in a non-hospital setting. Int J Radiat Oncol Biol Phys. 2013;85:1296–300.

7 Anesthesia for Robot-Assisted Laparoscopic Approaches for Pediatric Urologic Surgery

Vera Winograd-Gomez, Kalysa R. Porter, and Niekoo Abbasian

Learning Points

- Standard anesthesia monitoring is sufficient for most robot-assisted procedures in healthy children; however, children with significant comorbidities may benefit from arterial pressure monitoring and ability to perform frequent arterial blood gas analysis.
- Nitrous oxide should be avoided intraoperatively due to the risk of bowel distension from gas diffusion into the visceral lumen.
- Routine gastrointestinal decompression and Foley catheter placement are important to decrease the risk of inadvertent bowel perforation or other organ injury during initial access for insufflation.
- Use of a cuffed endotracheal tube and muscle relaxant help to facilitate ventilation. Pharmacologic paralysis also avoids inadvertent patient movement and risk of potential injury.
- Peritoneal insufflation and increased intra-abdominal pressure may create difficulties with ventilation. Peak inspiratory pressure (PIP) and respiratory rate (RR) should be adjusted to achieve tidal volumes between 6–8 mL/kg with $ETCO_2$ below 50 mmHg.
- Early fluid resuscitation aids in reducing the possibility of hypotension while also promoting the production of urine output throughout the surgery.
- Most pediatric robot-assisted laparoscopic procedures are performed in the supine or lateral decubitus position. The routine steep Trendelenburg positioning that is required for adult robotic surgery is usually not needed in children.
- Incisional pain can be well controlled with opioids, NSAIDs, and local anesthetic injection at the incision site. Caudal blockade and the use of transversus abdominis plane (TAP) block have been advocated by several authors, with mixed results. The use of aerosolized bupivacaine has been studied as an alternative to control pain from peritoneal insufflation.

Introduction

Since its introduction some three decades ago, minimally invasive surgery (MIS) has demonstrated its advantages in terms of quicker postoperative recovery, diminished postoperative pain, shorter length of stay, and improved cosmetic outcomes [1]. This has led to an increase in the popularity and widespread use of MIS. However, the steep learning curve and technical demand associated with laparoscopic MIS has to be taken into account [2]. The U.S. Food and Drug

V. Winograd-Gomez · K. R. Porter (✉) · N. Abbasian
Department of Anesthesiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA
e-mail: Vera.WinogradGomez@cchmc.org; Kalysa.Porter@cchmc.org; Niekoo.Abbasian@cchmc.org

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_7

Administration approved the use of robotic systems for assistance in laparoscopic surgery in the year 2000. Robotic surgery has since helped bridge the technical gap between traditional open and laparoscopic surgery. It provides magnified three-dimensional, stereoscopic visualization with enhanced precision of movement, and dexterity with a wrist-like mechanism. It also provides tremor filtration and improved ergonomics for the surgeon [3].

Since the publication of the first pediatric robot-assisted case series in 2001, the use of robot-assisted laparoscopy has exponentially increased to include a myriad of procedures and specialties [4]. The increase in scope of robot-assisted surgery in the management of urologic conditions has led the charge, representing the most frequently performed procedures [5]. For example, since its introduction in 2004, robotic-assisted laparoscopic ureteral reimplantation is one of the new minimally invasive procedures that has been increasingly adopted. The number of minimally invasive ureteral reimplantations increased from 0.3% in 2000 to 6.3% in 2012; of those, 81.2% were robot-assisted [6]. Robotic technology is currently being utilized to perform procedures such as pyeloplasty, ureteral reimplantation, total and partial nephrectomy, pyeloureterostomy, excision of ureteral and ureteropelvic junction polyps, as well as transplant to native ureteroureterostomy of renal allografts [7–10].

As robotic technology evolves, MIS will continue to be applied to the pediatric field and facilitate more complex procedures in pediatric urology. When faced with a robot-assisted urologic procedure, the anesthesia provider must consider not only the nuances and physiologic changes related to the laparoscopic approach but also the specific considerations related to the robot.

Anesthetic Considerations for the Pediatric Patient Undergoing Robotic Surgery

Pediatric robotic surgery for urological disease is performed using either a transperitoneal or retroperitoneal approach, usually the former. Access for robotic surgery using the transperitoneal approach requires insufflation of the abdomen to create a working space, comparable to that of traditional laparoscopic surgery. Once access has been obtained into the peritoneum, either via the Hasson technique with a small incision or by the use of a needle system to insufflate the abdomen with CO_2, the surgeon proceeds with placement of a port using a self-retracting bladed trocar. After gaining access, a laparoscope is introduced and careful inspection is performed to identify any hemorrhage or bowel, vascular, or other organ injury. Additional ports are then placed under direct visualization. The number and location of ports depends on the specific procedure being performed. Once the ports are placed, the robot is brought into the field and the robotic arms are engaged to each port [11].

Physiologic Changes Attributed to the Transperitoneal Approach

The transperitoneal approach requires insufflation of CO_2 into the peritoneal cavity in order to facilitate visualization and allow surgical intervention through the small ports. There are several physiologic changes associated with CO_2 pneumoperitoneum. This insufflation generates an increase in intra-abdominal pressure (IAP) that induces changes in several organ systems [12]. A complete understanding of these changes, and how they can and should be addressed during anesthetic and perioperative management, is of utmost importance to minimize any potential complications.

Pulmonary Effects

Increased IAP elevates the diaphragm and causes a decrease in functional residual capacity with an increase in airway resistance, physiologic dead space, and V/Q mismatch. CO_2 absorption through the peritoneum is highly dependent on IAP. At lower pressures (<10 mmHg) there is maximum absorption due to the high transmembrane gradient. When pressure is raised above venous pressure (>10 mmHg) absorption is decreased [13]. In healthy older children,

manipulation of ventilation parameters can easily offset these usually minimal changes [14]. However younger children, and those with significant pulmonary disease, may not tolerate high IAPs for extended periods of time. Plans should therefore be made with the surgical team to address this, perhaps by lowering IAPs during surgery [15]. Case reports have shown that CO_2 emboli can enter the bloodstream through inadvertent venous rupture. These may enter the arterial circulation via intrapulmonary shunting or a patent foramen ovale and potentially lead to significant hemodynamic compromise [16].

Cardiovascular Effects

The extent and severity of the cardiovascular changes depends on several variables. The volume of CO_2 absorbed, IAP, intravascular volume, ventilator technique, anesthetic agents used, and surgical conditions may all have differing effects on the cardiovascular changes seen during robotic surgery [17, 18]. Nevertheless, IAP and patient position are the two most important factors determining cardiovascular function during robotic intraperitoneal surgery. IAP levels below 15 mmHg cause an increase in venous return as the splanchnic venous bed is compressed, producing an increase in cardiac output [13]. Cardiac output may also increase as a result of sympathetically mediated peripheral vasoconstriction and increased filling pressures due to mechanical factors [19]. If the IAP elevates beyond 15 mmHg, inferior vena cava compression leads to diminished venous return. This, in turn, may cause decreased cardiac output and hypotension [20]. In children, a moderate-to-low IAP (<12 mmHg) is recommended by several studies, as this is the threshold for altered splanchnic perfusion [16]. IAPs below 12 mmHg will minimize organ dysfunction.

Several types of bradyarrhythmias may occur after placement of ports and insufflation of CO_2. These include profound bradycardia, AV dissociation, nodal rhythm, and asystole [21]. The most likely cause is vagal stimulation with needle placement and peritoneal stretch induced by pneumoperitoneum. These rhythm changes are seen more often in teenagers and young adults than in toddlers and school-aged children.

Initiating the insufflation in the horizontal position, rather than in the Trendelenburg or head-up position, may decrease the severity of hemodynamic changes associated with the induction of pneumoperitoneum. The variations in preload and afterload are usually well tolerated by most children with normal cardiovascular function. Those with cardiovascular disease, hypovolemia, or anemia require meticulous attention to IAP, insufflation pressure, positioning, and volume loading [20].

Physiologic Changes in Other Organ Systems

Cerebral Changes

Hypercapnia, increased IAP, increased systemic vascular resistance, and head-down position may lead to increased intracranial pressure and decreased cerebral perfusion pressure [22]. Because of this, special attention must be given to premature infants in whom significant ICP changes may lead to intraventricular hemorrhage.

Renal Changes

Pneumoperitoneum increases renovascular resistance and decreases flow through the renal vein due to direct compression of the renal parenchyma and vessels. This compression stimulates an increase in antidiuretic hormone and activates the renin-angiotensin system. Perioperative oliguria is common during these procedures and may last up to several hours post-operatively. Although generally transient and usually well tolerated with adequate intraoperative fluid administration, special attention must be given to guarantee generous intravascular volume loading in patients with compromised renal function [23].

Intraoperative Complications

The type and frequency of complications during robot-assisted urologic procedures varies greatly and depends on the type of procedure performed,

and the training and experience of the surgeon. The anesthesiologist should know the potential complications related to these procedures and be at the ready to expeditiously deal with them. During initial access, misplacement of the needle may lead to administration of CO_2 into the intravascular, subcutaneous, or preperitoneal spaces as well as the retroperitoneum, mesentery, omentum, or into abdominal and pelvic organs [13]. Catastrophic CO_2 embolism may occur after inadvertent intravascular needle placement. Since CO_2 is more soluble in blood than nitrous oxide or air, a greater volume of CO_2 can be tolerated. Pneumothorax, pneumomediastinum, or pneumopericardium can occur when gas traverses into the thorax, mediastinum, or pericardial space through a tear in the visceral peritoneum, forced entry of CO_2 into the mediastinum or pericardium through the inferior vena cava, or when CO_2 tracks through a defect in the diaphragm. Accidental insertion of the needle or trocar into a major vessel causing injury to the abdominal aorta, common iliac, inferior vena cava, or hepatic artery can lead to massive, frequently fatal hemorrhage requiring conversion to laparotomy for damage control. Minor vascular injuries of the vessels in the abdominal wall can often be managed during laparoscopy. Bowel and solid organ injuries involving the stomach, duodenum, small intestine, colon, liver, bladder, and spleen have also been reported [24]. Gastric and bladder decompression prior to needle placement has been demonstrated to reduce the incidence of stomach, bladder, and ureter injury [24]. A consistent approach to these procedures, and the development of treatment algorithms for the most common complications, is paramount. Algorithms have been developed for dealing with these common complications and have been validated in simulated and real-life scenarios to train surgeons, anesthesia providers, and nurses in the most effective methods to deal with these complications [25].

Anesthetic Management for Robotic Laparoscopic Surgery

Standard anesthesia monitoring is adequate for most robot-assisted procedures in healthy children. Patients with significant comorbidities, especially those with cardiovascular, renal, or respiratory compromise may benefit from arterial monitoring. In these patients, a significant V/Q mismatch may be present. If so, the gradient between arterial and expiratory CO_2 can become unpredictable and hypercarbia may only be detectable by direct $PaCO_2$ measurement with arterial blood gas analysis. Additionally, patients with renal compromise may benefit from serial measurement of electrolytes and base excess. These patients are at significant risk of sudden rise in potassium levels as they often have baseline total body hyperkalemia. This, combined with the respiratory and metabolic acidosis induced by the CO_2 pneumoperitoneum, may lead to symptomatic increases in serum potassium above 7–8 mEq/L, especially during long procedures [26].

Anesthetic Induction and Intraoperative Ventilator Management

The choice of anesthetic agents for induction and maintenance of anesthesia varies between centers [25, 27]. However, nitrous oxide should be avoided intraoperatively due to the risk of bowel distension from gas diffusion into the visceral lumen. The initial placement of two intravenous (IV) lines is important. Due to the positioning and draping of the patient, rapid placement of a second IV line during an emergency could be challenging. Furthermore, the second IV line may be used as a “draw line” by flushing it with heparinized saline so that electrolytes or hematocrit can be quickly and easily evaluated in the event of hemorrhage. Routine gastrointestinal decompression and foley catheter placement are important to decrease the risk of inadvertent bowel perforation during initial access for insufflation, especially if this is performed with the needle technique.

A cuffed endotracheal tube is always preferred as changes in IAP and patient positioning may compromise adequate ventilation. Muscle relaxants are administered to facilitate ventilation and avoid inadvertent patient movement and risk of potential injury. This is especially important during the initial placement of laparoscopic ports.

Atropine should always be readily available in case of sudden, significant bradycardia associated with vagal response induced by pneumoperitoneum [6].

In terms of ventilation parameters, the most effective strategy is adjustment of peak inspiratory pressure (PIP) and respiratory rate (RR) [27]. With this strategy, sudden increases in tidal volume are the first indicator of potential problems such as leakage of gas around the ports. PIP and RR are adjusted to achieve tidal volumes between 6–8 mL/kg with $ETCO_2$ below 50 mmHg. In children, ventilation with PIP below 20 is usually attainable since most healthy young patients have significant chest wall compliance. More ventilator adjustments are often required in infants and young children to effectively eliminate CO_2 due to their increased metabolism and increased CO_2 production. A close discussion with the surgeon should be initiated if PIP above 50% of baseline is required to achieve effective tidal volumes. In this case, lowering the IAPs may be necessary.

Early volume repletion is paramount in preventing adverse renal and cardiovascular effects associated with pneumoperitoneum. Early fluid resuscitation aids in reducing the possibility of hypotension but also promotes the production of urine output throughout the surgery. This is important in patients undergoing urologic procedures, especially ureteral surgery, since the appearance of small amounts of blood in urine aids in the detection of ureteral patency at the end of the procedure [25].

Positioning

Most pediatric robot-assisted surgeries are performed in the supine or lateral decubitus position. The routine steep Trendelenburg positioning that is required for adult robotic surgery is usually not needed in children. For some procedures, lateral tilting of the operating table is required to facilitate visualization [28]. This is often the case for robotic pyeloplasty, the most common pediatric robot-assisted procedure. Therefore, it is essential that patients are firmly secured to the operating table with safety straps, tape, etc. Although the robotic instruments are not heavy, they may be inadvertently placed on the patient's head. Routine placement of a foam ring or padding is suggested to prevent potential injury. It is also important to guarantee that the robotic arms are not in contact with the patient during motion. This can be easily accomplished by periodically checking under the drapes [29].

Perioperative Pain Management

Postoperative incisional pain is usually less after laparoscopic approach than traditional open surgery. However, it is important to note that contrary to open surgery, postoperative pain might happen after pneumoperitoneum. Insufflation of CO_2 into the peritoneal cavity has been associated with shoulder and diffuse abdominal pain in a significant number of patients. In adults, shoulder pain has been reported in up to 65% of cases [30]. The exact cause of this pain is not clear. This is most likely the result of diaphragm irritation and peritoneal desiccation with the dry CO_2 gas which is commonly utilized. Therefore, heating and humidifying the gas with isotonic saline has shown effectiveness in postoperative shoulder and diffuse abdominal pain control. Several humidification devices that are easily attached to the insufflation circuit have received FDA approval. Incisional pain can be well controlled with opioids, NSAIDs, and local anesthetic injection at the incision site [31]. Caudal blockade and the use of transversus abdominis plane (TAP) block have been advocated by several authors, with mixed results. Caudal blocks are shown to reduce the need for intraoperative opioid use as well as decrease postoperative nausea and vomiting [32]. Postoperative control of shoulder and diffuse abdominal pain can sometimes be more challenging. The use of aerosolized bupivacaine has been studied as an alternative to control this type of pain. The infusion of aerosolized local anesthetic in the closed, pressurized laparoscopic environment aids in augmentation of the surface area coverage and significantly reduces postoperative pain [33, 34].

Summary

Laparoscopic minimally invasive surgery has many perioperative advantages, but also an associated steep learning curve. Robotic surgery has the ability to bridge the gap between traditional open surgery and laparoscopic techniques. Robotic technology is currently being utilized to perform a myriad of procedures, principally in the field of pediatric urology. Robot-assisted laparoscopic procedures require specialized considerations of which anesthesia providers must be aware. Physiologic changes related to peritoneal insufflation can affect several organ systems and can lead to potential complications including difficulty with ventilation, decreased venous return leading to decreased cardiac output and hypotension, bradyarrhythmias, increased intracranial pressure and decreased cerebral perfusion pressure, and perioperative oliguria. Other potential complications of robot-assisted laparoscopic techniques include CO_2 embolism; pneumothorax, pneumomediastinum, or pneumopericardium; and vascular, bowel, or solid organ injury. Anesthesia providers should know the potential complications related to these procedures and prepared to expeditiously deal with them.

References

1. Trevisani L, Nguyen H. Current controversies in pediatric urologic robotic surgery. Curr Opin Urol. 2013;23:72–7. https://doi.org/10.1097/MOU.0b013e32835b0ad2.
2. Tomaszewski J, Casella D, Turner R, et al. Pediatric laparoscopic and robot-assisted laparoscopic surgery: technical considerations. J Endourol. 2012;26:602–13. https://doi.org/10.1089/end.2011.0252.
3. Camarillo D, Krummel T, Salisbury J. Robotic technology in surgery: past, present, and future. Am J Surg. 2004;188:2s–15s. https://doi.org/10.1016/j.amjsurg.2004.08.025.
4. Chaussy Y, Becmeur F, Lardy H, et al. Robot-assisted surgery: current status evaluation in abdominal and urological pediatric surgery. J Laparoendosc Adv Surg Tech A. 2013;23:530–8. https://doi.org/10.1089/lap.2012.0192.
5. Mahida J, Cooper J, Herz D, et al. Utilization and costs associated with robotic surgery in children. J Surg Res. 2015;199(1):169–76. https://doi.org/10.1016/j.jss.2015.04.087.
6. Baek M, Chest J. Lessons learned over a decade of pediatric robotic ureteral reimplantation. Investig Clin Urol. 2017;58:3–11. https://doi.org/10.4111/icu.2017.58.1.3.
7. Avery D, Herbst K, Lendvay T, et al. Robotic-assisted laparoscopic pyeloplasty: multi-institutional experience in infants. J Pediatr Urol. 2015;11:139.e1–5. https://doi.org/10.1016/j.jpurol.2014.11.025.
8. Li B, Liu D, Gong E. Robotic assisted laparoscopic transplant-to-native ureteroureterostomy of an intraperitoneal renal graft. J Pediatr Urol. 2018;14:356–7. https://doi.org/10.1016/j.jpurol.2018.06.008.
9. Oderda M, Caleris G, Allasia M, et al. Robot-assisted laparoscopic pyeloplasty in a pediatric patient with horseshoe kidney: surgical technique and review of literature. Urologia. 2017;84(1):55–60. https://doi.org/10.5301/uro.5000188.
10. Blanc T, Pio L, Clermidi P, et al. Robotic-assisted laparoscopic management of renal tumors in children: preliminary results. Pediatr Blood Cancer. 2019;66(Suppl. 3):e27867. https://doi.org/10.1002/pbc.27867.
11. Arlen A, Kirsch A. Recent developments in the use of robotic technology in pediatric urology. Expert Rev Med Dev. 2016;13(2):171–8. https://doi.org/10.1586/17434440.2016.1136211.
12. Means L, Green M, Bilal R. Anesthesia for minimally invasive surgery. Semin Pediatr Surg. 2004;13:181–7. https://doi.org/10.1053/j.sempedsurg.2004.04.006.
13. Gerges F, Kanazi G, Jabbour-Khoury S. Anesthesia for laparoscopy: a review. J Clin Anesth. 2006;18:67–78. https://doi.org/10.1016/j.jclinane.2005.01.013.
14. Bannister C, Brosius K, Wulkan M. The effect of insufflation pressure on pulmonary mechanics in infants during laparoscopic surgical procedures. Paediatr Anaesth. 2003;13:785–9. https://doi.org/10.1046/j.1460-9592.2003.01149.x.
15. Neira V, Kovesi T, Guerra L, et al. The impact of pneumoperitoneum and Trendelenburg positioning on respiratory system mechanics during laparoscopic pelvic surgery in children: a prospective observational study. Can J Anesth. 2015;62:798–806. https://doi.org/10.1007/s12630-015-0369-0.
16. Clark C, Weeks D, Gusdon J. Venous carbon dioxide embolism during laparoscopy. Anesth Analg. 1977;56:650–2. https://doi.org/10.1213/00000539-197709000-00010.
17. De Waal E, Kalkman C. Haemodynamic changes during low-pressure carbon dioxide pneumoperitoneum in young children. Paediatr Anaesth. 2003;13:18–25. https://doi.org/10.1046/j.1460-9592.2003.00973.x.
18. Sakka S, Huettemann E, Petrat G, et al. Transesophageal echocardio- graphic assessment of hemodynamic changes during laparoscopic herniorrhaphy in small children. Br J Anaesth. 2000;84:330–4. https://doi.org/10.1093/oxfordjournals.bja.a013434.
19. Solis-Herruzo J, Moreno D, Gonzalez A, et al. Effect of intrathoracic pressure on plasma arginine vaso-

pressin levels. Gastroenterology. 1991;101:607–17. https://doi.org/10.1016/0016-5085(91)90516-n.
20. Odeberg S, Ljungqvist O, Sevenberg T, et al. Haemodynamic effects of pneumoperitoneum and the influence of posture during anaesthesia for laparoscopic surgery. Acta Anaesthesiol Scand. 1994;38:276–83. https://doi.org/10.1111/j.1399-6576.1994.tb03889.x.
21. Yong J, Hibbert P, Runciman W, Coventry B. Bradycardia as an early warning sign for cardiac arrest during routine laparoscopic surgery. Int J Qual Healthcare. 2015;27:472–7. https://doi.org/10.1093/intqhc/mzv077.
22. De Waal E, de Vries J, Kruitwagen C. CJ. K. The effects of low-pressure carbon dioxide pneumoperitoneum on cerebral oxygenation and cerebral blood volume in children. Anesth Analg. 2002;94:500–5. https://doi.org/10.1097/00000539-200203000-00005.
23. Gomez Dammeiera B, Karanika E, Gluera S, et al. Anuria during pneumoperitoneum in infants and children: a prospective study. J Pediatr Surg. 2005;40:1454–8. https://doi.org/10.1016/j.jpedsurg.2005.05.044.
24. Larobina M, Nottle P. Complete evidence regarding major visceral injuries during laparoscopic access. Surg Laparosc Endosc Technol. 2005;5:119–23. https://doi.org/10.1097/01.sle.0000166967.49274.ca.
25. Munoz C, Nguyen H, Houck C. Robotic surgery and anesthesia for pediatric urologic procedures. Curr Opin Anaesthesiol. 2016;29(3):337–44. https://doi.org/10.1097/ACO.0000000000000333.
26. Dangle P, Akhavan A, Odeleye M, et al. Ninety-day perioperative complications of pediatric robotic urological surgery: a multi-institutional study. J Pediatr Urol. 2016;12(102):e1–6. https://doi.org/10.1016/j.jpurol.2015.08.015.
27. Bansal D, Cost N, Bean C, et al. Infant robot-assisted laparoscopic upper urinary tract reconstructive surgery. J Pediatr Urol. 2014;10(5):869–74. https://doi.org/10.1016/j.jpurol.2014.01.029.
28. Kapoor V, Elder J. Simultaneous bilateral robotic-assisted laparoscopic procedures in children. J Robot Surg. 2015;9:285–90. https://doi.org/10.1007/s11701-015-0528-x.
29. Spinoit A, Nguyen H, Subramaniam R. Role of robotics in children: a brave new world! Eur Urol Focus. 2017;3(2–3):172–80. https://doi.org/10.1016/j.euf.2017.08.011.
30. Bisgaard T, Klarskov B, Rosenberg J, Kehlet H. Characteristics and prediction of early pain after laparoscopic cholecystectomy. Pain. 2001;90:261–9. https://doi.org/10.1016/s0304-3959(00)00406-1.
31. Bisgaard T. Analgesic treatment after laparoscopic cholecystectomy: a critical assessment of the evidence. Anesthesiology. 2006;104:835–46. https://doi.org/10.1097/00000542-200604000-00030.
32. Faasse M, Lindgren B, Frainey B, et al. Perioperative effects of caudal and transversus abdominis plane (TAP) blocks for children undergoing urologic robot assisted laparoscopic surgery. J Pediatr Urol. 2015;11(121):e1–7. https://doi.org/10.1016/j.jpurol.2014.10.010.
33. Freilich D, Houck C, Meier P, et al. The effectiveness of aerosolized intraperitoneal bupivacaine in reducing postoperative pain in children undergoing robotic-assisted laparoscopic pyeloplasty. J Pediatr Urol. 2008;4:337–40. https://doi.org/10.1016/j.jpurol.2008.04.006.
34. Alkhamesi N, Peck D, Lomax D, Darzi A. Intraperitoneal aerosolization of bupivacaine reduces postoperative pain in laparoscopic surgery: a randomized prospective controlled double-blinded clinical trial. Surg Endosc. 2007;21:602–6. https://doi.org/10.1007/s00464-006-9087-6.

8 Anesthetic Management for Whole Lung Lavage in Patients with Pulmonary Alveolar Proteinosis

Kinjal M. Patel, Sandeep Krishnan, Ahmed S. Awad, Keyur Trivedi, and Ronak G. Desai

Key Learning Points

- Whole lung lavage is an uncommon procedure that requires careful planning and teamwork between the proceduralist and anesthesiology team to achieve consistent success.
- Invasive monitoring with an arterial line and placement of a double lumen endotracheal tube are necessary due to the potential for hypoxemia and need for lung isolation.
- Whole lung lavage should be done where access to extracorporeal membrane oxygenation can be provided if necessary.
- A total intravenous anesthetic reduces inhibition of hypoxic pulmonary vasoconstriction and improves hypoxemia.
- Complications of the procedure can include hypoxemia, hemodynamic instability, circulatory overload, hydrothorax, pneumothorax, and hypothermia.
- Patients are typically tracheally extubated a few hours post-procedure in the intensive care unit.

Introduction

Pulmonary alveolar proteinosis (PAP) is a rare lung syndrome in which the accumulation of phospholipoprotein (i.e. surfactant) in the lungs obstructs the alveoli, resulting in impaired gas exchange and hypoxemic respiratory failure. First described in 1958, PAP is thought to be the result of either disorders of surfactant production or a disorder of surfactant clearance [1]. A mutation of surfactant protein or granulocyte macrophage-colony stimulating factor (GM-CSF) receptor genes (hereditary or familial PAP) can cause respiratory failure in newborns due to abnormal surfactant production and accumulation. Disorders of surfactant clearance include primary PAP, where abnormal GM-CSF signaling interferes with surfactant removal. The most common variation of primary PAP (90% of cases) results from an autoimmune mechanism [2]; anti-GM-CSF antibodies block the activation of alveolar macrophages, resulting in surfactant accumulation. Inhalation of toxic substances or hematological disorders such as myelodysplasia

K. M. Patel (✉) · A. S. Awad · K. Trivedi · R. G. Desai
Department of Anesthesiology, Cooper Medical School of Rowan University, Cooper University Hospital, Camden, NJ, USA
e-mail: Patel-Kinjal@cooperhealth.edu; Awad-ahmed@cooperhealth.edu; Trivedi-keyur@cooperhealth.edu; Desai-ronak@cooperhealth.edu

S. Krishnan
Department of Anesthesiology, Wayne State University School of Medicine, St. Joseph Mercy Oakland Hospital, Pontiac, MI, USA

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_8

can also result in impaired surfactant clearance, resulting in secondary PAP [3].

Surfactant, a naturally occurring oily substance that functions to lower alveolar surface tension, is comprised of phospholipids, cholesterol, and proteins manufactured and secreted by type II pneumocytes. This, in turn, allows alveoli to remain patent, preventing end-expiratory alveolar collapse and allowing efficient gas exchange. In healthy patients, surfactant is routinely cleared by alveolar macrophages and type II pneumocytes, preventing a deleterious buildup [2]. In PAP, the balance between production and clearance is affected, leading to abnormally high amounts of surfactant in the lung. These abnormalities cause increased intrapulmonary shunting of blood through alveoli filled with proteinaceous material, leading to impaired gas exchange. Treatment decisions and prognosis are influenced by the particular surfactant disorder uncovered.

Common clinical presentations of PAP are non-specific and can include both dyspnea and cough, productive or non-productive. Chest pain, fatigue, fever and weight loss are rare. Most patients are male (70%) and the majority have an extensive smoking history [3]. Radiographic imaging (e.g. Chest X-ray and CT scan) typically demonstrates symmetric, bilateral ground-glass opacification, interlobular septal thickening and reticular densities described as "crazy paving" [3–5]. In most cases bronchoalveolar lavage, with characteristic findings of "milky" and opaque-rich fluid consisting of alveolar macrophages, or trans-bronchial biopsy are used to establish the diagnosis; however neither approach can definitively determine the cause of PAP [2]. Open lung biopsy is rarely warranted.

Spirometry from pulmonary function testing generally reveals a restrictive pattern of lung disease, but 10–30% of patients exhibit normal findings [2]. Obstructive patterns may also be seen in smokers. Reduced diffusion capacity of carbon monoxide (DLCO) with an increased alveolar-arterial gradient is seen in 40–50% of PAP patients [6, 7].

Whole-lung lavage (WLL) is widely considered the gold standard treatment for PAP due to its lasting treatment effects in the majority of patients [8]. It may, however, be less effective in patients with surfactant production disorders [8, 9]. The favorable physiologic response to WLL (improved oxygenation, increased DLCO, reduced need for supplemental oxygen) is attributed to the removal of lipoproteinaceous material from the alveolar space and removal of anti-GM-CSF antibody, as well as other possible immunologic effects on the effectors cells including alveolar macrophages or type II pneumocytes [10, 11].

The most common indications for WLL include declining lung function, worsening hypoxemia and deteriorating radiographic findings [12]. Newer off-label treatments include subcutaneous or inhaled GM-CSF and plasmapheresis with rituximab. These new therapies have efficacy in some cases of autoimmune PAP; however, the majority of patients will undergo WLL within 12 months of diagnosis [9, 13–15]. Due to the rarity of PAP and lack of randomized trials, no concrete guidelines exist that delineate best practices for performing therapeutic WLL under general anesthesia. However, a safe and effective protocol typically requires an experienced multidisciplinary lavage team that is fully aware of the risks and complications that can occur during WLL [16].

Anesthetic Monitoring and Equipment

WLL poses significant challenges for the anesthesia teams caring for these critically ill patients. Routine complications include hypoxemia and hemodynamic instability due to mediastinal shift; however, WLL is associated with many potential complications including pneumothorax/hydropneumothorax, pleural effusions, increased intrathoracic pressure, and hypotension caused by increased central venous pressure due to excess fluid administered during lavage [17]. As such, invasive intra-arterial monitoring, in addition to standard ASA monitoring, is recommended for this procedure. Patients with significant coexisting cardiac disease may require

the use of a pulmonary artery catheter or central venous catheter [16, 18].

Extracorporeal Membrane Oxygenation (ECMO) can be considered preemptively in patients who are unable to tolerate one-lung ventilation (paO_2 < 100 mmHg with FiO_2 100% [19]), or it can be used as an effective rescue tool for patients who undergo WLL and suffer from severe, refractory hypoxemia [18, 20]. The availability of extracorporeal circulation should be discussed as part of a multidisciplinary treatment plan prior to the procedure. Such preoperative planning and discussion can instill a level of confidence in the care team, leading to decreased early termination of WLL.

The principal objective of WLL is separation of the lungs to facilitate lavage while maintaining safe oxygen saturation and reducing cross-contamination between the two lungs. Thus, double lumen endotracheal tubes (DLT) are a mainstay of anesthetic management in adult patients undergoing WLL. DLTs allow for reliable separation of the lungs, and correct positioning can prevent spillage of lavage material from one lung into the other. Routine hypoxemia during one lung ventilation may require maneuvers to improve oxygenation that can only be achieved with a DLT (e.g. continuous positive airway pressure to the lavaged lung in between washings). Some variability does exist in methods of lung separation—case reports have described using different techniques including multiple endotracheal tubes to separate lungs (in patients in whom the smallest commercially available DLTs (26 Fr) are too large) [21] and using an endobronchial blocker through a DLT to isolate injured lung tissue and prevent hydrothorax during WLL [22].

Typically, placing a left-sided DLT is preferred as it has a greater margin of safety in positioning than a right-sided DLT [23]. Malposition of a right-sided DLT may lead to poor lung separation and leakage of lavage fluid into the contralateral lung [24]. Additionally, improper placement of a right-sided DLT may result in failure to adequately lavage the right upper lobe (RUL) if access to the RUL is obstructed by the misplaced right DLT. Fiberoptic bronchoscopy should be used to confirm appropriate positioning of DLTs and endobronchial blockers.

Procedural Details

Positioning

Once lung isolation is achieved, WLL can be successfully performed with patients in various positions. Positioning patients in supine, full-lateral, moderate-lateral, prone, reverse Trendelenburg, and Trendelenburg positions has been described in the literature [16, 24, 25]. In the lateral position, placing the lavaged lung in the dependent position can reduce the risk of fluid spillage into the ventilated lung. However, this can lead to an increased ventilation-perfusion (V/Q) mismatch that can contribute to hypoxemia [17, 24]. Placing the ventilated lung in the dependent position can improve V/Q matching and oxygenation by reducing blood flow to the lavaged lung; this reduces the incidence of hypoxemia but increases the risk of spillage of lavage fluid into the dependent lung [8, 22]. The majority of centers successfully utilize the supine and lateral positions; many place the patient in the reverse Trendelenburg position to facilitate instillation of the lavage fluid and the Trendelenburg position to improve recovery of the lavage fluid [12].

Anesthetic Induction and Maintenance

WLL is performed under general anesthesia, and induction of anesthesia is accomplished with a typical induction agent (propofol or etomidate if hemodynamic instability is expected), neuromuscular blocker, and an opioid. Patients with PAP undergoing WLL are routinely hypoxemic on room air, and often have mild respiratory distress. As a result, preoxygenation for several minutes with 100% oxygen is warranted. This denitrogenation of the lungs also serves to improve the efficacy of the WLL [17].

Maintenance of anesthesia after proper positioning can be achieved with either volatile anes-

thesia or total intravenous anesthesia (TIVA). Large case series have described the successful use of volatile anesthetics for decades in patients undergoing WLL. However, as volatile anesthetics are known to inhibit hypoxic pulmonary vasoconstriction in a dose-dependent fashion [26], recent practice has shifted towards TIVA for maintenance of anesthesia [16, 22, 27] in an effort to improve oxygenation during one lung ventilation (OLV). OLV should be instituted along with standard lung protective strategies used in patients with Acute Respiratory Distress Syndrome to reduce barotrauma—lower peak airway pressures (<30 cm H_2O), 4–6 mL/kg tidal volumes, and added positive end-expiratory pressure (10–12 cm H_2O) to achieve adequate oxygen saturation [16].

Whole-Lung Lavage: The Procedure

There is no single standardized approach to WLL and institutional practices vary widely [12]. Once OLV is established, the non-ventilated lung is connected to lavage tubing that has clampable inflow and outflow limbs. The inflow limb is connected to lavage fluid placed 30–100 cm above the patient [12, 16]; the outflow limb flows into a collecting chamber and is drained by gravity. The general consensus is that saline warmed to 37 °C should be instilled in 800–1000 mL aliquots, but significant variability exists in the total volume of fluid instilled per lung. Limiting the wash aliquots to 1 L is believed to reduce hydrotrauma and reduce the risk of lavage spillage into the contralateral lung [16]. Initial return to the collecting chamber is often thick and not able to be transilluminated. Once the majority of instilled fluid is returned into the collecting chamber, the process is repeated until the fluid return is clear and can be transilluminated [16, 27].

In cases where sequential bilateral WLL is being performed for PAP, recruitment maneuvers are often performed on the washed lung prior to resuming normal ventilation. Gentle suction can also be applied and patients can be placed in Trendelenburg position to aid in the removal of residual lavage fluid in the lung. Provided that the patient tolerates washing of the initial lung well, Smith et al. reported excellent success in proceeding with lavage of the contralateral lung [16]. Bilateral total lavage volume can range anywhere from 5–40 L [12].

In bilateral WLL, lavage is typically first performed on the side with more severe radiologic findings. If both lungs appear equally affected, the left lung is lavaged first because of its smaller size relative to the right lung and the potential for reduced hypoxemia [16, 18]. A majority of centers perform chest percussion during WLL to help emulsify PAP sediment [12].

WLL is typically performed by a critical care-trained physician; this is often another anesthesiologist. The proceduralist's extensive knowledge of cardiovascular and pulmonary physiology, and their ability to understand the needs of the anesthesiology team play a critical role in the successful completion of this procedure. Periods of hypoxemia are not uncommon during this procedure, and there are no well-described cutoff values of PaO_2 or SaO_2 at which the procedure should be terminated. Availability of a backup plan in case of emergency (e.g. ECMO), can increase the tolerance of hypoxemia by providers treating these patients. Constant communication between anesthesia providers and the proceduralist allows for effective perioperative care and reduces rates of early procedural termination due to hemodynamic instability or refractory hypoxemia [18].

Complications

WLL has been a therapeutic mainstay (since 1963) [28] for patients suffering from PAP. However, procedural and postoperative complications are not unusual and have been reported in 8–15% of patients [12, 16]. Fever (18%) and hypoxemia (14%) are the most commonly described complications [12]. Other procedural complications are described below.

Circulatory Overload

The aliquots of saline used for lavage do not fully drain from the lung and into the collecting chamber, resulting in significant absorption of saline when large volumes are used for lavage. Detailed records should be kept of the net fluid balance from each washing, and care must be taken during the procedure to reduce intravenous fluid administration. The patient should be carefully monitored for signs of circulatory overload postoperatively.

Spillage of Lavage Fluid

High lavage infusion pressures, insufficient lung isolation (due to poor DLT positioning or dislodgement), or washing with more than 1 L at a time have been implicated in the spillage of lavage fluid into the contralateral lung. Spillage of washed material into the ventilated lung can result in hypoxemia, increased peak airway pressures, sudden and severe bronchospasm, and increased V/Q mismatch. The appearance of bubbles in the lavage fluid draining from the lavage side, an increase in resistance to ventilation of the ventilated lung, and a sudden decrease in arterial oxygen saturation can suggest loss of lung isolation [17]. A large imbalance between saline instilled in the lung and saline recovered can also indicate loss of lung isolation [24, 29].

Hypothermia

Lavage fluid should be warmed to 37 °C for WLL and the intraoperative team must remain attentive to patient temperature during WLL. The large lavage volumes may lead to hypothermia if the fluid temperature is not adequately maintained and active warming devices are not utilized.

Pneumothorax/Hydrothorax

Barotrauma or hydrotrauma to the lungs during WLL can lead to pneumothorax and potentially hydrothorax. Barotrauma to the ventilated lung can be prevented by using tidal volumes in the 4–6 mL/kg range and reducing peak airway pressures. In a case series of 1110 WLLs, pneumothorax was rarely reported (0.8%) [12]. Hydrotrauma can occur if the lavage fluid is instilled too forcefully. Smith et al. proposed inflating the bronchial and tracheal cuffs of the DLT to 30 cm H_2O; this will allow fluid to leak back around the cuff if the lavage pressure increases above 30 cm H_2O, reducing the potential for application of large hydrostatic forces to the lung.

Postoperative Considerations

At the conclusion of WLL and after re-inflation of both lungs, oxygenation is typically improved [16, 27]. Residual lavage fluid in the lung or incompletely treated PAP may result in persistent hypoxemia. Therefore, many centers choose to extubate PAP patients in the intensive care unit (ICU) a few hours after completion of WLL [12]. The DLT can be exchanged for a single lumen endotracheal tube prior to transport to the ICU. Patients are often discharged from the ICU by post-procedure day 1, and occasionally several hours after tracheal extubation.

Most patients with PAP see an improvement in their symptomology after WLL, commonly manifested by a decreased need for supplemental oxygen. Physiologic signs of improvement are also seen including increases in forced vital capacity and forced expiratory volume, increased DLCO, and improved oxygenation both at rest and with exercise [16, 30–32].

Conclusions

WLL is an uncommon procedure for a disease that is rare but debilitating in nature. While conservative measures are often applied for the treatment of PAP, a significant portion of patients fail this therapy and present for WLL. Anesthesiologists caring for these patients must familiarize themselves with the intricate details of this procedure, as intra-pro-

cedural instability is common and complications are seen with relative frequency. Understanding the cardiopulmonary pathophysiology associated with PAP and WLL can help improve communication and perioperative planning between the anesthesia team and the proceduralist. As there are no established criteria for early termination of WLL due to hypoxemia or hemodynamic instability, the anesthesiologist and proceduralist must decide as a team when it is safe to continue, and when the procedure should be aborted. The prompt availability of extracorporeal circulation may allow for more complete washing of lungs and increase post-procedural benefit to patients. Providing anesthesia for WLL can at times prove to be challenging; however, effective communication and close attention to detail, combined with knowledge of the pathophysiology of WLL, can lead to successful outcomes.

References

1. Rosen SH, Castleman B, Liebow AA, et al. Pulmonary alveolar proteinosis. N Engl J Med. 1958;258:1123–42.
2. Borie R, Danel C, Debray M-P, et al. Pulmonary alveolar proteinosis. Eur Respir Rev. 2011;20:98–107. https://doi.org/10.1183/09059180.00001311.
3. Ishii H, Tazawa R, Kaneko C, et al. Clinical features of secondary pulmonary alveolar proteinosis: premortem cases in Japan. Eur Respir J. 2011;37:465–8.
4. Shah PL, Hansell D, Lawson PR, et al. Pulmonary alveolar proteinosis: clinical aspects and current concepts on pathogenesis. Thorax. 2000;55:67–77.
5. Trapnell BC, Whitsett JA, Nakata K. Pulmonary alveolar proteinosis. N Engl J Med. 2003;349:2527–39.
6. Delaval P, Brinchault G, Corre R, et al. Lipoprotéinose alvéolaire pulmonaire [Pulmonary alveolar phospholipoproteinosis]. Rev Pneumol Clin. 2005;61:186–92.
7. Briens E, Delaval P, Mairesse MP, et al. Lipoprotéinose alvéolaire pulmonaire [Pulmonary alveolar proteinosis]. Rev Mal Respir. 2002;19:166–82.
8. Beccaria M, Luisetti M, Rodi G, et al. Long term durable benefit after whole lung lavage in pulmonary alveolar proteinosis. Eur Respir J. 2004;23:526–31. https://doi.org/10.1183/09031936.04.00102704.
9. Seymour JF, Presneill JJ. Pulmonary alveolar proteinosis: progress in the first 44 years. Am J Respir Crit Care Med. 2002;166:215–35.
10. Perez A 4th, Rogers RM. Enhanced alveolar clearance with chest percussion therapy and positional changes during whole-lung lavage for alveolar proteinosis. Chest. 2004;125(6):2351–6.
11. Simpson RI, Ramsay MA, Millard MA, Capehart JE. Management of pulmonary alveolar proteinosis by repeated bronchoalveolar lavage. Proc (Baylor Univ Med Cent). 2000;13:119–20.
12. Campo I, Luisetti M, Griese M, et al. Whole lung lavage therapy for pulmonary alveolar proteinosis: a global survey of current practices and procedures. Orphanet J Rare Dis. 2016;11(1):115. https://doi.org/10.1186/s13023-016-0497-9.
13. Malur A, Kavuru MS, Marshall I, et al. Rituxmab therapy in pulmonary alveolar proteinosis improves alveolar macrophage lipid homeostasis. Respir Res. 2012;13:46.
14. Wylam ME, Ten R, Prakash UB, et al. Aerosol granulocyte-macrophage colony-stimulating factor for pulmonary alveolar proteinosis. Eur Respir J. 2006;27:585–93.
15. Kavuru MS, Sullivan EJ, Piccin R, et al. Exogenous granulocyte-macrophage colony-stimulating factor administration for pulmonary alveolar proteinosis. Am J Respir Crit Care Med. 2000;161:1143–8.
16. Smith BB, Torres NE, Hyder JA, et al. Whole lung lavage and pulmonary alveolar proteinosis: review of clinical and patient centered outcomes. J Cardiothorac Vasc Anesth. 2019;33:2453–61. https://doi.org/10.1053/jvca.2019.03.047.
17. Nandkumar S, Desai M, Butani M, Dwadia Z. Plumonary alveolar proteinosis with respiratory failure—anaesthetic management of whole lung lavage. Indian J Anaesth. 2009;53:362–6.
18. Tempe DK, Sharma A. Insights into anesthetic challenges of whole lung lavage. J Cardiothorac Vasc Anesth. 2019;33:2462–4. https://doi.org/10.1053/j.jvca.2019.04.033.
19. Claypool WD, Rogers RM, Matuschak GM. Update on the clinical diagnosis, management, and pathogenesis of pulmonary alveolar proteinosis (phospholipidosis). Chest. 1984;85:550–8.
20. Baumgartel M, Wurflein D, Neff U, et al. Bridging whole-lung lavage with venovenous extracorporeal life support for pulmonary alveolar proteinosis. J Cardiothorac Vasc Anesth. 2020;34:1115–7. https://doi.org/10.1053/j.jvca.2019.08.032.
21. Wilson CA, Wilmhurst S, Black AE. Anesthetic techniques to facilitate lung lavage for pulmonary alveolar proteinosis in children-new airway techniques and a review of the literature. Paediatr Anaesth. 2015;25(6):546–53. https://doi.org/10.1111/pan.12626.
22. Tan Z, Tan KT, Poopalalingam R. Anesthetic management for whole lung lavage in patients with pulmonary alveolar proteinosis. A A Case Rep. 2016;6(8):234–7. https://doi.org/10.1213/XAA.0000000000000283.
23. Benumof JL, Partridge BL, Salvatierra C, Keating J. Margin of safety in positioning modern double-

lumen endotracheal tubes. Anesthesiology. 1987;67(5):729–38.
24. Webb ST, Evans AJ, Varley AJ, Klein AA. Anaesthesia for serial whole lung lavage in a patient with severe pulmonary alveolar proteinosis: a case report. J Med Case Rep. 2008;2:360.
25. Awab A, Khan MS, Youness HA. Whole lung lavage-technical details, challenges and management of complications. J Thorac Dis. 2017;9(6):1697–706. https://doi.org/10.21037/jtd.2017.04.10.
26. Lumb AB, Slinger P. Hypoxic pulmonary vasoconstriction: physiology and anesthetic implications. Anesthesiology. 2015;122:932–46. https://doi.org/10.1097/ALN.0000000000000569.
27. Hunter Guevara LR, Gillespie SM, Klompas AM, Torres NE, Barbara DW. Whole-lung lavage in a patient with pulmonary alveolar proteinosis. Ann Card Anaesth. 2018;21(2):215–7. https://doi.org/10.4103/aca.ACA_184_17.
28. Ramirez J, Schultz RB, Dutton RE. Pulmonary alveoloar proetinosis: a new technique and rationale for treatment. Arch Intern Med. 1963;112:419–31.
29. Michaud G, Reddy C, Ernst A. Whole-lung lavage for pulmonary alveolar proteinosis. Chest. 2009;136(6):1678–81. https://doi.org/10.1378/chest.09-2295.
30. Mazone P, Thomassen MJ, Kavuru M. Our new understanding of pulmonary alveolar proteinosis: what an internist needs to know. Cleve Clin J Med. 2001;68(12):977–8.
31. Prakash UB, Barham SS, Carpenter HA, et al. Pulmonary alveolar phospholipoproteinosis: experience with 34 cases and a review. Mayo Clin Proc. 1987;62:499–518.
32. Xu Z, Jing J, Wang H, et al. Pulmonary alveolar proteinosis in China: a systematic review of 241 cases. Respirology. 2009;14:761–6. https://doi.org/10.1111/j.1440-1843.2009.01539.x.

Telehealth in Anesthesia, an Update

9

Kent Berg

Learning Points

- Telemedicine is defined as the remote delivery of healthcare services through audio-visual telecommunication systems. Telehealth also uses artificial intelligence, wearable technologies, and alternative strategies to enhance and personalize care.
- Telehealth promises many benefits, and the market for these services is expanding worldwide.
- While anesthesia staff have pioneered telehealth programs in perioperative settings, proper technical equipment, enhanced training, evolution of medical licensure and changes in reimbursement policy are necessary to expand telehealth in the practice of Anesthesiology.

Telemedicine Definition and Market Overview

According to the American Telemedicine Association (ATA), telemedicine is defined as the remote delivery of health care services and clinical information using telecommunications technology. Its close synonym and more current terminology, telehealth, also describes efforts to deliver health care services that utilize artificial intelligence (AI), virtual reality and behavioral economics in new and exciting ways [1]. As the Internet evolves and high-speed cable networks become more available, healthcare providers are exploring new mechanisms to accelerate care pathways, decentralize highly congested clinical environments, and reach more patients in remote areas. Certain specialties, like radiology, primary care, emergency medicine, and neurology have been practicing (and getting reimbursed for) telemedicine services for years. Other specialties, like dermatology and anesthesiology, are now venturing into these efforts as well. Using technology to expand capacity, patient access, and creative problem-solving is extremely important, especially as part of efforts to control pandemic infections like COVID-19.

Telehealth promises many benefits, including improved access, cost efficiencies, higher quality, and a better ability to address consumer demand. Regarding access, technology can bring together patients and providers across small and long distances, across urban and remote areas, and better match patients suffering from unique problems with world-class specialists that focus on their disease process. Telehealth has large potential to reduce the overall cost of healthcare, improve management of patients with chronic disease, create shared staffing models, and decrease time to travel between home and care locations.

K. Berg (✉)
Department of Anesthesiology, Sidney Kimmel Medical College and Thomas Jefferson University Hospital, Philadelphia, PA, USA
e-mail: Kent.Berg@Jefferson.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_9

Considering how patients perceive the quality of telehealth services, a growing number of studies have shown equivalency between telehealth and in-person health visits, and in some cases, such as mental health and Intensive Care Unit (ICU) care, telemedicine may show superior patient satisfaction and outcomes [1].

And finally, consumers continue to demand products or services that make it easier to manage their healthcare. Telemedicine allows patients to stay in their homes when they have an appointment, or place a video call on their lunchbreak from work, minimizing disruptions in their everyday lives. Patients can avoid the stressors of negotiating time off from their employer, arguing with other drivers in heavy traffic, or finding parking near their busy urban clinic.

Healthcare workers provide telehealth through a variety of services. Live videoconferencing describes a synchronous encounter where, for example, a patient is able to live-stream a conversation with a healthcare provider through the use of an application that is compliant with the Health Insurance Portability and Accountability Act (HIPAA) of 1996. Alternatively, a primary care provider may videoconference with a cardiology specialist in a different part of town or across the country. Store and forward services describe an asynchronous transfer of information, often digital images. For example, computed tomography (CT) or magnetic resonance imaging (MRI) scans can be captured and then sent to another provider for diagnosis or additional consultation. Remote patient monitoring is a telehealth service that uses wearable, implantable or other devices in close proximity to the patient to collect and transmit data to another location for evaluation. The pacemaker industry has utilized this service for years, but now new devices can measure continuous blood glucose [2] or capture simplified electrocardiogram (EKG) rhythm strips [3] and send them to healthcare professionals if patients opt-in to this service.

While the business market for telehealth is growing rapidly, the exact size is difficult to quantify. Of the data available, the ATA estimates that 200 telehealth networks exist in the United States (US), directly linking tertiary care centers with rural or suburban sites, across a total of nearly 3000 locations [1]. Meanwhile, the American Hospital Association (AHA) conducts annual surveys of its member institutions, including an assessment of their Information Technology (IT) systems. According to a 2019 AHA Fact Sheet on telehealth, the percent of US hospitals that had implemented a computerized telehealth system grew from 35% in 2010 to 76% in 2017 (Fig. 9.1) [4]. In addition, among US hospitals, use of remote patient monitoring has grown rapidly from 43.1% in 2015 to 61.2% in 2017 (Fig. 9.2) [4].

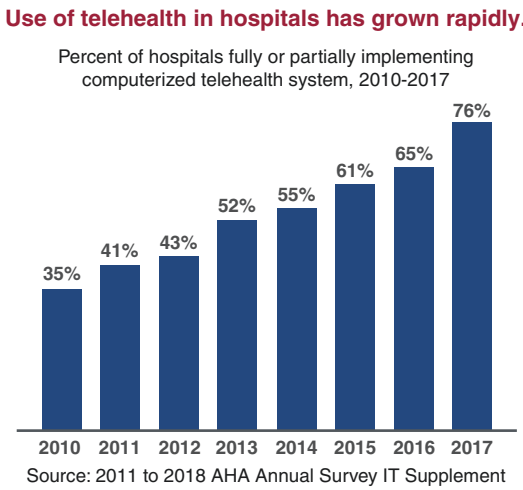


Fig. 9.1 Use of telehealth in US hospitals, 2010–2017 © Used with permission of American Hospital Association

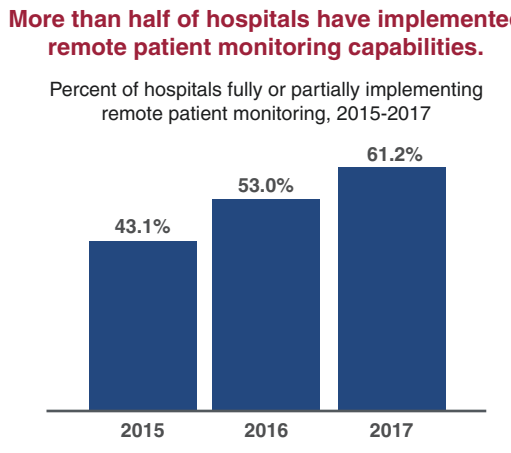


Fig. 9.2 Use of remote monitoring in US hospital, 2015–2017 © Used with permission of American Hospital Association

One of the main drivers of this increase in telehealth opportunities is the growing use of personal cellular devices, particularly smart phones (and tablet computers), which enable video-chat consultations to a much wider population of patients. Based on a 2019 survey conducted by the Pew Research Center, 96% of Americans own some form of a personal cell phone, and 81% of those are smartphones (assumingly with live video streaming capabilities) [5]. According to this same survey, while 53% of respondents over age 65 owned smart phones, 79% of respondents ages 50–64 owned them, pointing towards an increasing prevalence of smart phones as the 50–64 year-olds age into their Medicare-eligible years.

Further evidence is readily available to support the predicted growth of telehealth in the US and world-wide. In a 2016 Cable News Network (CNN) article, Mercy Hospital in St. Louis, MO, announced the opening of a $54-million facility, with 330 employees and no physical hospital beds [6]. The strategy of the Mercy's Virtual Care Center was to provide all eligible patients with Apple iPads, conduct live video consultations with patients, and review certain patients' vital signs and other physiologic activities with remote monitoring. This was part of a major initiative to personalize care for some of the health system's sickest patients in their own homes, in hopes to reduce rates of costly re-admissions. Several other health systems have also invested significant funds in telehealth ventures across the US and the globe. In addition, according to a 2018 analysis by Deloitte, consumers report that their #1 priority in healthcare is personalization of their care [7]. Telehealth is identified as a primary strategy for hospitals to achieve this goal, and to enhance the patient experience. This translates into wanting more transparency of patient data (e.g. lab results), easier ability to schedule live in-person visits with their providers when necessary, as well as more convenient patient-provider interactions like telehealth. This trend is also growing outside the US, as the international telemedicine industry is expected to exceed $40 billion by 2021 [8].

Examples of Telemedicine in Anesthesia: Intensive Care Unit, Pre-op, Intra-op, Post-op

Given the potential benefits of telehealth opportunities, it is appropriate to review how telehealth has been used to-date in Anesthesiology and Critical Care. Many studies claim improvements in overall survival outcomes, lower complication rates, and shorter length of stay (LOS) after implementing telemedicine programs. In a 2017 study, the authors described how implementing a telemedicine program in an ICU impacted their financial outcomes [9]. Researchers compared the baseline ICU patient group with a telemedicine-supported group, and later with a logistics center-supported group (supported by telehealth, as well as enhanced communication and standardized treatment protocols). By adding telemedicine and then a logistics center, this ICU was able to increase patient volume, decrease ICU LOS, and increase per case revenue relative to direct cost. Although the authors acknowledge that improvements in profitability seen in this study may be challenging to reproduce to the same degree after the implementation of the Affordable Care Act (ACA), they reported a $52.7 million improvement in total direct contribution margin. Even though the institution made an initial investment of $7.12 million to upgrade their IT infrastructure in the ICUs, they calculated that this amount was recouped in 2.75 months after ICU telemedicine was implemented.

While telehealth has gained momentum in ICU settings in the last 10–20 years, researchers from University Health Network in Toronto, Canada, were among the first to use telemedicine to perform pre-anesthesia assessments [10]. Authors stated that a significant percentage of Canadian patients (nearly 15%) live in remote areas far from tertiary care centers. Telemedicine showed promise to improve patient access to the healthcare system and reduce travel costs. As such, researchers then performed live video consultations on an initial ten patients. From a technical standpoint, live videoconference technology was installed at both the remote (patient) site and

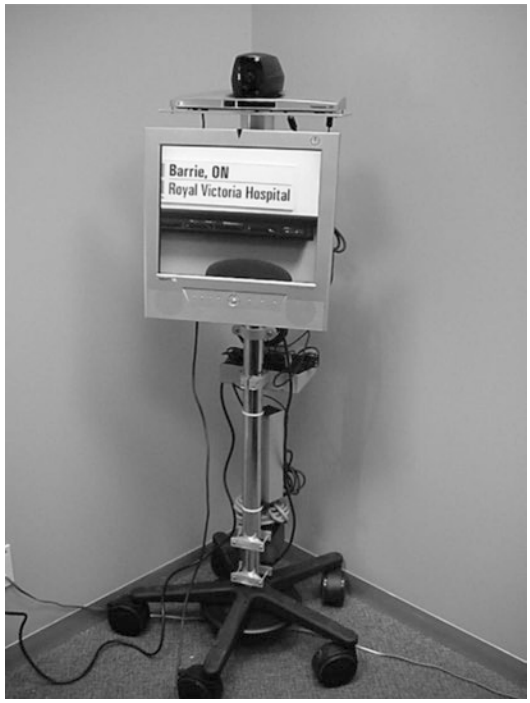


Fig. 9.3 Portable telemedicine unit with viewing monitor and camera mounted on the unit. © Used with permission of Wolters Kluwer Health, Inc. (*Anesthesiology*) and Copyright Clearance Center

the consultation (anesthesia preadmission clinic) site (Fig. 9.3), and the remote site also included a digital stethoscope to perform cardiac and pulmonary exams on the patient. The telecommunications network used for this study was operating with a bandwidth of 384 kilobytes per second (kbps). An anesthesiologist conducted the interview from the preadmission clinic, while the patient answered questions and underwent a stethoscope exam with a nurse's assistance at the remote site. The mean time needed to conduct the telemedicine consultation was 31 ± 7 min. While nine out of ten patients stated they were highly satisfied with the experience, eight out of ten anesthesiologists were also highly satisfied. Patients also reported happiness in avoiding time and cost that would have been associated with an in-person visit.

In a more recent 2018 study, researchers from Philadelphia, PA were concerned about extremely long times that patients spent in their preadmission testing center (PAT) [11]. A subset of 361 patients (out of 7803 total patients) were selected to receive a telemedicine screening visit, prior to their PAT appointment. Authors reported a statistically significant decrease in mean time spent in PAT from 121 ± 41 min to 72 + 24 min for patients that underwent a telemedicine screen prior to their scheduled PAT appointment. In addition, the patients pre-screened by telemedicine reported extremely high levels of satisfaction and reported no surgical case cancellations. Currently, a handful of healthcare institutions have already pioneered or are currently investigating telehealth consults to entirely replace in-person visits for pre-anesthesia assessments in select patient populations.

One of the most widely-referenced studies on telemedicine in anesthesia was published in 2009 [12]. Authors from Children's Hospital of Pennsylvania (CHOP) in Philadelphia, PA partnered with colleagues from Bangalore, India to provide live telemedicine consultation during two separate pediatric liver transplantations. Despite differences in time zones, anesthesiology staff members at CHOP provided consultation to the team in India during both the preoperative and intraoperative phases of care. Video cameras placed on surgeons' heads and lights above the surgical field allowed CHOP physicians to view key stages of the procedure in real time. Simultaneously, as vital signs and lab results became available in India, CHOP anesthesia staff recorded trends in Excel spreadsheets in Philadelphia. While both medical teams felt they benefited from this pioneering experience, authors stated that these live-streaming consultations raised significant concerns that could challenge the expansion of this technology in the medical field, and specifically in Anesthesiology. The technical aspects of live telecommunication across vast distances need to be tested in advance of the live consultation, and backup systems must be prepared. When a telemedicine consultation is completed, should the medical professional be licensed in her/his home US state, the state or country where the surgical procedure is being performed, or both? As part of this study, the hospitals in Philadelphia, PA and Bangalore, India had a pre-standing agreement that required the

Indian facility to take full responsibility of liability, but this topic is still hotly debated in the US today.

Regarding telemedicine use in the post-operative phase of care, authors from a 2017 study implemented a telemedicine model in the post-anesthesia care unit (PACU) during ICU surge levels [13]. Clinicians created a 4-bed virtual ICU (VICU), upgraded patient monitoring hardware, and increased nursing ratios (1 nurse per 2 VICU patients) in their PACU suite. During the 3.5-year study period (from 1 January 2008 to 31 July 2011), the ICU team cared for 1037 VICU patients, 28% of whom transitioned to the SICU for further critical care needs. Meanwhile, the large majority (72%) of VICU patients transitioned directly to floor unit beds, thereby decongesting the ICU beds for truly the highest acuity patients. Authors emphasized that appropriate patient selection for VICU assignment was critical to ensure patient safety and increase overall ICU care volume.

Equipment, Technical Support and Training

While the full technical requirements needed to implement a telehealth program are beyond the scope of this chapter, a 2019 textbook (hardcopy or online) called *Telemedicine in the ICU* [14] provides an expanded discussion on operational models for tele-ICU care, staff role definitions, and requirements for hardware and software. In general, a typical tele-ICU workstation would include a primary computer with telehealth software installed, a video camera, and several monitors for physiologic data (vital signs), access to radiologic imaging, and direct interface with the electronic medical record. A telehealth workstation for anesthesia use could be as complex as a tele-ICU system, or it could be scaled down for more basic usage.

In addition, as broad-band telecommunication networks evolve across the world, data is being transferred faster and in greater quantities than ever before. Video applications (such as Zoom, GoToMeeting, etc.) are becoming more prevalent, more accessible to the general population from desktop or mobile devices, and more HIPAA-compliant. These video applications open the door to telehealth opportunities for anesthesia providers. Again, to cite a 2009 study by Fiadjoe and colleagues [12], it is important to test backup communication systems prior implementing telemedicine programs. And on-call technical support needs to be available on a 24-h, 7-day-a-week basis, such as "share my screen" sessions between clinical and support staff.

With the expected increase in demand for telehealth services, some academic institutions have started formal training programs for telehealth. Regarding workflows to train an anesthetic pre-procedure evaluation, telehealth programs should define pathways to identify which patients are appropriate for telehealth or in-person consultations. Pre-implementation analysis should also include a review of hardware, software, data storage and data sharing policies. Finally, simulation of telehealth visits could yield high value to test the existing telecommunication network, provider workflows and other unknown factors, all without risk to actual patients.

Medical Licensure and Liability

Regarding their relevance to telehealth, medical licensure and liability are hotly debated topics among today's medical professional societies, governmental policy makers and health insurance leaders. By current law, each state issues its own medical license to practice within state boundaries. Does the provider's license cover telehealth services if these services are provided across state lines? If not, does the provider need to obtain licensure in the patient's state? The answer depends on each state's law. To address this issue, several state medical boards have joined together to form the Interstate Medical Licensure Compact (IMLC) [15]. As of March 25, 2020, 29 states, the District of Columbia (D.C.), and Guam have agreed allow licensed physicians practice across state lines within the IMLC if physicians meet the eligibility requirements, which is true for at least 80% of recent applicants [15]. Figure 9.4

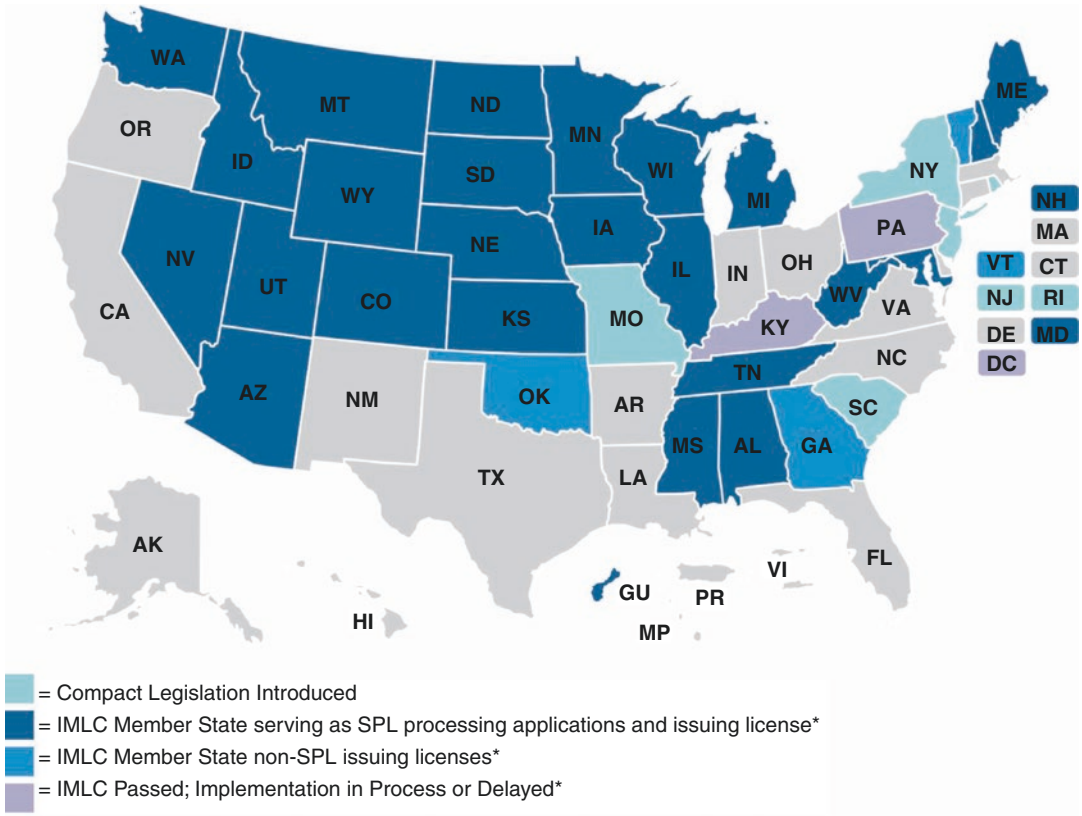


Fig. 9.4 Interstate Medical Licensure Compact (IMLC) participation, broken down by state. *SPL* state of primary licensure © Used with permission of Interstate Medical Licensure Compact

shows the current status of participation in the IMLC, broken down by state. Once a physician submits an application in her/his state of primary licensure (SPL), a new background check will be performed. A new qualified physician may then practice across state lines in any or all IMLC-participating states.

Unfortunately, telehealth liability is still contested in many medico-legal forums [16]. Who is responsible for managing a bad care outcome or medical error that results from a telehealth visit? If a plaintiff opens a legal suit, would both the local and remote providers be at risk of litigation? Does physician malpractice insurance cover telehealth services, and specifically if these services are delivered across state or national boundaries? The answers to these questions vary by state, by country, and by insurance provider. The key is to ask your group or institution's legal counsel to identify these answers in your practice jurisdiction.

Reimbursement for Telehealth

Do Medicare and Medicaid pay for telehealth services? Prior to COVID-19 exceptions, the answer is yes, in certain situations. The Center for Medicare & Medicaid Services (CMS) does reimburse for some current procedural terminology (CPT) codes for telehealth services in radiology, pathology and some cardiology [1]. Medicare Advantage (managed care) patients can use telehealth options if they are available from their practitioners. The Medicare Program, however, has very specific requirements that must be

met in order to qualify for reimbursement of telehealth services [17]. In general, the originating site (patient location) must be in a county outside a Metropolitan Statistical Area (MSA), or the physician office address must fall within a Health Professional Shortage Area (HPSA). Patients or physicians can see if Medicare is likely to offer telehealth reimbursement by entering the physician office address into the Medicare Telehealth Payment Eligibility Analyzer [18]: https://data.hrsa.gov/tools/medicare/telehealth.

In addition, while Medicaid programs in all 50 states and Washington D.C. provide some form of reimbursement for telehealth services, most commonly live-video, the full range of covered services vary greatly by state [19]. An excellent resource that reviews Medicare reimbursement for telehealth services, including current telehealth-related CPT codes, is the Medicare Learning Network Booklet on "Telehealth Services," most recently updated in March 2020 [17]. Another valuable resource is the Fall 2019 report by the Center for Connected Health Policy (CCHP), entitled "State Telehealth Laws & Reimbursement Policies" [19]. At the current time, unfortunately, there are no CPT codes specific to Anesthesia Telehealth services that qualify for CMS reimbursement. Moreover, very little additional information exists regarding private insurance coverage for Anesthesia Telehealth services.

The pre-surgical clinic, however, does represent an opportunity to expand anesthesia telehealth services. If pre-surgical clinics are supervised by Internal Medicine or Primary Care physicians, CMS will reimburse for some Part B services via telemedicine. This would provide funding to pay for direct and indirect costs associated with a pre-surgical clinic. Under current reimbursement regulations, unfortunately, if Anesthesia staff members complete pre-procedure consultations in a pre-surgery clinic, they cannot bill separately from the global Anesthesia fees that are charged on the day of surgery. Despite this obstacle, the value provided from an Anesthesia-supervised pre-surgical clinic may offset other institutional costs. An Anesthesia Telehealth consultation may be used as part of a strategy to enhance more personalized care, increase patient satisfaction scores, or decrease same-day surgical cancellation rates.

Now that we have reviewed the history of telehealth, its potential applications in Anesthesiology, medical licensure and liability, as well as current reimbursement policies, isn't it time for Anesthesiology practitioners to step forward and lobby for reimbursement for Anesthesia Telehealth services?

Key Telehealth Resources

Finally, several resources exist to provide education on telehealth issues. Table 9.1 contains current websites for several organizations or documents on telehealth.

COVID-19 Exceptions for Telehealth

As a response to the COVID-19 pandemic in March 2020, the US Department of Health and Human Services (HHS) is allowing physicians and other health care workers to practice across state lines [17]. This exception applies to the temporary reciprocity of medical licensure across state lines (even prior to full acceptance of IMLC participation by all 50 states). In addition, Medicare and Medicaid have also agreed to pay for an expanded list of telehealth services during the time of COVID-19 and social distancing practices [17]. Currently, this does not include additional approval to reimburse for Anesthesia Telehealth consultations or other services, but this may change as the public health response to COVID-19 evolves.

Funding and Conflict of Interest None

Table 9.1 Telehealth Resources

American Telemedicine Association	https://www.americantelemed.org
Center for Connected Health Policy	https://www.cchpca.org
International Society for Telemedicine and eHealth	https://www.isfteh.org
Center for Telehealth & eHealth Law	http://ctel.org

References

1. American Telemedicine Association. Telehealth basics. https://www.americantelemed.org/resource/why-telemedicine/. Accessed 17 March 2020.
2. Dexcom Continuous Glucose Monitoring. https://www.dexcom.com/g6-cgm-system. Accessed 18 March 2020.
3. AliveCor KardiaMobile. https://www.alivecor.com/kardiamobile. Accessed 18 March 2020.
4. American Hospital Association. Fact Sheet: Telehealth (Feb 2019). https://www.aha.org/system/files/2019-02/fact-sheet-telehealth-2-4-19.pdf. Accessed 20 March 2020.
5. Pew Research Center. Mobile Fact Sheet (12 June 2019). https://www.pewresearch.org/internet/fact-sheet/mobile/. Accessed 20 March 2020.
6. Julianne Pepitone. The $54 million hospital without any beds (13 September 2016). https://money.cnn.com/2016/09/12/technology/mercy-hospital-virtual-care/. Accessed 20 March 2020.
7. Deloitte. 2018 Global Healthcare Outlook: The evolution of smart healthcare. https://www2.deloitte.com/content/dam/Deloitte/global/Documents/Life-Sciences-Health-Care/gx-lshc-hc-outlook-2018.pdf. Accessed 20 March 2020.
8. The Future of Healthcare: How Healthcare Mobile App Trends are Changing in 2019. https://www.solutionbuilt.com/healthcare-mobile-apps/. Accessed 20 March 2020.
9. Lilly CM, Motzkus C, Rincon T, et al. ICU telemedicine financial outcomes. Chest. 2017;151(2):286–97.
10. Wong DT, Kamming D, Salenieks ME, et al. Preadmission anesthesia consultation using telemedicine technology: a pilot study. Anesthesiology. 2004;100:1605–7.
11. Mullen-Fortino M, Rising KL, Duckworth J, et al. Presurgical assessment using telemedicine technology: impact on patient efficiency, effectiveness, and patient experience of care. Telemed e-Health. 2019;25(2):137–42.
12. Fiadjoe J, Gurnaney H, Muralidhar K, et al. Anesth Analag. 2009;108(4):1212–4.
13. Collins TA, Robertson MP, Sicoutris CP, et al. Telemedicine coverage for post-op ICU patients. J Telemed Telecare. 2017;23(2):360–4.
14. Koenig M. Telemedicine in the ICU. Cham, Switzerland: Springer; 2019.
15. Interstate Medical Licensure Compact. https://imlcc.org. Accessed 25 March 2020.
16. Galvez JA, Rehman MA. Telemedicine in anesthesia. Curr Opin Anaesthesiol. 2011;24(4):459–62.
17. Centers for Medicare & Medicaid Services. Medicare Learning Network Booklet: Telehealth Services. https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNProducts/downloads/TelehealthSrvcsfctsht.pdf. Accessed 25 March 2020.
18. Health Resources & Services Administration. Medicare Telehealth Payment Eligibility Analyzer. https://data.hrsa.gov/tools/medicare/telehealth Accessed 25 March 2020.
19. Center for Connected Health Policy. State Telehealth Laws & Reimbursement Policies (Fall 2019). https://www.cchpca.org/sites/default/files/2019-10/50%20State%20Telehealth%20Laws%20and%20Reibmursement%20Policies%20Report%20Fall%202019%20FINAL.pdf. Accessed 25 March 2020.

10 Endoscopic Lung Volume Reduction Surgery: Anesthetic Challenges

Christopher Potestio, Karen Baddoura, Bhavi Patel, and Wissam Abouzghieb

Learning Points

- Even with successful control of symptoms with pharmacologic agents, COPD patients are known to have impaired quality of life which worsens over time. Lung Volume Reduction can improve pulmonary function, exercise capacity, and quality of life in patients with severe COPD and emphysema.
- Endoscopic Lung Volume Reduction is superior to the surgical approach because it limits the risk of postoperative pulmonary complications due to thoracotomy.
- General Anesthesia and Monitored Anesthesia Care are both acceptable anesthetic techniques for Endoscopic Lung Volume Reduction. If considering General Anesthesia, the anesthesiologist must weigh the benefits of controlled minute ventilation and reliable oxygen delivery against the risk of postoperative respiratory failure and prolonged mechanical ventilation.
- The most common postoperative complication after Endoscopic Lung Volume Reduction is pneumothorax. Most pneumothoraces occur in the first 48 h after the procedure, but have been described as late as 6 days post procedure.
- Endobronchial Valve deployment can also lead to COPD exacerbation, hemoptysis, and, rarely, valve migration. Any respiratory symptoms following Endobronchial Lung Volume Reduction with Endobronchial Valve should be investigated immediately with chest x-ray.

Introduction

Emphysema is defined as abnormal, permanent enlargement of air spaces distal to the terminal bronchioles, accompanied by the destruction of their walls and without obvious fibrosis [1]. Loss of elastic tissue leads to airway collapse and gas trapping in addition to impaired gas exchange in damaged acinar structures. The disease falls under the umbrella term "chronic obstructive pulmonary disease" (COPD) which also includes chronic bronchitis.

COPD is a leading cause of disability and death. The World Health Organization (WHO) estimates that 210 million people worldwide suffer from COPD and that COPD has led to approximately 5% of all deaths globally [2]. The majority of cases of COPD are the result of

C. Potestio (✉)
Division of Critical Care Medicine, Department of Anesthesiology, Cooper University Hospital, Camden, NJ, USA
e-mail: potestio-christopher@cooperhealth.edu

K. Baddoura
Department of Anesthesiology, Icahn School of Medicine, St. Lukes Roosevelt, New York, NY, USA

B. Patel · W. Abouzghieb
Department of Pulmonary Medicine, Cooper University Hospital, Camden, NJ, USA

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_10

cumulative destruction of lung tissue by tobacco smoke or other risk factor exposure.

COPD is a progressive disease – symptoms and clinical measures of disease activity increase over time [1]. Treatment options include smoking cessation, inhaled bronchodilators, pulmonary rehabilitation, annual influenza vaccination, and oxygen therapy. None of these therapies are curative, and none lead to significant reverse the disease process. Treatment strategy focuses on mitigating symptoms to allow for improved quality of life. Even with successful control of symptoms with pharmacologic agents, COPD patients are known to have impaired quality of life which worsens over time [3].

Emphysema can occur throughout the lung fields, but patients with predominantly upper lobe disease may benefit from lung volume reduction surgery [4]. Despite the clear benefit of lung volume reduction in patients with heterogeneous upper lobe emphysema and reduced exercise capacity, enthusiasm for the surgical management of patients with emphysema has remained low. COPD patients undergoing thoracic surgery are at high risk for postoperative pulmonary complications, which leads to increased post-operative mortality and an inherent degree of skepticism in the minds of surgeons [5].

Endobronchial Lung Volume Reduction: Mitigating Risk in a Vulnerable Population

Endobronchial lung volume reduction (ELVR) is an attractive option for COPD patients with significant emphysema because it offers a less invasive approach with superior recovery compared to LVRS. In fact, ELVR has been shown to improve pulmonary function, exercise capacity, and quality of life in patients with severe emphysema in any lobe of the lung and its benefit is not limited to upper lobe emphysema like SLVR [6]. ELVR with EBV has also been demonstrated to provide meaningful benefits of improved pulmonary function, exercise capacity, and quality of life in patients with both heterogeneous [7] and homogeneous emphysema [8].

Endobronchial valve (EBV) insertion is the most widely used procedure for ELVR procedures because of high success rate, ease of use, and low rate of complication compared to other endobronchial options. Although not discussed in this chapter, endobronchial coils, polymer sealants, and hot water vapor can be used for ELVR.

Endobronchial valves are inserted via fiberoptic bronchoscope into bronchi that lead to the most emphysematous part of the lung [5]. These are one-way valves that block inspired air from entering the portion of the lung distal to the valve. Over time, air and secretions leave during expiration, leading to local collapse of lung tissue and decreased gas trapping. Decreasing the volume in the most effected parts of the lung improves lung mechanics – it allows for increased overall lung elasticity and promotes healthier regions to expand and function more effectively [9]. Figure 10.1 depicts EBV insertion in a bronchus.

In the LIBERATE Trial, a multicenter randomized control trial, subjects who received EBV had significantly better pulmonary function at 12 months—48% of subjects had an improvement in FEV_1 greater than 15% compared to only 17% of subjects in the control group. Subjects receiving EBV also had an improvement in their 6-min walk test by 40 m [10].

While there are risks of endobronchial procedures, these risks are typically lower than the risks encountered during open thoracic surgery. The purpose of this chapter is to understand the preoperative aspects related to anesthesia, anesthetic management, intraoperative complications and postoperative challenges of ELVR.

Paranesthesia Evaluation with Reference to Emphysema

Patients with emphysema often suffer from a process of dynamic hyperinflation – easily collapsible airways result in significant air trapping. This air trapping makes the thorax less compli-

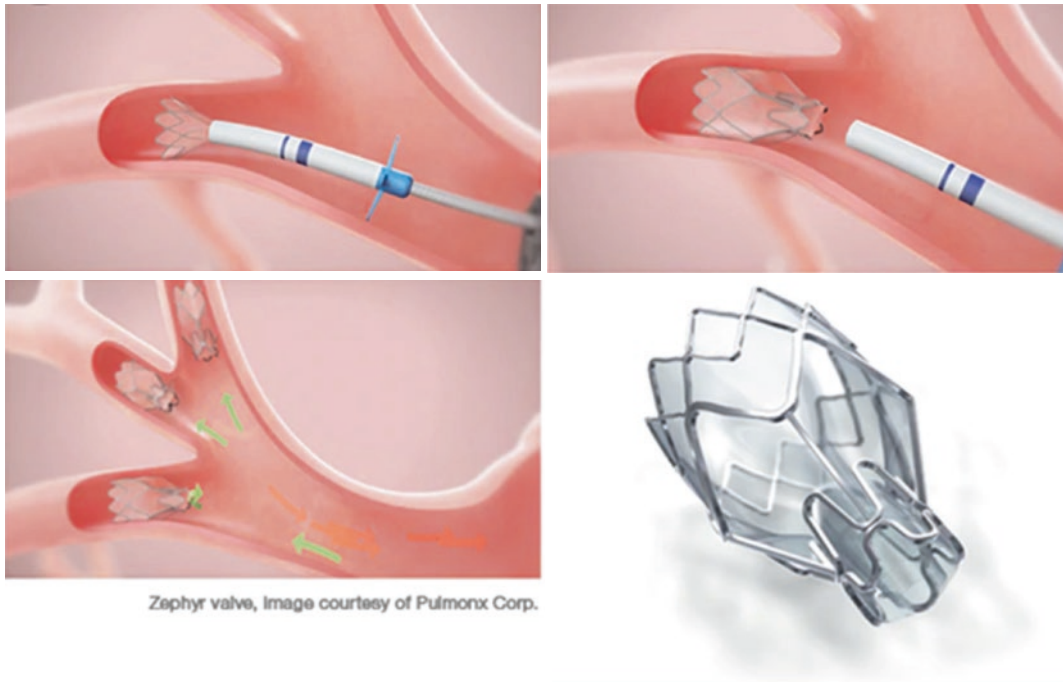


Fig. 10.1 Endobronchial valve placement. (**a**, **b**) Deployment of endobronchial valve in target bronchus. (**c**) Airflow directed to ipsilateral lobe. (**d**) Cage-like structure of deployed endobronchial valve

ant, and it becomes unable to respond to normal changes in lung volume during work of breathing. Air trapping is defined as increased residual volume and increased ratio of residual volume to total lung capacity. It is associated with the development of intrinsic positive end-expiratory pressure (PEEP). Air trapping and intrinsic PEEP lead to elevated expiratory airway resistance, expiratory airflow limitation, reduced elastic recoil, and diminished expiratory time due to increased ventilator rates. The combined effect of air trapping can lead to hypoxemia, hypercarbia, and severely limit exercise capacity and quality of life.

The diagnosis of COPD relies on spirometry, namely the ratio of post-bronchodilator forced expiratory volume in 1 s (FEV_1) to forced vital capacity (FVC). If this ratio (FEV_1/FVC) is less than 0.7, the patient has COPD and can be stratified into four categories from mild to very severe disease based on the magnitude of decrease of this ratio [11]. Because ELVR works by reducing lung hyperinflation, it is important to select for patients with hyper-inflated lungs. Patients are selected for ELVR according to generally agreed upon spirometry criteria—hyperinflation with residual volume >175% of predicted, and forced expiratory volume <50% of predicted [6].

In assessing risk for a patient undergoing anesthesia, the FEV_1/FVC ratio can be a useful marker of disease because it correlates with the degree of physical limitation and frequency of COPD exacerbations, although individual variation in symptom severity is to be expected. Exacerbations occur more frequently as the disease gets worse in most patients [12].

Exercise capacity is an important variable when assessing patients for ELVR. Patients with a 6-min walk distance (6MWD) between 100 and 500 m should be considered for EBV treatment. In patients with 6MWD below 200 m, reassessment should be considered after pulmonary rehabilitation [6]. Patients with severe hypercapneia (>60 mm Hg on room air) and/or severe hypoxemia (<45 mm Hg on room air) should be excluded from EBV treatment [6]. Noninvasive ventilation strategies may improve these numbers, especially the hypercapnia, so reassessment

after a trial of noninvasive ventilation is warranted.

There must be very little collateral ventilation for the procedure to be successful. The EBV will only be successful if it blocks the only pathway for inspired air. If the target segment of the lung received collateral ventilation from other bronchi, the procedure will be ineffective. Endobronchial flow catheters allow for precise measurement of the amount of collateral ventilation. These systems consist of a balloon catheter attached to a sensor. The balloon catheter is inserted into the bronchus of interest and inflated. The sensor then measures expiratory flow over time. If significant collateral ventilation is present, expiratory flow will persist despite balloon inflation limiting inspiratory flow. Quantitative CT analysis may be an alternative method for assessing collateral ventilation [13]. With quantitative CT, it patients have complete fissure integrity >80%, they can be screened in for further analysis or can be considered for ELVR.

Anesthesia Management

General anesthesia with endotracheal intubation and monitored anesthesia care (MAC) using sedation together with airway topicalization have both been described for these procedure [7, 14]. MAC confers the benefit of avoiding intubation. In patients with advanced COPD and emphysema, avoiding intubation and prolonged intubation may be the most important anesthetic concern so should be weighed heavily in assessing risk of anesthesia.

Dexmedetomidine is an appropriate choice for anesthetic as it will produce moderate level of sedation and the patient's respiratory drive will remain intact to facilitate recovery. Dexmedetomidine does not inhibit airway reflexes, so it must be used in conjunction with intravenous opioids or topical local anesthetic to ensure relaxation of vocal cords and pharyngeal muscles. Note that using opiates as part of your anesthetic plan may negate the benefit of using dexmedetomidine to maintain the patient's respiratory drive.

Ketamine, like dexmedetomidine, allows for moderate sedation with intact respiratory drive. Propofol will allow titration to a deep level of anesthesia which may help blunt airway reflexes, and may also maintain hypoxic pulmonary vasoconstriction [15], but using propofol adds the risk of respiratory depression during the case and in recovery.

Remifentanil infusion may be used to reduce the amount of anesthetic required. It can be administered in large doses without risk of accumulation and minimal effect on respiratory depression [14].

One downside to using MAC anesthesia is the inability to control minute ventilation in a spontaneously breathing patient. Many patients with severe COPD and chronic hypoxemia are at risk of World Health Organization Group III pulmonary hypertension. Respiratory acidosis may exacerbate pulmonary hypertension and increase risk of pulmonary hypertensive crisis.

General anesthesia (GA) via endotracheal tube (ETT) is an appropriate mode of anesthesia as well, although total intravenous anesthesia (TIVA) is the preferred maintenance strategy because of circuit leak during bronchoscopy. A secure ETT allows for paralysis during the case, which improves procedural conditions and makes it easier to deploy EBV. GA via ETT may also decrease the risk of endobronchial bleeding and pneumothorax that result from bronchoscope manipulation. If paralysis is used, sugammadex is the preferred reversal agent. These cases are short and may end before even one halflife of a nondepolarizing muscle relaxant such as rocuronium. Sugammadex allows for quick reversal and prevents residual neuromuscular blockade in these patients with compromised baseline respiratory function.

GA with supraglottic airway plus/minus the addition of paralytic may be used. This technique offers similar bronchoscopic conditions without needing to intubate. However, without a secure airway, repeated bronchoscopy may lead to trauma of the vocal cords and surrounding structures, or even displacement of the supraglottic device. These extra risks must be considered when choosing GA with supraglottic airway.

In a single center retrospective review by Thiruvenkatarajan and colleagues, 22 consecutive patients underwent ELVR, 10 patients received MAC anesthesia, with only one patient requiring conversion to general anesthesia due to refractory cough [9]. Of note, $PaCO_2$ trends were similar using both techniques. In this cohort, an increase in the anesthetic times of about 24 min were noted in the MAC group compared with the GA via ETT group (61 vs. 37 min). Though the size of this study is small, the large difference in anesthetic time demonstrates the difficult balance between optimum procedural conditions (blunting airway reflex, preventing laryngospasm) and maintaining spontaneous ventilation.

Airway topicalization with atomizing devices or nebulization of local anesthesia allows for passage of local anesthesia into the distal tracheobronchial tree. The benefit of suctioning must be weighed against the risk of causing airway edema and mucosal bleeding, both of which can affect the valve sizing judgements [6]. An antisialagoge such as glycopyrrolate may be considered preoperatively to prevent excessive secretions. An antisialagogue also prevents topical anesthesia from becoming diluted by secretions.

Pneumothorax

Pneumothorax is the most common complication of ELVR. Patients receiving EBVs are at particular risk for pneumothorax because, when the valve is deployed, inspired air is suddenly shunted to lobes adjacent to the target lobe, thus causing a sudden increase in volume and pressure in those lobes.

Pneumothorax can occur immediately, in the operating room or PACU and can be devastating, requiring emergent decompression with a chest tube or even needle thoracostomy. Incidence of pneumothorax is 15–25%. Approximately 80% occur in the first 48 h, but they can occur up to 6 days post-procedure [16, 17]. Post procedure bed rest and cough reduction may help decrease the incidence of pneumothorax [18]. Patients showing significant volume reduction on post procedure chext x-ray may be at an increased risk [6].

The occurrence of pneumothorax following ELVR with EBV usually involves the untreated ipsilateral lobe. It is hypothesized that the ipsilateral lobe expands into the space once occupied by the collapsed lobe [19]. Considering this potential mechanism for injury, the larger the target lobe, the more potential for pneumothorax. Rupture of blebs or preexisting pleural adhesions in the ipsilateral lung may also increase the risk of pneumothorax.

Respiratory Failure

Respiratory failure requiring prolonged mechanical ventilation is a devastating complication for these patients with poor pulmonary reserve. In a multicenter retrospective review of 423 cases of ELVR, 6 patients (1.4%) developed periprocedural respiratory failure [20]. This review demonstrates the safety of ELVR and the importance of patient selection. For patients with severe COPD, any procedure poses the risk of respiratory failure, let alone a procedure in the thorax.

COPD Exacerbation

After valve placement, up to 20% of patients can manifest acute bronchitis, pneumonia and/or lung infections within the first 3 months of the procedure [20]. Prophylactic antibiotics are often prescribed to prevent bacterial infection, and a short course of oral steroids may prevent COPD exacerbation.

Hemoptysis

Hemoptysis is a risk of any endobronchial procedure, especially during deployment of EBVs which can cause irritation to the mucosa. Hemoptysis occurs in approximately 2% of cases [20]. It can be minor due to granuloma formation,

requiring pharyngeal suctioning or major bleeding that may require embolization to stop the bleeding.

Valve Migration

Valve migration is rare, but should be suspected when a patient has an acute onset of coughing and/or dyspnea. If suspicion is high, CT scan and/or bronchoscopy is adequate to evaluate for valve migration and misplacement. The displaced valve should be removed and replaced immediately. Valve migration is more likely to occur if the initial valve has been seated incorrectly or is undersized.

Conclusions

Lung volume reduction for patients with severe COPD and emphysema can improve respiratory function and quality of life. ELVR is a superior technique to surgical LVR because it avoids the surgical incisions and postoperative pain. In patients at risk for postoperative respiratory failure, MAC is appropriate, although in patients with history of pulmonary hypertension, GA will allow the anesthesia provider better control of minute ventilation and more reliable oxygen delivery, thus decreasing risk of pulmonary hypertension crisis.

Funding and Conflicts of Interest
None

References

1. Kemp SV, Polkey MI, Shah PL. The epidemiology, etiology, clinical features, and natural history of emphysema. Thorac Surg Clin. 2009;19(2):149–58.
2. World Health Organization. Chronic obstructive pulmonary disease (COPD) fact sheet. World Health Organization. [Nov. 2017] http://www.who.int/en/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd).
3. Naunheim KS, Wood DE, Mohsenifar Z, Sternberg AL, Criner GJ, DeCamp MM, Deschamps CC, Martinez FJ, Sciurba FC, Tonascia J, Fishman AP. Long-term follow-up of patients receiving lung-volume-reduction surgery versus medical therapy for severe emphysema by the National Emphysema Treatment Trial Research Group. Ann Thorac Surg. 2006;82(2):431–43.
4. National Emphysema Treatment Trial Research Group. A randomized trial comparing lung-volume–reduction surgery with medical therapy for severe emphysema. N Engl J Med. 2003;348(21):2059–73.
5. Jarad N. Clinical review: Endobronchial valve treatment for emphysema. Chron Respir Dis. 2016;13(2):173–88.
6. Slebos DJ, Shah PL, Herth FJ, Valipour A. Endobronchial valves for endoscopic lung volume reduction: best practice recommendations from expert panel on endoscopic lung volume reduction. Respiration. 2017;93(2):138–50.
7. Davey C, Zoumot Z, Jordan S, McNulty WH, Carr DH, Hind MD, Hansell DM, Rubens MB, Banya W, Polkey MI, Shah PL. Bronchoscopic lung volume reduction with endobronchial valves for patients with heterogeneous emphysema and intact interlobar fissures (the BeLieVeR-HIFi study): a randomised controlled trial. Lancet. 2015;386(9998):1066–73.
8. Valipour A, Slebos DJ, Herth F, Darwiche K, Wagner M, Ficker JH, Petermann C, Hubner RH, Stanzel F, Eberhardt R. Endobronchial valve therapy in patients with homogeneous emphysema. Results from the IMPACT Study. Am J Respir Crit Care Med. 2016;194(9):1073–82.
9. Thiruvenkatarajan V, Maycock T, Grosser D, Currie J. Anaesthetic management for endobronchial valve insertion: lessons learned from a single centre retrospective series and a literature review. BMC Anesthesiol. 2018;18(1):1–8.
10. Criner GJ, Sue R, Wright S, Dransfield M, Rivas-Perez H, Wiese T, Sciurba FC, Shah PL, Wahidi MM, de Oliveira HG, Morrissey B. A multicenter randomized controlled trial of Zephyr endobronchial valve treatment in heterogeneous emphysema (LIBERATE). Am J Respir Crit Care Med. 2018;198(9):1151–64.
11. Vestbo J, Hurd SS, Agustí AG, Jones PW, Vogelmeier C, Anzueto A, Barnes PJ, Fabbri LM, Martinez FJ, Nishimura M, Stockley RA, Sin DD, Rodriguez-Roisin R. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med. 2013;187:347–65.
12. Hurst JR, Vestbo J, Anzueto A, Locantore N, Müllerova H, Tal-Singer R, Miller B, Lomas DA, Agusti A, MacNee W, Calverley P. Susceptibility to exacerbation in chronic obstructive pulmonary disease. N Engl J Med. 2010;363(12):1128–38.
13. Schuhmann M, Raffy P, Yin Y, Gompelmann D, Oguz I, Eberhardt R, Hornberg D, Heussel CP, Wood S, Herth FJ. Computed tomography predictors of response to endobronchial valve lung reduction treatment. Comparison with Chartis. Am J Respir Crit Care Med. 2015;191(7):767–74.

14. Hillier JE, Toma TP, Gillbe CE. Bronchoscopic lung volume reduction in patients with severe emphysema: anesthetic management. Anesth Analg. 2004;99(6):1610–4.
15. Van Keer L, Van Aken H, Vandermeersch E, Vermaut G, Lerut T. Propofol does not inhibit hypoxic pulmonary vasoconstriction in humans. J Clin Anesth. 1989;1(4):284–8.
16. Gompelmann D, Herth FJ, Slebos DJ, Valipour A, Ernst A, Criner GJ, Eberhardt R. Pneumothorax following endobronchial valve therapy and its impact on clinical outcomes in severe emphysema. Respiration. 2014;87(6):485–91.
17. Skowasch D, Fertl A, Schwick B, Schäfer H, Hellmann A, Herth FJ. LIVE Study Investigators. A Long-Term Follow-Up Investigation of Endobronchial Valves in Emphysema (the LIVE Study): study protocol and six-month interim analysis results of a prospective five-year observational study. Respiration. 2016;92(2):118–26.
18. Herzog D, Poellinger A, Doellinger F, Schuermann D, Temmesfeld-Wollbrueck B, Froeling V, Schreiter NF, Neumann K, Hippenstiel S, Suttorp N, Hubner RH. Modifying post-operative medical care after EBV implant may reduce pneumothorax incidence. PLoS One. 2015;10(5):e0128097.
19. Valipour A, Slebos DJ, De Oliveira HG, Eberhardt R, Freitag L, Criner GJ, Herth FJ. Expert statement: pneumothorax associated with endoscopic valve therapy for emphysema-potential mechanisms, treatment algorithm, and case examples. Respiration. 2014;87(6):513–21.
20. Fiorelli A, D'Andrilli A, Bezzi M, Ibrahim M, Anile M, Diso D, Cusumano G, Terminella A, Luzzi V, Innocenti M, Novali M. Complications related to endoscopic lung volume reduction for emphysema with endobronchial valves: results of a multicenter study. J Thoracic Dis. 2018;10(Suppl 27):S3315.

Anesthesia for Brachytherapy

11

Susanne IJmkers, Wouter Morshuis, and Eilish M. Galvin

Learning Points

- There are various brachytherapy treatment modalities which differ in length of treatment and degree of postoperative discomfort.
- A thorough preoperative assessment should be made with regards to comorbidity, hematologic and cardiac status post chemotherapy and the use of anticoagulant or antiplatelet agents.
- Neuraxial techniques are recommended for lower body brachytherapy, aside from providing periprocedural anesthesia they facilitate adequate pain relief during transportation and radio imaging. Catheter techniques can be used for prolonged analgesia.
- An image guided brachytherapy treatment session can take place in multiple locations. Close collaboration between anesthesiologist and radiation specialist is required to assure optimal care and workflow.

Introduction

Radiation therapy is an important treatment modality in the treatment of cancer since it was introduced over a century ago. Radiation therapy uses energy to damage cellular DNA which causes necrosis of the targeted cells. With both normal cells and cancer cells being affected by radiation there is a therapeutic challenge to gain tumor control while minimizing the risk of radiation induced complications in the normal tissue.

Brachytherapy, also known as internal radiation therapy (IRT), is a treatment where radioactive sources are placed within or close to the tumor as opposed to external beam radiation therapy (ERT) where the source is of radiation is externally projected onto the body. It allows for delivery of high doses of radiation with low penetrability, thus protecting the surrounding healthy tissue. Brachytherapy can be used as part of a multimodal cancer treatment regime or as a single treatment either with curative of palliative intent and can be used in patients unfit for major surgery or chemotherapy. With a decline in its use in the 1950s, novel techniques have made clinicians regain interest in in the use of brachytherapy in recent decades. Introduction of remote after-loading of catheters or applicators have reduced exposure hazard to practitioners. Innovative imaging modalities and treatment planning systems have assisted in positional accuracy allowing superior dose delivery. Brachytherapy has a defined role in the treatment of prostate cancer, gynaecologic malignancies, breast cancer, head and neck cancer, oesophageal cancer, bronchial cancer, bile duct cancer, penile cancer and skin cancer. It is also used in rarer

S. IJmkers · W. Morshuis · E. M. Galvin (✉)
Department of Anesthesiology, Erasmus Medical Center, Rotterdam, The Netherlands
e-mail: s.ijmkers@erasmusmc.nl; w.morshuis@erasmusmc.nl; e.galvin@erasmusmc.nl

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_11

types of cancer for example uveal cancer or soft tissue sarcoma [1].

Brachytherapy can be characterized by the duration of irradiation; radioactive sources may be placed permanently or temporarily. Permanent radioactive sources or seeds, are usually the size of a grain of rice and emit a low dose which travel only a few millimeters into the surrounding tumor tissue. Radioactive decay causes the seeds to become inactive while they remain in the treatment area. Temporary irradiation requires the placement of a non-radiating applicator or a number of small flexible catheters which after confirmation of correct placement with radio imaging, can be loaded with the radiation source. Placement of permanent seeds or a temporary applicator can be painful; therefore, the anesthesiologist has a vital role to play in brachytherapy treatment, enabling safe and optimal radiation source placement and contributing to patient satisfaction. With rising cancer incidence rates worldwide, there will be an increasing demand for anesthetic support whilst performing brachytherapy.

In this chapter, we will describe the anesthetic challenges for patients receiving brachytherapy and provide guidance for the anesthetic management for the most common types of brachytherapy.

General Anesthetic Management

Preoperative Evaluation

Brachytherapy can either be a first line treatment or can be used as a last resort in patients deemed unfit for other treatment modalities. Due to the variety of indications for brachytherapy, the patient population is heterogeneous. Each type of malignancy usually has its characteristic patient population with specific ranges in age and comorbidities [2].

A thorough preoperative assessment is indicated, including a full patient medical history, allergies and medication use, giving special considerations to cancer specific comorbidities. Patients with malignancies have an increased risk of developing thromboembolic complications and may use anticoagulants. Locally advanced or metastatic cancer can lead to loss of organ function, frailty due to weight loss, fractures, pain, infection and physical impairment. Patients who are being treated with concurrent chemotherapy may suffer from a wide variety of side effects, e.g. fatigue, nausea, vomiting, weight loss, dehydration, easy bruising and infection. Additional testing may be required such as laboratory testing to asses renal and hepatic function in addition to bone marrow activity. Some chemotherapeutic regimes require cardiac and/or pulmonary function tests to identify potential negative impact on these systems.

Procedure

As mentioned previously, brachytherapy is a treatment modality where a radioactive source is placed either in (interstitial) or near (intracavitary) a tumor. With intracavitary brachytherapy an applicator is placed in a pre-existing anatomical or surgical cavity. With interstitial brachytherapy, hollow needles are placed within the tumor and surrounding tissue, these needles the hold either radioactive seeds or temporary flexible catheters. Placement of these applicators or needles is usually performed in the operating theatre under some form of anesthetic management. After placement there is need to verify the correct position, usually with additional imaging. In some cases, this may require transport of the patient outside of the operating theatre for a CT or MRI scan. Catheter tubes placed in the tumor tissue are usually well secured in contrast to the applicator which requires gauze packing to maintain correct positioning. After confirming correct position, the catheters or applicator can be afterloaded with a radiation source.

Radiation sources can differ in intensity in general we distinguish two modalities: high dose rate and low dose rate. When using high dose radiation, the radiation session usually takes several minutes, after which the radiation source is removed. Following radiation treatment, the applicator or catheters can either be removed or

left in place for one or several concessive radiation treatments in the follow hours or days. Depending on the site of placement this may require immobilization to maintain correct positioning. In low dose radiation, a weak radiation source is placed in the catheters or applicator; the radiation can take from several hours to days. Some brachytherapy sessions are repeated weekly. National treatment guidelines and local facilities infrastructure make brachytherapy treatment variable between institutions.

From an anesthesia view point, brachytherapy is considered a low risk intervention and safe for patients with significant co-morbidities. Immediate complications following applicator positioning are rare and include mild bleeding at the applicator site. Hemorrhage requiring intervention is extremely rare.

Anesthetic Technique

To determine the optimal anesthetic technique there are multiple considerations to take into account. Firstly, patients may be unsuitable for specific anesthetic techniques due to comorbidities or medication use (e.g. use of anticoagulants), so a thorough preoperative assessment as mentioned previously is crucial.

Second, the target area and the type of brachytherapy technique that is to be used are important in determining the anesthetic approach. Upper body treatments are less suitable for regional techniques as opposed to lower body treatments where both regional/neuro-axial and general anesthesia can be used. Interstitial brachytherapy techniques are usually more painful compared to intracavitary tube placement; an important factor when deciding on postoperative pain management in the gynecologic setting. Length of the procedure (placement of the brachytherapy device) is important to determine whether a single shot neuraxial technique or a catheter technique is most suitable [3].

Third, if additional post placement imaging is necessary patients will generally need to be transported to other departments; depending on local hospital infrastructure this may present anesthetic challenges and can be time consuming. While the applicator is in place there is a need for analgesia and sometimes immobilization to maintain correct positioning of the applicator. Patient monitoring and access while in the MRI and/or radiotherapy room also present unique challenges.

Last but not least, patients often need multiple therapy sessions, so a positive patient experience is of utmost importance for treatment completion, therefore making the brachytherapy sessions as comfortable and non-traumatic as possible, while maintaining anesthesia safety is an important goal. Taking into account patients' wishes and respecting their autonomy is an essential element in compliance.

Monitoring

Pulse oximetry (SpO_2), noninvasive blood pressure, electrocardiography (ECG) and temperature are regarded as standard monitoring. For both general anesthesia and procedural sedation/analgesia capnometry is crucial. Additional monitoring may vary depending on specific procedures and comorbidities. Of course, when providing anesthesia for magnetic resonance imaging (MRI), compatible anesthetic equipment is needed.

Postoperative Management

Applicators, especially those used in gynecologic malignancies, cause discomfort while in situ. We recommend a well thought out pain management plan when the applicator remains in site for a longer period of time. Depending on patient factors and location of the procedure, regional catheter techniques, oral opioids or patient-controlled analgesia can be considered. Once the applicators are removed, pain is usually mild. Significant discomfort may also occur due to in bed immobilization in prostate brachytherapy.

Common Brachytherapy Indications and Anesthesia Management

Prostate Cancer

The two most used treatment modalities in brachytherapy for prostate cancer are permanent seed placement and high dose rate brachytherapy. Permanent seed placement is often used in localized prostate cancer. High dose rate brachytherapy is most commonly used in combination with external beam radiation to escalate radiation dose in intermediate to high risk prostate cancer [4, 5]. Patients are mostly older men with age correlated comorbidities. Both procedures are performed in lithotomy position using direct trans anal ultrasound, additional imaging is usually not required. In permanent seed placement a few dozen grain like radiation sources are placed through the perineum directly into the prostate. Operating time is approximately 90 min. The procedure can be performed under either general or single shot spinal anesthesia. These seeds are so small that they seldom cause postoperative discomfort.

In high dose rate brachytherapy 12–20 thin nylon catheters are placed through the perineum into the prostate (Photo 11.1). A radioactive source, usually iridium-192 or cecium-137, is placed in the catheters for the duration of several minutes, after which the radioactive source is removed. Usually, 1–4 radiation treatments are done over a period of 2 days with the catheters remaining in situ until treatment completion. Placement of the catheters may be performed under general or neuraxial anesthesia [2]. If the catheters are removed after only one radiation treatment, general anesthesia or single shot spinal anesthesia suffices. However, adequate analgesia is required when the catheters remain in place due to discomfort. This can be achieved with neuraxial catheter techniques such as a combined spinal epidural (CSE), however, in our experience, discomfort is usually due to bed confinement and the presence of a urinary catheter and is frequently well managed with oral analgesics. While there is a lack of comparative studies, a combination of paracetamol, oral or intravenous opioids and antispasmodics appear to be sufficient for the postoperative period while the catheters are in place [6]. Epidural catheters may be reserved for patients with contraindications to opioid use.

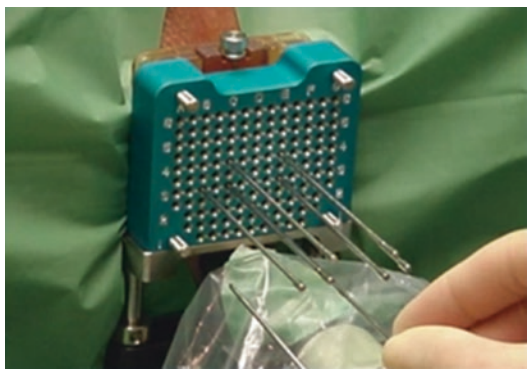


Photo 11.1 Prostate Brachytherapy applicator example

Gynecologic Cancer

In gynecologic oncology, brachytherapy is mostly used in cervical carcinoma and rarer in endometrial carcinoma and vulvar carcinoma. With a decreasing incidence in first world countries since the start of screening programs cervical cancer is still very common in developing countries [7]. Brachytherapy is a vital component in the treatment of local and locally advanced cervical cancer [8]. It can be used as monotherapy or in conjunction with external beam radiation, chemotherapy and hyperthermia. Brachytherapy has shown in multiple studies to improve patient survival with cervical cancer [9–12].

Patients with cervical cancer are often relatively young without significant comorbidity (ASA I-II). However, depending on tumor stage they may have been treated with chemotherapy and therefore preoperative assessment of hematological status is necessary.

In contrast to cervical cancer, brachytherapy in endometrial cancer is only used to treat patients unfit for a hysterectomy, which is the treatment of choice for non-metastatic disease stage [13]. Patients with endometrial cancer are usually older (>75 years) and may have significant comorbidities with higher ASA scores (III-IV). In these patients there is a high incidence of hypertension, obesity and diabetes mellitus [14].

Congestive heart failure and thromboembolic diseases are also frequently seen. Cardiac and pulmonary function tests should be performed where indicated.

A range of applicators exist for both malignancies; applicators for cervical cancer have a stabilizer (intrauterine tandem) inserted trans vaginally into the body of the uterus combined with either a vaginal ring, vaginal ovoids or a vaginal cylinder within the cervix (Photo 11.2). Applicators for endometrial cancer are placed solely within the cavity of the uterus and the position is maintained with vaginal gauze packing. Following applicator placement, additional imaging is necessary to confirm correct positioning. MRI-based image guided brachytherapy has become standard of practice in most institutions due to better tumor visualization when compared to CT-scan [15]. Post procedure MRI can be challenging as it requires transport of the patient to another location within the hospital and provision of adequate analgesia is essential.

High dose rate brachytherapy has largely replaced low dose rate in both cervical cancer and endometrial cancer and has the advantages of outpatient treatment [16]. In high dose rate treatments, usually only one radiation session is given over a period of several minutes after which the applicator can be removed. In rarer cases the applicator stays in situ for a second radiation session the next day. Procedure duration for applicator placement, MRI position check and radiation is approximately 300 min, but may vary between institutions depending on local infrastructure [17]. High dose rate brachytherapy is repeated in weekly sessions usually up to 3–4 times, with current techniques requiring applicator placement for each session.

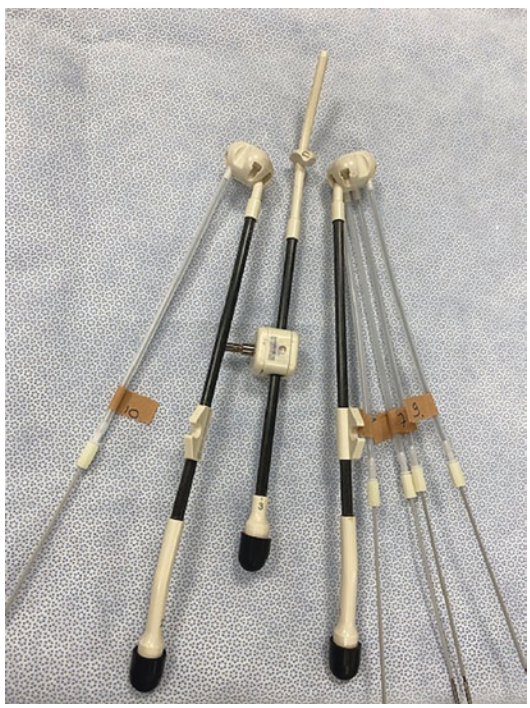


Photo 11.2 Gynecological Brachytherapy applicator example

For the choice of anesthetic technique, anesthesiologists should be aware that placement of the applicator is extremely painful. Uterine fundus and body stimulation result in stimulation of sympathetic afferent nerves from T10-L1. Cervical and vaginal distention cause stimuli to S2-4 parasympathetic afferent fibers, vaginal packing stimulates somatic pudendal nerve fibers. When performing neuro axial techniques, sensory nerve block should cover these areas. Insufficient analgesia may lead to discomfort in patients, while in the lithotomy position (image 1) causing movement leading to suboptimal applicator placement or interruption of the treatment session.

Neuro axial techniques have the advantage of providing postoperative analgesia during patient transport and radio imaging. A meta-analysis performed in 2020 found neuraxial techniques showed improved pain control, decreased opioid consumption and a similar rate of anesthesia complications when compared to general anesthesia [3]. The neuraxial techniques studied were spinal, epidural and combined spinal epidural, and there was no difference in discharge times. Often, patients receiving single shot spinal anesthesia required additional opioid during the hospital admission following wear off of the spinal block. This is also the experience in our hospital where either oral or intravenous opioids are offered via a patient-controlled analgesia device. Regional catheter techniques such as epidural or CSE may be considered, both provide excellent pain relief while the applicator is in situ.

Local anesthesia has been widely used in brachytherapy and although favorable results have been reported in gynecological studies, these were mainly placebo control studies. Even with a significant reduction in visual analogue score, moderate pain still persisted [18]. The frequent use of local anesthesia in some centers may be biased by the fact that medical radiotherapists can perform treatment without the need for anesthesia teams and without the use of hemodynamic monitoring. With high risk of periprocedural discomfort what may cause delay or even cessation of the treatment procedure, it is our opinion that local anesthesia has a limited role to play in present day anesthetic management.

In conclusion, there is a rationale for regional anesthesia for high dose brachytherapy in gynecologic malignancies. Aside from the positive effect on postoperative pain control, it may improve logistics for transportation and imaging. Local hospital infrastructure and the length of time the applicator remains in situ influence the choice between a neuraxial single shot or catheter technique. Local anesthesia may have a place in patients whose medical condition makes them unfit for other anesthetic techniques.

Breast Cancer

Whole breast irradiation following breast conserving surgery is the standard treatment for early stage breast cancer [19]. For selected cases, brachytherapy is used as part of accelerated partial-breast irradiation, which has gained in popularity in recent years due to the shorter treatment duration of just a few days compared to several weeks for whole breast irradiation [20]. There are two treatment modalities for brachytherapy for breast cancer: interstitial brachytherapy and intracavitary brachytherapy [21, 22]. With intracavitary brachytherapy a radiation delivery device is placed in the breast during lumpectomy surgery. With interstitial brachytherapy up to twelve small catheters are placed in the breast a few weeks after breast conserving surgery [23]. Correct placement is conformed using X-ray and ultrasound. Both high and low dose rates are used and catheters/devices remain in the breast for several days.

In terms of demographics, patients are of varying age groups with varying co-morbidities. Chemotherapy is usually given after surgery and radiation, although some patients receive chemotherapy prior to their surgery. The delivery device for intracavitary brachytherapy is placed during lumpectomy surgery under general anesthesia. While the device is in place, non-opioid analgesics usually suffice and removal of the device is not painful. Catheters for interstitial brachytherapy are placed under either general anesthesia or local anesthesia with or without conscious sedation. Choice of anesthetic management may depend on expertise, operating time, comorbidities and local logistics. While the catheters are in place, pain is usually mild and removal does not require anesthetic involvement.

Head and Neck Cancer

Brachytherapy for head and neck cancer can be used as monotherapy, offering a safe alternative for small T1-2 tumors with low risk of metastasis for patients unfit or unwilling to undergo radical surgery. It is also used in combination with external beam radiation or as adjuvant treatment in locally advanced cancer following surgery [24]. Despite relative low incidence in the western civilization, head and neck cancer is very common in South-East Asia and India [25].

Patients with head and neck cancer are usually older and may present with comorbidities related to nicotine and alcohol abuse [26]. Preoperative cardiac and pulmonary assessment is needed, as well as laboratory testing to assess renal and hepatic function. Careful evaluation of the oral cavity is necessary as there is potential for a difficult airway; some cohorts report up to 50% fiberoptic intubation these patients [2].

Patients almost exclusively receive high dose brachytherapy in the form of interstitial treatment. Tumor location can differ ranging from the lips, oral cavity, nasal cavity, nasopharynx or oropharynx. Depending on location, needles can either be placed under local anesthesia or under

general anesthesia. Where a potential difficult airway has been identified, adequate preoxygenation or high flow nasal oxygenation should be administered with a clear plan to secure the airway prior to induction of anesthesia. Endotracheal intubation is mandatory and access route depend on the situation. Due to tissue swelling after irradiation, a surgical tracheostomy may be indicated for specific tumor sites e.g. tongue base with epiglottal involvement [27]. Catheter placement is controlled with radio imaging. Catheters may stay in place up to a week, depending on the radiation treatment protocol [24]. For catheter placement in the oral cavity a nasogastric feeding tube may be required while the catheters are in place. While this may seem highly uncomfortable, pain is usually mild and tolerable with oral analgesics. Postoperative complications include bleeding, pulmonary complications and delirium, the latter may be related to thiamin deficiency [28].

Esophageal Cancer

Intraluminal brachytherapy for esophageal cancer can be used as a sole treatment or as a boost following external beam radiotherapy (EBRT) to improve local control in the curative setting [29]. It is also used as palliative care to reduce symptoms such as dysphagia, stenosis or tumor hemorrhage [30]. Compared to stent implantation, brachytherapy has longer lasting effects on health-related quality of life and dysphagia scores. Patients are frequently men above 60 years of age, and may have risk factors such as nicotine and alcohol abuse [31]. Cardiovascular comorbidities are more common in patients with esophageal cancer compared to patients with other malignancies. In the preoperative evaluation, thorough cardiac and pulmonary assessment is indicated. Patients often have an increased risk of aspiration due to gastroesophageal reflux disease, dysphagia or post esophageal resection.

Patients almost exclusively receive high dose brachytherapy. During endoscopy, tumor borders are marked with metal clips and the applicator is inserted over a guide wire followed by a CT scan. The procedure causes discomfort, but pain is limited and procedural sedation and analgesia usually suffices [29]. The challenge is to keep the patient spontaneously breathing with intact airway reflexes under sufficient sedation levels. Postprocedural, pain is usually mild.

Conclusion

Brachytherapy may be provided for a variety of different cancers and circumstances. Over time, techniques of radiotherapy delivery and regimes have evolved as has the heterogeneity of the patient population. While considered a low risk procedure from an intervention view point, patients may have complex comorbidities requiring careful anesthesia assessment and management. General, sedation and regional anesthesia may be used depending on the area undergoing treatment. Anesthesia care in the radiological department and/or during transport is frequently required. Discomfort or pain while the applicator devices remain in situ is common and requires careful attention to help ensure patient satisfaction and success of the brachytherapy treatment especially where treatments are recurrent.

Funding and Conflicts of Interest

None

References

1. Skowronek J. Current status of brachytherapy in cancer treatment—short overview. J Contemp Brachyther. 2017;9(6):581–9.
2. Benrath J, et al. Anaesthesia for brachytherapy--51/2 yr of experience in 1622 procedures. Br J Anaesth. 2006;96(2):195–200.
3. Petitt MS, et al. Anesthetic and analgesic methods for gynecologic brachytherapy: a meta-analysis and systematic review. Brachytherapy. 2020;19(3):328–36.
4. Justin EB, et al. Clinically localized prostate cancer: ASCO Clinical Practice Guideline Endorsement of an American Urological Association/American Society for Radiation Oncology/Society of Urologic Oncology Guideline. J Clin Oncol. 2018;36(32):3251–8.
5. Sanda MG, et al. Clinically localized prostate cancer: AUA/ASTRO/SUO Guideline. Part I: risk stratification, shared decision making, and care options. J Urol. 2018;199(3):683–90.

6. Doyle CA, Loadsman JA, Hruby G. An audit of analgesia requirements for high-dose-rate prostate brachytherapy. Anaesth Intensive Care. 2008;36(5):707–9.
7. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. CA Cancer J Clin. 2019;69(1):7–34.
8. Holschneider CH, et al. Brachytherapy: a critical component of primary radiation therapy for cervical cancer: from the Society of Gynecologic Oncology (SGO) and the American Brachytherapy Society (ABS). Brachytherapy. 2019;18(2):123–32.
9. Karlsson J, et al. Differences in outcome for cervical cancer patients treated with or without brachytherapy. Brachytherapy. 2017;16(1):133–40.
10. Logsdon MD, Eifel PJ. Figo IIIB squamous cell carcinoma of the cervix: an analysis of prognostic factors emphasizing the balance between external beam and intracavitary radiation therapy. Int J Radiat Oncol Biol Phys. 1999;43(4):763–75.
11. Tanderup K, et al. Curative radiation therapy for locally advanced cervical cancer: brachytherapy is NOT optional. Int J Radiat Oncol Biol Phys. 2014;88(3):537–9.
12. Viswanathan AN, et al. Increasing brachytherapy dose predicts survival for interstitial and tandem-based radiation for stage IIIB cervical cancer. Int J Gynecol Cancer. 2009;19(8):1402–6.
13. Colombo N, et al. Endometrial cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2013;24 Suppl 6:vi33–8.
14. Chao CK, et al. Brachytherapy-related complications for medically inoperable stage I endometrial carcinoma. Int J Radiat Oncol Biol Phys. 1995;31(1):37–42.
15. Viswanathan AN, et al. Computed tomography versus magnetic resonance imaging-based contouring in cervical cancer brachytherapy: results of a prospective trial and preliminary guidelines for standardized contours. Int J Radiat Oncol Biol Phys. 2007;68(2):491–8.
16. Patankar SS, et al. High versus low-dose rate brachytherapy for cervical cancer. Gynecol Oncol. 2015;136(3):534–41.
17. Frankart AJ, et al. Comparison of spinal and general anesthesia approaches for MRI-guided brachytherapy for cervical cancer. Brachytherapy. 2018;17(5):761–7.
18. Chen HC, et al. Local vaginal anesthesia during high-dose-rate intracavitary brachytherapy for cervical cancer. Int J Radiat Oncol Biol Phys. 1998;42(3):541–4.
19. Early Breast Cancer Trialists' Collaborative Group, et al. Effect of radiotherapy after breast-conserving surgery on 10-year recurrence and 15-year breast cancer death: meta-analysis of individual patient data for 10,801 women in 17 randomised trials. Lancet. 2011;378(9804):1707–16.
20. Strnad V, et al. 5-year results of accelerated partial breast irradiation using sole interstitial multicatheter brachytherapy versus whole-breast irradiation with boost after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: a randomised, phase 3, non-inferiority trial. Lancet. 2016;387(10015):229–38.
21. Dickler A, et al. The MammoSite breast brachytherapy applicator: a review of technique and outcomes. Brachytherapy. 2005;4(2):130–6.
22. Fijuth J. Brachytherapy in breast cancer. J Contemp Brachyther. 2009;1(2):117–20.
23. Strnad V, et al. ESTRO-ACROP guideline: Interstitial multi-catheter breast brachytherapy as Accelerated Partial Breast Irradiation alone or as boost—GEC-ESTRO Breast Cancer Working Group practical recommendations. Radiother Oncol. 2018;128(3):411–20.
24. Kovacs G, et al. GEC-ESTRO ACROP recommendations for head & neck brachytherapy in squamous cell carcinomas: first update—Improvement by cross sectional imaging based treatment planning and stepping source technology. Radiother Oncol. 2017;122(2):248–54.
25. Warnakulasuriya S. Global epidemiology of oral and oropharyngeal cancer. Oral Oncol. 2009;45(4-5):309–16.
26. Shaw R, Beasley N. Aetiology and risk factors for head and neck cancer: United Kingdom National Multidisciplinary Guidelines. J Laryngol Otol. 2016;130(S2):S9–S12.
27. Bhalavat R, et al. High-dose-rate interstitial brachytherapy in head and neck cancer: do we need a look back into a forgotten art—a single institute experience. J Contemp Brachyther. 2017;9(2):124–31.
28. Ghaffar ZA, et al. Brachytherapy of tongue carcinoma in a patient with difficult airway: anesthetic considerations. J Contemp Brachyther. 2018;10(6):573–6.
29. Lettmaier S, Strnad V. Intraluminal brachytherapy in oesophageal cancer: defining its role and introducing the technique. J Contemp Brachyther. 2014;6(2):236–41.
30. Skowronek J, Piotrowski T, Zwierzchowski G. Palliative treatment by high-dose-rate intraluminal brachytherapy in patients with advanced esophageal cancer. Brachytherapy. 2004;3(2):87–94.
31. Zhang Y. Epidemiology of esophageal cancer. World J Gastroenterol. 2013;19(34):5598–606.
32. Perera F, et al. Local resection and brachytherapy confined to the lumpectomy site for early breast cancer: a pilot study. J Surg Oncol. 1997;65(4):263–7; discussion 267–8

12 Anesthesia for Total Pancreatectomy with Islet Cell Autotransplantation (TPIAT)

Fernando Franco Cuadrado, Niekoo Abbasian, and Ximena Soler

Learning Points

- General anesthesia with endotracheal intubation is regarded as the standard of care for TPIAT.
- Postoperative pain management remains as one of the main challenges in the care of TPIAT patients. Although regional techniques have been described, a multimodal approach is common in pediatric patients. Regional techniques may be limited by surgical and patient factors such as goal directed postoperative anticoagulation regimens.
- Intraoperative management requires multiple parallel interventions to optimize long term surgical and intraoperative outcomes. These include CVP management, portal venous pressure monitoring, restrictive glycemic control, MAP goals, as well as anticoagulation administration and monitoring.
- Postoperative pain control requires aggressive treatment and close follow up. Opioid analgesia, adjuvants and opioid sparing techniques have been successfully described in the care of chronic pancreatitis patients. Pain management starts in the operating room and includes a combination of narcotics, ketamine, lidocaine and dexmedetomidine.

F. F. Cuadrado (✉) · N. Abbasian · X. Soler
Department of Anesthesiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA
e-mail: Fernando.cuadrado@cchmc.org; Niekoo.Abbasian@cchmc.org; Ximena.soler@cchmc.org

Introduction

Total pancreatectomy and islet cell transplantation (TPIAT) is indicated for patients with debilitating chronic pancreatitis (CP) refractory to therapy and complicated by chronic abdominal pain. It aims to improve quality of life by removing the pancreas, thought to be the primary source of abdominal pain, the most common indication for surgical intervention. TPIAT results in favorable short term outcomes including reduced opioid use, decreased need for parenteral nutrition with eventual discontinuation of insulin therapy in a number of patients long term [1]. Age dependent differences in outcomes have been observed. Children undergoing TPIAT between ages of 3 and 8 had favorable outcomes in a review of 17 patients by Bellin et al. [2]. Long term follow up (1–11 years after surgery) revealed that the majority of patients achieved resolution of pain, achieved narcotic and insulin independence. In the light of this and similar evidence, early intervention is likely to result in more favorable outcomes due to progressive deterioration of pancreatic function due to chronic inflammation.

Pediatric patients suffering from CP have significantly impaired quality of life compared to healthy patients as measured by health-related quality of life measures [3]. CP in pediatric patients is commonly a progressive disease that leads to significant morbidity when left untreated

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_12

due to poor nutritional intake, inability to participate in physical activity due to chronic pain.

Patients often suffer from CP resistant to multimodal pain management strategies. A number of patients may develop opioid dependence due long term treatment with opioid analgesics as part of a multimodal approach to pain management. The need for long term opioid therapy results in opioid tolerance with most patients reporting long term pain relief and narcotic independence after TPIAT [4]. Intraoperatively, patients undergoing TPIAT often require high and often unpredictable amounts of narcotic medications. Pain control remains a challenge in the operating room and in the postoperative phase of care. Regional techniques such as placement of paravertebral catheters, have been described for postoperative pain control in pediatric patients undergoing TPIAT. In one study by Hutchins et al., the use of paravertebral catheters resulted in reduced postoperative opioid consumption. However, no difference in the number of complications or length of stay was observed [5]. Thoracic epidurals provide excellent coverage to thoracic dermatomes with successful pain control described in pediatric surgery for major abdominal procedures. Thoracic epidurals are a powerful tool in the care of TPIAT patients when no contraindications are present due to the coverage of visceral pain they provide. Although thoracic epidurals are used in various centers around the country for TPIAT, widespread adoption has been limited. Institution dependent postoperative heparin administration regimens may pose a challenge given the risks of neuraxial complications. However, competing surgical and pain management priorities can be reconciled with a multidisciplinary approach. TPIAT patients are followed by a multidisciplinary care team that includes the acute pain service followed by medical pain service for long term follow up and medication management. Multimodal analgesia includes a combination of parenteral and enteral medications including α-2 agonists, methadone, lidocaine and ketamine infusions followed by an opioid based patient controlled analgesia (PCA) and additional adjuvants in the intensive care unit.

Preanesthesia Evaluation with Reference to Chronic Pain

Chronic Pancreatitis in Pediatrics

CP can be broadly classified as idiopathic, autoimmune, genetic, toxic/metabolic, obstructive and recurrent or severe acute. In general, the etiology guides patient selection. Genetic mutations or congenital anomalies in the biliary ductal system are the two most common etiologies in the pediatric population. Mutations of the PRSS1 gene have been described as one the most common causes of hereditary pancreatitis with the R122H mutation of the PRSS1 gene described by Howes et al. as the most common in Europe [6]. Other mutations associated with CP include, SPINK1, CFTR and CTRC [1].

Patient Selection and Indications

Patient selection is based on a risk benefit discussion. Symptoms interfering with quality of life, function, chronic abdominal pain, recurrent hospitalizations, and refractory pain syndromes often urge patients to seek more invasive options hoping for long term sustained improvement. TPIAT is indicated when the burden of pain from CP is considerable and significant to outweigh complications including, risk of short term surgical complications, lifelong pancreatic enzyme replacement and risk of insulin-dependent diabetes among other complications with variable degrees of morbidity. TPIAT is an extensive and invasive intervention, despite this, postoperative major complications remain uncommon [1].

The University of Minnesota has published selection criteria based on imaging findings, duration of pain, histopathology of the pancreas, narcotic dependence failure of maximal medical therapy including more invasive interventions [7]. Recent data suggests that performing TPIAT in patients with hereditary pancreatitis results in long term pain control (over 90%) with preservation of β-cell function. Chronic inflammation and fibrosis negatively impact the chances of successful islet cell autotransplantation resulting in

insulin independence and early intervention is often suggested [8].

Chronic Pain History

Initial treatment of pain for CP starts with titration of non-narcotic medications followed by gradual progression to neuromodulators and more invasive techniques including endoscopic interventions. It is our institutional experience that failure of pain management strategies and less invasive methods has occured by the time patients present for pre-anesthetic evaluation. It is common to encounter complex pain medication regimens and escalating narcotic doses accompanied by severe refractory pain and opioid tolerance. A thorough evaluation is necessary to formulate an effective plan for each patient. Obtaining a detailed medication history including opioids, non-opioid medications and adjuvants is necessary. Furthermore, gaining an understanding of individual comorbid psychiatric disorders, when present, is crucial to ensure effective follow up and to optimize postsurgical outcomes.

Anesthetic Management

Management of the anesthetic care is guided by three main principles, intraoperative general anesthesia, pain management, and specific interventions aimed at improving the necessary conditions for graft survival. Patients with CP undergoing TPIAT will require general anesthesia with additional procedures such as central and arterial line placement. General anesthesia can be achieved with a combination of an inhalational or intravenous agents, opioids, adjuvants, and muscle relaxants. Although regional techniques have been described, widespread adoption has been limited by the administration of heparin and avoidance of possible hemodynamic effects intraoperatively. There is no significant data supporting a specific anesthetic technique, making the individualized formulation of an anesthetic plan an essential aspect of the anesthetic care for TPIAT [9].

Adequate intravenous access with large bore intravenous catheters is standard. Including the ability to transfuse with warmed blood products rapidly if needed. Although major blood loss is uncommon in TPIAT, the risk is nevertheless considerable. A discussion with the patient and family regarding the need for blood product availability with its risks and benefits in the perioperative period must take place.

Maintenance of Anesthesia and Pain Management

Inhalational anesthesia is standard in TPIAT in combination with additional intravenous medications for general anesthesia. There are no known contraindications to total intravenous anesthesia for TPIAT. Prompt and effective treatment of intraoperative nociception and postoperative pain can be achieved with a multimodal approach. A multimodal approach to acute pain management is extensively supported by current evidence. In patients without a history of chronic pain, multimodal analgesia has been shown to decrease time to return of gastrointestinal function, reduce cardiac and pulmonary complications and result in shorter length of stay [10].

The use of non-steroidal anti inflammatory drugs (NSAIDs) and acetaminophen is limited in TPIAT. NSAIDs, while effective for inflammatory pain, may increase the risk of postoperative bleeding and are generally avoided in the presence of alternative agents [11]. The parenteral preparation of acetaminophen (Ofirmev ®) contains mannitol (38.5 mg of mannitol per mL) which may impair glucose monitoring depending on the equipment available [12].

Pre-existing opioid doses should be continued at their parenteral equivalents to avoid narcotic withdrawal. A long acting opioid such as methadone is encouraged due to its favorable pharmacokinetics. Additional doses of opioids such as fentanyl, hydromorphone, morphine are administered once baseline opioid requirements are met.

Ketamine and lidocaine infusions are included in our multimodal intra-operative approach and are routinely employed in the care of TPIAT patients. Dexmedetomidine can be used for post-operative sedation and is likely to decrease opioid requirements.

Methadone provides sustained analgesia perioperatively and its use has been investigated in the perioperative period when it serves the role as a long acting opioid agonist and NMDA receptor antagonist [13]. Due to its long half life, methadone provides a sustained effect on the mu receptor and may help prevent severe episodes of pain exacerbations in the postoperative period. Intraoperative administration of methadone 0.1 mg/kg up to 5 mg, has been shown to be effective in the ambulatory care setting compared to clonidine or placebo [14]. Furthermore, NMDA receptor antagonism plays an important role in addressing opioid induced hyperalgesia, and opioid tolerance. Methadone can be given intraoperatively for TPIAT after evaluation of QTc in the preoperative evaluation.

Ketamine, started in the operating room with a bolus dose of 0.3–0.5 mg/kg IV followed by an infusion of 0.1–0.5 mg/kg/h, has been shown to be effective in the treatment of chronic pain characterized by opioid tolerance [15]. In our institution, a ketamine bolus of 1 mg/kg is given followed by 0.2 mg/kg/h to be continued postoperatively. Limited evidence has revealed small differences in postoperative nausea and pain at rest when combined with an opioid based PCA. In addition, ketamine has been shown to prevent opioid induced hyperalgesia most likely due to its activity at the NMDA receptor [16]. In the absence of relatively severe side effects at the doses administered, the benefits of continuing a ketamine infusion postoperatively should be considered.

Lidocaine is also a known adjuvant in the multimodal approach, albeit with more limited evidence compared to ketamine. Intravenous lidocaine administered as an infusion is thought to reduce the need for opioid consumption as described in a meta analysis in 2018 by Weibel et al. Other outcomes such as gastrointestinal recovery, nausea, and postoperative pain were included with limited evidence to support its efficacy. Additionally the utility of lidocaine in the reduction of pain scores appears to be limited to the initial 24 h in the perioperative period [17]. There is very limited data for its use in children and dosing regimens not well defined. However, when no contraindications exist, it is our approach to run a lidocaine infusion at 20 μg/kg/min and to discontinue it 8 h after initiation.

Alpha-2 (α-2) agonists including clonidine and dexmedetomidine, are important tools in the chronic pain management armamentarium. Although, the exact analgesic mechanism of α-2 agonists remains unknown, the analgesic properties of α-2 agonists have been reported, especially when co-administered with opioids [18]. The use of α-2 agonists in the operating room can potentially have opioid sparing properties while providing a potent sedative effect in the intensive care unit. On a more practical note, dexmedetomidine administration is not commonly initiated during the intraportal infusion of islet cells, when significant hemodynamic fluctuations can be expected.

Choice of Muscle Relaxant

TPIAT is a long surgical procedure with a reported median surgical time of 757 min [1]. The use of non-depolarizing neuromuscular blockers such as rocuronium or vecuronium is common with special consideration given to patients with co-existing renal impairment where cisatracurium can be a more practical choice. The need for immobility becomes more acute as the surgeon approaches vital intra-abdominal organs and blood vessels. Intermittent redosing of large doses of rocuronium and vecuronium is necessary to maintain paralysis and avoid patient initiated breaths, sudden movements or bucking. The use of an intraoperative infusion of a non-depolarizing neuromuscular blocker such as rocuronium or vecuronium can be considered. Succinylcholine can be used safely in the absence of contraindications followed by administration of non-depolarizing muscle relaxants if a rapid sequence intubation (RSI) is indicated.

Alternatively, rocuronium at doses of 1–1.2 mg/kg on induction can be used for RSI and will result in long lasting muscle relaxation after induction. Large doses of non-depolarizing muscle relaxants can be administered at the start of surgery given the ability to rapidly reverse blockade when sugammadex is available.

Choice of Endotracheal Tube

The majority of patients undergoing TPIAT are admitted to the intensive care unit postoperatively. A cuffed endotracheal tube is needed which remains in place for transport to the intensive care unit. Extubation can be considered and performed in a smallnumber of patients prior to transport to the intensive care unit. Special attention to the size of the tube can be advantageous should a prolonged intubation be necessary. Larger tubes are more practical in order to prevent obstruction secondary to secretions and optimize pulmonary hygiene in the intensive care unit.

Monitoring

Standard monitors are employed intraoperatively. These include capnography, pulse oximetry (SpO_2), blood pressure (arterial line or non-invasive cuff), electrocardiography (ECG), temperature and urine output via foley catheter. Additional monitoring is employed for TPIAT. These include central venous pressure and the capacity to transduce portal pressures intraoperatively. Portal pressures are measured at multiple times to address portal hypertension and reduce the risk of portal vein thrombosis during islet cell infusion. Given the need for intensive intraoperative glycemic control a glucometer is essential.

TPIAT has a substantial risk for intraoperative metabolic derangements, mainly glucose homeostasis, and insidious bleeding during dissection. Point of care blood gas analysis is commonly employed to detect intraoperative anemia and additional metabolic derangements. Although intraoperative major blood loss is uncommon in TPIAT, a type and crossmatch with compatible blood products immediately available is necessary.

Specific Interventions to Optimize Surgical Outcomes

Glycemic control is crucial to optimize islet cell autograft survival. There is considerable variability in the rates of insulin independence even when islet cell infusion mass is optimal. Reduced function can be attributed to impaired islet cell survival. The majority of infused islet cells are lost [19] during infusion and aggressive interventions are aimed at reducing loss and enhancing engraftment. Constant measurement of glucose in the operating room is necessary to maintain glucose in the range of 80–120 mg/dL. At the start of the procedure care is taken to ensure that medications are not in dextrose containing solutions to avoid unaccounted glucose administration. Glucose infusion rates of 2–4 mg/kg/min are necessary for islet homeostasis, and intraoperative euglycemia (80–120 mg/dL) is necessary to avoid graft distress. Insulin protocols vary, however we initiate an insulin infusion when glucose measurements exceed 120 mg/dL. Dosing must be individualized but we start an insulin infusion in the range of 0.3 U/kg/h with follow up adjustments intraoperatively.

Intraportal islet infusions trigger an inflammatory response that may negatively influence islet cell survival. Although additional methods have been described, the intraportal route has been extensively studied and remains as the most common site for islet cell autotransplantation. Portal vein thrombosis is a risk, given the inflammatory response that ensues.

Transducing portal pressures during the islet infusion may prevent portal thrombosis and is part of the intraoperative care for TPIAT patients in our institution. Iincreases above 30 mmHg force the discontinuation of the intraportal infusion [20]. Heparin can be mixed with the islet transfusate or given separately as an IV bolus dose to reach an activated coagulation time

(ACT) goal in the range of 140 s. A mean arterial pressure must be kept within physiologic range during this process as well.

Follow-Up Post TPIAT Patients

Pain control remains as one of the most important goals of TPIAT. Pain, narcotic use or narcotic independence is an important postsurgical outcome. Pain outcomes are favorable after TPIAT. Reduced narcotic use after TPIAT has been reported in 90 day outcomes [1] and long term narcotic use is significantly reduced or eliminated in most patients long term after TPIAT. Most pediatric patients report long term pain relief after TPIAT [21]. Short term post surgical gastrointestinal complications have been reported and are relatively uncommon, however nutritional status improves after TPIAT as pancreatic enzyme supplementation continues.

Various quality of life measurements are difficult to interpret at this time due to the lack of standardization across multiple studies. However, current data shows that overall, patients report a global improvement in quality of life after TPIAT. Pain relief, arguably the most influential outcome in quality of life measures, resolves after TPIAT in long term follow up.

Special consideration is given to the impact of insulin-dependent diabetes in long term outcomes after TPIAT. The Collaborative Islet Cell Transplantation Registry (CITR), a voluntary registry of allogeneic islet cell transplantation patients, defines Insulin independence as no exogenous administration of insulin after 14 days. Insulin independence can be achieved if the number and quality of autologous islet cells transplanted is adequate [20]. Approximately two third of patients who had TPIAT from 1990–1999 were insulin independent for 1 year [22].

Conclusions

TPIAT has been extensively described in the surgical care of adult patients suffering from CP for over 40 years. Since the 1990s pediatric hospitals started developing the intraoperative techniques aimed at improving outcomes for children suffering from debilitating CP. TPIAT, pioneered at the University Of Minnesota Medical School, has resulted in favorable short and long term outcomes in pediatric patients. More recently, our institution is experiencing increased demand for this surgical alternative. It has redefined the care of children suffering from CP, long limited to medical management and previously destined to an inevitable decline in function and quality of life. A more preventative approach is also evolving. Earlier intervention is aimed at reducing morbidity secondary to CP while addressing common challenges associated with pancreatic inflammation and fibrosis. Long standing CP makes islet cell preservation more difficult mainly due to worsening pancreatic histopathology. It is our institutional experience that a multidisciplinary approach in the care of TPIAT patients is the path to successful postoperative outcomes.

Unprecedented progress in the field of genetics has helped in the detection of patients at increased risk and early intervention with autotransplantation is becoming more common. Insulin independence is an important post surgical outcome linked to improvements in quality of life. Early intervention aims to reduce the degree of pancreatic deterioration including islet cell mass destruction, an important element influencing insulin independence after TPIAT. The intraoperative management will directly affect the environment for graft survival; the need for anticoagulation to prevent thrombosis in small vessels has influenced the way we care for this unique patient population. It is important to introduce multimodal pain management strategies early to provide an effective alternative to the advantages neuraxial and regional techniques offer. Intensive glucose management defines intraoperative care in TPIAT and continues in the intensive care unit in a joint effort to reduce insulin dependence. Pain management teams, social workers, gastroenterologists, endocrinologists, anesthesiologists, pathologists, and intensivists play a crucial role in ensuring good outcomes before, during and after TPIAT.

Funding and Conflicts of Interest

None

References

1. Kotagal M, Slusher J, Ahmad S, et al. In-hospital and 90-day outcomes after total pancreatectomy with islet autotransplantation for pediatric chronic and acute recurrent pancreatitis. Am J Transplant. 2019;19:1187–94.
2. Bellin MD, Forlenza GP, Majumder K, et al. Total pancreatectomy with islet autotransplantation resolves pain in young children with severe chronic pancreatitis. J Pediatr Gastroenterol Nutr. 2017;64:440–5.
3. Pohl JF, Limbers CA, Kay M, Harman A, Rollins M, Varni JW. Health-related quality of life in pediatric patients with long-standing pancreatitis. J Pediatr Gastroenterol Nutr. 2012;54:657–63.
4. Bondoc AJ, Abu-El-Haija M, Nathan JD. Pediatric pancreas transplantation, including total pancreatectomy with islet autotransplantation. Semin Pediatr Surg. 2017;26:250–6.
5. Hutchins J, Castro C, Wang Q, Chinnakotla S. Postoperative pain control with paravertebral catheters after pediatric total pancreatectomy and islet autotransplantation: a retrospective cohort study. Paediatr Anaesth. 2016;26:315–20.
6. Howes N, Lerch MM, Greenhalf W, et al. Clinical and genetic characteristics of hereditary pancreatitis in Europe. Clin Gastroenterol Hepatol. 2004;2:252–61.
7. Bellin MD, Freeman ML, Schwarzenberg SJ, et al. Quality of life improves for pediatric patients after total pancreatectomy and islet autotransplant for chronic pancreatitis. Clin Gastroenterol Hepatol. 2011;9:793–9.
8. Chinnakotla S, Radosevich DM, Dunn TB, et al. Long-term outcomes of total pancreatectomy and islet auto transplantation for hereditary/genetic pancreatitis. J Am Coll Surg. 2014;218:530–43.
9. Farrell C, McConaghy P. Perioperative management of patients taking treatment for chronic pain. BMJ. 2012;345:e4148.
10. Bonnet F, Marret E. Postoperative pain management and outcome after surgery. Best Pract Res Clin Anaesthesiol. 2007;21:99–107.
11. Forsyth MG, Clarkson DJ, O'Boyle CP. A systematic review of the risk of postoperative bleeding with perioperative non-steroidal anti-inflammatory drugs (NSAIDs) in plastic surgery. Eur J Plast Surg. 2018;41:505–10.
12. Ofirmev—FDA prescribing information, side effects and uses. In: Drugs.com. https://www.drugs.com/pro/ofirmev.html. Accessed 27 Mar 2020.
13. Murphy GS, Szokol JW. Intraoperative methadone in surgical patients: a review of clinical investigations. Anesthesiology. 2019;131:678–92.
14. Simoni RF, Cangiani LM, Pereira AMSA, Abreu MP, Cangiani LH, Zemi G. Efficacy of intraoperative methadone and clonidine in pain control in the immediate postoperative period after the use of remifentanil. Rev Bras Anestesiol. 2009;59:421–30.
15. Schwenk ES, Viscusi ER, Buvanendran A, Hurley RW, Wasan AD, Narouze S, Bhatia A, Davis FN, Hooten WM, Cohen SP. Consensus guidelines on the use of intravenous ketamine infusions for acute pain management from the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists. Reg Anesth Pain Med. 2018;43:456–66.
16. Laulin J-P, Maurette P, Corcuff J-B, Rivat C, Chauvin M, Simonnet G. The role of ketamine in preventing fentanyl-induced hyperalgesia and subsequent acute morphine tolerance. Anesth Analg. 2002;94:1263–9, table of contents.
17. Weibel S, Jelting Y, Pace NL, Helf A, Eberhart LH, Hahnenkamp K, Hollmann MW, Poepping DM, Schnabel A, Kranke P. Continuous intravenous perioperative lidocaine infusion for postoperative pain and recovery in adults. Cochrane Database Syst Rev. 2018;6:CD009642.
18. Omote K, Kitahata LM, Collins JG, Nakatani K, Nakagawa I. Interaction between opiate subtype and alpha-2 adrenergic agonists in suppression of noxiously evoked activity of WDR neurons in the spinal dorsal horn. Anesthesiology. 1991;74:737–43.
19. Watkins JG, Krebs A, Rossi RL. Pancreatic autotransplantation in chronic pancreatitis. World J Surg. 2003;27:1235–40.
20. Bellin MD, Gelrud A, Arreaza-Rubin G, et al. Total pancreatectomy with islet autotransplantation: summary of an NIDDK workshop. Ann Surg. 2015;261:21–9.
21. Chinnakotla S, Bellin MD, Schwarzenberg SJ, et al. Total pancreatectomy and islet autotransplantation in children for chronic pancreatitis: indication, surgical techniques, postoperative management, and long-term outcomes. Ann Surg. 2014;260:56–64.
22. Bretzel RG, Hering BJ, Schultz AO, Geier C, Federlin K. International islet transplant registry report. In: Yearbook of Cell and Tissue Transplantation 1996–1997. New York: Springer; 1996. p. 153–60.

13 Anesthetic Management for Small Bowel Transplantation

Adam Thaler and Devin Harkins

Introduction

Small bowel transplantation has become the standard of care for irreversible intestinal failure in patients who are unable to continue total parenteral nutrition (TPN) therapy. Irreversible intestinal failure is defined as the inability of the gastrointestinal system to maintain adequate nutrition, hydration, and electrolyte homeostasis from oral support [1]. The most common cause of irreversible intestinal failure is secondary to the surgical removal or congenital absence of a significant length (>70%) of small bowel leading to short-gut syndrome [2].

American Society of Transplantation and the Centers for Medicare and Medicaid Services recommend intestinal transplantation for patients that meet certain conditions including TPN failure, high risk of death, severe short bowel syndrome, frequent hospitalizations, narcotic dependency, pseudoobstruction, and unwillingness to accept long-term home parenteral nutrition [3]. There are additional clinical criteria for patients with TPN failure. Vanishing vein syndrome is seen in patients with TPN failure and can lead to lack of central venous access. This generally involves thrombosis of two or more of the major central venous channels (jugular, subclavian, or femoral veins). Frequent line infections, sepsis, and recurrent episodes of dehydration despite intravenous fluid administration are also clinical signs associated with TPN failure [4]. Impending liver failure is another very serious manifestation of TPN failure. Prolonged TPN administration may induce cholestatic liver disease, which can eventually lead to intestinal failure associated liver disease (IFALD). Laboratory results show a persistent elevation of serum transaminases 1.5 times the upper limit of normal in the presence of short bowel syndrome [5]. Other markers of impending liver failure include elevated serum bilirubin, splenomegaly, thrombocytopenia, gastroesophageal varices, coagulopathy, stomal bleeding, and hepatic cirrhosis/fibrosis. Development of these complications associated with TPN failure is associated with a high 1-year mortality, especially in patients with decompensated cirrhosis [6].

Small bowel transplant grafts can be isolated or combined with the liver, duodenum, and/or pancreas [7]. Multi-visceral transplantation is reserved for patients who develop cholestatic liver disease from chronic TPN use. Combined liver and intestinal transplantation have been shown to have an increased risk of mortality at 6 months compared to an isolated intestinal graft [8].

A. Thaler (✉) · D. Harkins
Department of Anesthesiology, Thomas Jefferson University Hospital, Philadelphia, PA, USA
e-mail: adam.thaler@jefferson.edu; devin.casey2@jefferson.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_13

The number of patients undergoing small bowel transplantation is much lower compared to other types of organ transplants. Advancements in surgical technique, immunosuppressive agents, intraoperative anesthesia, and postoperative care have all helped to increase both the viability of small bowel grafts and the total number of transplants occurring worldwide. The shortage of appropriate deceased donors is currently the limiting factor in performing small bowel transplantation, however with this may be improved by the increased use of live donors [4].

Recipient and Donor Selection

Irreversible intestinal failure without IFALD is the main indication for isolated small bowel transplantation in addition to one of the following criteria: (1) recurrent catheter-related sepsis (2) thrombosis of 2 of the 6 major venous access sites (jugular, femoral, or subclavian) (3) failure of growth and development in pediatric patients [7]. Short-gut syndrome (SGS) is the most common cause of irreversible intestinal failure and is commonly seen secondary to multiple surgeries, trauma, or Crohn's disease. Vascular anomalies, defective motility, and conditions that impair absorptive capacity can also cause irreversible intestinal failure. Vascular anomalies can lead to SMA infarction and SMA/SMV thrombosis. Defective motility is seen in Hirschsprung's disease and pseudoobstruction. Inflammatory bowel disease, radiation induced bowel injury, neoplasms, massive intestinal polyposis, and mesenteric desmoid tumors are all examples of conditions that result in impaired absorptive capacity [9]. Table 13.1 contains a more comprehensive list of frequent causes of irreversible intestinal failure.

There are many contraindications to small bowel transplantation including the presence of active infection, life-threatening illness unrelated to the gastrointestinal tract, advanced neurological disorders (especially those involving cerebral edema), and disseminated malignancy. Additional contraindications to this procedure are major psychiatric illness or non-compliant patient behavior, congenital or acquired immune deficiencies (including advanced human immune deficiency virus infection), any co-morbidity that would restrict life expectancy to <5 years, and multisystem organ failure [9, 10].

There are two types of donors available for small bowel transplantation: deceased and living. Cadaveric intestinal donors are generally ABO-identical brain dead donors with no intestinal pathology. Intestinal grafts from donors who have died secondary to cardiac death are not usually harvested due to the increased susceptibility to ischemic injury [11, 12]. Donors must be <45 years old, <75 kg, and are matched to the recipient's height to provide a graft that is 25–50% smaller than would be expected. This reduces the space requirement in a likely contracted abdomen [9].

Grafts from living donors are becoming increasingly more common. Living donation provides advantages such as optimal timing, short ischemia time, and good leukocyte antigen matching. Grafts from living donors have also been associated with lower postoperative complications [13]. In order to harvest the graft, a segment of the terminal ileum is removed 20 cm proximal to ileocaecal valve. At least 60% of the small intestine remains intact in the donor.

Preoperative Considerations

It is crucial to have the patient assessed by a multi-disciplinary team preoperatively, including by not limited to the transplant surgeon and coordinating team, anesthesia provider, hepatologist/gastroenterologist, cardiologist, dental surgeon, dietician, and psychiatrist/psychologist [14].

Cardiovascular assessment is dependent on patient risk factors, age, and coexisting diseases. It is important to obtain a thorough medical history. If the patient is young (≤40 years old), has no cardiovascular risk factors, no exercised limitation, and no abnormalities found on cardiac physical exam then a baseline EKG and 2D echocardiogram should be obtained. In older patients, with cardiac risk factors/medical history, or physical exam consistent with cardiovascular disease

Table 13.1 Causes of irreversible intestinal failure

Short-gut syndrome	Vascular anomalies	Defective intestinal motility	Impaired absorptive capacity	Gastrointestinal neoplasm
Crohn's disease	SMA infarction	Hirschsprung's disease	Inflammatory bowel disease	Gardener's syndrome
Necrotizing enterocolitis	SMA or SMV thrombosis	Pseudoobstruction	Microvillus inclusion disease	Mesenteric desmoid tumor
Intestinal atresia			Selective autoimmune enteropathy	Massive intestinal polyposis
Midgut volvulus			Radiation enteritis	
Gastroschisis				
Abdominal trauma				
Multiple surgeries (surgical adhesions)				
Mesenteric vascular thrombosis				

additional evaluation for both cardiac ischemia and valvular disease (dobutamine stress echocardiogram) should be considered [15]. If stress test results show possible ischemia, percutaneous coronary intervention may be warranted prior to transplantation. If the patient qualifies for intestinal transplantation secondary to intestinal ischemia, then it might also be beneficial to screen for a patent foramen ovale. There has been an associative, although not causal, relationship reported between the presence of a patent foramen ovale and mesenteric artery occlusion leading to gut ischemia [2].

Evaluation of central venous access should be completed preoperatively as difficulty with access is a known complication of irreversible intestinal failure. Many of these patients require chronic indwelling central venous catheters for extended TPN administration. The presence of chronic catheters can lead to thrombosis and obstruction of central vessels eventually leading to vanishing vein syndrome. Catheter related infections can also lead to challenges obtaining access. Contrast venography is recommended preoperatively to evaluate central venous patency and has been shown to be a more reliable method than ultrasonography [16, 17].

Investigating coagulation status is of great importance preoperatively. Many patients presenting for small bowel transplantation have SGS secondary to vascular injury or thrombosis. In these patients it may be beneficial to consider preoperative low-dose anticoagulation with either heparin or enoxaparin. Traditional clotting studies, including prothrombin time, activated partial thromboplastin time, international normalized ration, and platelet count, may show normal clotting or hypercoaguable state. In patients with inflammatory bowel disease increased levels of anti-cardiolipin antibodies, decreased protein S levels, increased factor V Leiden levels, and increased active protein C resistance have all been reported [18, 19]. Some practitioners believe that the hypercoagulability seen in this patient population is potentially due to a lack of intestinal heparin [4].

Other serological studies that are routinely obtained prior to transplantation include cytomegalovirus, Epstein Barr virus, human immune deficiency virus, hepatitis B virus, and hepatitis C virus. Blood typing human leukocyte antigen (HLA) is also completed for crossmatching purposes [14].

An additional purpose of the preoperative evaluation is to determine whether the patient qualifies for an isolated intestinal transplant or combined intestinal and liver or multivisceral transplantation. Combined intestinal and liver transplantation is reserved for patients with intestinal failure and end-stage liver disease. Multivisceral transplantation is reserved for patients with intestinal failure and the presence of neuropathy or extensive mesenteric thrombosis [20].

It is essential to consider the best postoperative pain management strategy prior to completion of the surgery. Patient controlled analgesia with fentanyl or morphine has been reported as an option. Additional analgesia coverage involves placement of a thoracic epidural preoperatively. The catheter is generally placed at the T6–T9 interspaces. Ropivicaine or bupivicaine are the most common local anesthetic agents used with or without the addition of low dose opiates [21]. A consideration of risks and benefits should be discussed regarding placement and use of an epidural. Local anesthetic administration through the epidural could induce vasodilation, which can potentially compound episodes of hypovolemia and cardiovascular instability. It is also not uncommon for patients to develop a significant coagulopathy during the perioperative period. The benefits of epidural use, however include reduced risk of respiratory and thromboembolic complications, potentially facilitate earlier extubation, and provide superior postoperative analgesia [9].

Intraoperative Management

Routine equipment required to safely anesthetize a patient for any surgery should be utilized (ventilator, capnography, and standard ASA monitors). Additionally, one may require rapid infusion devices, blood salvaging devices, thromboelastography analyzer, and transesophageal echocardiogram (TEE). TEE can be used to assess myocardial function, diagnose a thrombotic event, and aid in volume status management [22]. It is crucial to have 10 units of pRBCs and 10 units of FFP prepared by the blood bank and available for use prior to the start of the procedure [4]. Bispectral index (BIS) monitoring is also recommended to ensure adequate depth of anesthesia as hypotension may require decreased concentrations of inhaled anesthetics.

Patients presenting for small bowel transplant commonly have minimal or no accessible central veins. It is important to both review prior studies that have been performed to assess central venous access and reevaluate the patient on presentation for the procedure. Ideally, two large bore (8.5 or 9 French) introducer catheters should be placed for central venous access. This will allow for volume administration and pulmonary artery catheterization. Additionally, the anesthesia provider will be able to continuously monitor cardiac output, central venous pressure (CVP), mean pulmonary pressure (PAP), pulmonary capillary wedge pressure (PCWP), mixed venous oxygen saturation (SVO2), right ventricular ejection fraction, right ventricular end-diastolic volume, and blood temperature. To facilitate blood sampling and close blood pressure monitoring, two arterial catheters should also be placed (radial and femoral arteries) [4].

Increased success of intestinal transplantation has been made possible in part by advances in immunosuppression. Induction immunosuppression should be started once it has been reconfirmed that the patient will be proceeding with the transplant. Immunosuppressant agents include daclizumab (Zenepax), anti-thymocyte globulin (Thymoglobulin), or alemtuzumab (Campath). It is important to administer these medications slowly (over 4 h) to minimize adverse side effects [23, 24]. Broad spectrum antibiotics are also initiated prior to incision. Prophylaxis consists of aztreonam (1 g Q8 h), vancomycin (1 g Q12 h), metronidazole (500 mg Q12 h), and amphotericin B (5 mg/kg/24 h). Patients additionally require premedication with acetaminophen 1000 mg PO, diphenhydramine 25 mg IV, and methylprednisolone 1 g IV. An additional dose of methylprednisolone should be given once the donor intestinal graft is present in the surgical field [4]. Table 13.2 lists these important medications required for small intestine transplantation.

Many of the patients presenting for small bowel transplantation likely suffer from delayed gastric emptying. As a result, a rapid sequence induction should be utilized and the anesthesia provider should plan to use succinylcholine, as long as there are no contraindications, to facilitate endotracheal intubation. Etomidate or sodium thiopental have been reported as the preferred medications for induction of anesthesia. Ketamine and propofol are rarely administered

Table 13.2 Medications required for small bowel transplantation

Premedication	Antibiotics	Immunosuppressants	Vasoactive drugs
Acetaminophen (1000 mg PO)	Aztreonam (1 g Q8 h)	Methylprednisolone[a] (1 g IV)	Epinephrine
Diphenhydramine (25 mg IV)	Vancomycin (1 g Q12 h)	Zenepax, Campath, OR Thymoglobulin	Dopamine
Methylprednisolone (1 g IV)	Metronidazole (500 mg Q12 h)	FK 506	Prostaglandin E1 (Alprostadil)
	Amphotericin B (5 mg/kg/24 h)		

[a]A second dose of methylprednisolone is administered when the donor intestinal graft is brought to the surgical field

for this purpose. Maintenance of anesthesia includes a combination of volatile anesthetic delivered in an air-oxygen mixture, narcotics, benzodiazepines, and muscle relaxants [4].

Following induction, special care should be taken with positioning, especially in such a lengthy procedure. The patient will remain supine with both arms either positioned at the patient's side or abducted to a maximum of 70° to protect against brachial plexus injury. It can be difficult to maintain normothermia secondary to the large exposed surgical site and extensive surgical incision, so it is recommended that both upper body and lower body forced hot air warming blankets are utilized. Calf compression devices should also be considered, but should be removed during the anastomotic phase while the aorta is partially clamped [9]. Additionally, a nasogastric tube (NGT) is placed following induction and is maintained into the postoperative period.

Throughout the procedure is it important to monitor blood gases, acid-base status, electrolytes, hematocrit, coagulation, metabolic status, and hemodynamics every hour to ensure optimal management of the patient [25]. This becomes especially critical immediately prior to reperfusion of the graft.

In order to monitor coagulation status, thromboelastography (TEG) is recommended. TEG can also aid in guiding transfusion of blood products, specifically platelets and FFP [26]. TEG is a comprehensive test of whole-blood coagulation. It measures the initial formation of fibrin strands by reaction time (r) within 10–14 min. Clot formation rate (α) measures the speed at which the clot forms (normal: 53°–67°) and is determined by fibrinogen and platelet function. A decreased α can be treated with cryoprecipitate administration. K is a measurement of the speed the clot reaches certain strength. Prolonged K values can be managed by FFP administration. Maximum amplitude (MA) is a direct function of the maximum dynamic properties of fibrin and platelet bonding. Platelet transfusion can be used to treat abnormally low values of MA. Additionally, fibrinolysis can be diagnosed using TEG. If fibrinolysis proves to be clinically significant, then treatment involves small doses of aminocaproic acid or transexamic acid [27]. Clinical observations have shown that patients presenting for small bowel transplantation behaved hypercoaguable, which has been confirmed with TEG [28]. In these patients TEG showed both a significant reduction in r time and an increase in α angle.

Intraoperative hemodynamic stability is influenced by many factors including intravascular volume status, compression/clamping of major vessels, blood loss, and release of endotoxins from isolated or loculated abdominal infections. Intravascular volume status should be closely monitored as there can be large intraoperative fluid shifts and massive extravasation of fluid throughout the procedure and can last 10–15 h. Third spacing of fluid eventually results in intravascular depletion [29, 30]. The goal of fluid management is to maintain hemodynamic stability while avoiding abdominal visceral edema. Edema can potentially lead to abdominal compartment syndrome and cause additional problems, such as difficulty with ventilation and renal failure. It is recommended to use a 50:50 ratio of 0.9% sodium chloride and 5% albumin to maintain intravascular volume. The use of vasoactive agents is also important to maintain adequate

perfusion pressure and support cardiac function. Epinephrine and dopamine are generally the vasopressors of choice for small bowel transplantation [4].

The goal of red blood cell replacement therapy is to maintain a hematocrit of 28–30%. This allows for optimal oxygen delivery, prevents increased viscosity, and increases survival postoperatively in critically ill patients [31, 32]. If massive transfusion is required, then close monitoring of ionized calcium is warranted. Avoidance of hypocalcemia is essential as it can lead to hypotension and myocardial depression. Most patients present as hypercoaguable by TEG analysis as mentioned above, so minimal FFP and platelets should be administered throughout the procedure [4].

Surgical Phases

Dissection Phase (Stage I)

During the dissection stage, the surgeon must isolate the recipient's infrarenal aorta and a segment of either the portomesenteric venous system or infrarenal inferior vena cava (IVC) for vascular anastomosis. The dissection can be difficult as patients typically have extensive abdominal adhesions from previous operations and a contracted abdomen. Less commonly, portal hypertension or splanchnic vascular thrombosis may occur. This stage is often also associated with the greatest blood loss [33].

Vascular Anastomosis Phase (Stage II)

First, the superior mesenteric artery of the donor intestine is anastomosed to the recipient's infrarenal aorta during the vascular anastomosis phase. In order to facilitate this step, partial clamping of the aorta is required. Partial clamping will cause dampening of the femoral artery catheter waveform. Then, the donor superior mesenteric vein is anastomosed to the recipient's superior mesenteric vein, confluence with the splenic vein, side of the portal vein, or IVC. Lastly, reperfusion is initiated [33].

It is recommended to obtain a blood sample 3–5 min prior to reperfusion in order to assess hematocrit, acid-base status, ionized calcium concentration, and electrolytes in order to treat appropriately. It is important to pay special attention to potassium levels. Potassium levels should be <4 mEq/L before reperfusion of the donor intestine, which helps to avoids potential cardiac dysrhythmias associated with elevations in potassium seen during reperfusion. Increased serum potassium levels are observed during reperfusion due to the output of metabolic products by the donor intestine [34]. Patients with difficult potassium levels to control or have renal failure may need to be treated with potassium lowering agents including insulin-glucose solutions, sodium bicarbonate, washing blood prior to transfusion, or potentially intraoperative hemodialysis [4].

There are many hemodynamic changes that can occur during this phase and require consideration. An increase in mean PAP, CVP, and PCWP has been observed during stage II and immediately after reperfusion. Generally a return to baseline is seen within the first hour of reperfusion [25]. Systemic vascular resistance (SVR) decreases by 20% from baseline approximately 2 h after incision and is the lowest at reperfusion (40% below baseline). SVR continues to remain low throughout the remainder of the procedure (30–40% below baseline) [4].

"Post-reperfusion Syndrome" (PRS) is a major complication that is seen in 47% of small bowel transplant patients and is defined as a mean arterial pressure (MAP) <60 mm Hg [35]. PRS can be seen as result of hyperkalemia, acidosis, sudden hypothermia, and release of vasoactive substances (free radicals, endotoxins, inflammatory cytokines, and acidotic compounds) by the graft intestine during reperfusion [36]. Acidosis in particular is a prominent contributor to PRS. During reperfusion, acid load from the ischemic bowel enters the systemic circulation causing pH to decrease significantly. This is accompanied by a rise in PaCO2 and is likely due to the increased metabolic activity of the new

organ. Severe metabolic acidosis can be treated by administration of sodium bicarbonate or tromethamine and intravenous fluids [34].

Intestinal ischemia-reperfusion injury (IRI) can additionally be seen during the phase. During reperfusion, damage to the graft can be caused by intestinal inflammation leading to structural deterioration and increased permeability [37]. Platelet function may be affected by ischemia and reperfusion injury due to activation of neutrophils. IRI is also closely related to early postoperative complications such as sepsis and acute rejection [38]. One study has shown that preconditioning with remifentanil can reduce intestinal IRI and the subsequent systemic inflammatory response in mice. Remifentanil can be given as either a bolus or continuous infusion, however a single bolus prior to tissue ischemia offers more protection against intestinal IRI. It may be beneficial to prophylax with remifentinal in cases involving IRI [39].

Some patients may require continuous infusion of prostaglandin E1 (PGE1, Alprostadil) after reperfusion. The infusion can be administered at 0.1–0.6 μg/kg/h and facilitates blood flow to the donor intestinal graft. PGE1 can protect against IRI and minimizes platelet adhesion to vascular endothelium. Unfortunately, PGE1 can cause systemic hypotension, so addition of an epinephrine or dopamine infusion may be required to maintain adequate blood pressures [4].

Intestinal Reconstruction Phase (Stage III)

At stage III, the surgeon will anastomose the proximal jejunum of the donor intestine to the recipient's jejunum, duodenum, or stomach. The distal end of the donor intestine is then anastomosed to the recipient's native ileum, transverse colon, descending colon, or rectum. A jejunostomy and ileostomy are created in order to allow endoscopic monitoring and retrieval of biopsies of the donor intestinal graft. A gastrostomy is also created [29]. Figure 13.1 illustrates the implanted donor intestine in an isolated small bowel transplantation.

Abdominal wall closure can be especially difficult in these patient secondary to previous multiple surgeries, recurrent infections, scar formation, and a contracted abdominal cavity. Closure can be obtained with temporary mesh, Gore-Tex grafts, or rotation flaps for particularly difficult cases. It is important to monitor intra-abdominal pressures postoperatively [9].

Postoperative Management

Due to the extensive length of the procedure and the potential fluid shifts, most patients remain intubated postoperatively and require admission to the intensive care unit (ICU). Patients are then extubated at a later time while in the ICU. Early postoperative goals include maintenance of adequate perfusion and oxygenation of the intestinal graft, prevention of secondary infections, and continuation of immunosuppressive therapy. Additionally nutrition is started initially via TPN as NGT output is often high in the first 24–48 h following the procedure. Enteral feeding tends to be started around postoperative day 3–7. Jejunal feeding has been reported at a median of 83 days [9].

There are many complications that can arise in the postoperative period, the most common being renal function impairment. Renal failure is seen in more than 50% of small bowel transplant patients. Risk factors include dehydration due to the presence of an ileostomy with potential for high output, hypovolemia, renal impairment prior to transplantation, anemia, use of calcineurin inhibitors, and nephrotoxicity caused by antibiotics and immunosuppressive medications [40].

Technical complications such as bleeding, thrombosis, and anastomotic leaks can also be seen in the postoperative period. Infectious complications secondary to intra-abdominal sepsis, catheter-related sepsis, or sepsis related to bacterial translocation from the graft are also reported and remain the most common cause of death in the postoperative period. Prophylaxis to prevent infection is routinely administered. Regimens include trimethoprim-sulfamethoxazole for prevention of P. jirovecci, fluconazole/nystatin/

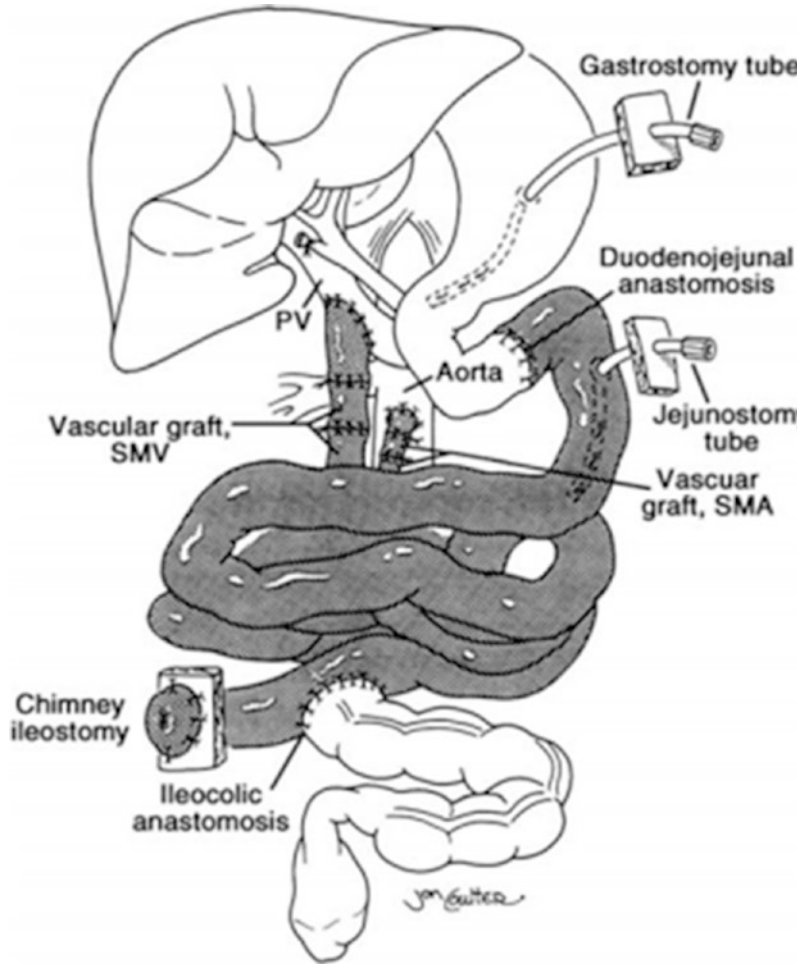


Fig. 13.1 Implanted donor intestine in an isolated small bowel transplantation. *SMA* small mesenteric artery, *SMV* small mesenteric vein, *PV* portal vein. Reproduced with permission from Planinsic [4]

clotrimazole for fungal prophylaxis, and ganciclovir IV or valganciclovir PO for CMV prophylaxis [14].

Post-transplant lymphoproliferative disease is another postoperative complication that occurs in 30% of intestinal transplant recipients. It is often associated with Epstein Barr virus. Treatment involves decreasing the immunosuppression regimen and starting antiviral therapy.

Graft rejection at any postoperative stage is an extremely worrisome complication. The incidence of acute rejection in intestinal transplantation is higher when compared with other organ transplants. Graft loss occurs in virtually all patients with severe rejection despite treatment with aggressive immunosuppressive therapy [41, 42]. Patients typically present with increased stoma output, fever, abdominal pain, distention, and ileus. Acute rejection predisposes patients to sepsis secondary to bacterial translocation and fungal infections. Early postoperative serial endoscopies via the stoma and intestinal biopsies are crucial to monitor the graft for any signs of rejection. Rejection is most common is the 3 weeks following transplantation. Multiple measures have been investigated to reduce the rate of rejection including irradiating donor grafts, infusing donor bone marrow, and leukocyte depletion prior to transplantation. Irradiation, however, is not used routinely due to risk of radiation-induced small bowel injury [14]. Additionally it has been reported that the addition of a liver transplant may help achieve immunologic tolerance to small bowel grafts [43].

Chronic rejection is observed in approximately 8% of intestinal transplantation patients. Isolated intestinal transplant versus small bowel-liver grafts, acute rejection within the first month, multiple acute rejection episodes, recipients of older age, recipients of non-Caucasian race, and Caucasian donor to non-Caucasian recipient transplant have all been factors associate with chronic rejection. Patients present with poor oral intake or lack of appetite requiring enteral feeding. Patients may also experience intestinal obstruction after repeated episodes of chronic rejection [44, 45].

Graft-versus-host disease (GVHD) is an additional major postoperative complication worth discussing. Small bowel transplants are particularly vulnerable to GVHD due to the concentrated amount of lymphocytes and mesenteric lymph nodes present in the small intestine. Patients present with skin rash, mouth or tongue lesions, diarrhea, gastrointestinal ulcerations, liver dysfunction, and bone marrow suppression [46].

Survival Outcomes

There has been an increase in the number of small bowel transplants performed worldwide during the past two decades. Growth rates are slow, however, due to organ shortage, lack of expertise, and inability to obtain health insurance coverage. The Intestinal Transplant Registry, an international registry for intestinal transplant centers, reported in 2016 that 3194 patients had received intestinal transplants [47]. Based on Organ Procurement and Transplantation network (OPTN) data as of March 23, 2020 there have been a total of 3099 intestinal transplants performed in the United States between 1990 and 2019 with 81 in 2019.

Improvement in survival rates have been reported worldwide. 1- and 5-year survival rates after 1995 were 61% and 42% respectively. Data from the Intestinal Transplant Registry reported in 2001 an overall survival rate of 51% for all intestinal transplants [4]. A single center study in the United States reported that from 1990 to 2000 165 intestinal transplants were performed in 155 consecutive patients. In this study the survival rate was 75% at 1 year, 54% at 5 years, and 42% at 10 years. Full nutritional autonomy was achieved in 90% of survivors. It was also noted that recipients of liver-intestinal grafts had best prognosis for continued survival beyond 5 years [48].

Based on the 2018 Annual Report provided by OPTN, graft failure has plateaued over the past decade. Patients status post small intestine transplantation with or without a liver (2011–2013) had a survival rate at 1- and 5-year of 74.2% and 51.1%, respectively. More specifically 1- and 5-year graft survival was 76.2% and 47.0%, respectively, for intestine recipients, and 72.9% and 55.8%, respectively, for intestine-liver recipients [49]. The most important predictor of graft survival has been determined to be the recipient's functional status. Homebound recipients had 68% survival rate at 2 years, while hospitalized patients had 42% survival at 2 years. This reflects the increased severity of the underlying gastrointestinal disease and additional comorbidities in the hospitalized patient [14].

References

1. William K, Lewis JF, Davis G, Geiser EA. Dobutamine stress echocardiography in patients undergoing liver transplant evaluation. Transplantation. 2000;69(11):23–54.
2. De'Atha HD, Sabharwal NK, Ormerod O, Vaidya A. Patent foramen ovale and gut ischemia in potential intestinal transplant recipients. Transplantation. 2014;98:e60–1.
3. Buchman AL, Scolapio J, Fryer J. AGA technical review on short bowel syndrome and intestinal transplantation. Gastroenterology. 2003;124:1111.
4. Planinsic RM. Anesthetic management for small bowel transplantation. Anesthesiol Clin North Am. 2004;22:675–85.
5. Abu-Wasal B, Molinari M. Liver disease secondary to intestinal failure. Biomed Res Int. 2014;2014:968357.
6. Reyes JD. Intestinal transplantation: an unexpected journey. J Pediatr Surg. 2014;49:13–8.
7. Bhamidimarri KR, Beduschi T, Vianna R. Multivisceral transplantation: where do we stand? Clin Liver Dis. 2014;18:661.
8. Dopazo C, Gupte GI, Sharif K, et al. Combined liver-intestine grafts compared with isolated intestinal

transplantation in children: a single center experience. Transplantation. 2012;94:859–65.
9. Lomax S, Klucniks A, Griffiths J. Anesthesia for intestinal transplantation. Contin Educ Anesth Crit Care Pain. 2001;1:1–4.
10. Abu-Elmagd KM. Intestinal transplantation for short bowel syndrome and gastrointestinal failure: current consensus, rewarding outcomes, and practical guidelines. Gastroenterology. 2006;130:S132.
11. Roskott AM, van Haaften WT, Leuvenink HG, et al. Histopathologic and molecular evaluation of the Organ Procurement and Transplantation Network selection criteria for intestinal graft donation. J Surg Res. 2014;189:143–51.
12. Berg CL, Steffick DE, Edwards EB, et al. Liver and intestine transplantation in the United States 1998–2007. Am J Transplant. 2009;9:907–31.
13. Dalal A. Intestinal transplantation: the anesthesia perspective. Transplant Rev. 2016;30:100–8.
14. Khan F, Selvaggi G. Overview of intestinal and multivisceral transplantation. UpToDate 2018.
15. Middleton SJ, Pither C, Gao R, et al. Adult small intestinal and multivisceral transplantation: lessons through the "retroscepcto-scope" at a single UK centre from 1991 to 2013. Transplant Proc. 2014;46:2114–8.
16. Aggarwal S, Abu-Elmagd K, Amesur N, Thaete FH, Planinsic RM, Zak M. Patency of the central vein system in the epatients undergoing SBTx: ultrasonogrphy versus contrast venography [abstract]. Anesth Analg. 2002;95:S79.
17. Sakai T, Matsusaki T, Abu-Elmagd K, et al. The role of ultrasonography in determining central venous patency in patients undergoing bowel transplantation. Clin Transpl. 2012;26:E78–83.
18. Koutrabakis IE, Sfiridaki A, Mouzas IA, et al. Resistance to activated protein C and low levels of free protein S in Greek patients with inflammatory bowel disease. Am J Gatroenterol. 2000;95(1):190–4.
19. Novacek G, Miehsler W, Kapotis S. Thomboembolism and resistance to activated protein C in patients with inflammatory bowel disease. Am J Gatroenterol. 1999;94(3):685–90.
20. Fiel MI, Sauter B, Wu HS, et al. Regression of hepatic fibrosis after intestinal transplantation in total parenteral nutrition liver disease. Clin Gastroenterol Hepatol. 2008;6:926.
21. Siniscalchi A, Begliomini B, De Pietri L, et al. Pain management after small bowel/multivisceral transplantation. Transplant Proc. 2002;34:969–70.
22. Gologorsky E, De Wolf A, Scott V, et al. Intracardiac thrombus formation and pulmonary thromboembolism immediately after graft reperfusion in 7 patients undergoing liver transplantation. Liver Transpl. 2001;7(9):783–9.
23. Abu-Elmagd K, Bond JJ, Reyes J, Fung J. Intestinal transplantation: a coming of age. Adv Surg. 2002;36:65–101.
24. Zeevi A, Bentlejewski C, Gouspari D, Halfhill J, Harris C, Bond J, et al. The impact of immunosuppression weaning on T cell function in small bowel recipients as assessed by the cylex immune cell function assay. Am J Transplant. 2003;3:S192.
25. Planinsic RM, Nicolau-Radueu R, Aggarwal S, Hilmi I, Abu-Elmagd K. Hemodynamic and metabolic changes during small bowel transplantation [abstract]. Anesthesiology. 2003;99(4):A-214.
26. Whitten CW, Greilich PE. Thromboelastography: past, present, and future. Anesthesiology. 2000;95(5):1226.
27. Dalal A, Lang JD Jr. In: Hesham A, editor. Anesthetic considerations for patients with liver disease, hepatic surgery. 2013.
28. Planinsic RM, Milroy SJ, Aggarwal S, Hilmi I, Boucek C, Chalansani AJ, et al. Hypercoagulability in small bowel transplant recipients as demonstrated by thromboelastography [abstract]. Anesth Analg. 2002;94(Suppl 2):S114.
29. Siniscalchi A, Spedicato S, Dante A, et al. Fluid management of patients undergoing intestinal and multivisceral transplantation. Transplant Proc. 2008;40:2031–2.
30. Ronald AS, Giogono AW. Fluid and electrolyte physiology, chapter 45. In: Miller RD, editor. Anesthesia, vol. 1. 5th ed. Philadelphia: Churchill Livingstone. p. 1586–613.
31. Sunder-Plassmann L, Klovenkorn WP, Holper K, et al. The physiological significance of acutely induced hemodilution. In: Proceedings of the 6th European Conference on Microcirculation, Basel; 1970. p. 23.
32. Czer LS, Shoemaker WC. Optimal hematocrit value in critically ill postoperative patients. Surg Gynecol Obstet. 1978;147:363.
33. Abu-Elmagd K, Fung J, Bueno J, Martin D, Madariaga JR, Mazariegos G, et al. Logistics and technique for procurement of intestinal, pancreatic, and hepatic graft from the same donor. Ann Surg. 2000;232(5):680–7.
34. Siniscalchi A, Piraccini E, Cucchetti A, et al. Analysis of cardiovascular, acid-base status, electrolyte, and coagulation changes during small bowel transplantation. Transplant Proc. 2006;38:1148–50.
35. Planinsic RM, Nicolau-Radueu R, Aggarwal S, Hilmi I, Abu-Elmagd K. Post reperfusion changes during Small Bowel Transplantation. Transplantation. 2004;78(2):P606.
36. Siniscalchi A, Cucchetti A, Miklosova Z, et al. Post-reperfusion syndrome during isolated intestinal transplantation: outcome and predictors. Clin Transpl. 2012;26:454–60.
37. Thuijls G, de Haan JJ, Derikx JP, et al. Intestinal cytoskeleton degradation precedes tight junction loss following hemorrhagic shock. Shock. 2009;31:164.
38. Varga J, Stasko P, Toth S, Pristasova Z, Bujdos M, Pomfy M. Development of jejunal graft damage during intestinal transplantation. Ann Transplant. 2009;14:62–9.
39. Cho SS, Rudloff I, Berger PJ, et al. Remifentanil ameliorates intestinal ischemia-reperfusion injury. BMC Gatroenterol. 2013;13:69.
40. Calvo Pulido J, Jimenez Romero C, Morales Ruiz E, et al. Renal failure associated with intestinal

transplantation: our experience in Spain. Transplant Proc. 2014;46:2140–2.
41. Wu T, Abu-Elmagd K, Bond G, et al. A schema for histologic grading of small intestine allograft acute rejection. Transplantation. 2003;75:1241.
42. Selvaggi G, Gaynor JJ, Moon J, et al. Analysis of acute cellular rejection episodes in recipients of primary intestinal transplantation: a single center, 11-year experience. Am J Transplant. 2007;7:1249.
43. Wu G, Cruz RJ. Liver inclusion improves outcomes of intestinal retransplantation in adults. Transplantation. 2015;99:1265.
44. Parizhskaya M, Redondo C, Demetris A, et al. Chronic rejection of small bowel grafts: pediatric and adult study of risk factors and morphologic progression. Pediatr Dev Pathol. 2003;6:240.
45. Lauro A, Oltean M, Marino IR. Chronic rejection after intestinal transplant: where are we in order to avert it? Dig Dis Sci. 2018;63:551.
46. Mazariegos GV, Abu-Elmagd K, Jaffe R, et al. Graft versus host disease in intestinal transplantation. Am J Transplant. 2011;91:219.
47. Lacaille F. Thirty years after the first intestinal transplantation in 1987: which indications are left in 2018? Curr Opin Organ Transplant. 2018;23:196.
48. Abu-Elmagd K, Reyes J, Bond JJ, Mazariegos G, Wu T, et al. Clinical intestinal transplantation: a decade of experience at a single center. Ann Surg. 2001;234(3):404–17.
49. 2018 Annual Report of the U.S. Organ Procurement and Transplantation Network and the Scientific Registry of Transplant Recipients: Transplant Data 2011–2018. Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation, Rockville, MD; United Network for Organ Sharing, Richmond, VA; University Renal Research and Education Association, Ann Arbor, MI.

The Nuss Procedure and Anesthetic Implications

14

Fatimah Habib, Michael R. Schwartz, and Amal Amir

Introduction

Pectus excavatum (PE) is a chest wall deformity where the sternum is depressed, thereby compressing the thoracic cavity. The deformity is often congenital (about one third of cases), but can become more prominent during the rapid growth phase associated with puberty [1]. It occurs in about every 8 per 1000 live births, making it the most common congenital chest wall abnormality [2]. It can be found concomitantly with other congenital diseases, but more often, these patients are otherwise healthy. The most common associated abnormality appears to be scoliosis [3]. Potential symptoms include dyspnea on exertion, decreased exercise capacity, and even chest pain depending on the severity of the deformity. With severe malformation, patients can develop irreversible restrictive lung disease and are at risk for cardiac arrhythmias and right ventricular volume reduction, leading to decreased cardiac output. These children also often face the psychosocial stress associated with their deformity [1, 3, 4]. Image 14.1 shows a normal sternum versus a depressed sternum in a supine patient.

Surgical correction of PE has been ongoing since the early twentieth century. However at that time, an open, anterior chest wall approach was both painful and not reliably successful. With time, new approaches developed, such as rib resection with sternal osteotomy, costal cartilage resection with mobilization of the sternum, and a wide chest resection surgery [1, 3]. No technique provided a high success rate and low complication rate, along with ease of procedure. The most common surgical correction prior to the Nuss procedure was the Ravitch procedure. It consisted of resection of all costal cartilages that were abnormal, excision of the xiphoid, sternal osteotomy with anterior fixation [2], and occasional placement of a retrosternal bar. The Ravitch technique was an open, more invasive option, however after many years of experience with the procedure, outcomes were mostly favorable from a cosmetic and morbidity standpoint.

In 1998, Donald Nuss published a 10 year review of a minimally invasive technique for correction of PE, which involved placing a curved steel bar behind the sternum and anterior to the pericardium in the pleural space, turning the bar 180° to force the sternum into an anterior deflection, and stabilization of the bar laterally to the rib cage on either side [5]. Initially, as the technique started becoming more popular, complica-

F. Habib (✉) · M. R. Schwartz
Cooper University Hospital, Cooper Medical School of Rowan University, Camden, NJ, USA

A. Amir
Rowan University School of Osteopathic Medicine, Monroe, NJ, USA

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_14

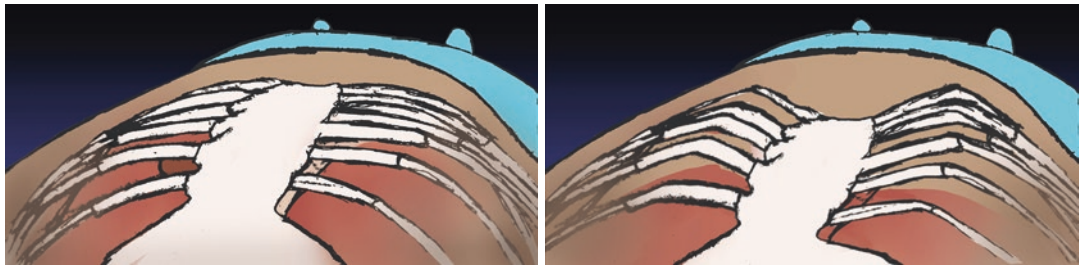


Image 14.1 Normal chest vs. pectus excavatum (Illustration credit: Jadila Majid, MA)

tion rates and outcomes were not significantly more favorable than the original open approaches, especially since providers were not yet experienced with the technique. Since then, the technique has been modified for efficiency, efficacy and safety, particularly with the addition of thoracoscopy to guide bar placement. Instruments have been modified and customized, and postoperative pain techniques have been improved.

The new "Nuss procedure" was revolutionary because of its minimally invasive nature, not requiring a large incision or any rib or cartilage resection. Towards the end of the study, Nuss et al. started to obtain chest computed tomography (CT) scans preoperatively to determine severity of the deformity and to identify any other complications. This allowed them to utilize the Haller index (HI) to quantify severity of the chest wall deformity. The HI was introduced by Haller et al. in 1987, and is often still used today. The HI is calculated by dividing the transverse diameter of the chest wall by the anterior-posterior diameter at the level of the greatest depression (Image 14.2). A value of greater than 3.25 correlates to indication/need for surgical correction [6]. In the 1998 Nuss study, the majority of surgically corrected patients had an HI of greater than 4 [5].

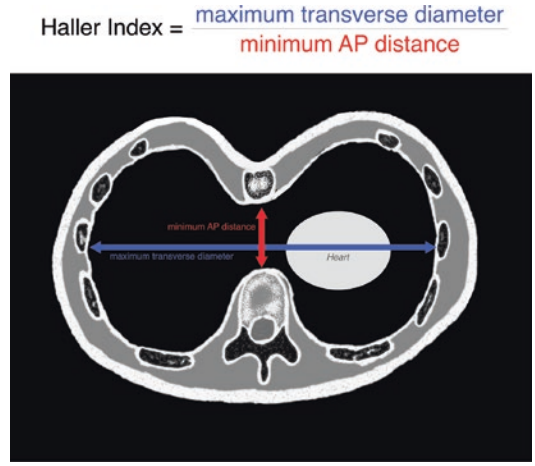


Image 14.2 Haller index. (Illustration credit: Jadila Majid, MA)

Preoperative Planning and Operative Selection Criteria

The etiology of PE remains unclear, however suggested mechanisms include congenital abnormalities, cartilaginous insufficiency due to connective tissue disorders, and acquired deformity via mechanical forces, among others. Consequently, the severity of deformity and symptoms in PE can also be highly varied. The morphology of chest wall deformity includes focal and cup-shaped, broad and shallow saucer shaped, or asymmetric and trench-like [7]. The anatomical diversity in presentation can explain the physiologic changes and varying symptomatology as well [3]. Patients can experience pain, shortness of breath, exercise intolerance, diminished pulmonary and cardiac function, arrhythmias, and body image disturbances [8].

Managing PE is dependent on the severity of the presenting illness. Mild to moderate PE is treated conservatively with exercise, physical therapy and posture programs, however severe deformity and symptomatic PE can suggest need for surgical correction [9]. Indications for surgical management of PE include severe deformity, pain, pulmonary or cardiac abnormalities, HI greater than 3.25, history of failed repairs, and

Table 14.1 Operative selection criteria

Operative selection criteria
Surgical candidates should have two or more of the following criteria • Severe deformity on clinical exam • Symptomatic pain • Haller index greater than 3.25 on chest CT • Evidence of pulmonary compression on chest CT • Evidence of cardiac compression on chest CT or echocardiogram • Pulmonary function tests indicating restrictive and/or obstructive lung patterns • Mitral valve prolapse • Cardiac conduction abnormalities • History of failed repairs • Significant disturbance due to body image

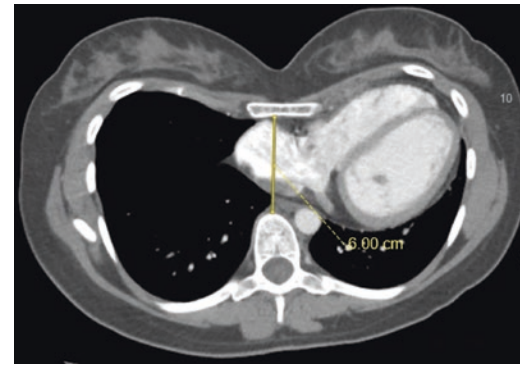


Image 14.3 Preoperative axial view of a patient who had a good result with decrease in dyspnea from cardiac compression. (Image Credit: D. Shersher, MD)

psychological disturbance [3, 7, 9–11]. The operative selection criteria is displayed in Table 14.1. Other important factors include the maturity and motivation of the patient to undergo the procedure.

Preoperative evaluation of morphology, cardiac abnormalities and pulmonary function is necessary in order to determine need for surgical intervention. Chest wall dimensions and the HI can be obtained using chest radiographs, chest CT, or magnetic resonance imaging (MRI) [7, 8, 10, 11]. A greater HI, indicating severe deformity, is associated with changes in cardiac and pulmonary function [10]. Many practitioners prefer a preoperative CT scan as the optimal imaging study. It is ideal in determining chest dimensions, calculating HI, visualizing bony and cartilaginous deformities, assessing other bone details such as sternal shape and the craniocaudal extent of deformity, and the degree of cardiac compression. An echocardiogram report may not mention cardiac compression, though it can be clearly visualized in a chest CT scan [3]. Being able to review a CT scan with the patient and their family preoperatively can reduce family preoperative anxiety and set reasonable expectations for recovery. MRI is an alternative to reduce radiation exposure, however there are clear benefits with a CT scan. Electrocardiograms and echocardiograms are used to establish baseline cardiac function. The predominant cardiac abnormalities with severe malformation include right bundle branch block, mitral valve prolapse and right ventricular compression to name a few [2, 8, 9, 12]. Severe cardiac compromise can be seen in patients with severe pectus in which cardiac compression leads to diminished stroke volume and decreased cardiac function. The clinical picture associated with such changes include chest pain on activity, arrhythmias, decreased exercise capacity, and dyspnea on exertion. Image 14.3 shows a preoperative CT scan of a patient with cardiac compression from PE.

Pulmonary function tests (PFTs) are also obtained preoperatively, often displaying restrictive and less commonly obstructive disease in patients with PE [2, 3, 8, 12, 13]. The PFTs generally show a 10–20% decrease below the average population, with a decrease in overall lung volumes as well [3]. A number of different studies show a statistically and clinically significant decrease in the FEV1 (forced expiratory volume over 1 s time), FVC (forced vital capacity), as well as FEF 25–75% (forced expiratory flow in mid-exhalation between 25 and 75% exhalation time). PFTs were initially obtained to try to find an explanation for the decrease in exercise capacity often seen in patients with PE [3]. Repeat findings of statistically significant decrease in PFTs from the expected average can be a reasonable additional cause for decrease in exercise capacity.

In addition to the components of the preoperative evaluation that determine operative eligibility, age and allergies are considered in order to reduce risk of reoperation after the Nuss procedure [7].

Nuss Procedure

The Nuss procedure is known as a minimally invasive approach to repairing pectus excavatum (MIRPE). The original procedure according to Nuss's 10 year review published in 1998 describes a transverse thoracic incision bilaterally between the anterior and posterior axillary lines [5]. A tunnel is made directly under the sternum using a long Kelly clamp, until it emerges on the other side. The tunnel is carefully widened as needed. Through the tunnel, umbilical tape is pulled through, which then is used to pull in a steel bar, shaped ahead of time to the exact desired curvature of the patient's chest. Once in place across the mediastinum and immediately posterior to the sternum, with the convexity facing posteriorly, the bar is rotated 180°. After rotation, the convexity faces anteriorly, effectively pushing the sternum into the desired curvature (refer to Image 14.4). The bar is then stabilized to the lateral chest wall on either side. On occasion, a second bar is needed superiorly or inferiorly. The second bars are also stabilized laterally [5]. In 2016, Nuss et al. published an update on the Nuss procedure, in which they described the most current version of the procedure in great detail [13].

Originally, these patients remained heavily sedated to prevent the bar from moving, and remained hospitalized for days. The patients would return after approximately 2–3 years to have the bar removed [5]. The Nuss procedure does not include any cartilage resection, rib resection or sternal osteotomy. The surgical treatment options prior to Nuss included "open" approaches which were more invasive with little added benefit. In fact, the complication rate and infection rate were considerably higher. Some approaches were abandoned because they simply were ineffective. Others were abandoned because they were harmful. For example, resection of costal cartilages at a young age led to an inflexible chest wall which was not able to grow appropriately, leading to the development of a severe restrictive lung defect [3].

Since then, many modifications have been made to the technique itself which has allowed shorter hospital stays, immediate emergence and extubation postoperatively, safer techniques, and more effective pain management strategies. The procedure is now done using thoracoscopy, which allows for direct visualization of the rod as it is passed across the mediastinum and decreasing risk of vascular damage, pericardial injury, or cardiac injury [13]. Direct visualization via thoracoscopy is used throughout the surgery, in order to maintain a visual for every portion of the procedure, including the pericostal suture placement, and one last check of all major thoracic structures and organs before closing skin. Bar displacement incidence has decreased significantly because of the addition of pericostal

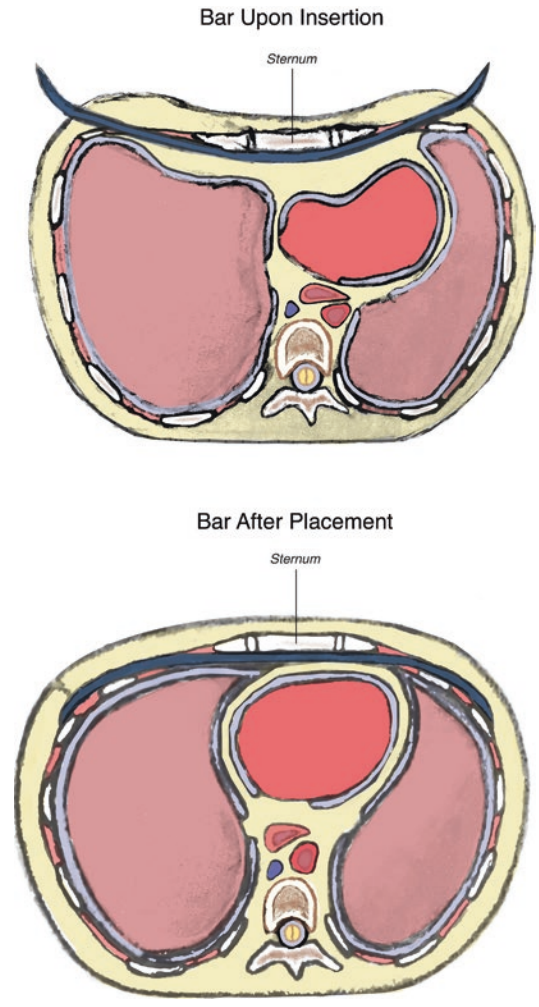


Image 14.4 Bar placement in chest (Illustration credit: Jadila Majid, MA)

sutures, along with lateral stabilizers to keep the bar in place. This addition has reduced the bar displacement rate to less than 1% [13, 14]. Some institutions have begun utilizing a third point of fixation as well [15]. Special bars are now made for asymmetric pectus vs. symmetric pectus, or with extra convexity for increased resistance to pressure [16]. Platinum bars are now available for patients with allergic reaction to nickel, which is a component of the traditional steel bar. Allergy testing is routinely done preoperatively to prevent any bar allergy complications which often require treatment with prednisone, or removal of the stainless steel bar [13]. Sternal elevation prior to mediastinal dissection has become a popular technique to facilitate the mediastinal dissection and to decrease risk of cardiac injury, with different tools and methods created to complete the sternal elevation safely [13, 15–17]. Sternal elevation has become standard of practice in many centers due to the many advantages including: improving visibility of the area behind the sternum, increasing the space for dissection, putting more room between the heart and the sternum, increasing ease of dissection, and decreasing risk of injury to mediastinal structures [15].

With all the advances and new techniques to modify the Nuss procedure, the patients are typically no longer kept sedated for a prolonged time. The patients are extubated postoperatively in the operating room (OR). They are encouraged to ambulate on postoperative day (POD) one, and typically discharged between POD 4–6. The discharge criteria include being able to ambulate independently, successful transition to an oral pain regiment and no evidence of postoperative complications such as pleural effusions, pneumothorax or bar displacement. The ideal recovery times are displayed in Table 14.2.

The bar is scheduled for removal usually about 2–3 years after insertion. Bar removal is done under general anesthesia with an endotracheal tube. Recovery time is shorter than with placement and expected postoperative pain is considerably less. Patients often go home the same day or within 1–2 days postoperatively. The risk of life threatening bleeding from a potential complication still exists. Therefore, large bore IV access, blood consent, and preparation for large volume blood transfusion is required. Images 14.5 and 14.6 are postoperative images of a patient who had a good results post MIRPE.

Table 14.2 Postoperative goals timeline [13]

Timeline	Postoperative goals
4–5 days postoperatively	Discharge from the hospital: Ambulating independently, PO pain regimen, aggressive incentive spirometry usage, normal followup chest x-ray
1–2 weeks postoperatively	Oral narcotics and sedatives weaned
2–4 weeks postoperatively	Oral inflammatories weaned
3 weeks postoperatively	Return to school
6 weeks postoperatively	Return to sports, return to normal activities, safe for heavy lifting if necessary
3 months postoperatively	Return to competitive sports

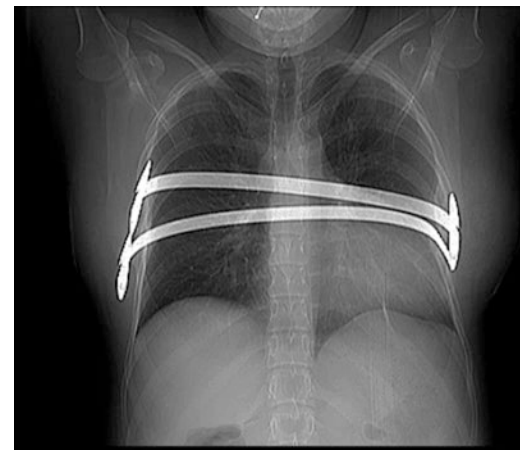


Image 14.5 Postoperative CXR of a patient who had a good result post MIRPE with decrease in dyspnea from cardiac compression (Image Credit: D. Shersher, MD)

Anesthetic Management

The Nuss procedure is done under general anesthesia, most commonly with an endotracheal (ETT) tube in place. A laryngeal mask airway has been used successfully in place of an ETT [18]. Some institutions utilize double lumen ETTs in

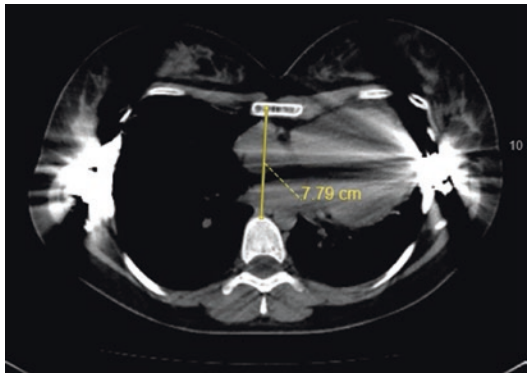


Image 14.6 Postoperative CT scan 1 year post MIRPE, displaying increased AP diameter of the chest as compared to the same patient preoperatively in Image 14.1 (Image Credit: D. Shersher, MD)

order to provide lung isolation on the side of thoracoscopy. Other institutions place the thoracoscope bilaterally for better visualization. General ETT anesthesia is most commonly provided, and large bore IV access is obtained. Patients' preoperative plan includes the necessary blood work and imaging, so the patients present to the OR with a full thorough workup already completed. Blood consent, preoperative blood typing, and having type and crossed blood available in the operating room is necessary to ensure adequate preparation in the event of an emergency. Though emergencies and complications are less common, the potential for severe and rapid blood loss exists; therefore precautions are in place. The patient is positioned supine with both arms abducted and above the head, using appropriate padding. Further advanced monitoring with an arterial line or central venous access may be placed on a case by case basis, assuming appropriate indications exist.

Intraoperative complications usually occur in relation to certain parts of the operation. Once the thoracoscope is inserted by the surgeon, a track is created behind the sternum prior to placing the bar. During track creation and bar insertion, there is risk of injury to vital thoracic and mediastinal structures. Intercostal vessels or the internal mammary artery may be injured and bleed during track creation or insertion of the thoracoscope. There is a risk of direct lung parenchymal injury, which can lead to bleeding and/or air leak. Most seriously, the pericardium or heart can be directly injured, potentially requiring sternotomy and cardiopulmonary bypass. There should be awareness by the surgeons and anesthesia providers, along with effective communication between both teams at all times.

The biggest challenge for the anesthesiologist is intraoperative and postoperative pain control, as these patients experience significant pain postoperatively. All patients generally receive multimodal analgesia which will be discussed later in the chapter. At the end of the surgery, the anesthesiologist helps the surgeon remove any remaining intrathoracic air by providing valsalva breaths, which also aids in recruiting any atelectatic areas of the lung. In most centers, patients are extubated immediately postoperatively, with no further need for prolonged intubation and sedation. They may remain hospitalized up to 4–5 days postoperatively, and occasionally require initial monitoring in an intensive care setting. If the patients have other baseline comorbidities such as congenital heart disease or connective tissue disease, they may be monitored in an ICU setting for a longer course.

The most common postoperative complication after the Nuss procedure is bar dislocation, which can occur within days to months after the procedure. Other common complications include pneumothorax, hemothorax, infection and rib fractures. A list of rare reported complications as well as more commonly seen complications are listed in Tables 14.3 and 14.4 respectively. Not all

Table 14.3 Rare but reported complications of repair of pectus excavatum using a minimally invasive approach [11, 19, 20]

Rare complications based on case reports
• Life threatening hemorrhage from pulmonary arterial vessel bleed after bar removal
• Fatal arrhythmia developed 3 years post repair in a patient with congenital heart disease
• Cardiac perforation/cardiac injury (on placement of bar and removal)
• Development of incarcerated diaphragmatic hernia requiring emergent repair
• Sternoclavicular dislocation leading to recurrence of funnel chest, requiring reoperation
• Laceration in the adventitial layer of the ascending aorta leading to bleeding, cardiac tamponade and cardiogenic shock, requiring emergent repair and bar removal
• Pericarditis and pneumonia requiring antibiotics and anti-inflammatories

Table 14.4 Common complications of repair of pectus excavatum using a minimally invasive approach [15, 19]

More commonly seen complications
• Bar dislocation or migration
• Pneumothorax
• Post-operative chronic pain
• Recurrent funnel chest needing reoperation
• Wound infection
• Pleural effusions
• Allergic reaction

adverse outcomes are reported so a true rate of severe life-threatening complications is unknown. Based on the current literature, the incidence of life-threatening complications is estimated at about 0.1% [15]. Awareness of the risks of the procedure, experience with the procedure and recognition of any potential complications as early as possible can help continue to keep the incidence of complications low [15].

Pain Management

Postoperative pain tends to be greater after MIRPE [21]. This can lead to complications including increased morbidity, decreased satisfaction, decreased functional status and quality of life, poor wound healing, delayed recovery time, increased length of stay (LOS), increased opioid consumption and duration, risk for chronic pain, and higher costs [22, 23]. Katz et al. looked at thoracotomy patients and concluded that early post-operative pain was the one factor that significantly predicted long-term pain [24]. Aggressive management of early postoperative pain may reduce long-term pain, unnecessary interventions, and costs.

The American Society of Anesthesiologists (ASA) has developed the Perioperative Surgical Home (PSH), which is a patient-centric, team-based model of care to help meet the demands of a rapidly approaching health care paradigm that will emphasize gratified providers, improve population health, reduce care costs, and satisfy patients [25]. According to the Centers for Disease Control and Prevention (CDC) website, over 67,000 drug overdose deaths occurred in the United States in 2018 with synthetic opioids being the main driver of these deaths [26]. Recent approaches in pain management focus on multimodal analgesia along with a multidisciplinary team approach to reduce opioids, side effects, and LOS. Enhanced Recovery After Surgery (ERAS) protocols help to achieve these goals. Numerous studies have shown improvement in pain outcomes when implementing protocols for various pediatric surgeries [27–30]. Despite improvements, there are still challenges to implementing them [31–35].

Preoperatively, patients and families should be counseled on pain expectations. Counseling has been shown to improve pain, outcomes, and satisfaction [36, 37]. Another non-pharmacological intervention which may improve pain is preoperative self-hypnosis therapy (SHT). Manworren et al. showed SHT along with epidural infusions helped reduce pain scores, morphine equivalents over time and LOS [38]. More research is needed, but SHT is an easy, safe intervention with minimal if any costs and side effects.

Preoperative pharmacological interventions should focus on non-opioid medications. Gabapentin, acetaminophen and clonidine patches are often given preoperatively. Gabapentin has been shown to help reduce pain, opioid use and their side effects, however it may not be helpful for chronic postsurgical pain [39–42]. Cyclooxygenase(COX)-2 selective nonsteroidal anti-inflammatory drugs (NSAIDs), such as celecoxib, are used to treat many conditions involving pain and inflammation [43]. Acetaminophen has been shown to reduce postoperative pain when given preoperatively [44]. Clonidine, may help reduce pain through its effects on the central nervous system. Transdermal clonidine, in addition to oral gabapentin postoperatively, showed improved functional outcomes, reduced opioid usage, and shorter LOS for posterior spinal fusion surgeries [45].

Constipation and postoperative nausea and vomiting (PONV) can cause strain and retching leading to pain, discomfort and complications with surgical site healing. Antibiotics and operative sterility help prevent surgical site infection (SSI) which can cause pain and possible reoperation. ERAS protocols focus on multimodal anal-

gesia to reduce side effects of opioids, but also include medications that directly counter these issues. Management of constipation consists of preoperative bowel regimen with stool softeners, followed by a postoperative clear diet that is advanced as tolerated. Medications that work on different chemoreceptors, such as scopolamine, aprepitant, ondansetron, dexamethasone, promethazine, prochlorperazine, droperidol and haloperidol can reduce PONV [46, 47].

Intraoperative analgesia for PE surgeries used to be opioid-based. Over time neuraxial anesthesia has been incorporated for pain management. Thoracic epidural catheters (TEC) were the neuraxial procedure preferred by anesthesiologists and surgeons. TECs can provide better analgesia than when IV opioids are used alone, and can help reduce postoperative ileus, pulmonary complications, and need for mechanical ventilation [48]. TECs may be placed in children under local anesthesia, sedation or under general anesthesia safely [49]. Although rare, TECs do have complications and side effects including: placement failure (5–35%), infections, dural puncture, epidural abscesses/hematomas, nerve damage, nausea, vomiting, pruritus, hypotension, urinary retention, sedation, and respiratory depression [48, 50]. Studies show there is no difference in pain outcomes between ropivacaine and bupivacaine in TECs [51, 52]. However, ropivacaine may reduce motor block and urinary retention and has less neurotoxicity and cardiotoxicity [53, 54]. The addition of opioids with local anesthetics has been shown to improve analgesia [51, 55]. TEC infusions can be started during MIRPE and continued and managed postoperatively.

Ultrasound imaging has led to nerve blocks being proposed and performed in lieu of TECs. Paravertebral nerve blocks (PNB) had equal analgesia with less opioid consumption, side effects and complications compared to TECs [56–60]. The incidence of pneumothoraces is low at 0.5% [61]. Ultrasound-guided bilateral intercostal nerve blocks (INB) have been shown to lower subjective pain scores, opioids administered and incidences of side effects compared to patient-controlled IV analgesia [62]. INBs also have a low incidence of pneumothorax [63]. One study using single-shot bilateral serratus anterior plane blocks noted decreased pain and opioid consumption but was not clear how effective they were on deeper intercostal muscles, which might result in pain while coughing [64]. Regional anesthesia is often provider dependent and may increase OR time. However, one study showed PNBs only prolonged OR time by 4 min compared to TEC placement [60].

Another option is for surgeons to directly place chest wall catheters (CWC) or perform cryoablation during surgery. Jaroszewski et al. showed no significant differences between TECs and CWCs in terms of pain, opioid usage or LOS [65]. Kabagambe et al. had pain scores slightly higher but clinically insignificant with CWCs [66]. Choudry et al. showed CWCs had slightly higher pain only on POD#0 but had the benefits of lower PONV, with shorter total OR and anesthesia times, and shorter LOS [67]. Cryoablation had reduced opioid requirements and shortened LOS [68, 69]. Cryoablation may increase OR times and costs, and removal of pain sensation may contribute to bar displacement due to increased postoperative activity [69].

Non-opioid medications should be used as analgesic adjuncts. If not given already, IV acetaminophen and ketorolac may be given intraoperatively. Despite concerns, studies have shown that perioperative bleeding or impaired bone healing are not increased [70–72]. Ketamine, when used as an infusion, has been shown to help reduce opioids [73, 74]. Ketamine can also be used postoperatively to reduce opioids [75, 76]. Methadone has been shown to be effective in lowering opioid consumption [77]. A retrospective study by Singhal et al. showed methadone was associated with lower total opioids, time with uncontrolled pain, and shortest LOS [77]. Side effects of methadone include sedation, respiratory depression, and QT prolongation. However, respiratory depression and prolonged sedation were not clinically significant at smaller doses. Although studies showed prolonged QT in some patients, there were no episodes of torsades de pointes [77]. Providers should consider getting a preoperative electrocardiogram if using methadone. Diazepam, a benzodiazepine, can be

used to prevent and treat muscle spasms, however there is no evidence of its effect as an analgesic adjuvant [78]. Diazepam can be started preoperatively, intraoperatively or postoperatively, but no studies were found comparing each phase. Dexamethasone can help reduce pain and opioid consumption after surgery [79, 80]. Dexamethasone simultaneously helps reduce the incidence of PONV. Concerns for postoperative surgical site infection and poor wound healing with dexamethasone are likely not warranted [81]. If a clonidine patch was not used, IV clonidine or clonidine placed with a block, may help reduce opioids and limit their side effects [82, 83]. Dexmedetomidine can also be added in blocks or separately as an infusion to help limit opioids and their side effects [84, 85]. Providers must be aware of serious potential side effects, such as hypotension and bradycardia, when using dexmedetomidine [84].

Postoperatively, patients should be maintained on their scheduled multimodal regimen. If available, multidisciplinary teams including an acute pain management specialist, should follow each patient. TECs or CWCs should be maintained and adjusted as needed to help reduce opioid use. Depending on protocols, some patients may be discharged with CWCs. Most patients will receive patient-controlled opioid analgesia, but focus should be on maintaining scheduled non-opioid medication with goals to convert to oral medications as soon as tolerated. Providers should continue to focus on advancing diet, preventing PONV, constipation, SSI, thromboembolism and maintaining aggressive pulmonary toilet. All patients should be placed on a recovery floor with ability to monitor respiratory status. Despite aggressive pain management, chronic postoperative pain may develop. Besides chronic pharmacologic treatment, there may be other options for pain control. One case report showed that bilateral paravertebral nerve radiofrequency thermoablation stopped pain in a patient until scheduled bar removal [86]. More studies may be needed to evaluate the best method of managing chronic pain.

No definitive pain management guidelines have been created for MIRPE. A multidisciplinary and multimodal analgesic regimen is likely to help reduce pain, complications, and costs while also increasing patient and family satisfaction. Institutes should develop and implement protocols, as well as inform patients and staff about expectations, in order to achieve these goals. Example of an ERAS protocol is shown in Table 14.5. Protocols and training can help reduce variations in care, which can help determine what changes can be made for improvement. Further prospective studies may allow for practitioners to optimize their practices to benefit patients [87].

Outcomes

The Nuss procedure has become a standard of care in surgically correcting PE as it has proved to be effective and safe, with good psychological results. The outcomes of the procedure have been documented through measuring anatomic surgical results after bar removal, improved postoperative cardiac and/or pulmonary function, patient satisfaction, recurrence rate, and incidence of complications. Anatomic surgical outcome was reported to be good or excellent in 95.3% of patients in a 2010 report by Kelly RE et al., with similar outcomes cited in other reports [9, 12, 88]. In addition, striking improvement in postoperative cardiac output and PFTs are evident in many reports [4, 7, 9].

Patient and caretaker satisfaction rates measured via questionnaires and postoperative evaluations indicate positive results. Examples of criteria examined by surveys aimed at identifying physical and psychosocial results include satisfaction with the surgery overall, satisfaction with the physical appearance, number of missed school days and improvement in exercise capacity. Questionnaires concerning physical limitation and psychosocial functioning indicated high satisfaction scores from both patients and parents [4]. In a review of 251 cases, patient satisfaction was rated as excellent or good in 96.5% of surveyed cases [10].

Recurrence rates after the Nuss procedure are approximately 1–2% as indicated in many publi-

Table 14.5 Theoretical MIRPE enhanced recovery after surgery (ERAS) protocol

Theoretical MIRPE enhanced recovery after surgery (ERAS) protocol	
Prior to ERAS initiation	Create a plan at your institute that can be agreed upon amongst the surgeons, anesthesiologists, and multidisciplinary teams
	Provide intensive training to all members who will be taking care of MIRPE patients
Preoperative	Preoperative assessment, including educating patients and family of pain management methods and goals
	Consider using non-medication strategies including child life experts and other coping methods
	Bowel regimen, including clear liquids up until 2 h prior to procedure and stool softeners
	PONV prophylaxis
	Multimodal analgesia prior to OR, focusing on non-opioid medications: NSAIDs, acetaminophen, gabapentin, diazepam, etc.
Intraoperative	Prevention of SSI: Timely antibiotic prophylaxis, thromboprophylaxis, maintain normothermia
	Continue PONV prophylaxis
	Continue multimodal analgesia which may include medications such as ketamine, dexmedetomidine, methadone with opioid administration as needed
	Neuraxial anesthesia, which may include thoracic epidurals, chest wall catheters, paravertebral or sub-paraspinal blocks, intercostal nerve blocks, serratus anterior plane blocks, cryoablation
Postoperative	Continue multimodal pain management, including patient controlled analgesia
	If available, utilize a pain management service to manage neuraxial anesthesia
	Plan to start oral medications by postoperative day (POD) 1
	Prevent SSI including continuing antibiotics, early ambulation utilizing physical therapy, aggressive incentive spirometry
	Promote gastrointestinal (GI) motility by starting clear diet early and advancing as tolerated, promote early ambulation, start GI prophylaxis, continue PONV medications as needed
	Goal for discharge on POD 2–3
	Appropriate followup, including pain management if continuous chest wall infusions are still being used

cations from around the world. Reports of higher recurrence rates are associated with elective or early bar removal and younger age at time of repair. However they remain lower than the recurrence rates of the open Ravitch procedure [4, 7]. The literature reports 2–20% incidence of complications, both minor and major. The most common complications include bar displacement, pneumothorax, infection, pleural effusion, and hemorrhage [2, 4, 9–12, 88]. In 2018, a publication discussing the complications and mortality associated with the Nuss procedure reported incidence of life-threatening complications to be approximately 0.1% of the 50,000 cases estimated to have been performed in the past 20 years [15]. The incidence of complications was higher closer to the time of introduction of the new procedure. As experience with the procedure increased over time, complications rates correspondingly decreased.

Conclusion

PE is the most common congenital chest wall deformity, occurring in about 0.008% of live births. Since Donald Nuss introduced the MIRPE technique in 1998, the procedure has been revised and improved to make it a safe and effective method, no longer requiring prolonged hospital stays. More than a cosmetic deformity, there are pulmonary, cardiac and psychosocial sequelae of the disease. These limitations are all indications to proceed with surgery. The most up-to-date

Nuss procedure includes: thoracoscopy to visualize into the chest, placement of a uniquely curved bar behind the sternum in the anterior mediastinum avoiding the heart and vital thoracic organs, rotation of the bar to position the curve anteriorly and below the point of maximal depression in order to elevate the sternum into the desired location, and secure stabilization of the bar in place to prevent displacement. General ETT anesthesia with large bore IV access and blood typing are required, as well as an effective intraoperative and postoperative pain plan in place. The bar is typically removed after 2–3 years. Although the incidence of complications has decreased with time, the potential for life threatening complications still exists. However, with experience and improvements in technique, the incidence of these complications remains extremely low. The Nuss procedure has proved to be a safe and effective technique to treat PE with obvious physical, physiologic, and psychosocial benefits.

Acknowledgements The authors would like to express their gratitude to Ms. J. Majid for her contribution of illustrations and to Dr. D Shersher for his contribution of images to the chapter.

References

1. Mayer OH. Pectus excavatum: treatment. In: Redding G, Hoppin AG editors. UpToDate. Waltham, MA: UpToDate; 2019 [cited 2019 Dec 3].
2. Molik KA, Engum SA, Rescorla FJ, West KW, Scherer LR, Grosfeld JL. Pectus excavatum repair: experience with standard and minimal invasive techniques. J Pediatr Surg. 2001;36(2):324–8.
3. Kelly RE Jr. Pectus excavatum: historical background, clinical picture, preoperative evaluation and criteria for operation. Semin Pediatr Surg. 2008;17(3):181–93.
4. Kelly RE Jr, Daniel A. Outcomes, quality of life, and long-term results after pectus repair from around the globe. Semin Pediatr Surg. 2018;27(3):170–4.
5. Nuss D, Kelly RE Jr, Croitoru DP, Katz ME. A 10-year review of a minimally invasive technique for the correction of pectus excavatum. J Pediatr Surg. 1998;33(4):545–52.
6. Haller JA, Kramer SS, Lietman SA. Use of CT scans in selection of patients for pectus excavatum surgery: a preliminary report. J Pediatr Surg. 1987;22(10):904–6.
7. Nuss D, Kelly RE Jr. Indications and technique of Nuss procedure for pectus excavatum. Thorac Surg Clin. 2010;20(4):583–97.
8. Singhal NR, Jerman JD. A review of anesthetic considerations and postoperative pain control after the Nuss procedure. Semin Pediatr Surg. 2018;27(3):156–60.
9. Kelly RE Jr, Goretsky MJ, Obermeyer R, Kuhn MA, Redlinger R, Haney TS, et al. Twenty-one years of experience with minimally invasive repair of pectus excavatum by the Nuss procedure in 1215 patients. Ann Surg. 2010;252(6):1072–81.
10. Hebra A, Swoveland B, Egbert M, Tagge EP, Georgeson K, Othersen HB Jr, et al. Outcome analysis of minimally invasive repair of pectus excavatum: review of 251 cases. J Pediatr Surg. 2000;35(2):252–7.
11. Leonhardt J, Kubler JF, Feiter J, Ure BM, Petersen C. Complications of the minimally invasive repair of pectus excavatum. J Pediatr Surg. 2005;40(11):e7–9.
12. Zhang DK, Tang JM, Ben XS, Xie L, Zhou HY, Ye X, et al. Surgical correction of 639 pectus excavatum cases via the Nuss procedure. J Thorac Dis. 2015;7(9):1595–605.
13. Nuss D, Obermeyer RJ, Kelly RE. Nuss bar procedure: past, present and future. Ann Cardiothorac Surg. 2016;5(5):422–33.
14. Nuss D. Minimally invasive surgical repair of pectus excavatum. Semin Pediatr Surg. 2008;17(3):209–17.
15. Hebra A, Kelly RE, Ferro MM, Yuksel M, Campos JRM, Nuss D. Life-threatening complications and mortality of minimally invasive pectus surgery. J Pediatr Surg. 2018;53(4):728–32.
16. Park HJ, Lee SY, Lee CS, Youm W, Lee KR. The Nuss procedure for pectus excavatum: evolution of techniques and early results on 322 patients. Ann Thorac Surg. 2004;77(1):289–95.
17. Park HJ, Kim KS, Lee S, Jeon HW. A next-generation pectus excavatum repair technique: new devices make a difference. Ann Thorac Surg. 2015;99(2):455–61.
18. Mao S, Du X, Ma J, Zhang G, Cui J. A comparison between laryngeal mask airway and endotracheal intubation for anaesthesia in adult patients undergoing NUSS procedure. J Thorac Dis. 2018;10(6):3216–24.
19. Hoel TN, Rein KA, Svennevig JL. A life-threatening complication of the Nuss procedure for pectus excavatum. Ann Thorac Surg. 2006;81(1):370–2.
20. Marusch F, Gastinger I. Life-threatening complication of the Nuss-procedure for funnel chest. A case report. Zentralbl Chir. 2003;128(11):981–4.
21. Papic JC, Finnell SM, Howenstein AM, Breckler F, Leys CM. Postoperative opioid analgesic use after Nuss versus Ravitch pectus excavatum repair. J Pediatr Surg. 2014;49(6):919–23; discussion 923. https://doi.org/10.1016/j.jpedsurg.2014.01.025.
22. Hanna WC, Ko MA, Blitz M, Shargall Y, Compeau CG. Thoracoscopic Nuss procedure for young adults with pectus excavatum: excellent midterm results and patient satisfaction. Ann Thorac Surg. 2013;96(3):1033–6; discussion 1037–8. https://doi.org/10.1016/j.athoracsur.2013.04.093.

23. St Peter SD, Weesner KA, Weissend EE, Sharp SW, Valusek PA, Sharp RJ, Snyder CL, Holcomb GW 3rd, Ostlie DJ. Epidural vs patient-controlled analgesia for postoperative pain after pectus excavatum repair: a prospective, randomized trial. J Pediatr Surg. 2012;47(1):148–53. https://doi.org/10.1016/j.jpedsurg.2011.10.040.
24. Katz J, Jackson M, Kavanagh BP, Sandler AN. Acute pain after thoracic surgery predicts long-term post-thoracotomy pain. Clin J Pain. 1996;12(1):50–5.
25. Kash BA, Zhang Y, Cline KM, Menser T, Miller TR. The perioperative surgical home (PSH): a comprehensive review of US and non-US studies shows predominantly positive quality and cost outcomes. Milbank Q. 2014;92(4):796–821. https://doi.org/10.1111/1468-0009.12093.
26. Hedegaard H, Miniño AM, Warner M. Drug overdose deaths in the United States, 1999–2018. NCHS Data Brief no 356. Hyattsville, MD: National Center for Health Statistics. p. 2020.
27. Leeds IL, Boss EF, George JA, Strockbine V, Wick EC, Jelin EB. Preparing enhanced recovery after surgery for implementation in pediatric populations. J Pediatr Surg. 2016;51(12):2126–9. https://doi.org/10.1016/j.jpedsurg.2016.08.029.
28. Varadhan KK, Neal KR, Dejong CH, Fearon KC, Ljungqvist O, Lobo DN. The enhanced recovery after surgery (ESR) pathway for patients undergoing major elective open colorectal surgery: a meta-analysis of randomized trials. Clin Nutr. 2010;29(4):434–40. https://doi.org/10.1016/j.clnu.2010.01.004.
29. West MA, Horwood JF, Staves S, Jones C, Goulden MR, Minford J, Lamont G, Baillie CT, Rooney PS. Potential benefits of fast-track concepts in pediatric colorectal surgery. J Pediatr Surg. 2013;48(9):1924–30. https://doi.org/10.1016/j.jpedsurg.2013.02.063.
30. Reismann M, Dingemann J, Wolters M, Laupichler B, Suempelmann R, Ure BM. Fast-track concepts in routine pediatric surgery: a prospective study in 436 infants and children. Langenbecks Arch Surg. 2009;394(3):529–33. https://doi.org/10.1007/s00423-008-0440-1.
31. Wren AA, Ross AC, D'Souza G, Almgren C, Feinstein A, Marshall A, Golianu B. Multidisciplinary pain management for pediatric patients with acute and chronic pain: a foundational treatment approach when prescribing opioids. Children (Basel). 2019;6(2):E33. https://doi.org/10.3390/children6020033.
32. Odell S, Logan DE. Pediatric pain management: the multidisciplinary approach. J Pain Res. 2013;6:785–90. https://doi.org/10.2147/JPR.S37434.
33. Friedrichsdorf SJ, Postier A, Eull D, Weidner C, Foster L, Gilbert M, Campbell F. Pain outcomes in a US children's hospital: a prospective cross-sectional survey. Hosp Pediatr. 2015;5(1):18–26. https://doi.org/10.1542/hpeds.2014-0084.
34. Vidaurri LD, Hoang SQ. Pediatric ERAS: big ideas for the smallest patients. ASA Monitor. 2020;84(3):26–8.
35. Litz CN, Farach SM, Fernandez AM, Elliott R, Dolan J, Nelson W, Walford NE, Snyder C, Jacobs JP, Amankwah EK, Danielson PD, Chandler NM. Enhancing recovery after minimally invasive repair of pectus excavatum. Pediatr Surg Int. 2017;33(10):1123–9. https://doi.org/10.1007/s00383-017-4148-6.
36. Kiecolt-Glaser JK, Page GG, Marrucha PT, MacCallum RC, Glaser R. Psychological influences on surgical recovery perspectives from pscychthoreumoimmunology. Am Psychol. 1996;53:1209–18.
37. Anderson KO, Masur FT. Psychological preparation for invasive medical and dental procedures. J Behav Med. 1983;6(1):1–40.
38. Manworren RCB, Anderson MN, Girard ED, Ruscher KA, Verissimo AM, Palac H, Weiss R, Rader C, Hight D. Postoperative pain outcomes after Nuss procedures: comparison of epidural analgesia, continuous infusion of local anesthetic, and preoperative self-hypnosis training. J Laparoendosc Adv Surg Tech A. 2018;28(10):1234–42. https://doi.org/10.1089/lap.2017.0699.
39. Sills GJ. The mechanisms of action of gabapentin and pregabalin. Curr Opin Pharmacol. 2006;6(1):108–13.
40. Han C, Kuang MJ, Ma JX, Ma XL. The efficacy of preoperative gabapentin in spinal surgery: a meta-analysis of randomized controlled trials. Pain Physician. 2017;20(7):649–61.
41. Khan ZH, Rahimi M, Makarem J, Khan RH. Optimal dose of pre-incision/post-incision gabapentin for pain relief following lumbar laminectomy: a randomized study. Acta Anaesthesiol Scand. 2011;55(3):306–12.
42. Dauri M, Faria S, Gatti A, Celidonio L, Carpenedo R, Sabato AF. Gabapentin and pregabalin for the acute post-operative pain management. A systematic-narrative review of the recent clinical evidences. Curr Drug Targets. 2009;10(8):716–33.
43. Derry S, Moore RA. Single dose oral celecoxib for acute postoperative pain in adults. Cochrane Database Syst Rev. 2013;10:CD004233. https://doi.org/10.1002/14651858.CD004233.pub4.
44. Remy C, Marret E, Bonnet F. Effects of acetaminophen on morphine side-effects and consumption after major surgery: meta-analysis of randomized controlled trials. Br J Anaesth. 2005;94(4):505–13.
45. Choudhry DK, Brenn BR, Sacks K, Shah S. Evaluation of gabapentin and clonidine use in children following spinal fusion surgery for idiopathic scoliosis: a retrospective review. J Pediatr Orthop. 2019;39(9):e687–93. https://doi.org/10.1097/BPO.0000000000000989.
46. McCracken GC, Montgomery J. Postoperative nausea and vomiting after unrestricted clear fluids before day surgery: a retrospective analysis. Eur J Anaesthesiol. 2018;35(5):337–42. https://doi.org/10.1097/EJA.0000000000000760.
47. Höhne C. Postoperative nausea and vomiting in pediatric anesthesia. Curr Opin Anaesthesiol. 2014;27(3):303–8. https://doi.org/10.1097/ACO.0000000000000073.
48. Manion SC, Brennan TJ. Thoracic epidural analgesia and acute pain management. Anesthesiology. 2011;115(1):181–8.

49. Polaner DM, Taenzer AH, Walker BJ, Bosenberg A, Krane EJ, Suresh S, Wolf C, Martin LD. Pediatric regional anesthesia network (PRAN): a multi-institutional study of the use and incidence of complications of pediatric regional anesthesia. Anesth Analg. 2012;115(6):1353–64. https://doi.org/10.1213/ANE.0b013e31825d9f4b.
50. St Peter SD, Weesner KA, Sharp RJ, et al. Is epidural anesthesia truly the best pain management strategy after minimally invasive pectus excavatum repair? J Pediatr Surg. 2008;43:79–82. [discussion]
51. Macias A, Monedero P, Adame M, Torre W, Fidalgo I, Hidalgo F. A randomized, double-blinded comparison of thoracic epidural ropivacaine, ropivacaine/fentanyl, or bupivacaine/fentanyl for postthoracotomy analgesia. Anesth Analg. 2002;95(5):1344–50.
52. Walaszczyk M, Wiench R, Copik M, Karpe J, Lowicka M, Pioro A, Knapik P, Misiolek H. Ropivacaine has no advantage over bupivacaine in thoracic epidural analgesia for patients with pectus excavatum undergoing the Nuss procedure—a single blind randomized clinical trial comparing efficacy and safety. Pol J Cardiothorac Surg. 2018;15(1):5–9. https://doi.org/10.5114/kitp.2018.74668.
53. Girsberger SA, Schneider MP, Löffel LM, Burkhard FC, Wuethrich PY. Effect of thoracic epidural Ropivacaine versus bupivacaine on lower urinary tract function: a randomized clinical trial. Anesthesiology. 2018;128(3):511–9. https://doi.org/10.1097/ALN.0000000000001980.
54. McClellan KJ, Faulds D. Ropivacaine: an update of its use in regional anaesthesia. Drugs. 2000;60(5):1065–93.
55. Block BM, Liu SS, Rowlingson AJ, Cowan AR, Cowan JA Jr, Wu CL. Efficacy of postoperative epidural analgesia: a meta-analysis. JAMA. 2003;290(18):2455–63.
56. Davies RG, Myles PS, Graham JM. A comparison of the analgesic efficacy and side-effects of paravertebral vs epidural blockade for thoracotomy: a systematic review and metaanalysis of randomized trials. Br J Anaesth. 2006;96(4):418–26.
57. Daly DJ, Myles PS. Update on the role of paravertebral blocks for thoracic surgery: are they worth it? Curr Opin Anaesthesiol. 2009;22(1):38–43.
58. Powell ES, Cook D, Pearce AC, Davies P, Bowler GM, Naidu B, Gao F. UKPOS investigators: a prospective, multicentre, observational cohort study of analgesia and outcome after pneumonectomy. Br J Anaesth. 2011;106(3):364–70.
59. Hall Burton DM, Boretsky KR. A comparison of paravertebral nerve block catheters and thoracic epidural catheters for postoperative analgesia following the Nuss procedure for pectus excavatum repair. Paediatr Anaesth. 2014;24(5):516–20. https://doi.org/10.1111/pan.12369.
60. Bryskin R, Robie D, Mansfield F, Freid E, Sukumvanich S. Introduction of a novel ultrasound-guided extrathoracic sub-paraspinal block for control of perioperative pain in Nuss procedure patients. J Pediatr Surg. 2017;52(3):484–91.
61. Lönnqvist PA, MacKenzie J, Soni AK, Conacher ID. Paravertebral blockade. Failure rate and complications. Anaesthesia. 1995;50(9):813–5.
62. Luo M, Liu X, Ning L, Sun Y, Cai Y, Shen S. Comparison of ultrasonography-guided bilateral intercostal nerve blocks and conventional patient-controlled intravenous analgesia for pain control after the Nuss procedure in children: a prospective randomized study. Clin J Pain. 2017;33(7):604–10. https://doi.org/10.1097/AJP.0000000000000449.
63. Moore DC. Intercostal nerve block for postoperative somatic pain following surgery of thorax and upper abdomen. Br J Anaesth. 1975;47(suppl):284–6.
64. Hammerback H, Venkatachalam S, Rashid A. Serratus plane block and rib fractures. Anaesthesia. 2016; 77 (In-Reply).
65. Jaroszewski DE, Temkit M, Ewais MM, Luckritz TC, Stearns JD, Craner RC, Gaitan BD, Ramakrishna H, Thunberg CA, Weis RA, Myers KM, Merritt MV, Rosenfeld DM. Randomized trial of epidural vs. subcutaneous catheters for managing pain after modified Nuss in adults. J Thorac Dis. 2016;8(8):2102–10. https://doi.org/10.21037/jtd.2016.06.62.
66. Kabagambe SK, Goodman LF, Chen YJ, Keller BA, Becker JC, Raff GW, Stark RA, Stephenson JT, Rahm A, Farmer DL, Hirose S. Subcutaneous local anesthetic infusion could eliminate use of epidural analgesia after the Nuss procedure. Pain Manag. 2018;8(1):9–13. https://doi.org/10.2217/pmt-2017-0042.
67. Choudhry DK, Brenn BR, Sacks K, Reichard K. Continuous chest wall ropivacaine infusion for analgesia in children undergoing Nuss procedure: a comparison with thoracic epidural. Paediatr Anaesth. 2016;26(6):582–9. https://doi.org/10.1111/pan.12904.
68. Morikawa N, Laferriere N, Koo S, Johnson S, Woo R, Puapong D. Cryoanalgesia in patients undergoing Nuss repair of pectus excavatum: technique modification and early results. J Laparoendosc Adv Surg Tech A. 2018;28(9):1148–51. https://doi.org/10.1089/lap.2017.0665.
69. Keller BA, Kabagambe SK, Becker JC, Chen YJ, Goodman LF, Clark-Wronski JM, Furukawa K, Stark RA, Rahm AL, Hirose S, Raff GW. Intercostal nerve cryoablation versus thoracic epidural catheters for postoperative analgesia following pectus excavatum repair: preliminary outcomes in twenty-six cryoablation patients. J Pediatr Surg. 2016;51(12):2033–8. https://doi.org/10.1016/j.jpedsurg.2016.09.034.
70. Gobble RM, Hoang HL, Kachniarz B, Orgill DP. Ketorolac does not increase perioperative bleeding: a meta-analysis of randomized controlled trials. Plast Reconstr Surg. 2014;133(3):741–55. https://doi.org/10.1097/01.prs.0000438459.60474.b5.
71. Strom BL, Berlin JA, Kinman JL, Spitz PW, Hennessy S, Feldman H, Kimmel S, Carson JL. Parenteral ketorolac and risk of gastrointestinal and operative

site bleeding. A postmarketing surveillance study. JAMA. 1996;275(5):376–82.
72. Pradhan BB, Tatsumi RL, Gallina J, Kuhns CA, Wang JC, Dawson EG. Ketorolac and spinal fusion: does the perioperative use of ketorolac really inhibit spinal fusion? Spine (Phila Pa 1976). 2008;33(19):2079–82. https://doi.org/10.1097/BRS.0b013e31818396f4.
73. Himmelseher S, Durieux ME. Ketamine for perioperative pain management. Anesthesiology. 2005;102(1):211–20.
74. Gorlin AW, Rosenfeld DM, Ramakrishna H. Intravenous sub-anesthetic ketamine for perioperative analgesia. J Anaesthesiol Clin Pharmacol. 2016;32(2):160–7. https://doi.org/10.4103/0970-9185.182085.
75. Cha MH, Eom JH, Lee YS, Kim WY, Park YC, Min SH, Kim JH. Beneficial effects of adding ketamine to intravenous patient-controlled analgesia with fentanyl after the Nuss procedure in pediatric patients. Yonsei Med J. 2012;53(2):427–32. https://doi.org/10.3349/ymj.2012.53.2.427.
76. Min TJ, Kim WY, Jeong WJ, Choi JH, Lee YS, Kim JH, Park YC. Effect of ketamine on intravenous patient-controlled analgesia using hydromorphone and ketorolac after the Nuss surgery in pediatric patients. Korean J Anesthesiol. 2012;62(2):142–7. https://doi.org/10.4097/kjae.2012.62.2.142.
77. Murphy GS, Szokol JW. Intraoperative methadone in surgical patients: a review of clinical investigations. Anesthesiology. 2019;131(3):678–92.
78. Seki H, Ideno S, Ishihara T, Watanabe K, Matsumoto M, Morisaki H. Postoperative pain management in patients undergoing posterior spinal fusion for adolescent idiopathic scoliosis: a narrative review. Scoliosis Spinal Disord. 2018;13:17. https://doi.org/10.1186/s13013-018-0165-z.
79. De Oliveira GS Jr, Almeida MD, Benzon HT, McCarthy RJ. Perioperative single dose systemic dexamethasone for postoperative pain: a meta-analysis of randomized controlled trials. Anesthesiology. 2011;115(3):575–88. https://doi.org/10.1097/ALN.0b013e31822a24c2.
80. Waldron NH, Jones CA, Gan TJ, Allen TK, Habib AS. Impact of perioperative dexamethasone on postoperative analgesia and side-effects: systematic review and meta-analysis. Br J Anaesth. 2013;110(2):191–200. https://doi.org/10.1093/bja/aes431.
81. Polderman JAW, Farhang-Razi V, Van Dieren S, Kranke P, DeVries J, Hollmann MW, Preckel B, Hermanides J. Adverse side-effects of dexamethasone in surgical patients—an abridged Cochrane systematic review. Anaesthesia. 2019;74(7):929–39. https://doi.org/10.1111/anae.14610.
82. Samantaray A, Rao MH, Chandra A. The effect on post-operative pain of intravenous clonidine given before induction of anaesthesia. Indian J Anaesth. 2012;56(4):359–64. https://doi.org/10.4103/0019-5049.100817.
83. Cucchiaro G, Adzick SN, Rose JB, Maxwell L, Watcha M. A comparison of epidural bupivacaine-fentanyl and bupivacaine-clonidine in children undergoing the Nuss procedure. Anesth Analg. 2006;103(2):322–7.
84. Tang C, Xia Z. Dexmedetomidine in perioperative acute pain management: a non-opioid adjuvant analgesic. J Pain Res. 2017;10:1899–904. https://doi.org/10.2147/JPR.S139387.
85. Schnabel A, Meyer-Frießem CH, Reichl SU, Zahn PK, Pogatzki-Zahn EM. Is intraoperative dexmedetomidine a new option for postoperative pain treatment? A meta-analysis of randomized controlled trials. Pain. 2013;154(7):1140–9. https://doi.org/10.1016/j.pain.2013.03.029.
86. Ladenhauf HN, Stundner O, Likar R, Schnöll J, Metzger RP. Successful treatment of persistent pain after pectus excavatum repair using paravertebral nerve radiofrequency thermoablation. AA Case Rep. 2017;8(1):18–20.
87. Boric K, Dosenovic S, Jelicic Kadic A, Batinic M, Cavar M, Urlic M, Markovina N, Puljak L. Interventions for postoperative pain in children: an overview of systematic reviews. Paediatr Anaesth. 2017;27(9):893–904. https://doi.org/10.1111/pan.13203.
88. Miller KA, Woods RK, Sharp RJ, Gittes GK, Wade K, Ashcraft KW, et al. Minimally invasive repair of pectus excavatum: a single institution's experience. Surgery. 2001;130(4):652–7.
89. Singhal NR, Jones J, Semenova J, Williamson A, McCollum K, Tong D, Jerman J, Notrica DM, Nguyen H. Multimodal anesthesia with the addition of methadone is superior to epidural analgesia: a retrospective comparison of intraoperative anesthetic techniques and pain management for 124 pediatric patients undergoing the Nuss procedure. J Pediatr Surg. 2016;51(4):612–6. https://doi.org/10.1016/j.jpedsurg.2015.10.084.

15 Congenital Chest Wall Abnormalities and Anesthetic Challenges

Michael R. Schwartz and Erin W. Pukenas

Introduction

In the normal anatomic variant, the chest wall is composed of the rib cage and vertebral column, with the diaphragm forming the inferior border. An intact chest wall is vital to maintaining normal cardiorespiratory physiology. Congenital defects can be minor, causing only cosmetic concerns, but can be more severe causing major physiologic dysfunction in patients. Abnormalities range from common defects to very rare ones that may cause significant morbidity and mortality. Chest wall abnormalities may be seen in isolation, but are often associated with other syndromes which may present providers with additional concerns. Providers must be aware of these issues and the challenges they may experience when taking care of these patients.

Pectus Deformities: Pectus Excavatum, Pectus Carinatum, Pectus Arcuatum

Pectus deformities comprise approximately 95% of congenital chest wall abnormalities and include pectus excavatum (PE), pectus carinatum (PC), and pectus arcuatum (PA). While there is no consensus on the etiology of pectus deformities, it is thought they are due to abnormal or defective growth of the cartilage, ribs and sternum [1–4]. The majority of pectus deformities are minor, and often the greatest concern amongst patients relates to cosmetic appearance. However, each pectus deformity can have a spectrum of presentations, including cardiorespiratory compromise. Surgery is dependent on patients desire for cosmetic improvement as well as comorbid conditions caused by the severity of the defect.

PE is a chest wall deformity characterized by a sunken chest and is sometimes referred to as "funnel chest". PE accounts for almost 90% of pectus deformities [5]. PE occurs in 1 in every 300–1000 live births and is more common in males than females [5, 6]. Pectus carinatum (PC), also known as "pigeon chest", is a protrusion deformity of the chest wall. PC is less common than PE occuring in 1 per 1500 live births with 80% male predominance [2]. PC is also more common in Caucasian and Hispanic populations [7]. Pectus arcuatum (PA) also known as pouter pigeon chest, is an even rarer wave-like deformity with a mixed form of excavatum and carinatum features.

Pectus deformities are usually solitary and sporadic but may have a genetic component with familial incidence ranging from 25 to 45% [2, 8]. Pectus deformities may also be associated with other diseases including connective tissue

M. R. Schwartz (✉) · E. W. Pukenas
Cooper University Health Care, Cooper Medical School of Rowan University, Camden, NJ, USA
e-mail: schwartz-michael@cooperhealth.edu; pukenas-erin@cooperhealth.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_15

Table 15.1 Other diseases associated with pectus excavatum, carinatum and arcuatum

Connective tissue disorders [9, 10]	Neuromuscular/muscular disorders [11]	Other genetic disorders [12]
• Marfan syndrome • Ehlers-Danlos syndrome • Osteogenesis imperfecta • Poland syndrome • MASS (mitral valve prolapse, not progressive aortic enlargement, skeletal and skin alterations) • Loeys–Dietz syndrome	• Spinal muscular atrophy • Facio-scapulo-humeral muscular dystrophy • Duchenne muscular dystrophy • Rigid spine syndrome • Non-Fukuyama CMD • Multi-minicore disease • Nemaline myopathy • Congenital myopathy • Multicore disease • Myotubular (centronuclear) myopathy • Minimal change myopathy • Actin myopathy (congenital)	• Multiple endocrine neoplasia type 2b • Noonan syndrome • Turner syndrome • Cardiofaciocutaneous syndrome • Holt-Oram syndrome • Morquio syndrome • Coffin-Lowry syndrome

disorders, neuromuscular disorders and genetic disorders as seen in Table 15.1 [9–12]. PE may present in infancy in one third of cases but most cases, as with PC and PA, present and worsen in puberty due to natural growth spurts [3, 13, 14].

Clinically, most pectus deformities have no or minimal symptoms. Non-operative treatment of pectus deformities may include exercise and physical therapy. PE may be treated with vacuum bell therapy, while PC can be treated with bracing [15–17]. The decision to perform surgery may be cosmetic due to psychosocial stress or due to functional limitations [13, 18, 19]. As pectus deformities worsen, they may cause symptoms which include shortness of breath, dyspnea, fatigue, respiratory infections, and, in severe cases, restrictive lung disease, cardiac compression and arrhythmias [3]. More severe symptoms typically occur in pectus disorders associated with severe scoliosis or associated syndromes [9].

Preoperative evaluation of pectus disorders depends on the degree of the abnormality. A thorough history and physical can help to elicit the degree of the deformity. On examination, patients should be observed for dyspnea and tachypnea. Cardiac auscultation may reveal tachycardia and murmurs due to conduction defects or heart displacement and obstruction [20]. Imaging, including x-ray and computed tomography (CT), can determine the severity of the deformity. Surgeons use the pectus severity index (PSI), also known as the Haller Index, to determine the degree of the deformity. This is calculated by dividing the width of the chest by the distance between the sternum and spine. A normal PSI value is 2.54. A higher PSI correlates with more severe deformity in PE, whereas a lower PSI in PC indicates more severity [3, 7].

Additional testing is usually not warranted unless there are symptomatic concerns or patients have other syndromes associated with cardiopulmonary defects. Despite subjective respiratory symptoms, pulmonary function testing (PFT) only shows abnormalities in about a third of cases [21]. PFTs more often show restrictive and less commonly obstructive patterns, often times with decreased lung volumes [13]. Electrocardiogram may show axis deviation and ST depression, likely from rotation rather than intrinsic heart defects [3]. Further cardiac testing such as echocardiogram and exercise stress tests may be performed. However, these are usually only indicated if severe disease or associated conditions with underlying heart defects.

PE was originally repaired via the Ravitch technique, which required the sub-perichondrial resection of all deformed costal cartilages, xiphoid excision and sternal osteotomy, with anterior fixation of the sternum [22]. The Modified Ravitch procedure is a modification, consisting of resection of the subperichondrial cartilage, a sternal osteotomy underneath the angle of the PE, and temporary internal fixation

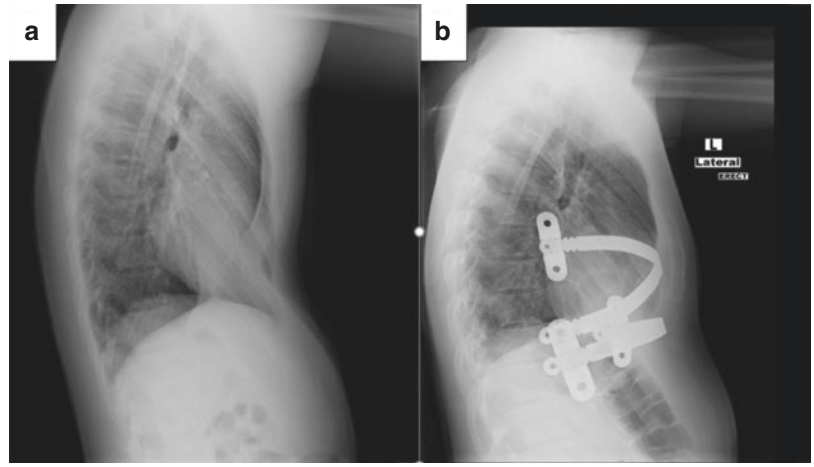


Fig. 15.1 (**a**) Preoperative lateral chest x-ray. (**b**) Postoperative lateral chest x-ray. Permission: Bowen F. (2017) Camden, NJ: Cooper University Hospital

to support the sternum [23]. In 1998 Dr. Nuss created an alternative method, now known as the Nuss procedure, which is a minimally invasive technique that involves two small cuts in the side of the chest. One or more steel bars are inserted behind the sternum using a thoracoscope. The surgeon then turns the bars, raising the sternum, and the bar is then fixed in place [23]. Procedural changes on chest x-ray can be seen in Fig. 15.1. This has become the preferred treatment for PE the past 25 years.

Since PC repair is usually cosmetic, no other testing is usually necessary. However, if there are associated syndromes, severe scoliosis causing cardiorespiratory compromise or functional limitations, then other tests such as electrocardiogram, echocardiogram or PFTs may be indicated. Surgery is usually reserved for patients with more severe forms of PC or those unable to adhere to bracing. Patients with PC usually undergo the modified Ravitch procedure or a minimally invasive repair similar to that created by Dr. Nuss [23–26]. The Ravitch operation still has a critical role in the correction of chest wall deformity in cases of PC, PA and asymmetric PE [27].

The most common procedure for pectus repair is the Nuss procedure. Anesthetic management during the Nuss procedure is done under general anesthesia with standard ASA monitors. Need for additional monitors, equipment and access is dependent on the severity of the deformity and patient comorbidities. Risks and complications associated with the Nuss procedure include but are not limited to injury to the heart, pericardium and great vessels causing rapid blood loss, as well as pneumothorax and hemothorax [28–30]. The anesthesia team must be attentive to the intricacies of the procedure and remain acutely aware as to what part of the procedure is being performed in order to anticipate possible complications. Pain associated with the Nuss procedure is one of the biggest concerns to care providers. Most institutes treat these patients via multimodal and multidisciplinary pain management strategies that incorporate nerve blocks along with opioid and non-opioid medications. For more information about the Nuss procedure and pain management strategies refer to Chap. 47: Anesthesia For Nuss Procedures.

Poland Syndrome

Poland syndrome (PS), was first reported in 1841 by Dr. Alfred Poland, and is a congenital chest wall dysplasia typically associated with hypoplasia or aplasia of the pectoralis major muscle. The deformity is most often right-sided. PS is often associated with thoracic anomalies and upper limb deformities [31, 32]. Lower extremity deformities are rare [33].

The incidence of PS has been reported between 1:30,000 and 1:80,000 with a higher incidence in males [34]. However, there may be a

genetic component to PS as described by Vaccari et al. [35]. The embryogenesis of PS is still misunderstood, but is possibly related to decrease in embryonic blood supply during the first trimester. This may be due to hypoplasia of the ipsilateral subclavian artery or one of its branches, as well as possible intrauterine exposure to teratogens [36]. PS may have an association with other disorders such as Moebius, Parry-Romberg and Adams-Oliver syndromes [37–39].

In addition to the chest wall, other organ systems may be affected. PS may predispose patients to developing scoliosis [40]. Scoliosis in PS may be due to multiple factors, including involvement of thoracic and spinal musculature, as well as hemi-vertebrae deformities [41, 42]. Pulmonary function may be compromised due to lung hypoplasia on the side of the deformity. Respiratory muscle function may be decreased which could lead to perioperative lung dysfunction. PS can also have cardiovascular manifestations, including dextrocardia and congenital heart defects [43–46]. The incidence of dextrocardia may range from 5.6 to 11.5%, but it is unknown which anomaly occurs first [43, 47]. When dextrocardia is present, it usually occurs with left-sided defects [43]. PS may also be associated with renal hypoplasia and aplasia which is often asymptomatic [48, 49]. One case report identified potential gynecological involvement in a patient with premature ovarian failure, but this may have been coincidental [50]. There may also be an association with PS and malignancy, but the relationship is controversial. Case reports have shown an increased incidence of leukemia and lymphoma, as well as gastric, breast and lung cancers with PS [51–61]. A list of conditions associated with PS can be found in Table 15.2.

Table 15.2 Organ systems affected by Poland syndrome [40–61]

System	Associated defects
Musculoskeletal	Pectoralis major muscle hypoplasia/aplasia, rib and cartilage aplasia/hypoplasia, syndactyly, hemivertebrae, scoliosis
Cardiac	Dextrocardia, atrial septal defects
Vascular	Interruption of subclavian arteries
Pulmonary	Lung hypoplasia, pulmonary hypertension
Airway	Not increased risk for difficult ventilation or intubation unless associated with other syndromes
Neurologic	No known defects or learning disabilities
Renal	Kidney aplasia
Hematology	Cancer, leukemia, lymphoma
Gynecological	Ovarian failure (one case report)

Surgeries associated with PS depend on the degree of the deformity and other associated conditions. Romanini et al. proposed the management of the different PS types with an algorithm according to the phenotypical features of each PS patient. Based on the algorithm, surgeons can determine the need for the appropriate procedures [62]. For rib aplasia, a two stage procedure, including rib defect repair followed by a muscle flap transposition, may be performed as well as vertical expandable prosthetic titanium rib (VEPTR) placement. Female patients may require muscle flap transposition combined with breast augmentation after they reach puberty. These patients may also require specific surgeries to correct syndactyly and other associated muscle and breast deformities [63–65]. Operations are usually performed by or in combination with thoracic, plastic and orthopedic surgeons.

Due to the possible impact on the cardiorespiratory system, a thorough history and physical should be performed preoperatively. Chest x-rays should be obtained to evaluate for cardiac positioning, rib deformities, and the degree of scoliosis. CT and MRI imaging can also be used to further evaluate the extent of the deformities. Renal function tests should be obtained due to incidence of renal anomalies. Additional tests, such as electrocardiogram, echocardiography, PFTs, and arterial blood gases, should be based on clinical findings and symptoms. Unless the patient has severe underlying cardiopulmonary disease or an associated syndrome that predisposes to a difficult airway, premedication to help with anxiety is suitable.

Despite muscle dysfunction and theoretical concerns, no episodes of malignant hyperthermia (MH) have been reported in patients with PS. In a review of MH susceptibility, PS was not found to be an indicator for MH [66]. Despite the lack of

evidence, in most case reports and studies providers opted to perform total intravenous anesthesia (TIVA) and avoid triggering agents [67–69]. However, in one case report a patient received both succinylcholine and halothane without incidence [70]. Another reason to consider TIVA is the association of PS with Moebius syndrome, which is associated with facial musculature paralysis, abducens and related nerve palsies [37]. Succinylcholine may be avoided due to its relative contraindication with degenerative diseases of cranial motor nuclei [71].

When performing a procedure that requires general endotracheal anesthesia, standard ASA monitors should be applied. Every patient should have temperature monitored considering the theoretical risk of MH. Anesthetic induction and maintenance will be based on underlying cardiopulmonary function and any associated syndromes or abnormalities present. Patients presenting with only PS do not appear to have an increased risk for difficult mask ventilation or intubation. Endotracheal intubation with controlled ventilation is preferred in these patients as they may experience paradoxical lung movement due to chest wall defects. This may lead to hypoventilation and hypoxia. Depending on the type of surgery and degree of lung hypoplasia, lung isolation may be indicated [72]. Positive end-expiratory pressure (PEEP) may be beneficial to prevent atelectasis [73]. Insertion of additional vascular access, including peripheral, arterial and central lines, should be based on patient factors. Pain management is imperative to prevent splinting, hypoventilation and hypoxia. Anatomical differences may make regional anesthesia difficult or less reliable, but multimodal analgesia, with a goal to reduce opioid use, may be beneficial to prevent systemic side effects of opioids [67].

Jeune Syndrome

Jeune syndrome (JS), also known as asphyxiating thoracic dystrophy, is a rare congenital skeletal dysplasia syndrome occurring in approximately 1 in 100,000 to 300,000 live births [74]. It was first described by Jeune et al. in 1955 [75]. The syndrome is autosomal recessive with mutations found on the locus of chromosome 15q13 [76]. Skeletal dysplasia involves the chest wall and limb abnormalities. The thorax is usually small, narrow and bell-shaped, with short, horizontally sloping ribs, elevated clavicles and asymmetrical costochondrial junctions, leading to respiratory complications. Patients also often have postaxial polydactyly and hypoplastic phalanges in both upper and lower extremities [77]. JS is usually a clinical diagnosis, but can be discovered prenatally via ultrasound [78]. Common surgeries performed for patients include anterior chest wall reconstruction, VEPTR placement and tracheostomy due to ventilator dependence [79–82]. In addition to respiratory and skeletal dysfunction, JS may affect numerous other organ systems. The kidneys are most likely involved outside of the pulmonary system and can lead to progressive kidney failure requiring transplant [75, 83–85]. Other organs that may be affected include the heart, liver, spleen, pancreas, intestines and eyes [75, 86–91].

Patients with JS are more likely to experience respiratory distress in the first few years of life, as well as increased risk for respiratory infections. As patients grow, the thoracic defect becomes less prominent and the risk of respiratory problems decreases. A retrospective study examining 13 patients with the syndrome found that most of the patient's respiratory dysfunction improved after 2 years of age, with only two patients requiring further supplemental oxygen [75]. There have been reports of acquired JS after pectus repair [77, 92]. However, with recommendations to perform surgery at a later age and remove less cartilage, the incidence has dropped [3].

When evaluating patients for surgery, anesthesia providers will complete a thorough history and physical with a targeted focus on the respiratory system. Patients should be asked about prior respiratory issues including infections, need for intubation and mechanical ventilation, and associated respiratory diseases such as asthma or sleep apnea. An understanding of the patient's current respiratory function including coughs, fevers, wheezing, use of respiratory medications

and oxygen support is important for planning anesthetic management. Imaging studies including radiographs and CT should be reviewed. Depending on respiratory function, PFTs may not be reliable in younger patients, but should be considered for patients who can perform them. PFTs will most likely show a restrictive pattern with a decreased FVC and a normal FEV1/FVC ratio. Restrictive lung disease results in reduced lung volumes, ventilation/perfusion mismatching, progressive hypoxemia, and hypercarbia. Baseline arterial blood gas values may be considered. Depending on the degree of chronic hypoxia and hypercarbia, a cardiology consult or echocardiogram may be considered to evaluate for pulmonary hypertension. Renal disease usually occurs after the second year of life and renal function tests should be obtained. Although hepatomegaly and splenomegaly is common, blood tests are usually normal and clinical symptoms are infrequent so routine testing may not be warranted unless symptomatic. As with the liver and spleen, pancreatic dysfunction is uncommon and testing should be based on clinical findings. Ocular manifestations are common and any vision issues should be documented prior to anesthesia.

Despite respiratory concerns, no studies or case reports have shown any incidence of difficult ventilation or intubation. However, providers should be aware of peak pressures during mask ventilation due to lung hypoplasia. After intubation, parameters for mechanical ventilation should attempt to keep inspiratory pressures as low as possible while maintaining adequate tidal volumes in order to prevent barotrauma, impaired venous return and decrease in cardiac output [93]. Lung protective strategies, including low tidal volumes (6 cc/kg by ideal body weight) and PEEP, may be beneficial but ventilation may need to be tailored to each individual patient [94–96]. To maintain normocapnia, higher respiratory rates may be needed. If cor pulmonale and pulmonary hypertension are present it is vital to prevent hypercapnia. An arterial line may be beneficial. However placement may be difficult due to limb abnormalities, so preventing increases in end-tidal CO2 is important. Depending on baseline lung function and the type of surgery, postoperative ventilation may be required.

Providers should be aware of any renal and hepatic dysfunction. Drugs requiring hepatic or renal metabolism should be titrated accordingly. Qualitative, or preferably quantitative peripheral nerve stimulators should be used to appropriately administer muscle relaxants and reversal agents. Positioning of patients may be difficult due to skeletal anomalies, and all pressure points should be padded. Due to limb dysplasias, placement of blood pressure cuffs, intravenous and arterial lines and peripheral nerve monitors may be challenging. Providers should consider multimodal anesthesia to reduce opioid administration which can lead to respiratory depression. Thoracic epidural blocks have successfully been used for postoperative pain control [93].

Postoperatively, patients may require intensive care unit (ICU) admittance. There is an up to 60% decrease in spirometry variables in patients with scoliosis, many of whom have severe restrictive lung diseases. This may contribute to prolonged postoperative mechanical ventilation. The peak fall in lung volumes occurs on the third day after surgery, and recovery to baseline levels may take up to 2 months [97]. If patients require postoperative ventilation, lung protective strategies should continue into the ICU. Incentive spirometry can help reduce pulmonary complications, whereas few trials support the usefulness of prophylactic respiratory physiotherapy [98, 99]. Pain management is important to prevent splinting and atelectasis, as well as improve ambulation and prevent infections and thromboembolism. Goals for these patients include optimization of medical therapy, pain management, limiting mechanical ventilation time and early mobilization to prevent respiratory complications.

Sternal Malformations

Sternal malformations can be classified as cleft sternum, thoracic ectopia cordis (EC), cervical EC, and thoracoabdominal EC [100]. Cleft sternum is the most common and is estimated to occur in 1:50,000 to 1:100,000 live births [101].

A simple sternal cleft consists of an orthotopic heart, intact pericardium and normal skin coverage. Clefts can be classified as either complete or partial, with partial clefts being further divided into superior, medium or inferior [102]. Inferior partial clefts are the rarest type and are usually associated with thoracoabdominal EC as part of Pentalogy of Cantrell [103]. Pentalogy of Cantrell is a newborn syndrome that involves bifid sternum, ectopia cordis, anterior diaphragmatic hernia, upper omphalocele and intracardiac anomalies [104]. The sternum is usually embryologically formed by the end of the tenth week of gestation [105]. Disruption in this process leads to sternal malformation. There may be genetic and teratogenic associations to these defects [105–107].

Cleft sternum is diagnosed postnatally with visualization of mediastinal viscera exposed through the defect, usually when the patient is crying or coughing. Surgical repair is usually performed within the first 6 months. EC, on the other hand, is diagnosed prenatally via ultrasound during the second trimester. Unlike cleft sternum, these are surgical emergencies. The infants are often delivered by planned Cesarean section to protect vital organs and they are usually intubated immediately and undergo initial neonatal resuscitation [103].

Surgical correction is most commonly performed in patients under 1 year of age, and preferably in the neonatal period because of compliance and flexibility of skeletal and cardiopulmonary structures [102]. Cleft sternum repair has the highest success rate, whereas cervical EC repair is incompatible with life, so no repair is indicated [106, 108]. There are varying results for thoracic and thoracoabdominal EC repair, with EC still associated with high mortality and significant long-term morbidity [109].

Preoperatively sternal cleft patients are usually stable from a cardiovascular standpoint despite concerns of visceral protrusion from the cleft. Sternal clefts may be associated with PHACES syndrome which is characterized by Posterior fossa malformations, facial Hemangiomas, Arterial anomalies, Cardiac defects, Eye abnormalities, Sternal cleft and Supraumbilical raphe [110]. Because of this, patients should have a thorough workup to determine the existence and extent of any of these associations. This should include an electrocardiogram and transthoracic echocardiogram. Patients with sternal clefts associated with more severe symptoms or associated CHDs may benefit from management by a pediatric cardiac anesthesiologist, as well as cardiopulmonary bypass (CPB) available on standby.

Preoperative labs should include a complete blood count and a type and screen. Blood should be available, as injury to the heart and great vessels may occur causing acute blood loss.

Patients undergoing cleft repair who are otherwise stable can receive preoperative anxiolytics, and the decision to place an IV catheter before induction at the discretion of the provider. Most patients can receive either an intravenous or inhalation induction. If inhalation induction is performed, then intravenous access should be obtained once the patient is asleep. At least one large bore IV should be obtained, in case blood transfusion is required. Arterial line placement is helpful to diagnose possible compression of great vessels and changes in hemodynamics during closure. Transesophageal echocardiogram may be beneficial to determine heart function after sternal closure. Providers should be alert to rapid changes in hemodynamics which may be due to cardiovascular injury, vessel compression or elevated intrathoracic pressures. Continuous communication between the anesthesia and surgical teams is necessary to recognize any issues that may arise. Assuming an uneventful surgery, patients may be extubated in the operating room. As with all surgeries, appropriate pain management is necessary to help reduce postoperative complications. Multimodal analgesia including a combination of NSAIDs, antipyretics, local and/or regional anesthesia can be used successfully to help reduce opioid use for cleft repair [103].

Management of thoracic and thoracoabdominal EC requires more complex care than that of simple clefts. Underlying cardiac anomalies require a comprehensive workup which may begin in utero. Pentalogy of Cantrell, is commonly associated with EC and often occurs with

Table 15.3 Cardiac anomalies associated with pentalogy of cantrell [111–115]

- Situs solitus
- Dextrocardia
- Double-outlet right ventricle
- Malposition of the great vessels
- Left superior vena cava to the coronary sinus
- Left ventricular diverticulum
- Absence of pericardium
- Ventricular septal defect
- Atrial septal defect
- Tetralogy of Fallot
- Pulmonary stenosis

complex cardiac defects as seen in Table 15.3 [111–115]. A multidisciplinary team including cardiac anesthesia, cardiothoracic surgery, neonatology and obstetrics should develop a plan for delivery and subsequent operations. Case reports show patients have undergone uneventful pregnancies and deliveries, however Cesarean section is more feasible for both preventing damage to organs and planning care [103, 111, 112].

Patients with Pentalogy and EC have a poor prognosis, and cause of death is usually due to arrhythmias, hypotension due to acute bleeding, diverticulum rupture, sepsis, and heart failure [116, 117]. Providers should be well prepared for hemodynamic instability during any operation. Intubation will likely occur at birth, even while the patient is still under placental circulation. Difficult intubation should be expected, especially if the heart is directed caudad which could impede technique and visualization. Once the airway is secured, peripheral, arterial and central access should be obtained. Blood and CPB should be readily available. The main goal at delivery is to stabilize the patient with fluid resuscitation and to protect exposed organs, often with a silo. Constant communication between the surgeon and anesthesia team is necessary, since rapid hemodynamic changes may occur during surgical manipulation. Providers should be aware of ongoing fluid and blood losses, increased abdominal and thoracic pressures, and sudden cardiac arrhythmias and collapse. Surgeons will often need to perform multiple procedures on known defects prior to any attempts for sternal closure. Patients usually remain intubated and mechanically ventilated, with recovery in the ICU and expectations of coming back to the OR repeatedly.

References

1. Park CH, Kim TH, Haam SJ, Lee S. Rib overgrowth may be a contributing factor for pectus excavatum: evaluation of prepubertal patients younger than 10 years old. J Pediatr Surg. 2015;50(11):1945–8. https://doi.org/10.1016/j.jpedsurg.2015.07.010.
2. Shamberger RC. Congenital chest wall deformities. In: Grosfeld JL, Coran AG, Caldamone AA, O'Neill Jr JA, Fonkalsrud EW, editors. Pediatric surgery. 6th ed. St. Louis, MO: Mosby; 2006. p. 894.
3. Fonkalsrud EW. 912 open pectus excavatum repairs: changing trends, lessons learned: one surgeon's experience. World J Surg. 2009;33:180–90.
4. Haje SA, Harcke HT, Bowen JR. Growth disturbance of the sternum and pectus deformities: imaging studies and clinical correlation. Pediatr Radiol. 1999;29(5):334–41.
5. Fokin AA, Steuerwald NM, Ahrens WA, Allen KE. Anatomical, histologic, and genetic characteristics of congenital chest wall deformities. Semin Thorac Cardiovasc Surg. 2009;21(1):44–57. https://doi.org/10.1053/j.semtcvs.2009.03.001.
6. Abdullah F, Harris J. Pectus excavatum: more than a matter of aesthetics. Pediatr Ann. 2016;45(11):e403–6.
7. Fonkalsrud EW. Surgical correction of pectus carinatum: lessons learned from 260 patients. J Pediatr Surg. 2008;43(7):1235–43. https://doi.org/10.1016/j.jpedsurg.2008.02.007.
8. Leung AK, Hoo JJ. Familial congenital funnel chest. Am J Med Genet. 1987;26(4):887–90.
9. Behr CA, Denning NL, Kallis MP, Maloney C, Soffer SZ, Romano-Adesman A, Hong AR. The incidence of Marfan syndrome and cardiac anomalies in patients presenting with pectus deformities. J Pediatr Surg. 2019;54(9):1926–8. https://doi.org/10.1016/j.jpedsurg.2018.11.017.
10. Tocchioni F, Ghionzoli M, Messineo A, Romagnoli P. Pectus excavatum and heritable disorders of the connective tissue. Pediatr Rep. 2013;5(3):e15. https://doi.org/10.4081/pr.2013.e15.
11. Finsterer J, Strobl W. Orthopaedic abnormalities in primary myopathies. Acta Orthop Belg. 2011;77(5):563–82.
12. Kotzot D, Schwabegger AH. Etiology of chest wall deformities—a genetic review for the treating physician. J Pediatr Surg. 2009;44(10):2004–11. https://doi.org/10.1016/j.jpedsurg.2009.07.029.
13. Kelly RE Jr. Pectus excavatum: historical background, clinical picture, preoperative evaluation and criteria for operation. Semin Pediatr Surg. 2008;17(3):181–93.

14. Humphreys GH 2nd, Jaretzki A 3rd. Pectus excavatum. Late results with and without operation. J Thorac Cardiovasc Surg. 1980;80(5):686–95.
15. St-Louis E, Miao J, Emil S, Baird R, Bettolli M, Montpetit K, Goyette J, Laberge JM. Vacuum bell treatment of pectus excavatum: an early north American experience. J Pediatr Surg. 2019;54(1):194–9. https://doi.org/10.1016/j.jpedsurg.2018.10.011.
16. Obermeyer RJ, Cohen NS, Kelly RE Jr, Ann Kuhn M, Frantz FW, McGuire MM, Paulson JF. Nonoperative management of pectus excavatum with vacuum bell therapy: a single center study. J Pediatr Surg. 2018;53(6):1221–5. https://doi.org/10.1016/j.jpedsurg.2018.02.088.
17. Colozza S, Bütter A. Bracing in pediatric patients with pectus carinatum is effective and improves quality of life. J Pediatr Surg. 2013;48(5):1055–9. https://doi.org/10.1016/j.jpedsurg.2013.02.028.
18. Kelly RE Jr, Goretsky MJ, Obermeyer R, Kuhn MA, Redlinger R, Haney TS, et al. Twenty-one years of experience with minimally invasive repair of pectus excavatum by the Nuss procedure in 1215 patients. Ann Surg. 2010;252(6):1072–81.
19. Mayer OH. Pectus excavatum: treatment. In: Redding G, Hoppin AG, editors. UpToDate. Waltham, MA: UpToDate; 2019 [cited 2019, Dec 3].
20. Brochhausen C, Turial S, Müller FK, Schmitt VH, Coerdt W, Wihlm JM, Schier F, Kirkpatrick CJ. Pectus excavatum: history, hypotheses and treatment options. Interact Cardiovasc Thorac Surg. 2012;14(6):801–6.
21. Redding GJ, Kuo W, Swanson JO, Phillips GS, Emerson J, Yung D, Swanson JW, Sawin RS, Avansino JR. Upper thoracic shape in children with pectus excavatum: impact on lung function. Pediatr Pulmonol. 2013;48(8):817–23. https://doi.org/10.1002/ppul.22660.
22. Ravitch MM. The operative treatment of pectus excavatum. Ann Surg. 1949;129(4):429–44.
23. Nuss D, Kelly RE, Croitoru DP, et al. A 10-year review of a minimally invasive technique for the correction of pectus excavatum. J Pediatr Surg. 1998;33:545–52.
24. Robicsek F. Surgical treatment of pectus carinatum. Chest Surg Clin N Am. 2000;10(2):357–76, viii.
25. Abramson H, D'Agostino J, Wuscovi S. A 5-year experience with a minimally invasive technique for pectus carinatum repair. J Pediatr Surg. 2009;44:118–24.
26. Hock A. Minimal access treatment of pectus carinatum: a preliminary report. Pediatr Surg Int. 2009;25:337–42.
27. Kim SY, Park S, Kim ER, Park IK, Kim YT, Kang CH. A case of successful surgical repair for pectus arcuatum using chondrosternoplasty. Korean J Thorac Cardiovasc Surg. 2016;49(3):214–7. https://doi.org/10.5090/kjtcs.2016.49.3.214.
28. Leonhardt J, Kubler JF, Feiter J, Ure BM, Petersen C. Complications of the minimally invasive repair of pectus excavatum. J Pediatr Surg. 2005;40(11):e7–9.
29. Hoel TN, Rein KA, Svennevig JL. A life-threatening complication of the Nuss procedure for pectus excavatum. Ann Thorac Surg. 2006;81(1):370–2.
30. Marusch F, Gastinger I. Life-threatening complication of the Nuss-procedure for funnel chest. A case report. Zentralbl Chir. 2003;128(11):981–4.
31. Poland A. Deficiency of the pectoral muscles. Guy Hosp Rep. 1841;6:191–3.
32. "Poland syndrome". Genetic and Rare Diseases Information Center (GARD)—an NCATS Program. 2016. Retrieved October 16, 2018, from https://rarediseases.info.nih.gov/diseases/7412/poland-syndrome
33. Silengo M, Lerone M, Seri M, Boffi P. Lower extremity counterpart of the Poland syndrome. Clin Genet. 1999;55(1):41–3.
34. Lantzsch T, Lampe D, Kantelhardt EJ. Correction of Poland's syndrome: case report and review of the current literature. Breast Care. 2013;8(2):139–42. https://doi.org/10.1159/000350778.
35. Vaccari CM, Tassano E, Torre M, Gimelli S, Divizia MT, Romanini MV, Bossi S, Musante I, Valle M, Senes F, et al. Assessment of copy number variations in 120 patients with Poland syndrome. BMC Med Genet. 2016;17(1):89.
36. Bavinck JN, Weaver DD. Subclavian artery supply disruption sequence: hypothesis of a vascular etiology for Poland, Klippel-Feil, and Möbius anomalies. Am J Med Genet. 1986;23(4):903–18.
37. Chopan M, Sayadi L, Laub D. Mobius syndrome and Poland syndrome presenting together in a single patient. Eplasty. 2015;15:ic12.
38. Dintiman BJ, Shapiro RS, Hood AF, Guba AM. Parry-Romberg syndrome in association with contralateral Poland syndrome. J Am Acad Dermatol. 1990;22(2 Pt 2):371–3.
39. Der Kaloustian VM, Hoyme HE, Hogg H, Entin MA, Guttmacher AE. Possible common pathogenetic mechanisms for Poland sequence and Adams-Oliver syndrome. Am J Med Genet. 1991;38(1):69–73.
40. Inklebarger J, Leddy J, Galanis N, Gyer G, Michael J, Anand P, Abbas B, Krishnaswamy K, Kumar D, Roberts A. Poland's syndrome associated with thoracic spine scoliosis—a case report. IJMSCI [Internet]. 2018 [cited 2020 Mar 22];5(7):3931–3. Available from: https://valleyinternational.net/index.php/ijmsci/article/view/1360
41. Cobben JM, Robinson PH, van Essen AJ, van der Wiel HL, ten Kate LP. Poland anomaly in mother and daughter. Am J Med Genet. 1989;33(4):519–21.
42. Bainbridge LC, Wright AR, Kanthan R. Computed tomography in the preoperative assessment of Poland syndrome. Br J Plast Surg. 1991;44(8):604–7.
43. Torre M, Baban A, Buluggiu A, Costanzo S, Bricco L, Lerone M, Bianca S, Gatti GL, Sénès FM, Valle

M, Calevo MG. Dextrocardia in patients with Poland syndrome: phenotypic characterization provides insight into the pathogenesis. J Thorac Cardiovasc Surg. 2010;139(5):1177–82. https://doi.org/10.1016/j.jtcvs.2009.08.024.
44. Hanka SS, Fox V. Letter: dextrocardia associated with Poland's syndrome. J Pediatr. 1975;86(2):312.
45. Matsui A, Nakagawa M, Okuno M. Association of atrial septal defect with Poland-Moebius syndrome: vascular disruption can be a common etiologic factor. A case report. Angiology. 1997;48(3):269–71.
46. Samant AR, Sridhar S, Desser KB, Benchimol A. Association of atrial septal defect with Poland's syndrome. Am Heart J. 1983;106(1 Pt 1):159–61.
47. Fraser FC, Teebi AS, Walsh S, Pinsky L. Poland sequence with dextrocardia: which comes first? Am J Med Genet. 1997;73(2):194–6.
48. Hedge HR, Leung AKC. Aplasia of pectoralis major muscle and renal anomalies. Am J Med Genet. 1989;32(1):109–11.
49. Assadi F, Salem M. Poland syndrome associated with renal agenesis. Pediatr Nephrol. 2002;17(4):269–71.
50. Derman O, Gold MA. Poland's syndrome and premature ovarian failure. J Pediatr Adolesc Gynecol. 2004;17(6):389–92.
51. Hoefnagel D, Rozycki A, Wurster-Hill D, Stern P, Gregory D. Leukaemia and Poland's syndrome. Lancet. 1972;2(7785):1038–9.
52. Hershatter BW, Montana GS. Poland's syndrome and lymphoma. Am J Dis Child. 1983;137(12):1211–2.
53. Kurt Y, Demirbas S, Uluutku AH, Akin ML, Celenk T. Poland's syndrome and gastric cancer: report of a case. Eur J Cancer Prev. 2006;15(6):480–2.
54. Khandelwal A, O'Hea BJ, Garguilo G. Breast cancer in a patient with Poland's syndrome. Am Surg. 2004;70(6):491–5.
55. Ji J, Zhang S, Shao C, Xu M, Chen S, Lu C, Wang Z, Zhao Z, Fan X, Tu J. Poland's syndrome complicated with breast cancer: mammographic, ultrasonographic, and computed tomographic findings. Acta Radiol. 2008;49(4):387–90. https://doi.org/10.1080/02841850801922904.
56. Okamo H, Miura K, Yamane T, Fujii H, Matsumoto Y. Invasive ductal carcinoma of the breast associated with Poland's syndrome: report of a case. Surg Today. 2002;32(3):257–60.
57. Katz SC, Hazen A, Colen SR, Roses DF. Poland's syndrome and carcinoma of the breast: a case report. Breast J. 2001;7(1):56–9.
58. Havlik RJ, Sian KU, Wagner JD, Binford R, Broadie TA. Breast cancer in Poland syndrome. Plast Reconstr Surg. 1999;104(1):180–2.
59. Fukushima T, Otake T, Yashima R, Nihei M, Takeuchi S, Kimijima II, Tsuchiya A. Breast cancer in two patients with Poland's syndrome. Breast Cancer. 1999;6(2):127–30.
60. Tamiolakis D, Venizelos D, Antoniou C, Tsiminikakis N, Alifieris E, Papadopoulos N. Breast cancer development in a female with Poland's syndrome. Onkologie. 2004;27(6):569–71.
61. Ahn MI, Park SH, Park YH. Poland's syndrome with lung cancer. A case report. Acta Radiol. 2000;41(5):432–4.
62. Romanini MV, Calevo MG, Puliti A, Vaccari C, Valle M, Senes F, Torre M. Poland syndrome: a proposed classification system and perspectives on diagnosis and treatment. Semin Pediatr Surg. 2018;27(3):189–99. https://doi.org/10.1053/j.sempedsurg.2018.05.007.
63. Bairov GA, Fokin AA. Surgical treatment of Poland's syndrome in children. Vestn Khir Im I I Grek. 1994;152(1–2):70–2.
64. Drebov RS, Katsarov A 2nd. Poland syndrome: use of vertical expandable prosthetic titanium Rib system before walking age—a case report. Surg J. 2016;2(3):e91–5. https://doi.org/10.1055/s-0036-1593354.
65. Fijałkowska M, Antoszewski B. Surgical treatment of patients with Poland's syndrome—own experience. Pol Przegl Chir. 2011;83(12):662–7. https://doi.org/10.2478/v10035-011-0106-5.
66. Litman RS, Griggs SM, Dowling JJ, Sheila RS. Malignant hyperthermia susceptibility and related diseases. Anesthesiology. 2018;128(1):159–67. https://doi.org/10.1097/ALN.0000000000001877.
67. Gui L, Shen S, Mei W. Anaesthesia for chest wall reconstruction in a patient with Poland syndrome: CARE-compliant case report and literature review. BMC Anesthesiol. 2018;18(1):57. https://doi.org/10.1186/s12871-018-0518-4.
68. İnce I, Aksoy M, Ahıskalıoğlu A, Çömez M, Kaciroğlu A. Anaesthesia in Poland syndrome: a case report. J Clin Exp Invest. 2014;5(4):608–9. https://doi.org/10.5799/ahinjs.01.2014.04.0468.
69. Kabukcu HK, Sahin N, Kanevetci BN, Titiz TA, Bayezid O. Anaesthetic management of patient with Poland syndrome and rheumatic mitral valve stenosis: a case report. Ann Card Anaesth. 2005;8(2):145–7.
70. Sethuraman R, Kannan S, Bala I, Sharma RK. Anaesthesia in Poland syndrome. Can J Anaesth. 1998;45(3):277–9.
71. Küpper HJ. Anesthesia in Poland syndrome. Can J Anaesth. 1999;46(5 Pt 1):513–4.
72. Urschel HC. Poland's syndrome. Chest Surg Clin N Am. 2000;10(2):393–403, viii.
73. Neumann P, Rothen HU, Berglund JE, Valtysson J, Magnusson A, Hedenstierna G. Positive end-expiratory pressure prevents atelectasis during general anaesthesia even in the presence of a high inspired oxygen concentration. Acta Anaesthesiol Scand. 1999;43(3):295–301.
74. den Hollander NS, Robben SG, Hoogeboom AJ, Niermeijer MF, Wladimiroff JW. Early prenatal sonographic diagnosis and follow-up of Jeune syndrome. Ultrasound Obstet Gynecol. 2001;18(4):378–83.
75. de Vries J, Yntema JL, van Die CE, Crama N, Cornelissen EA, Hamel BC. Jeune syndrome: description of 13 cases and a proposal for follow-up

protocol. Eur J Pediatr. 2010;169(1):77–88. https://doi.org/10.1007/s00431-009-0991-3.
76. Morgan NV, Bacchelli C, Gissen P, Morton J, Ferrero GB, Silengo M, Labrune P, Casteels I, Hall C, Cox P, et al. A locus for asphyxiating thoracic dystrophy, ATD, maps to chromosome 15q13. J Med Genet. 2003;40(6):431–5.
77. Phillips JD, van Aalst JA. Jeune's syndrome (asphyxiating thoracic dystrophy): congenital and acquired. Semin Pediatr Surg. 2008;17(3):167–72. https://doi.org/10.1053/j.sempedsurg.2008.03.006.
78. Mistry KA, Suthar PP, Bhesania SR, Patel A. Antenatal diagnosis of Jeune syndrome (asphyxiating thoracic dysplasia) with micromelia and facial dysmorphism on second-trimester ultrasound. Pol J Radiol. 2015;80:296–9. https://doi.org/10.12659/PJR.894188.
79. Sacco Casamassima MG, Goldstein SD, Salazar JH, Papandria D, McIltrot KH, O'Neill DE, Abdullah F, Colombani PM. Operative management of acquired Jeune's syndrome. J Pediatr Surg. 2014;49(1):55–60; discussion 60. https://doi.org/10.1016/j.jpedsurg.2013.09.027.
80. Campbell RM Jr. VEPTR: past experience and the future of VEPTR principles. Eur Spine J. 2013;22(Suppl 2):S106–17. https://doi.org/10.1007/s00586-013-2671-2.
81. Kotoda M, Ishiyama T, Okuyama K, Matsukawa T. Anesthetic management of a child with Jeune syndrome for tracheotomy: a case report. AA Case Rep. 2017;8(5):119–21. https://doi.org/10.1213/XAA.0000000000000444.
82. Salik I, Genis A, Barst S. Anesthetic management of an infant with Jeune syndrome and severe pulmonary hypertension for tracheostomy. J Clin Anesth. 2019;52:76–7. https://doi.org/10.1016/j.jclinane.2018.09.018.
83. Hennekam RC, Beemer FA, Gerards LJ, Cats BP. Thoracic pelvic phalangeal dystrophy (Jeune's syndrome). Tijdschr Kindergeneeskd. 1983;51(3):95–100.
84. Amirou M, Bourdat-Michel G, Pinel N, Huet G, Gaultier J, Cochat P. Successful renal transplantation in Jeune syndrome type 2. Pediatr Nephrol. 1998;12(4):293–4.
85. Bernstein J, Brough AJ, McAdams AJ. The renal lesion in syndromes of multiple congenital malformations. Cerebrohepatorenal syndrome; Jeune asphyxiating thoracic dystrophy; tuberous sclerosis; Meckel syndrome. Birth Defects Orig Artic Ser. 1974;10(4):35–43.
86. Labrune P, Fabre M, Trioche P, Estournet-Mathiaud B, Grangeponte MC, Rambaud C, Maurage C, Bernard O. Jeune syndrome and liver disease: report of three cases treated with ursodeoxycholic acid. Am J Med Genet. 1999;87(4):324–8.
87. Hudgins L, Rosengren S, Treem W, Hyams J. Early cirrhosis in survivors with Jeune thoracic dystrophy. J Pediatr. 1992;120(5):754–6.
88. Yerian LM, Brady L, Hart J. Hepatic manifestations of Jeune syndrome (asphyxiating thoracic dystrophy). Semin Liver Dis. 2003;23(2):195–200.
89. Karjoo M, Koop CE, Cornfeld D, Holtzapple PG. Pancreatic exocrine enzyme deficiency associated with asphyxiating thoracic dystrophy. Arch Dis Child. 1973;48(2):143–6.
90. Allen AW Jr, Moon JB, Hovland KR, Minckler DS. Ocular findings in thoracic-pelvic-phalangeal dystrophy. Arch Ophthalmol. 1979;97(3):489–92.
91. Bard LA, Bard PA, Owens GW, Hall BD. Retinal involvement in thoracic-pelvic-phalangeal dystrophy. Arch Ophthalmol. 1978;96(2):278–81.
92. Haller JA Jr, Colombani PM, Humphries CT, Azizkhan RG, Loughlin GM. Chest wall constriction after too extensive and too early operations for pectus excavatum. Ann Thorac Surg. 1996;61(6):1618–24. discussion 1625
93. Saletti D, Grigio TR, Tonelli D, Ribeiro Júnior OD, Marini F. Case report: anesthesia in patients with asphyxiating thoracic dystrophy: Jeune syndrome. Rev Bras Anestesiol. 2012;62(3):424–31. https://doi.org/10.1016/S0034-7094(12)70142-3.
94. O'Gara B, Talmor D. Perioperative lung protective ventilation. BMJ. 2018;362:k3030. https://doi.org/10.1136/bmj.k3030.
95. Hedenstierna G, Edmark L. Protective ventilation during anesthesia: is it meaningful? Anesthesiology. 2016;125(6):1079–82.
96. Goldenberg NM, Steinberg BE, Lee WL, Wijeysundera DN, Kavanagh BP. Lung-protective ventilation in the operating room: time to implement? Anesthesiology. 2014;121(1):184–8. https://doi.org/10.1097/ALN.0000000000000274.
97. Yuan N, Fraire JA, Margetis MM, Skaggs DL, Tolo VT, Keens TG. The effect of scoliosis surgery on lung function in the immediate postoperative period. Spine (Phila Pa 1976). 2005;30(19):2182–5.
98. do Nascimento JP, Módolo NS, Andrade S, Guimarães MM, Braz LG, El Dib R. Incentive spirometry for prevention of postoperative pulmonary complications in upper abdominal surgery. Cochrane Database Syst Rev. 2014;2014(2):CD006058. https://doi.org/10.1002/14651858.CD006058.pub3.
99. Pasquina P, Tramèr MR, Walder B. Prophylactic respiratory physiotherapy after cardiac surgery: systematic review. BMJ. 2003;327(7428):1379–0.
100. Shamberger RC, Welch KJ. Sternal defects. Pediatr Surg Int. 1990;5:156–64. https://doi.org/10.1007/BF00179653.
101. Ashok RJ, Mathevan G, Mathiarasan K, Ramasubramaniam P. Closing the cleft over a throbbing heart: neonatal sternal cleft. BMJ Case Rep. 2014;2014:bcr2014204529. https://doi.org/10.1136/bcr-2014-204529.
102. Acastello E, Majluf R, Garrido P, Barbosa LM, Peredo A. Sternal cleft: a surgical opportunity. J Pediatr Surg. 2003;38(2):178–83.

103. Nichols JH, Nasr VG. Sternal malformations and anesthetic management. Paediatr Anaesth. 2017;27(11):1084–90. https://doi.org/10.1111/pan.13253.
104. Colambani PM. Recurrent chest wall anomalies. Semin Pediatr Surg. 2003;12(2):94–9.
105. van der Merwe AE, Weston DA, Oostra RJ, Maat GJ. A review of the embryological development and associated developmental abnormalities of the sternum in the light of a rare palaeopathological case of sternal clefting. Homo. 2013;64(2):129–41. https://doi.org/10.1016/j.jchb.2013.01.003.
106. Engum SA. Embryology, sternal clefts, ectopia cordis, and Cantrell's pentalogy. Semin Pediatr Surg. 2008;17(3):154–60. https://doi.org/10.1053/j.sempedsurg.2008.03.004.
107. Soper SP, Roe LR, Hoyme HE, Clemmons JJ. Trisomy 18 with ectopia cordis, omphalocele, and ventricular septal defect: case report. Pediatr Pathol. 1986;5(3–4):481–3.
108. Douglas DM. Cervical ectopia cordis; report of a case in which surgical treatment was attempted. Scott Med J. 1958;3(1):43–5.
109. Escobar-Diaz MC, Sunderji S, Tworetzky W, Moon-Grady AJ. The fetus with ectopia cordis: experience and expectations from two centers. Pediatr Cardiol. 2017;38(3):531–8. https://doi.org/10.1007/s00246-016-1545-x.
110. Patil SJ, Moray AA, Kiran VS, Battu RR. PHACE/S syndrome: a syndromic infantile segmental hemangioma. Indian J Pediatr. 2010;77(8):911–3. https://doi.org/10.1007/s12098-010-0136-8.
111. de Rubens FJ, Sosa Cruz EF, Díaz García L, Carrasco DD. Cardiac malformations in patients with pentalogy of Cantrell and ectopia cordis. Rev Esp Cardiol. 2011;64(7):615–8. https://doi.org/10.1016/j.recesp.2010.07.010.
112. Kaouthar H, Jihen A, Faten J, Hela M, Fatma O, Lilia C, Rafik B. Cardiac anomalies in Cantrell's pentalogy: from ventricular diverticulum to complete thoracic ectopia cordis. Cardiol Tunis. 2013;9(1):94–7.
113. Abdallah HI, Marks LA, Balsara RK, Davis DA, Russo PA. Staged repair of pentalogy of Cantrell with tetralogy of Fallot. Ann Thorac Surg. 1993;56(4):979–80.
114. Morales MJ, Patel SG, Duff JA, Villareal RL, Simpson JW. Ectopia cordis and other midline defects. Ann Thorac Surg. 2000;70(1):111–4.
115. Vazquez-Jimenez JF, Muehler EG, Daebritz S, Keutel J, Nishigaki K, Huegel W, Messmer BJ. Cantrell's syndrome: a challenge to the surgeon. Ann Thorac Surg. 1998;65(4):1178–85.
116. Diaz JH. Perioperative management of neonatal ectopia cordis: report of three cases. Anesth Analg. 1992;75(5):833–7.
117. Jones AF, McGrath RL, Edwards SM, Lilly JR. Immediate operation for ectopia cordis. Ann Thorac Surg. 1979;28(5):484–6.

16 Anesthesia Considerations for Adolescent Bariatric Surgery

Haig Minassian, Mario DeAngelis, and Michael S. Green

Introduction

Pediatric obesity has rapidly emerged as a public health crisis in the United States [1]. The national prevalence of pediatric obesity increased from 5% to about 17% within the past 50 years, with the fastest-growing subset being "super obese" (i.e., BMI over 50) children [2, 3]. In this time period, there has emerged a correlation between not only pediatric obesity and progression to adult obesity, but also pediatric obesity and premature onset of adult obesity-related comorbidities such as hypertension, obstructive sleep apnea, and diabetes. As a consequence of children displaying obesity related co-morbid conditions at ages younger than ever before seen, a significant burden to provide adequate medical resources will be placed on our already taxed healthcare system.

Bearing in mind the scope of this epidemic, aggressive and sustainable treatment is of paramount importance. Pediatric obesity is unfortunately highly recalcitrant to dietary and medical management alone [4] and is therefore often treated with bariatric surgery in rigorously selected patients. The purpose of surgical intervention is not only attaining rapid, significant, and sustained weight loss, but also reducing the burden of obesity-related comorbidities [5].

Since the first reported adolescent bariatric surgical series in 1975, significant clinical modifications have been made to optimize the efficacy of surgical weight loss programs. Globally speaking, the most effective programs are multidisciplinary and thus able to accommodate the diverse physical and psychological needs of this population [6]. In terms of specific surgical approaches, three primary adolescent bariatric operations have emerged, which are the Roux-en-Y gastric bypass, the sleeve gastrectomy, and the adjustable gastric band. Short-term outcomes for these procedures are promising and fairly comparable to those in adult bariatric surgeries, but concerns about long-term outcomes and the many known safety risks, including post-operative complications and impaired nutrition, remain largely unassuaged [7].

As anesthesia providers, it is incumbent upon us to understand the impact that pediatric obesity has on almost every aspect of perioperative care. Regardless of the guarded optimism that bariatric surgical outcomes may provide us, we inherit these patients prior to them receiving the full benefit of combined medical, behavioral, and surgical intervention and must therefore know how to manage all of the resultant anesthetic challenges. In this chapter, we will begin

H. Minassian · M. DeAngelis (✉) · M. S. Green
Department of Anesthesiology, Thomas Jefferson University Hospital, Philadelphia, PA, USA
e-mail: Haig.Minassian@jefferson.edu; Mario.Deangelis@jefferson.edu; Michael.green2@jefferson.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_16

with a discussion of the comorbidities of pediatric obesity, a framework upon which considerations for each phase of perioperative care can be understood.

Comorbidities of Pediatric Obesity

Obesity is a systemic disease that impacts every organ system and leads to earlier onset of adult obesity-related diseases. The degree of comprehensive comorbid disease burden varies from patient to patient, but there is a significant increase in cardiovascular and metabolic risk in patients whose weight falls above the threshold of 99th percentile [8, 9]. It also appears that "obesity duration"—that is, the severity and longevity of obesity—is predictive of comorbid disease risk [10].

Cardiovascular Comorbidites

As is the case in obese adults, obese children are at increased risk for developing many cardiovascular diseases, including hypertension, metabolic syndrome, atherosclerosis, and left ventricular hypertrophy [11].

Hypertension is particularly common in obese pediatric patients, with a prevalence of 4%. Moreover, the prevalence of prehypertension is estimated to be as high as 10% [12]. Obese children have a threefold risk of having hypertension compared to normal-weight peers, and there is a direct correlation between hypertension and BMI percentile [13].

Metabolic syndrome, by adult criteria (elevated waist circumference plus any two of the following: elevated triglyceride levels, reduced HDL-C, hypertension, and impaired fasting glucose), is ever increasing and has an estimated prevalence of 5–40% [14].

A multitude of studies have shown that arterial plaque deposition begins in childhood, and is accelerated under the presence of multiple cardiovascular risk factors, with obesity being one of the strongest risk factors. In a 1998 NEJM study, 204 autopsies of individuals aged 2–39 revealed a significant correlation between atherosclerotic lesions in the coronary arteries and aorta in subjects and elevated BMI [15].

Cardiovascular remodeling is common in obese children, with the most common manifestation being left ventricular hypertrophy (LVH). Remodeling is commonly subclinical, but overt cardiac dysfunction including diastolic dysfunction and reduced contractility have also been observed. LVH is strongly associated with "obesity duration", and it exhibits reversibility with bariatric surgery [16, 17].

Childhood obesity predisposes patients to increased lifetime risk of major adverse cardiac events (MACE), as well as earlier onset of cardiovascular disease [18]. Perioperative MACE is relatively infrequent in pediatric patients as a whole, but the risk is certainly increased in obese children. Asymptomatic children who meet or exceed the 99th percentile weight threshold may have significant underlying cardiovascular disease that becomes unmasked by the stress of anesthesia and surgery.

There is a cascade of cardiac remodeling that occurs in bariatric surgery patients who have obstructive sleep apnea syndrome (OSAS). Hypoxia and hypercapnia associated with nocturnal apneic events cause pulmonary artery hypertension and intimal wall thickening, progressing to right ventricular hypertrophy and eventually right heart failure due to increased right ventricular afterload. In patients who have left heart dysfunction, as many bariatric surgery patients do, the onset of these changes can be seen in childhood [19].

Respiratory Comorbidities

Both adult and pediatric obese patients exhibit diminished pulmonary function. Depending on the overall burden and distribution of excess adipose tissue, both upper and lower respiratory mechanics can be impaired.

Obstructive sleep apnea syndrome (OSAS) is about five times more common in obese children than in non-obese children. Its prevalence also directly correlates with BMI percentiles, approaching 50% in the heaviest cohort.

Establishing an accurate diagnosis usually requires polysomnography, as detection via history and physical alone is poor [20, 21].

Given the known adverse health risks of longstanding, untreated OSAS, moderate to severe OSAS in children is in fact a strong indication for bariatric surgery. Pulmonary hypertension is one of the feared sequelae, and it has been discovered in patients referred for bariatric surgery. The presence of pulmonary hypertension secondary to OSAS significantly elevates one's risk for perioperative hypoxemia by virtue of both airway obstruction and impaired oxygen exchange [5].

Persistent sleep apnea in obese children who undergo tonsillectomy and adenoidectomy for nocturnal airway obstruction suggests that these patients may also exhibit a component of central sleep apnea. Central sleep apnea in pediatric obesity is an area of ongoing research [22].

Severely obese children typically demonstrate a restrictive lung pattern on pulmonary function testing. Reduced functional residual capacity and forced vital capacity, along with supine positioning during anesthesia, greatly increases the risk of hypoxemia in obese children [23].

A few studies have illustrated a weak correlation between pediatric obesity and asthma. The pathophysiological relationship between these two diseases is poorly understood. However, their concomitant presence in children referred for bariatric surgery presents a high-risk patient subset that is increasingly prone to upper and lower airway hyperreactivity events that are poorly responsive to traditional therapies [24].

Gastrointestinal Comorbidities

Obesity is the strongest risk factor for pediatric nonalcoholic fatty liver disease (NAFLD). NAFLD is present in up to 40% of obese children, and it is the most common cause of chronic liver disease in children. Nonprogressive hepatic steatosis and nonalcoholic steatohepatitis (NASH) are predisposing factors for hepatocellular carcinoma and liver failure, and as such are strong indications for bariatric surgery in children. NAFLD can impact hepatic function and drug metabolism, but these effects are usually not clinically relevant. No specific guidelines exist for pediatric drug dosing in NAFLD, and anesthetic management per se is typically not significantly modified [8, 25].

Gastroesophageal reflux disease (GERD) is twice as common in obese children as in non-obese children. However, barring the presence of gastrointestinal motility disorders, GERD by itself does not pose a substantial risk of perioperative aspiration [26].

Endocrine Comorbidities

Pediatric obesity and Diabetes Mellitus 2 (DM-2) are intimately linked. Thirty-five percent of children with DM-2 are obese, and DM-2 has a prevalence of 0.2% in obese children. Presence of established DM-2 is a strong indication for bariatric surgery in obese children. Patients with poor glycemic control are at risk for postoperative morbidity with respect to surgical site infections and acute kidney injury [27].

Overt hypothyroidism is the most common cause of endocrine-related obesity in children. Overall, its incidence in obese children is rare, but it requires optimization and treatment to reduce perioperative morbidity. Subclinical hypothyroidism, on the other hand, is quite common, though not as clinically relevant [28].

Renal Comorbidities

Obesity increases the risk of perioperative acute kidney injury (AKI) in adults, and may pose similar risk in obese children. Presence of other risk factors like ACE-I or ARB use, DM-2, preoperative renal dysfunction, hypertension, and long operative times are commonly seen in pediatric bariatric surgery patients, and intuitively further increase AKI risk. Perioperative rhabdomyolysis may contribute to the development of AKI as well [29].

Pediatric obesity can lead to chronic renal dysfunction through multiple mechanisms, including obesity-related glomerulonephropathy,

insulin resistance, and over-activation of the renin-angiotensin-aldosterone system [30].

Hematologic Comorbidities

Venous thromboembolism is significantly associated with pediatric obesity. An underlying mechanism for this may be a chronic pro-inflammatory state as evidenced by elevated C-reactive protein and interleukin-6 levels [31].

Musculoskeletal Comorbidities

Obese children are predisposed to a variety of orthopedic issues, including acute fractures, degenerative joint disease, and slipped capital femoral epiphysis (SCFE), osteoarthritis, and lower back pain. Self-reported joint dysfunction and pain can worsen perioperatively [32].

Neurologic and Psychiatric Comorbidities

Obese adolescents are developing intracranial hypertension, pseudotumor cerebri, and multiple sclerosis more frequently. Pseudotumor cerebri in particular is a strong indication for bariatric surgery [33].

Psychiatric comorbidities such as anxiety, depression, and eating disorders are common in pediatric bariatric surgery patients. A 2009 review by Pratt et al. outlined a variety of psychosocial eligibility criteria for adolescent weight loss surgery, including treatment of comorbid psychiatric conditions, evidence of social support, and evidence of motivation and ability to comply with requisite lifestyle changes after surgery [26].

Pre-operative Phase

Patient Selection

Selection of appropriate surgical candidates is an important aspect of pre-operative evaluation in pediatric bariatric surgery. Given that long-term outcomes in pediatric bariatric surgery patients are unknown, the inherent risks of these surgeries must be weighed against the potential benefits of improved quality and length of life. Until long-term outcome studies render new insights, patients must exhibit comorbidities to qualify for surgery.

The International Pediatric Endosurgery Group published 2009 criteria that consider both BMI cut-offs and the severity of patient comorbidities. Children with a BMI above 35, who have "severe" comorbidities, meet criteria for adolescent bariatric surgery. Children with "mild" comorbidities must have a BMI above 40. Comorbidities that are considered "severe" include moderate to severe sleep apnea, DM-2, and pseudotumor cerebri. "Mild" comorbidities include hypertension, dyslipidemia, and mild obstructive sleep apnea. Additional requirements for surgery are near-full physical (95% of adult skeletal stature) and sexual (Tanner stage 4 or greater) development, motivation to comply with lifestyle changes and long-term follow-up, ability to consent to surgery and surgical program, commitment to psychological evaluation and optimization perioperatively, and a stable psychosocial environment including a positive support system [34–36].

Contraindications to bariatric surgery, aside from patient and/or family refusal, include obesity that is medically correctable, current or planned pregnancy and/or breastfeeding, a documented substance abuse problem, and inability and/or unwillingness to adhere to postoperative treatment [37].

Efforts to select a patient for pediatric bariatric surgery and mobilize multidisciplinary teams should be long initiated by the time an anesthesia provider interfaces with the patient. However, a thorough understanding and familiarity with patient selection is a shared responsibility that, if neglected, can lead to negative patient outcomes.

Pre-operative Testing

Given that adolescent bariatric surgery is elective and reserved for patients with comorbidities, the pre-anesthesia evaluation should include a thor-

ough history and physical examination that identifies obesity-related diseases. It should also be initiated well in advance of surgery to allow for disease optimization. There are currently no nationally standardized protocols for pre-anesthesia assessment, as evidence-based recommendations for ordering supplementary diagnostic tests are lacking. Therefore, diagnostic tests and studies should be performed on a case-by-case basis, in patients with known or suspected comorbid disease burden.

Close attention to cardiopulmonary symptoms and exercise tolerance is essential. If cardiac disease is suspected, a preoperative electrocardiography is generally recommended. Echocardiography can also be considered in the context of known or suspected cardiac disease, or sub−/acute development of cardiopulmonary symptoms [8].

Antihypertensive therapy may be initiated in patients with severe disease burden. Withholding ACE-inhibitors and angiotensin receptor blocking mediations on the day of surgery is recommended, given the potential for significant perioperative vasoplegia and hypotension [30].

Attempts to improve the shortcomings of clinical questionnaires and screening tools for OSAS are ongoing, and therefore many institutions rely heavily on polysomnography (PSG) to screen high-risk patients who lack an established diagnosis. The utility of PSG is its ability to quantify OSAS severity, which determines the need for initiation of continuous positive airway pressure (CPAP) and bilevel airway pressure therapy (BIPAP). CPAP and BIPAP should be continued through the postoperative period. There are no standard criteria for postoperative admission and continuous postoperative monitoring in pediatric patients with suspected OSAS [21].

Serologic studies such as hemoglobin A1c (HbA1c), thyroid function tests, metabolic panels, and complete blood counts (CBC) are also part of the pre-operative work-up in patients with known or suspected disease. HbA1c testing is recommended in diabetic patients or patients with abnormal glucose tolerance at baseline. Preoperative glycemic control to a goal HbA1c less than 6.5–7.0% is recommended and associated with decreased surgical site infections and AKI [8].

Anesthetic Considerations

Vascular Access, Monitoring

All pediatric bariatric surgery patients require peripheral venous access prior to induction of anesthesia. Obese children are at greater risk for requiring multiple insertion attempts for peripheral lines than their lean counterparts [38]. Anesthesia providers should see patients allot adequate time to obtain intravenous access to prevent procedural delays, and there should be a low threshold to use ultrasound. Ideally, a second peripheral intravenous catheter should be obtained for the procedure as well.

Multiple studies have demonstrated that ultrasound improves success of first cannulation and reduces the time to cannulation in pediatric patients with history of difficult access [39]. Ultrasound can reliably identify vessels in the forearm and antecubital fossa; however, the distance between the skin and target vessel is often increased due to excess subcutaneous tissue. A linear high-frequency probe can be used to identify the vein in cross section, and the tip of the needle can be followed into the vessel lumen by either rotating the probe 90° and seeing the vessel longitudinally, or maintaining a dynamic cross section view. Longer cannulas are preferred to reduce the risk of catheter dislodgement and resultant extravasation. Many institutions recommend ultrasound confirmation of adequate catheter in the vessel after cannulation.

Central venous access is not routinely recommended, especially with the widespread use of ultrasound guided peripheral access. Arterial access may be necessary in patients with significant cardiopulmonary disease [40].

Pediatric bariatric surgery patients often require large cuff sizes for accurate non-invasive blood pressure monitoring. Alternative cuff sites, including forearm and calf, are commonly utilized, as the upper arm cuff can be compressed by

the patient's axillary and truncal tissue. In cases where the arms are tucked at the patient's sides, blood pressure cuffs have given inaccurate measurements when surgical personnel lean against the cuff. Consider arterial line access where non-invasive blood pressure measurements are unreliable.

Other Preoperative Interventions

All morbidly obese patients are at increased risk of developing perioperative deep venous thromboses (DVT), including fatal DVT's. To this end, patients should receive both chemical and mechanical thromboprophylaxis. Compression boots can be placed while the patient is awake [40].

Airway Management Plan

A comprehensive induction and airway plan that anticipates the degree of difficulty of mask ventilation, laryngoscopy, intubation, and extubation is essential in the pediatric bariatric surgery patient.

Obesity is an independent risk factor for difficult mask ventilation. However, barring the presence of other anatomic risk factors elucidated on standard airway physical exam, obesity alone does not appear to be a risk factor of difficult intubation. With ramping that positions the tragus above the level of the sternal notch, a majority of pediatric bariatric surgery patients reported in the literature were successfully intubated using routine direct laryngoscopy. These results, while reassuring, do not excuse a lack of a thorough evaluation. In the case of a potentially difficult airway, it is advisable to include video laryngoscopy or flexible bronchoscopy as backup plans, as well as emergency airway equipment on standby [30, 41, 42].

Likelihood of safe extubation should be assessed in advance. Extubation should be done in the operating room with the same positioning that led to successful intubation. Given the high risk of laryngospasm in pediatric patients, and airway obstruction in morbidly obese and sleep apneic patients, the anesthesia provider must be thoroughly prepared for resuscitation and re-intubation, with emergency medications and airway equipment within close reach [30, 41, 42].

Patient Positioning

The hallmarks of appropriate patient positioning are increasingly important in pediatric bariatric patients. These patients are at increased risk for position-related injuries, both because of challenging body habitus and because of long operative duration [40].

Surgical beds, safety straps, and transfer devices that accommodate high weight patients are indispensable to the prevention of catastrophic injuries. Attention should be devoted to immobilizing the pannus to prevent injuries while tilting the bed throughout the case. Bariatric surgery positioning is usually supine with varying degrees of Trendelenburg and reverse Trendelenburg positioning. Head and neck position should be neutral to prevent brachial plexopathy, upper extremities should be abducted less than 90°, and forearms should be supinated to prevent ulnar neuropathy. Pressure points should be padded. Eyes should be free from compression, and confirming eye safety throughout the case is mandatory especially in laparoscopic cases where surgical instruments can cause significant patient injury [40]. Pre-operative consultation with the surgical team to assess their positioning needs, and communicating intraoperatively if and when issues arise, is a recommended practice.

Reverse Trendelenburg is often used to facilitate upper abdominal surgery, especially in laparoscopic surgeries. Main challenges with reverse Trendelenburg positioning include hypotension and reduced cardiac output due to venous pooling in the lower extremities, reduced cerebral perfusion pressure, patient injury from sliding, and cerebral air embolism. Optimizing cardiac output by adequate pre-hydration is recommended. If significant hemodynamic instability or need for frequent blood pressure

readings is required, consideration of arterial line access is warranted [43].

Laparoscopic surgery in supine position, when combined with Trendelenburg position, can complicate respiratory mechanics by virtue of decreased respiratory system compliance, ventilation-perfusion mismatching, and endotracheal tube malposition. Hemodynamic instability can occur due to several mechanisms, including most notably decreased venous return secondary to increased intra-abdominal pressure. In a patient with limited hemodynamic reserve, the anesthesia provider can request slower insufflation to mitigate this effect [40].

Medication Dosing

Pharmacokinetics in obese children are complex and unpredictable due to high variance in volume of distribution and drug clearance. As a result, these patients are at increased risk of medication overdose and underdose. Volume of distribution is the major determinant of loading doses, and clearance determines maintenance or infusion dosing.

Dosing can be planned, at the anesthesia provider's discretion, by total body weight (TBW), lean body weight (LBW), or ideal body weight (IBW), depending on the specific medication and whether it is being administered as a bolus or an infusion. Due to the unpredictable pharmacokinetics of infusions in obese patients, it is recommended that intraoperative electroencephalogram be employed in TIVA cases [40].

For many anesthetic drugs, LBW is the appropriate choice. Interestingly, Olutoye et al. demonstrated that obese children require significantly less propofol for loss of consciousness on a per kilogram basis than normal weight children [44]. Therefore, induction doses of propofol can be dosed by LBW, whereas infusions can be dosed by total body weight. If complete neuromuscular paralysis is desired for ideal laryngoscopy and intubating conditions, a large total body weight dose of succinylcholine is recommended [45].

The clinical behavior of volatile anesthetic agents in the pediatric population is not as well described as in the adult population. Several studies have demonstrated faster emergence with sevoflurane and desflurane as compared to isoflurane, whereas the differences between sevoflurane and desflurane are equivocal. For longer case durations, desflurane may yield a more rapid emergence and return to normal cognition, which can theoretically prevent post-operative delirium and all of its undesirable sequelae [46].

In order to optimize the maintenance and emergence phases, MAC-sparing anesthetic adjuncts should be considered in every patient when clinically appropriate. Dexmedetomidine and ketamine are two popular agents, as they are potent analgesics that can reduce intraoperative narcotic requirements and do not cause significant respiratory depression. Dexmedetomidine is particularly favorable in children who are at increased risk for postoperative delirium, and in TIVA cases, as there are no confounding effects on BIS monitoring (as there are with ketamine).

Crystalloid administration should be conservative, with a target of euvolemia. Anticipated blood loss is minimal [40].

Postoperative nausea and vomiting is fairly common, and aggressive antiemesis with at least one agent is preferred [40].

Analgesia

Every attempt to minimize opioids and their adverse effects should be made via the implementation of multimodal analgesia. Pediatric bariatric surgery patients have heightened sensitivity to opioids, increased prevalence of OSAS, and tenuous bowel function in the immediate postoperative period, making opioid sparing a critical component of every anesthetic plan.

In patients with extensive open abdominal incisions, epidural catheters devoid of opioids can provide significant postoperative relief [47, 48]. Many patients require inpatient admission after surgery and do not have medical contraindications to neuraxial anesthesia. Therefore, every effort should be made to offer regional and neuraxial anesthetics when clinically appropriate, especially in patients who are opioid tolerant or

who may be surgically complex. For patients with anatomical landmarks that are indiscernible for epidural anesthesia, ultrasound has been shown to be effective [47].

Truncal blocks, most commonly transversus abdominis plane (TAP) blocks, have been widely used in laparoscopic cases, but the benefits in terms of improving pain scores and reducing opioid consumption are conflicting [49].

An array of non-opioid analgesic medications should be offered in the absence of contraindications, to combat the various modes of postoperative pain signaling. NSAID medications are particularly useful at relieving not just inflammatory pain, but also visceral pain [50–53]. NSAIDs are also well-known for their opioid sparing effects, and their synergistic effects with other pain medications [51]. Concerns have been expressed over possible adverse effects of ketorolac on bleeding (surgical and gastrointestinal) and healing of anastomoses [50].

Regularly scheduled intravenous acetaminophen has been shown to decrease postoperative opioid requirements in obese children [51].

Gabapentinoids, particularly preoperative pregabalin, decrease opioid requirements in morbidly obese patients after laparoscopic bariatric surgery. Low-dose gabapentin is not as effective in this regard [47, 54]. In fact, recent evidence suggests that routine administration of gabapentin as part of a multimodal analgesia regimen in total hip and knee arthroplasties increased postoperative pulmonary complications, including naloxone administration, noninvasive ventilation, and invasive mechanical ventilation [55].

As previously described, ketamine and dexmedetomidine are used not only as anesthetic adjuncts, but also as analgesics. Subanesthetic dosing of ketamine demonstrates significant opioid sparing and synergistic properties when used with opioids, and it can reduce opioid induced hyperalgesia [56]. Ketamine infusion can be initiated intraoperatively and continued postoperatively. Dexmedetomidine infusion similarly decreases postoperative pain scores, opioid requirements, and need for rescue pain medications [57].

Conclusion

Obesity is an increasingly common and debilitating chronic illness in children and adolescents that causes significant morbidity and reduction in quality of life. In appropriately selected patients, bariatric surgery provides a potentially disease modifying and life-extending treatment. Anesthetic management of pediatric bariatric surgery patients should be planned with an attention to obesity related comorbidities in every phase of care.

Funding and Conflicts of Interest

None.

References

1. Wang G, Dietz WH. Economic burden of obesity in youths aged 6 to 17 years: 1979–1999. Pediatrics. 2002;109:e8. https://doi.org/10.1542/peds.109.5.e81.
2. Ogden CL, Carroll M, Curtin LR, et al. Prevalence of high body mass index in US children and adolescents, 2007–2008. JAMA. 2010;303(3):242–9.
3. Sturm R. Increases in clinically severe obesity in the United States, 1986–2000. Arch Intern Med. 2003;163:2146–8.
4. Dansinger ML, Tatsioni A, Wong JB, Chung M, Balk EM. Meta-analysis: the effect of dietary counseling for weight loss. Ann Intern Med. 2007;147(1):41–50.
5. Michalsky M, Reichard K, Inge T, Pratt J, Lenders C. ASMBS pediatric committee guidelines. Surg Obes Relat Dis. 2012;8:1–7.
6. Zitsman JL, Inge TH, Reichard KW, Browne AF, Harmon CM, Michalsky MP. Pediatric and adolescent obesity; management, options for surgery, and outcomes. J Pediatr Surg. 2014;49(3):491–4.
7. Frank P, Crookes PF. Short- and long-term surgical follow-up of the postbariatric surgery patient. Gastroenterol Clin N Am. 2010;39(1):135–46.
8. Ortiz VE, Kwo J. Obesity: physiologic changes and implications for preoperative management. BMC Anesthesiol. 2015;15:97.
9. Freedman DS, Mei Z, Srinivasan SR, et al. Cardiovascular risk factors and excess adiposity among overweight children and adolescents: the Bogalusa Heart Study. J Pediatr. 2007;150:12–7.
10. Abdullah A, Stoelwinder J, Shortreed S, et al. The duration of obesity and the risk of type 2 diabetes. Public Health Nutr. 2011;14:119–26.
11. Kelly AS, Barlow SE, et al. Severe obesity in children and adolescents: identification, associated health risks, and treatment approaches. Circulation. 2013;128:1689–712.

12. Gurnani M, Birken C, Hamilton J. Childhood obesity. Pediatric Clin North Am. 2015;62:821–40.
13. Sorof J, Daniels S. Obesity hypertension in children: a problem of epidemic proportions. Hypertension. 2002;40:441–7.
14. Weiss R, et al. What is metabolic syndrome, and why are children getting it? Ann N Y Acad Sci. 2013;1281:123–40.
15. Berenson GS, Srinivasan SR, Bao W, et al. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study. N Engl J Med. 1998;338:1650–6.
16. Crowley DI, Khoury PR, Urbina EM, et al. Cardiovascular impact of the pediatric obesity epidemic: higher left ventricular mass is related to higher body mass index. J Pediatr. 2011;158:709–14.
17. Michalsky MP, Raman SV, Teich S, et al. Cardiovascular recovery following bariatric surgery in extremely obese adolescents; preliminary results using cardiac magnetic resonance (CMR) imaging. J Pediatr Surg. 2013;48:170–7.
18. Shah RV, Abbasi SA, et al. Myocardial tissue remodeling in adolescent obesity. J Am Heart Assoc. 2013;2:e.000279.
19. Donat A. Bariatric surgery, sleep apnea and pulmonary hypertension. Surg Obes Relat Dis. 2017:1581–6. https://doi.org/10.26226/morressier.58f5b030d462b80296c9e56c.
20. Mathew JL, Narang I. Sleeping too close together: obesity and obstructive sleep apnea in childhood and adolescence. Paediatr Respir Rev. 2014;15:211–8.
21. Patino M, Sadhasivam S, Mahmoud M. Obstructive sleep apnoea in children: perioperative considerations. Br J Anaesth. 2013;111(S1):A18–32.
22. Mitchell RB, Kelly J. Outcome of adenotonsillectomy for obstructive sleep apnea in obese and normal-weight children. Otolaryngol Head Neck Surg. 2007;137:43–8.
23. Hans GA, Lauwick S, Kaba A, et al. Postoperative respiratory problems in morbidly obese patients. Acta Anaesthesiol Belg. 2009;60:169–75.
24. Berardis S, Sokal E. Pediatric non-alcoholic fatty liver disease: an increasing public health issue. Eur J Pediatr. 2014;173:131–9.
25. Grazia Clemente M, Mandato C, et al. Pediatric non-alcoholic fatty liver disease: recent solutions, unresolved issues, and future research directions. World J Gastroenterol. 2016;22(36):8078–93.
26. Pulgaron ER. Childhood obesity: a review of increased risk for physical and psychological comorbidities. Clin Ther. 2013;35(1):A18–32.
27. Puldaron ER, Delameter AM. Obesity and type 2 diabetes in children: epidemiology and treatment. Curr Diab Rep. 2014;14:508.
28. Barreca M, Renzi C, et al. Is there a role for enhanced recovery after laparoscopic bariatric surgery? Preliminary results from a specialist obesity treatment center. Surg Obes Relat Dis. 2016;12:119–26.
29. Ding W, Cheung WW, Mak RH. Impact of obesity on kidney function and blood pressure in children. World J Nephrol. 2015;4(2):223–9.
30. Maxwell BG, Ingrande J, et al. Perioperative management of the morbidly obese adolescent with heart failure undergoing bariatric surgery. Pediatr Anesth. 2012;22:476–82.
31. Shah AS, Dolan LM, et al. Severe obesity in adolescents and young adults is associated with subclinical cardiac and vascular changes. J Endocrinol Metab. 2015;100(7):2751–7.
32. Paulis WD, Silva S, et al. overweight and obesity are associated with musculoskeletal complaints as early as childhood: a systematic review. Obes Rev. 2014;15:52–67.
33. Langer-Gould A, Brara SM, et al. Childhood obesity and risk of pediatric multiple sclerosis and clinically isolated syndrome. Neurology. 2013;80:548–52.
34. Gastrointestinal surgery for severe obesity: National Institutes of Health Consensus Development Conference Statement. Am J Clin Nutr. 1992;55(2 suppl):615S–9S.
35. Pratt JS, Lenders CM, Dionne EA, et al. Best practice updates for pediatric/adolescent weight loss surgery. Obesity (Silver Spring). 2009;17(5):901–10.
36. Ibele AR, Mattar SG. Adolescent bariatric surgery. Surg Clin North Am. 2011;91(6):1339–51.
37. Brandt ML, Harmon CM, Helmrath MA, Inge TH, McKay SV, Michalsky MP. Morbid obesity in pediatric diabetes mellitus: surgical options and outcomes. Nat Rev Endocrinol. 2010;6(11):637–45.
38. Nafiu OO, Burke C, Cowan A, Tutuo N, Maclean S, Tremper KK. Comparing peripheral venous access between obese and normal weight children. Paediatr Anaesth. 2010;22:449–54.
39. Doniger SJ, Ishimine P, Fox JC, Kanegaye JT. Randomized controlled trial of ultrasound-guided peripheral intravenous catheter placement versus traditional techniques in difficult-access pediatric patients. Pediatr Emerg Care. 2009;25:154–9.
40. Mecoli M, et al. Pediatric obesity: anesthetic implications and perioperative considerations for weight loss surgery. Curr Anesthesiol Rep. 2017;7(2):125–34. https://doi.org/10.1007/s40140-017-0211-z.
41. Tait AR, Voepel-Lewis T, et al. Incidence and risk factors for perioperative adverse respiratory events in children who are obese. Anesthesiology. 2008;3(108):375–80.
42. Samuels PJ. Anesthesia for adolescent bariatric surgery. Int Anesthesiol Clin. 2006;44(1):17–31.
43. Hsia DS, et al. Adolescent bariatric surgery. Arch Pediatr Adolesc Med. 2012;166(8):757. https://doi.org/10.1001/archpediatrics.2012.1011.
44. Olutoye OA, Yu X, Govindan K, et al. The effect of obesity on the ED(95) of propofol for loss of consciousness in children and adolescents. Anesth Analg. 2012;115:147–53.
45. Lemmens HJM, Brodsky JB. The dose of succinylcholine in morbid obesity. Anesth Analg. 2006;102:438–42.

46. Juvin P, Vadam C, Malek L, Dupont H, Marmuse JP, Desmonts JM. Postoperative recovery after desflurane, propofol, or isoflurane anesthesia among morbidly obese patients: a prospective, randomized study. Anesth Analg. 2000;91(3):714–9.
47. Alvarez A, Singh PM, Sinha AC. Postoperative analgesia in morbid obesity. Obes Surg. 2014;24:652–9.
48. Zotou A, Siampalioti A. Does epidural morphine loading in addition to thoracic epidural anglesia benefit the postoperative management of morbidly obese patients undergoing open bariatric surgery? A pilot study. Obes Surg. 2014;24:2099–108.
49. Albrecht E, Kirkham KR, Endersby RV, et al. Ultrasound-guided transversus abdominis plane (TAP) block for laparoscopic gastric bypass surgery: a prospective randomized controlled double-blinded trial. Obes Surg. 2013;23(8):1309–14.
50. Caesar Y, Sidlovskaja I, et al. Intraabdominal pressure and postoperative discomfort in laparoscopic Roux-en-Y gastric bypass (RYG6) surgery: a randomized study. Obes Surg. 2016;26:2168–72.
51. Saurabh S, Smith JK, et al. Scheduled intravenous acetaminophen reduces postoperative narcotic analgesia demand and requirement after laparoscopic Roux-en-Y gastric bypass surgery. Surg Obes Relat Dis. 2015;11:424–30.
52. Ziemann-Gimmel P, Hensel P, Koppman J, et al. Multimodal analgesia reduces narcotic requirements and antiemetic rescue medication in laparoscopic Roux-en-Y gastric bypass surgery. Surg Obes Relat Dis. 2013;9(6):975–80.
53. Andersen LP, Werner MU, et al. Analgesic treatment in laparoscopic gastric bypass surgery: a systematic review of randomized trials. Obes Surg. 2014;24:462–70.
54. Hassani V, Pazouki A, et al. The effect of gabapentin on reducing pain after laparoscopic gastric bypass surgery in patients with morbid obesity: a randomized controlled trial. Anesth Pain Med. 2015;5(1):e22372.
55. Ohnuma T, et al. Effects of acetaminophen, NSAIDs, gabapentinoids, and their combinations on postoperative pulmonary complications after total hip or knee arthroplasty. Pain Med. 2020;21:2385–93. https://doi.org/10.1093/pm/pnaa017.
56. Wang L, Johnston B, et al. Ketamine added to morphine or hydromorphone patient-controlled analgesia for acute postoperative pain in adults: a systematic review and meta-analysis of randomized trials. Can J Anesth. 2016;63:311–25.
57. Salama AK, Abdallah NM. Multimodal analgesia with pregabalin and dexmedetomidine in morbidly obese patients undergoing laparoscopic sleeve gastrectomy: a prospective randomized double blind placebo controlled study. Egypt J Anesth. 2016;32:293–8.

Anesthesia for Surgical Procedures in Conjoined Twins

17

Helena Karlberg and Premal M. Trivedi

Learning Points

One of the goals of the authors is to initiate the reader in general aspects of anesthesia in the context of conjoined twin separation surgery. The following are highlights of general learning seen as valuable to medical professionals providing anesthesia care for children, and to others with an interest in this subject.

- An institutional multidisciplinary specialty team is of the essence for the extensive and protracted planning required for the execution of the separation of conjoined twins.
- A successful separation of conjoined twins greatly depends on the nature and extent of shared organs, in particular when cardiac, vascular and cranial structures are involved.
- Planning and preparing the operating suite for the separation demands duplicate setups and color coding of anesthesia staff, as well as all equipment, medication, anesthesia machines, iv-tubing, blood coolers, sample tubing and order forms in conformance with original twin identification.
- Biomedical Engineering and Information Technology services are essential for operational functionality, including network capability and electronic medical record data flow for the operation of two anesthesia workstations.
- During the separation process immediate access, presence and availability of physicians from all specialty teams including transfusion medicine is critical.
- Hemodynamic and respiratory stability must be established prior to transportation to a second operating room following separation and to the intensive care unit after completion of surgery.
- Preparatory procedures will be performed on the twins while conjoined and several corrective procedures will be needed for a long period after separation.

Introduction

Successful separation of conjoined twins strongly depends on nature and extent of shared organs, in particular when cardiac, vascular and cranial structures are involved. Availability of a multidisciplinary specialty team with expertise and experience in supporting extensive pre-operative investigations, evaluations, procedural preparation and the implementation of these highly complex surgical procedures is crucial. Such a team comprises multiple surgical pediatric specialties, pediatric anesthesia specialists, transfusion medi-

H. Karlberg (✉) · P. M. Trivedi
Department of Anesthesiology, Perioperative and Pain Medicine, Texas Children's Hospital, Baylor College of Medicine, Houston, TX, USA
e-mail: hxkarlbe@texaschildrens.org; pxtrived@texaschildrens.org

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_17

cine and radiology teams, and close support from biomedical engineering, information technology and simulation staff.

Clinical History

This section highlights certain surgical landmarks involving conjoined twin separation chronicled over many centuries into more recent times. Many more cases, too many to enumerate here, have been performed during the latter portion of the twentieth century and the beginning of the twenty-first.

Possibly the earliest case of separating conjoined twins took place in Constantinople around 945 AD, when separation of 30 year old ischiopagus twins joined at the pelvis was attempted. According to the records emergency surgery was performed after one twin had died, in an attempt to save the other twin who survived for only another 3 days.

The first successful separation of female conjoined twins was conducted in 1689 in Basel, Switzerland by the highly regarded surgeon Johannes Fatio (1649–1691) who separated xiphoomphalopagus twins, joined at the xiphoid process, umbilicus and the abdomen. However, most of Dr. Fatio's documents were confiscated and burned during political unrest. Fortunately the event was captured in his only surviving book, *Der Arzney Doctor*, *The Helvetic (Swiss) Reasonable Midwife,* published 61 years after his death [1].

Fast forward, the first separation of Craniopagus twins, fused at the skull, occurred in 1952 at the University Medical Center in Chicago. The male twins were 20 months old at the time of separation. During the procedure it was discovered that the twins shared the sagittal sinus. One of the twins did not regain consciousness, dying 34 days later. The other survived surgery with neurological damage and subsequently died at 11 years of age.

The first successful separation of Craniopagus twins, where both female twins were long-lived was performed at Mercy Hospital in Chicago in 1955 [2] by Dr. Harold Voris. In 1963, about 8 years after separation the larger girl was reported as developing normally but the smaller was permanently impaired.

In 1957 Dr. Bertram Katz and his team at Northside Hospital in Youngstown, Ohio, separated omphalopagus twins joined at the umbilicus and abdomen, who shared the liver, becoming the world's first successful separation of conjoined twins sharing a vital organ.

In the latter part of the twentieth century and early twenty-first there has been an upswing in number of cases involving separation of conjoined twins. Separation surgeries have been performed in institutions with long-standing experience, such as Great Ormond Street Hospital in London, The Red Cross War Memorial Children's Hospital in Cape Town, King Abdullah Specialist Children's Hospital in Riyadh, Children's Hospital of Philadelphia, Texas Children's' Hospital in Houston as well as a few cases in other institutions worldwide [3].

Epidemiology

Conjoined twins represent a rare developmental accident of monoamniotic, monochorionic and monozygotic twinning believed to result from incomplete fission at the embryonic axis [3]. The lack of division of the fertilized egg is likely caused by a delay of fission to post conception day 12–15 from the normal 4–12 days after fertilization.

Incidences of conjoined twins are estimated to occur in between 1:30,000 to 1:100,000 births, 1:900 twin pregnancies and 1:200 monozygotic twin pregnancies [2, 3]. Conjoined twins are always identical, symmetrical and of same sex with a higher incidence of conjoined twinning in females with a ratio of 3:1. Conjoined twinning is associated with a high perinatal mortality, especially in females, premature infants and neonates with low birth weight. The rate of still-born and early death of conjoined twins has been reported between 70 and 80%, with 10% of live born twins surviving to undergo surgical separation, which has a 60–80% survival rate [1, 3]. Live birth survival rate has been reported as 12–13.6%, with overall survival rates at 7.5–8.3% [3–5].

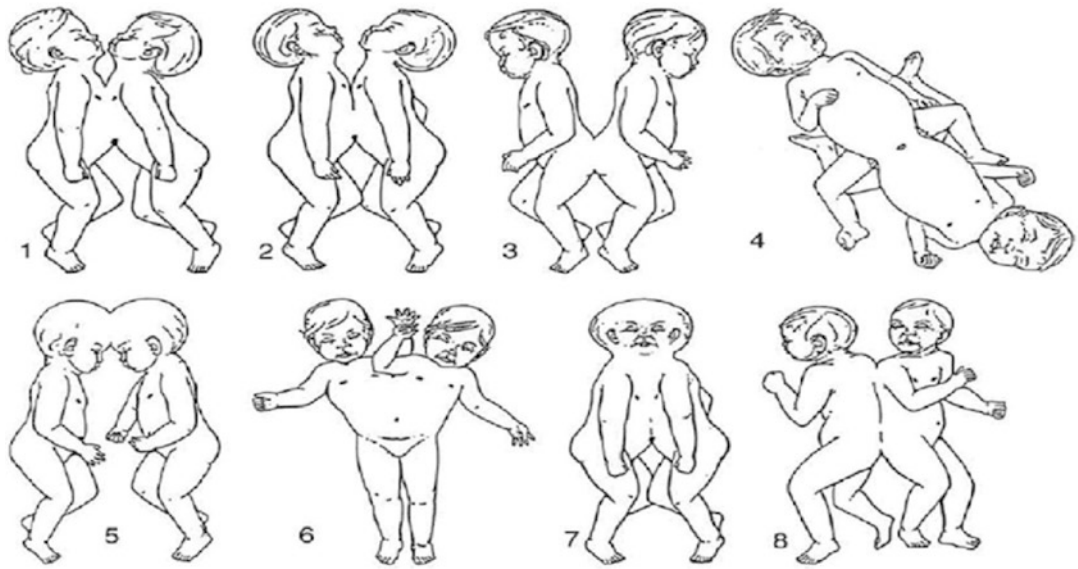
There has been no single factor identified as predicting or predisposing cause for conjoined twinning, although links to assisted reproductive techniques have been suggested. Neither has one been able to point to any specific genetic, environmental or demographic causes, however, high rates in Central Africa and increased trends in South America have been reported [2, 6].

The preeminent French surgeon Ambroise Pare' (1510–1590), considered one of the fathers of surgery issued a leaflet of illustrations depicting several types of conjoined twins. In 1832 French naturalist Etienne Geoffroy Saint-Hilaire published the classification of conjoined twins still used to this day [7]. Conjoined twin types are classified by the most prominent site of union, with the suffix pagus from the Greek pa'gos meaning joined. The number of legs can vary between two, three and four, i.e. bipus, tripus and tetrapus, respectively.

Different types of conjoined twin fusions are illustrated in Fig. 17.1 and described in the following in regards to union sites, shared structures and rate of incidence. The variations discussed are: *Thoracopagus, Omphalopagus, Xiphopagus, Pygopagus, Ischiopagus, Craniopagus, Cephalopagus, Rachipagus, Parapagus, Parasitic and non-classified* types. This is based on data from the Worldwide Collaborative Epidemiological Study of the International Clearinghouse for Birth Defects Surveillance and Research, a multicenter worldwide research program including the largest sample of conjoined twins studied, in addition to that of imaging and surgical publications [3, 8, 9].

Thoracopagus

Thoracopagus twins are joined at the thorax and upper abdomen. This is the most common twinning (42%), observed predominantly in female conjoined twins. The overall prognosis and success of separation is determined by the extent of cardiac fusion. If pumping heart structures are shared separation is not achievable, resulting in the loss of one or both conjoined twins. Thoracopagus twins are positioned face-to-face, sharing the upper thorax, with a common sternum, diaphragm, upper abdominal wall, including umbilicus and liver with a jointed biliary tree in 25% of the cases. Nearly 90% share a pericar-



1. Thoracopagus, 2. Omphalopagus, 3. Pygopagus, 4. Ischiopagus, 5. Craniopagus, 6. Parapagus, 7. Cephalopagus, 8. Rachipagus

Fig. 17.1 Schematic drawing of types of conjoined twins

dial sac and 85% share cardiac structures. The twins can have a common small intestine (50%) but separate large intestines, pelvis, urinary tracts and separate sets of limbs.

Omphalopagus

Omphalopagus twins are joined at the umbilicus and abdomen, with an incidence of 5.5%.

Heart structures are never involved, but the pericardium may be shared. Most twins (80%) share one common liver. The stomach and proximal small intestines are usually separate, and each twin has a rectum. The intestines usually join at the Meckel diverticulum. The terminal ileum and colon are shared, while the colon divides distally and each twin has separate rectums. The twins also have separate pelvises, urinary tracts and separate sets of limbs.

Xiphopagus

Xiphopagus twins are joined at the xiphoid cartilage, with an incidence of 3%.

They are usually linked by only cartilage and soft tissue. They may share the liver, but no other vital organs.

Pygopagus

Pygopagus twins share the sacrum and have an incidence is 1%.

The twins are fused posteriorly and are facing away from each other. There is a common sacrum, coccyx, part of the pelvic bone and perineum. Spinal cords are often separate, although if fused separation may not be feasible. They have a common anus and one or two rectums and sometimes a shared bladder. Proximal intestines are separate.

Ischiopagus

Ischiopagus twins share the pelvis and have an incidence of 1.8%.

They are facing each other or connected end-to-end. They are fused from the level of umbilicus caudally to a duplicated fused pelvis. They share lower gastrointestinal (70%) and genitourinary tracts (50%) and have complex urogenital and orthopedic anatomy.

Craniopagus

Craniopagus twins are fused at the skull and have an incidence of 5%.

They share skull, meninges, and venous sinuses but rarely (33%) brain cortex. The union can be occipital, frontal, temporo-parietal or parietal but does not include the base of the skull, the face or the trunk.

Cephalopagus

Cephalopagus twins are joined at the maxillofacial structure and have an incidence of 5.5%.

They have a fused head and often a fused thorax. The single fused head may have two faces (janiceps), which are facing away from each other or one face may be rudimentary. These types of twins are nonviable.

Rachipagus

Rachipagus twins are joined at the spine and have an incidence of 1.0%.

They are dorsally fused, faced away from each other. They have vertebral anomalies and neural tube defects. Rachipagus twins may involve the dorso-lumbar vertebral column but rarely the cervical vertebrae or the occipital bone.

Parapagus

Parapagus twins are fused laterally, side-by-side, and regularly share the pelvis. The incidence is 14.5%. Involves extensive side-to-side fusion. Parapagus dithoracic twins have fused abdomen and pelvis, whereas the thorax is not fused. Parapagus dicephalus twins share one

trunk and have two heads. Parapagus diprosopic twins share trunk and head with two faces. The number of limbs varies from four to a maximum of seven [10].

Parasitic

Parasitic twins are joined at any location and have an incidence of 3.0%. An incomplete twin can be attached to the other twin at any location. This is the only asymmetric type of conjoined twins.

Other Symmetric Non-classified

The incidence is 21.4%.

Thoracopagus type fusion is almost four times more common in females, and parapagus and parasitic types are significantly more common in males [3]. All twins are symmetrical and joined at the same site except for parasitic twins [3].

Perioperative Management

Conjoined twins are delivered mostly by planned cesarean section. Survival and successful separation of conjoined twins strongly depend on the nature and extent of shared organs, in particular when cardiac, vascular and cranial structures are involved.

An estimated 70% of conjoined twins die in utero, or in the early neonatal period from causes such as the nature of twinning, prematurity or low birth weight. A significantly higher mortality rate observed in female conjoint twins has been linked to the fact that most thoracopagus twins are female, and 90% of thoracopagus twins share a pericardial sac and 85% share cardiac structures. About 10% of all live born twins survive to undergo surgical separation with a 60–80% survival rate [2, 3].

Separation of conjoined twins is a challenging and complex undertaking which requires extensive and detailed planning by multiple specialties. Consequently these procedures are often performed at centers that have the resources to provide multi-disciplinary teams capable of supporting an extensive pre-operative investigation, evaluation, procedural preparation and not the least, implementation of these complex surgeries. Examples of commonly involved teams include pediatric anesthesia and the surgical specialties: general pediatric surgery, reconstructive plastic surgery, pediatric cardiac surgery, liver surgery, urology, gynecology, orthopedics and neurosurgery. Radiology departments with experienced radiologists and state-of-the-art equipment and instrumentation can further provide essential information and data through detailed imaging of the anatomy and physiology of the twins. This is commonly accomplished via CT, CT angiography, MRI, MRI angiography (MRA) and 3D-imaging and -printing. Amongst other important contributors to a successful outcome are teams specializing in pediatric cardiology, transfusion medicine, neonatal and critical care medicine, biomedical engineering, information technology and the simulation.

Prior to the separation the twins may be subject to preparatory procedures such as vascular access in the radiology imaging suites, sedation for CT, MRI and angiography, general anesthesia for placement and removal of tissue expanders, corrective and palliative procedures and urgent surgery for intestinal obstruction, colostomies and necrotizing enterocolitis [8]. These procedures provide the anesthesiology teams, in preparation for the separation surgery, opportunities to evaluate the airways and physiology of each twin and to learn and practice the set-up and logistics of working with two anesthesia teams simultaneously.

In the following sections, attention will be given to five important areas of support in preparation for separation surgery, as examples of how recent modern technology and innovation have enhanced the ability to prepare, plan and execute this complex surgical procedure. Such are the roles of advanced imaging, simulation, transfusion medicine, biomedical engineering and information technology services.

Role of Imaging

Early and accurate diagnosis of a conjoined twin pregnancy is possible with two-dimensional (2D) ultrasonography as early as 7 weeks of pregnancy, although false positive cases are common before 10 weeks' gestation [11]. Timely prenatal diagnosis is advisable to avoid potential maternal complications due to late termination. Early prenatal diagnosis and categorization of conjoined twins allows for counseling based on predictions of survivability of fetuses and newborn neonates, and in determining whether to terminate or to maintain the pregnancy. After 18–20 weeks, surgical termination with cesarean section may often be necessary.

A diagnosis of the anatomy of shared organs and the presence of additional malformations is essential for counseling families regarding outcome and planning of postnatal surgical separation [11]. Whereas 2D ultrasound is instrumental to prenatally diagnose conjoined twinning, 3D imaging allows for spatial understanding of organs and is instrumental for superior planning of surgery. The preoperative evaluation includes a detailed 3D ultrasound examination at 18–20 weeks and an ultrafast 3D MRI reconstruction and/or CT imaging which provide superior imaging quality and additional information as an adjunct to the 3D ultrasound. A fetal echocardiogram provides essential knowledge of cardiac anatomy and is critical for the process of forecasting survival and feasibility of pursuing separation surgery.

Postnatal imaging is vital to model skin coverage, confirm and provide further detail on the extent of organ sharing, and map the visceral and vascular anatomy for optimal planning of the surgical separation. MRI, 3D-MRI, and CT are essential to these goals. MRI and 3D-MRI provide additional information on the parenchymal anatomy of the areas of concern, whereas a triple phase CT can accurately delineate the cardiovascular and coronary anatomy, arteries in the chest and liver, visceral anatomy of the abdomen, and the vascular anatomy of the abdomen and pelvis. A 2015 study by Dr. Krishnamurthy at Texas Children's Hospital, Houston, Texas, further described how CT imaging combined with 3D printing could greatly facilitate planning of separation [10]. For these patients, the CT imaging results of skeletal structures, hearts, livers, kidneys, ureters and bladders were printed as a color-coded 3D model with simulated surgical planes identified between viscera and an avascular zone of separation marked in the liver. The 3D model was designed such that it could be assembled together or separated during surgical planning [8, 10, 12], (Figs. 17.2 and 17.3).

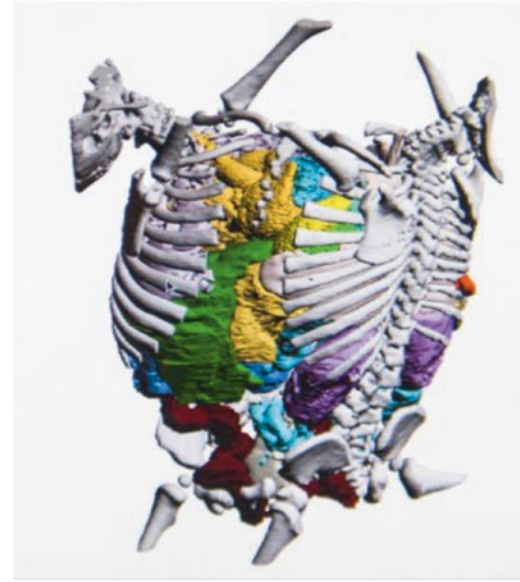


Fig. 17.2 Color coded CT-3D Image of skeletal, cardiovascular, arterial, and visceral structures

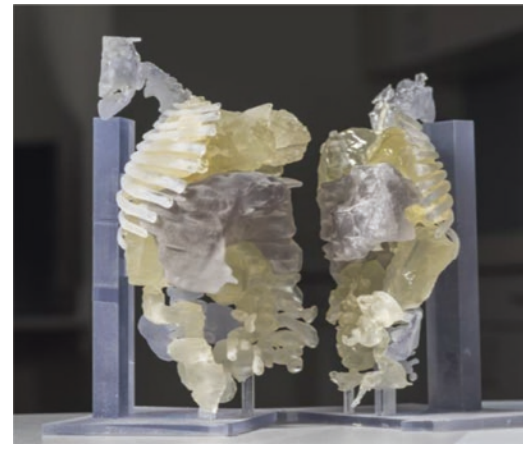


Fig. 17.3 3D Printed Model with detachable cardiac and visceral structures

Additional studies that can be performed include perfusion studies that are useful for assessing and estimating the amount of vascular shunting, cross circulation and exchange of blood volume between the twins. Cardiac evaluation includes echocardiography, cardiac angiography and/or MRA. If spinal cord fusion is suspected clinically and by electromyography further assessment by angiography and MRI is necessary to assess viability of separation [8]. A group at the University of Minnesota Masonic Children's Hospital used virtual reality to simulate a surgery to separate conjoined twins where new findings change the surgical plan [13].

Simulation

Modern medical simulation has been part of health care since the late twentieth century. Today simulation is a highly technically developed tool for education, training and testing in medical schools and teaching hospitals. Simulation-based in-situ clinical rehearsal (SbCR) provides a unique opportunity to safely practice and prepare for rare, complex and patient specific clinical procedures and scenarios [14, 15]. Repeated clinical simulation rehearsals with all participating team members provides an opportunity to attain familiarity with all essential equipment, to practice logistics of different stages of patient care including resuscitation in emergency scenarios, to improve communication, and to identify potential problems and roles. High fidelity life-size realistic mannequin twins provide opportunities to evaluate spatial orientation and optimal positioning of the twins during airway management, placement of vascular access, and surgery itself. Simulation also allows for familiarization with colour coding and labelling of the anesthesia teams and equipment [15].

Transfusion Medicine

Transfusion experts are essential for maintaining euvolemia and preventing coagulopathies during this lengthy procedure. Their presence in the operating room assures individualized and instant handling of laboratory tests and results, and expert guidance for real-time transfusion plans including replacement of necessary blood components and products of hemostasis. The risk for massive blood loss is also high, and they can further help to coordinate massive transfusion should it be needed. Of note, even if the twins have the same red blood cell group it is important to issue blood products individually such as in case of coagulopathy, a blood transfusion reaction or a massive blood loss in only one of the twins. The blood products as well as the coolers should be color-coded to avoid confusion of error.

Biomedical Engineering and Information Technology Service

The separation of conjoined twins in the current era of electronic charting demands early planning and in-situ modifications of the infrastructure of the operating room. In preparation for separation surgery, the operating room should be equipped with two anesthesia workstations (AWS) with network capabilities, electronic medical record data flow, and appropriate gas lines, scavenging, and suction for both work stations. Furthermore, should ECMO be needed, a third independent set of gas lines would be required. It should also be verified that the room can provide sufficient electrical power and outlets for all equipment involved. In addition, custom mounts for patient data monitors in order to optimize the anesthesiologist's work areas should be considered. Additional data jacks for a second patient workstation may have to be installed if not available initially. The biomedical engineering department oversees these needs and processes and validates data flow across the network.

Required Procedures Prior to Final Separation

Imaging studies during the pre-separation phase can mostly be carried out with the twins awake or light sedation. However, even light sedation for an MRI can be relatively unsafe unless their

airways are considered "easy", presenting challenges of monitoring, limited space and remoteness. General anesthesia in the MRI or CT suites with a double anesthesia setup is not a realistic undertaking. Pre-separation surgeries such as establishing vascular access and the placement of tissue expanders require general anesthesia and present an opportunity for the anesthesia team to become familiar with patient management and a double set-up in the operating room. An assessment of the following is valuable information for the planning of the upcoming separation procedure; optimal positioning, degree of difficulty to establish peripheral and central vascular access, airway access and intubation difficulties, respiratory capacity and hemodynamic stability, drug response and the degree of cross circulation evident on induction. The plastic surgery team places the tissue expanders only after necessary imaging procedures are completed. The expanders are gradually stretched with normal saline injection up until the separation surgery, a timespan of approximately 1 month.

Anesthesia Planning and Set-Up

Regular preparatory planning meetings with the necessary surgical specialists should be initiated early on in the process and continued through the date of surgery. Additional essential services likely to be involved include pediatric radiology, transfusion medicine, biomedical engineering, information technology, neonatal and critical care medicine and the simulation service. A chief anesthesiologist should early on commence anesthesia specific planning and preparation in anticipation of a lengthy and complex surgical procedure. Perioperative concerns and specific medical specialty-related considerations are itemized in Table 17.1.

The elective separation is usually scheduled at around 4–12 months of age to allow for sufficient growth, physiological development and maturation of the babies so that they can gain the strength and size to better tolerate the separation [2, 16]. Detailed information and understanding of the degree of fusion of visceral organs is imperative prior to surgery and is obtained from MRI, CT

Table 17.1 Peri-operative concerns and considerations for separation of conjoined twins

Cardiac concerns
- Patent ductus arteriosus
- Shared pericardial sac
- Shared pumping heart structures
- Cardiac decompensation
- Arrhythmia
- Cardiac arrest
- Inadequate chest cavity depth to accommodate heart after separation

Hemorrhage
- Massive bleeding during separation of cardiac, liver and cranial structures
- Coagulopathy

Respiratory concerns
- Nasal intubation
- Securing endotracheal tube
- Pulmonary reserve

Vascular access
- Difficult venous access
- Abnormal central vascular anatomy

Crosscirculation
- Degree of cross-circulation determines distribution and effects of medication on the other twin

Fluid balance
- Large fluid losses due to third spacing and evaporation

Thermostasis
- High possibility of hypothermia due to intra-operative exposure of large body surface area and long duration of procedure
- Adjust ambient temperature in operating room
- Place heating blanket under sterile drapes

Positioning and padding
- Patient positioning, adjusted as needed is key to optimal surgical exposure and access
- Risk of developing pressure ulcers during lengthy surgery requires careful and appropriate padding

Team fatigue
- Provide opportunities for scheduled breaks for rest, hydration and nutrition, by recruiting sufficient number of team members

Overcrowding, traffic control
- Access to other than essential intra-operative medical staff should be avoided for optimal infection control, and to minimize distraction, and accidental interference

Transport
- Arrange for safe and sterile transport of stabilized post-separated twin to second operating room
- Ensure safe transport to PICU in stable condition for postoperative care

Fig. 17.4 Duplicate anesthesia set-up in the operating room

and 3D-imaging and -printing. Access to a 3D model is an invaluable tool used for planning of the procedure and can further benefit the separation as it allows for pre-operative familiarization and clarification of critical anatomy and organ relationships, as well as opportunities for informal rehearsals to the surgeons and the other members of the operative team.

Anesthesiology management led by a chief anesthesiologist consists of two anesthesiology teams, one for each member of the conjoined twins. Each team consisting of two to three members should care for its respective designated twin throughout the entire course of hospitalization. The anesthesia teams are color coded in conformance with the colors already assigned to each child. The set-up of color-coded drugs, airway equipment, intravenous fluids and tubing, monitoring devices and anesthesia machines are labeled accordingly (Fig. 17.4). The equipment list is documented in Table 17.2 and the intra-operative set-up is described in Table 17.3.

Time out procedures are mandated at the beginning of surgery with all surgical specialties to be involved present and at each time another surgical specialty team begins their part of this multi-specialty complex surgery. Post-separation, one child will remain in place and the other will be moved to an adjacent surgical suite. Detailed plans for safe and sterile post-separation transfer of this twin should be made. Furthermore plans to control potential overcrowding and minimization of team fatigue should be instituted.

Techniques for anesthesia induction can be either inhalation based, intravenous, or a combi-

Table 17.2 Anesthesia equipment available for each twin at separation surgery

• Standard ASA monitors • Sterile pulse oximetry probe(s) • Five lead EKG with sterile coverage if in the sterile field. • Near-infrared spectroscopy (NIRS) monitor to measure tissue oxygenation of the brain • Peripheral intravenous fluids • Fluid warmer • Blood transfusion sets • Central venous line pressure transducer • Arterial line pressure transducer	• Short laryngoscope handle • Afrin nose drops • Difficult airway equipment • Infusion pumps • Manifold attached to central line • Anesthesia work station • Ultrasound equipment • Oxygen tank and bag mask ventilation system • Intraoperative communication sheet • Pediatric critical event checklist • Code sheet

Table 17.3 Intraoperative set-up

Anesthesia drugs
• Standard induction drugs, e.g. Propofol, midazolam, Rocuronium, fentanyl, sevoflurane • Antibiotic: In compliance with institutional protocol • Antifibrinolytic agent: Tranexamic acid; as a bolus dose combined with a continuous infusion when extensive blood loss is expected • Vasopressor infusions: Dopamine, vasopressin and epinephrine
Emergency setup
• Cardiac emergency drugs drawn up for immediate availability • Defibrillator and external defibrillator pads • Internal cardiac defibrillator paddles on the operating room table • Extracorporeal membrane oxygenation (ECMO) standby

nation of the two. Induction will begin with the twin of lesser cardio-pulmonary reserves. Meanwhile the other twin is managed with O_2 support and evaluated for signs of any cross circulation evidenced by sedation or apnea. Following intubation of the first twin, anesthesia induction of the second twin will begin. All intravenous agents administered are weight based and calculated by the total weight of the twins and divided equally between the two. Airway management and intubation can be challenging especially if both heads are close together resulting in limited airway access. Nasal intubation is preferred when long-term intubation is expected. During surgery the endotracheal tube is sutured in place to avoid accidental extubation. Adequate peripheral venous access and arterial lines are established under ultrasound guidance, secured and sutured in place before commencement of surgery. Surgeons will place additional venous lines for central access on the sterile field.

Following the completion of surgical separation and plastics closure, the patients will be transferred to the critical care unit where they will have separate rooms in close vicinity to each other. Onwards they will remain hospitalized for an extended period of time. During hospitalization and also after discharge they will require many corrective surgeries and long-term physical and occupational therapy. Interdisciplinary palliative care, plays an important role in supporting families regarding the planned course of treatment and to aid in developing goals of care and to guide decision-making by promoting communication between the medical team and the family [17].

Ethical Considerations

The separation of conjoined twins poses not only technical and medical challenges but also ethical ones. Once the diagnosis is made the parents should be counseled in detail regarding short and long-term prognosis and options. The viability of the fetus, the feasibility of surgical separation and the expected degree of disability and long-term quality of life should be addressed. The viability of the pregnancy and the newborn neonate and a successful surgical outcome strongly depends on the nature and extent of the shared organs. Conjoined twins sharing the heart cannot be separated unless one twin is sacrificed. Decision-making should consider the family's values and goals and what is ethically justifiable in the context of the prognosis of the procedure, the chance of survival of both twins, a necessity to sacrifice one twin for the other twin's survival and degree of expected disability and long-term quality of life comparing the outcome of no intervention to that of surgical separation.

Many parents choose early termination of the pregnancy. The despair experienced by families unable to secure a surgical correction for their conjoined twins can be devastating, however, there are examples of permanently conjoined twins living a satisfying life without the desire to be surgically separated, even at the time one twin is dying [18, 19].

Conjoined twinning is a complex socio-medical problem, which presents unique medical, ethical and palliative care challenges.

Conclusions

The intent of this chapter is to provide insights into the complexities associated with conjoined twin separation surgery. As a background a review of the anatomy and physiology of the categories of twinning types encountered were presented. It is clear that the types of twinning with its implications to specific organs, and to what degree such organs are shared, as well as the presence of other anomalies are factors determining the feasibility of separation. Consequently the rationale and strategy of performing a conjoined twin separation is inherently a case-by-case decision. At the onset a significant time should be allocated to careful consideration of patients' conditions and anticipated preparedness and optimal timing of the intended surgical separation procedure. Assessment and planning call for multispecialty surgical, medical and anesthesiology experts, aided by state-of-the-

art technology such as 3D-imaging, -printing and -modelling tools, and in-situ clinical simulation rehearsals prior to actual surgery. From the anesthesiologist's perspective, the operating room must be equipped with duplicate Anesthesia Work Stations with networking capabilities to ensure seamless electronic record data flow for each twin. A designated anesthesia team is assigned to each twin. The teams and all their equipment are color coded to avoid confusion and errors.

Surgical separations of conjoined twins are without doubt complicated and variable in their degrees of difficulty. Their complexity is greatly dependent on the duality, adaptability and surgical wiring of critical organs that allow for viability post-separation. In spite of the noted challenges, attempts at surgical separation have produced groundbreaking successes around the world, increasing the quality of life for many. It is foreseeable that this specialty, through continual progress and advances in surgical medicine, science and engineering, will evolve to successfully deal with cases of increasing complexity.

Acknowledgements I would like to express my thanks and gratitude to Dr, Steven Stayer for his trust and confidence in appointing me to lead the anesthesia team in prepararing and implementing the separation of the Mata twins.

Funding and Conflicts of Interest None.

References

1. Inglis-Arkell E. The tragic story of the first man who separated conjoined twins. https://io9.gizmldo.com
2. El-Agwany AMS, et al. Thoraco-omphalopagus: a case of conjoined twin with a single heart. https://www.ecronic.com/ecgy/gynecology
3. Mutchinik OM, et al. Conjoined twins: a worldwide collaboration epidemiology study of the international clearinghouse for birth defects surveillance and research. Am J Med Genet C Semin Med Genet. 2011;150(4):274–87.
4. De Lourdes Brizot M, et al. Prenatal diagnosis, delivery and postnatal outcome. Rev Bras Ginecol Obstet. 2011;33(5):211–8.
5. Brizot DL, et al. Conjoined twins pregnancies: experience with 36 cases from a single center. Prenat Diagn. 2011;31(12):1120–5.
6. Kaufman MH. The embryology of conjoined twins. Childs Nerv Syst. 2004;20(8–9):508–25.
7. Cuillier F, et al. History, classifications, and two cases of conjoined twins. 2017. https://sonoworld.com/fetus/
8. Mathew RP. Conjoined twins-role of imaging and recent advances. J Ultrason. 2017;17:259–66.
9. Lewis S, et al. Conjoined twins. Pediatric surgery. 7th ed. ScienceDirect. 2012. https://www.sciencedirect.com
10. HospiMedica International staff writers. 3D printing aids surgical separation of Siamese twins. Posted December 13, 2015. https://mobile.hospimedica.com
11. Yalcin SE, et al. Prenatal sonography diagnosis of cephalopagus conjoined twins at 14 weeks of pregnancy. J Clin Ultrasound. 2018;46:408–11.
12. Gedikbasi A, et al. Prenatal diagnosis of conjoined twins: four cases in a prenatal center. J Turk Ger Gynecol Assoc. 2010;11(4):174–7.
13. Advisory Board. August 9, 2017. https://advisory.com/daily briefing/2017/08/09
14. Hyun WG, et al. Advanced medical use of three-dimensional imaging in congenital heart disease: augmented reality, mixed reality, virtual reality and three-dimensional printing. Korean J Radiol. 2020;21(2):133–45.
15. Parmekar S, et al. Role of simulation in preparation for the care of conjoined twins-prenatal preparation to separation. Semin Perinatol. 2018;42:329–39. www.seminperinat.com
16. Almond PS, et al. Intraoperative management of the neonate. conjoined twins. Assisted ventilation of the neonate. 5th ed. 2011. https://www.sciencedirect.com
17. Thomas A, et al. An ethical-justifiable, practical approach to decision-making surrounding conjoined-twin separation. Semin Perinatol. 2018;42(6):381–5.
18. Quigley, C. Conjoined twins, body, identity, and disability. Encyclopedia of applied ethics. 2nd ed. 2012. https://www.sciencedirect.com
19. Armstrong J. A dividing issue: can the girls be separated? The Globe and Mail, April 27, 2007.

18 Anesthesia for Conjoined Twins-Basic Principles

Meenakshi Atteri, Mario Patino, and Lori A. Aronson

Learning Points

- Anesthesia for the conjoined twins requires rigorous planning, coordination, cooperation, and communication of a multidisciplinary team during all stages.
- Advanced preparation includes tabletop simulation, task assignments with specific role designation, duplication and color-coding of all equipment, medications, and personnel for anesthetizing two infants in one operating room, as well as addressing overcrowding.
- Conjoined twins' physiology is complicated by cross-over circulation, distribution of blood volume, organ sharing and positioning challenges resulting in unique anesthetic implications.

Introduction

Conjoined twins are a rare type of monoamniotic twinning in which their bodies are physically joined in utero. The reported incidence is estimated at 1: 50,000 to 1: 100,000 live births, but the true incidence is much smaller at 1:250,000 as 60% succumb in utero [1]. Although, more case reports have been reported in the last years, there is still a paucity of publications regarding the anesthetic management of conjoined twins. The low incidence of such surgeries and anatomical variations in each type of conjoined twinning makes each separation surgery a unique experience.

Embryology

The embryologic etiology of conjoined twins remains unclear; however, it is generally considered an abnormal form of monozygotic twinning. Twins are divided into two types: dizygotic and monozygotic twins. Dizygotic twins originate from two separate independently fertilized ova. Monozygotic twins, on the other hand, occur due to the splitting of one embryo into two identical embryos. They are classified based on the extent of amniotic and chorionic cavity shared between the fetuses. Timing of post fertilization division of the zygote determines placentation in twins. Monoamniotic, monochorionic placentation occurs with division at post conception day 8–12; conjoined twins result from division at post conception day 13–17. Conjoined twins are always monozygotic, monochorionic and monoamniotic [2].

M. Atteri (✉)
Department of Pediatric Anesthesiology, Arkansas Children's Hospital, Little Rock, AR, USA
e-mail: matteri@uams.edu

M. Patino · L. A. Aronson
Department of Pediatric Anesthesiology, Cincinnati Children's Hospital, Cincinnati, OH, USA
e-mail: Mario.Patino@cchmc.org; Lori.Aronson@cchmc.org

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_18

Two contradicting theories exist to explain the origins of conjoined twins: fission and fusion. Fission, the more accepted theory, states the fertilized egg splits partially between days 13 and 17 following fertilization. Fusion suggests that the fertilized egg splits completely, but a secondary union of two separate embryonic discs/stem cells takes place at 3–4 weeks' gestation.

Conjoined twins are always the same gender with a male to female ratio of 1:3. Although conjoined twins are genetically identical, they usually vary in size, appearance, and internal anatomy based on degree of organ-sharing and duplication. Contrary to conjoined twins, parasitic twins are asymmetrical twins in which one of the twins stops development leading to the full development of one twin with physical parts of the underdeveloped twin attached to the viable twin.

Classification

A general classification of conjoined twins is determined by the ventral or dorsal aspect of conjunction. The most common classification is given by the site of union of their body parts with thoracopagus, joined by the thorax, as the most common. Omphalopagus are joined at the lower abdomen, pyopagus at the sacrum, ischiopagus by the pelvis, craniopagus by the skull, cephalopagus at the face and torso, rachiopagus posteriorly at the spine, and parapagus laterally [3]. Each type of conjoined twinning poses challenges specific to their type of conjunction.

Perinatal Considerations

Advancement in techniques of antenatal diagnosis and fetal imaging enables early diagnosis and reasonably accurate assessment of union type, shared organs and associated co-morbidities. Congenital anomalies are commonly present in conjoined twins and require the performance of multiple diagnostic studies, including fetal ultrasound and MRI. Conjoined twins can be diagnosed as early as the eleventh week of gestation. As a result, delivery is usually Caesarean, and postnatal care of conjoined twins can frequently be planned. Two neonatal resuscitation teams and two anesthesiologists should be available for immediate intervention. If intubation is required, it must be done sequentially. Moreover, some cases may require ex utero intrapartum treatment (EXIT) procedure, especially if there is concern for a difficult airway due to an anomaly.

Successful outcome mandates a close collaboration of a multidisciplinary team (MDT) consisting of pediatric surgeons, anesthesiologists, neonatologists, operating room and intensive care nurses, anesthesia technicians, subspecialty pediatric and surgical services as indicated, hospital management and public relations.

If the conjoined twins are stable, allowing them to continue their physiologic development, to gain weight and to thrive are crucial before attempting separation surgery. Typically, separation surgery is planned between 4 and 11 months. This allows the anatomy and physiology to be more clearly defined. At the same time, it ensures adequate tissue expansion for better closure of the skin defect. However, emergency separation surgery may be required in cases in which one twin is stillborn or is critically ill thus endangering the second twin's life. It is also required if there is severe injury to the connecting bridge during delivery or when one twin has a correctable life-threatening congenital anomaly (e.g. intestinal obstruction, ruptured exomphalos). Many of the principles of management are similar for both elective and emergency separation, but given the nature of the emergency separation, it carries considerably higher risks.

Presurgical Planning and Evaluation

The management of anesthesia for conjoined twins poses unique anatomical, physiological, and logistic challenges. Their rarity contributes to the additional challenge of gaining experience in their management. The overall success depends on meticulous planning and detailed preparation with an MDT. As mentioned, the team includes

representatives from pediatric anesthesiology, pediatric surgery (general, plastic surgery, cardiothoracic, orthopedic, neurosurgical, urologic as indicated), nursing, intensivists, and operating room support staff. The initial anesthetic care of conjoined twins often begins with the performance of multiple diagnostic studies including CT, MRI, contrast studies, and angiography to better delineate the surgical planning and prognosis.

Various screening methods used for preoperative evaluation of cross-circulation include angiographic/radioisotope imaging, MRI and CT imaging. Unfortunately, CT imaging may miss vascular connections. The degree of cross-circulation is dynamic, highly dependent on both twins' relative systemic vascular resistance and thus could be missed during a contrast study, especially in the presence of congenital heart disease [4].

Once all organ systems have been evaluated and vascular territories have been established, the MDT meets on several occasions to review the information and plan for separation [5]. Accurate diagnosis of anatomy along with three-dimensional organ models available at preoperative discussions are very helpful in understanding physiology and pathology for each member of the team. MDT sessions include discussions of surgical plan, anesthesia plan, staffing, location of anesthesia and surgical equipment, patient positioning, the order in which surgical specialties will operate, locations where intravenous lines may or may not be placed, plan for repositioning after physical separation and anticipated problems or concerns. Decisions are made regarding the order of organ separation, anesthetic management an access, monitoring of vital signs, wound closure, including plans for preoperative tissue expansion and postoperative care. Additionally, discussions should address resuscitation plans in the event of a code event.

Finally, complete rehearsals of the separation procedure allow each member of the team to be familiar with his or her role throughout the anesthetic and surgery so that the actual operation proceeds as smoothly as possible. Simulation also offers a safe environment to run a variety of logistics in how to prepare surgically and to accomplish the myriad steps that nursing, surgical, and anesthesia personnel must perform. Teamwork principals including leadership and communication play a key role in ensuring safe and effective patient care. Thus, they should be stressed during these meetings. Specific anesthesia, surgical and nursing team assignments must be coordinated, including identifying a team leader by service and overall point person, that synchronizes the care and interventions of the various teams. This primary lead physician can also oversee the performance of both teams and review the clinical status of both twins [6].

Parental involvement and support are equally important as decisions in care are made. Psychology and social work resources should be available throughout for the family. Maintaining the privacy of the conjoined twins and their family is of critical importance.

General Principles and Challenges Specific for Anesthetic Care of Conjoined Twins

Anesthesia is required for a variety of pre-separation procedures including diagnostic imaging, invasive diagnostic procedures, and tissue expanders. Basic principles of anesthesia during the care of neonates and infants apply to the care of conjoined twins. We describe the challenges and principles that are unique during the anesthetic care of conjoined twins.

Pre-anesthesia Planning

The anesthetic management of conjoined twins requires two dedicated anesthesia teams, one for each infant. The dual team usually consists of two senior anesthesiologists, preferably those who have taken care of these cases previously, two additional anesthesia providers, be they fellows, residents, or nurse anesthetists, and two anesthesia technicians. Based on physiology, a pediatric cardiac anesthesiologist may be warranted. It is beneficial to carry rehearsals in the

operating room pre-operatively with all staff and anesthesia teams present. It helps each team member to understand his or her role and activities [6].

Anesthesia debriefing should include the sequence of twin induction, the method of induction and intubation, equipment availability and planning for potential difficulties with airway management, the need for invasive monitoring, and obtaining appropriate intravenous accesses. A printed checklist is very useful to follow during these procedures. The preoperative planning must include life threatening scenarios if the condition of one of the conjoined twins deteriorates.

The team should ensure the availability of a double supply of all necessary equipment, including supply of two sources of medical gases, suctioning, scavenging, anesthesia machines, monitors, infusion pumps, fluid warmers and temperature control devices. Clinical engineering may be required to outfit the location to facilitate monitor capture when using an electronic medical record.

As space is limited, if a drug cart is shared by the two anesthesia teams, the medications should be color-coded and drawn up independently for each infant. All personnel, equipment, monitoring and intravenous lines must be also color-coded and specific for each twin. The operating room should be arranged to suit the type of twins; with thoracopagus and craniopagus twins, it is helpful to have the anesthetic machines at the same end of the table; whereas with ischiopagus twins, it may be necessary to have the machines at opposite ends of the operating table. If procedures are taking place in an off-site location such as MRI, then dual equipment will need to be available both inside and outside the scanner as induction, airway manipulation and emergency scenarios should take place outside the MRI room.

Induction of Anesthesia

Sequential induction is preferable over simultaneous induction as it gives more control and time in inducing each twin safely. Choice of anesthetic induction technique depends, as usual, on the factors such as presence of IV access before induction, presence of difficult airway, hemodynamic stability of each infant, comorbidities, and the preferences of the attending anesthesiologists. However, given the potential for a rapid deterioration during the induction, the pre-induction presence of an intravenous access is important. In twins with potentially difficult airways, spontaneous respiration with inhalational induction with sevoflurane or the intravenous use of ketamine is helpful.

The presence or absence of cross-circulation is an important determining factor in planning the induction. In case of cross-circulation there is a passage of drugs from one twin to the other which may cause sedation and airway obstruction in the second twin. Prior to induction, the administration of atropine or glycopyrrolate to one twin and assessing the changes in heart rate and time required for the change in each twin can help predict the timing of further medication affects related to cross-circulation [7].

Usually the presence of cross-circulation is more significant in thoracopagus and craniopagus twins than in other types; therefore, unpredictable drug responses can occur. In general, the administration of a muscle relaxant is avoided until ventilation is confirmed and provided to both infants as a muscle relaxant given to one infant could reach to the other one by cross-circulation [8, 9].

Furthermore, one must consider the existing comorbidities of the two infants. Traditionally, if there is associated complex congenital heart disease or other reasons for one infant to be significantly more fragile than the other, the sicker infant should be induced first [10].

Airway Management

In general, airway management of most ventral and craniopagus conjoined twins is more difficult as the heads face each other and are close together. This position leads to a very limited space to manipulate and to place instruments in the airway. In the case of thoracopagus twins, mask ventilation has to be provided in a gentle

manner since changes in the intrathoracic pressure can lead to significant deviation of shared structures in the other twin, potentially causing rapid deterioration. Thus, positive pressure ventilation in the case of thoracopagus twins must occur simultaneously and in a synchronized fashion. The rotation of the head from the lateral position to near sagittal in order to facilitate intubation may obstruct the upper airway or distort anatomy. Exaggerated lordosis in thoracopagus twins leads to hyperextension of the head and neck. It is safer to intubate these twins on their side rather than one above the other to avoid possible hemodynamic compromise from auto transfusion particularly in conjoined twins with significant cross-circulation. If frequent position changes are anticipated during surgery, then nasal intubation may be preferable to minimize risk of inadvertent extubation [10, 11].

Regardless, the teams should be prepared for potential difficult airway management and intubation. Size appropriate oropharyngeal airways and LMAs should be immediately available. Difficult airway carts should be present with fiberoptic bronchoscopy supplies for both infants. Flexible extension tubing attached to the mask may be necessary to avoid crowding near the faces during airway management. Consideration for consultation with ENT and the need for rigid bronchoscopy should have been addressed during pre-planning.

Vascular Access

Obtaining peripheral and central access may be challenging due to limited space, infant positioning and ease of access to vessels as well as deviation of normal anatomic relationships of arteries and veins. The neck anatomy is especially concerning in craniopagus twins; consequently, femoral access is preferred. Separation of conjoined twins is a prolonged procedure that lasts multiple hours; thus, invasive monitoring with arterial and central lines are of paramount importance. The use of ultrasound is a very helpful modality to assist in obtaining access for invasive monitoring. Minimizing multiple vascular access points prior to separation surgery can help preserve vessels. Avoiding arterial and central access for imaging procedures and tissue expander surgery should be considered. Additionally, PICC placement earlier in their hospital course may preserve peripheral veins for larger IV access at time of separation [11, 12].

Medications

The responses of conjoined twins to medications are unpredictable, as vascular shunts and cross-circulation cause mixing of their blood. Regardless of the degree of the cross-circulation, medications should be administered as they would be for two separate individuals. Recommended intravenous doses of anesthetic agents for the combined body weight of the twins are usually halved and then divided into two equal doses to be administered to each twin. The routine drugs available should include analgesics, anesthetic agents, muscle relaxants, and inotropes. Emergency drugs to have prepared as weight specific doses include atropine, epinephrine, phenylephrine, sodium bicarbonate and calcium. The drugs for each infant should be separated, color-coded and labeled [11, 12].

Color-Coding

In order to increase the safety of conjoined twins during anesthesia and separation surgery, each of the twins and their equipment should be color-coded. These designations have usually been made in the neonatal intensive care unit and designated for Twin A and Twin B. Intraoperative color-coding should follow the predetermined designation. Color-coding should be placed on the anesthesia machine and circuit, endotracheal tube, monitoring cables, multiple points along IV tubing (especially access points), arterial lines, drugs, infants' limbs, and the respective staff. A vast majority of separation surgeries requires several changes of twins' positions on the operating table which requires disconnecting and reconnecting equip-

ment and color-coding is very helpful at these points to prevent any mistakes.

Circulation

The blood pressure values of the twins can be different and arterial blood tends to shunt from the twin with higher blood pressure to the one with a lower pressure. Increasing the concentration of anesthetics to lower the blood pressure in one twin can cause an overdose of anesthetic in the other twin. Applying mechanical maneuvers such as continuous positive airway pressure (CPAP) to the twin with the higher blood pressure can reduce cardiac filling and blood pressure of this twin and cardiac filling of the twin with a lower blood pressure is improved and pressure is increased. Especially with thoracopagus twins, over vigorous ventilation of one may compromise the other because of the chest contents moving across into the chest cavity of the other [7, 12].

The presence of a third anesthesia provider during these circumstances is important since vigilance and monitoring the physiologic state of both infants can detect the impairment of one of the infants due to the physiologic changes into the other infant. These changes may be missed by the providers that are assigned to a specific infant. For example, managing FIO_2 to regulate vascular resistance, especially in the presence of congenital heart disease can impact cross-circulation. Communication between teams is essential so as not to result in over- or under-circulation of either twin. Conjoined twins with cardiac abnormalities, have less favorable outcomes, and if the hearts are fused, mortality is considerably higher [12–14].

Blood Loss and Transfusion

Vascular structures are not always predictable, and blood loss may be sudden, especially during separation surgery. Blood loss can reach up to five times each infant's estimated blood volume. Highest risks for blood loss during separation includes craniopagus sharing vascular structures such as venous sinuses, thoracopagus sharing major vascular structures, omphalopagus sharing liver parenchyma, and ischiopagus with the performance of osteotomies [13–15].

Due to cross-circulation of blood between twins, it is difficult to determine a precise percentage of blood loss from each twin. Generally, half of the estimated volume of the blood lost is transfused to each child. A rational order of blood and blood products based on calculation of anticipated blood and fluid losses should be done [16]. Monitoring of blood gases, hemoglobin, electrolytes and lactate regularly using point-of-care testing is important, as well as monitoring coagulation tests. In the presence of large blood volume loss, thromboelastography can guide transfusion requirements. Clamping and separation of vascular shunts can potentially eliminate the cross-circulation early during separation surgery and prevent hypovolemic shock from loss of blood volume through the shared vessels [17–19].

Positioning

A vast majority of separation surgeries require several changes in the position of the conjoined twins. It needs careful forethought and innovative planning to accommodate changes needed by different surgical specialties and to avoid loss of airway or vascular access. Positioning a conjoined twin higher than the other one can result in autotransfusion between twins and cardiovascular disturbances, especially in twins with limited cardiovascular reserve. To avoid postural hypotension, it is recommended to position both twins in the same horizontal plane. Appropriate positioning requires the use of various protective rolls and supports to minimize pressure injury [15].

Once the twins are separated, the predetermined twin is moved to an adjoining operating room. This requires using a sterile surface on the transport table, temporary sterile cover for the baby, and full monitoring and ventilation for the transfer and repositioning of the child in the new operating theater. All color-coded lines, medica-

tions and monitoring must be situated and appropriate repositioning secured [16, 18].

Temperature

Maintenance of normothermia during the surgical procedures in conjoined twins is another challenge due to the extensive surgical wound, which increases heat loss by evaporation, radiation, and convection. To reduce losses by radiation and convection, the room temperature should be regulated to at least 24 °C and active forms of heat transfer such as thermal blanket, water mattress, and heated solutions should be used. Heat lamp may be necessary to maintain normothermia during induction and vascular access [17].

Crowd Control

Control of traffic in the operating room is essential. Privacy and infection risks need to be regulated; thus, non-essential personnel should not be present despite medical interest. Therefore, strict guidelines established by operating room staff and hospital management must be in place prior to embarking on any surgical procedure performed in conjoined twins. Procedures may need to be initiated earlier than regular scheduled times to allow for privacy during transportation [14, 17, 19].

Conclusion

The anesthetic management of conjoined twins is challenging and demanding. Anesthesia presence is required during planning and coordination as a critical part of the MDT during all stages from pre-delivery through surgical separation. Preoperative meetings to collect information, coordinate proceedings, formulate an agenda and develop a plan of action are vital. The conduct of the anesthesia requires attention to safe airway management, intravascular access, color-coding, careful medication and intravascular volume management, temperature maintenance and positioning. Meticulous anesthetic management is a vital component to the successful perioperative management of these children and contributes significantly to their survival.

References

1. Coran A. Paediatric surgery, chapter 131. In: Spitz L, Kiely EM, Pierro A, editors. Conjoined twins. 7th ed. Philadelphia: Elsevier Saunders; 2012. p. 1725–38.
2. Kaufman MH. The embryology of conjoined twins. Childs Nerv Syst. 2004;20:508–25.
3. O'Neill JA Jr, Holcomb GW 3rd, Schnaufer L, Templeton JM Jr, Bishop HC, Ross AJ 3rd, et al. Surgical experience with thirteen conjoined twins. Ann Surg. 1988;208(3):299–312.
4. Kingston CA, McHugh K, Kumaradevan J, Kiely EM, Spitz L. Imaging in the preoperative assessment of conjoined twins. Radiographics. 2001;21:1187–208.
5. Thomas JM, Lopez JT. Conjoined twins—the anaesthetic management of 15 sets from 1991–2002. Paediatr Anaesth. 2004;14:117–29.
6. Singh M, Jacob R, Naik V, Baines D. Separation of thoraco-omphalopagus twins in a rural secondary hospital: perioperative management. Indian J Anaesth. 2012;56(5):442–7.
7. Toyoshima M, Fujihara T, Hiroki K, Namatame R, Ka K, Ooe K. [Evaluation of cross circulation in conjoined twins]. Masui. 1993; 42:1347–50.
8. Szmuk P, Rabb MF, Curry B, et al. Anesthetic management of thoracopagus twins with complex cyanotic heart disease for cardiac assessment: special considerations related to ventilation and cross-circulation. BJA. 2006;96:3341–5.
9. Bloch EC, Karis JH. Cardiopagus in neonatal thoracopagus twins: anesthetic management. Anesth Analg. 1980;59:304–7.
10. Harrison VL, Keneally JP, Gold PD, Malcom PS, Overton JH. Anaesthesia for separation of conjoined twins in the neonatal period. Anaesth Intensive Care. 1985;13:82–5.
11. Diaz JH, Furman EB. Perioperative management of conjoined twins. Anesthesiology. 1987;67:965–73.
12. Thomas JM. Anaesthesia for conjoined twins. Childs Nerv Syst. 2004;20:538–46.
13. Brown DI, Holubec DM, Towle DJ, et al. Anesthetic management of thoracopoagus twins undergoing cardiopagus separation. Anesthesiology. 1985;62:679–82.
14. Wong KC, Ohmura A, Roberts TH, Webster LR, Cook GL. Anesthetic management for separation of craniopagus twins. Anesth Analg. 1980;59:883–6.
15. Leelanukrom R, Somboonviboon W, Bunburaphong P, Kiatkungwanklai P. Anaesthetic experi-

ences in three sets of conjoined twins in King Chulalongkorn Memorial Hospital. Paediatr Anaesth. 2004;14:176–83.
16. Spitz L, Kiely EM. Experience in the management of conjoined twins. Br J Surg. 2002;89:1188–92.
17. Chalam KS. Anaesthetic management of conjoined twin's separation surgery. Indian J Anaesth. 2009;53:294–301.
18. Kaniyil S, et al. Anaesthetic challenges in conjoined twins' separation surgery. Indian J Anaesth. 2016;60(11):852–5.
19. Stuart GM, et al. The anaesthetic management of conjoined twins. Semin Pediatr Surg. 2015;24(5):224–8.

19 Anesthesia for Transjugular Intrahepatic Portosystemic Shunt (TIPS) Procedures

Niraj K. Agarwalla

Learning Points

1. Given the complexity and duration of the procedure, general anesthesia with endotracheal intubation is typically preferred. However, the procedure can be performed under monitored anesthesia care (MAC) in carefully selected patients.
2. With severe portal hypertension, abdominal ascites may be present. Rapid sequence induction should be considered in patients undergoing TIPS to minimize aspiration. Alternatively, paracentesis can be performed prior to induction of anesthesia to mitigate aspiration risk.
3. TIPS often can worsen hepatic encephalopathy, and therefore the presence of baseline encephalopathy is considered a relative contraindication to the procedure.

Introduction

A TIPS procedure creates a shunt between the portal and systemic venous circulations. This may be performed for a number of disease states including but not limited to complications from portal hypertensive disease such as refractory ascites, variceal bleeding, hepatorenal syndrome and Budd-Chiari syndrome.

The origin of the TIPS procedure dates back to the 1960s, however its widespread use in humans as a portal decompressive technique was not seen until the 1990s [1]. Prior to this, open surgical porto-caval shunt procedures associated with high morbidity and mortality were the predominant approach. TIPS was further refined over the subsequent decades with regards to stent technology and advances in imaging.

The most recent practice guidelines updated by the American Association for the Study of Liver Diseases (AASLD) discuss the role of TIPS in the management of portal hypertension. They clarify technical aspects of the procedure, further expanding on its utility as compared with surgical shunts, and review the considerations for TIPS in specific hepatic disease states [2]. Tables 19.1 and 19.2 include indications and contraindications for TIPS as outlined by the AASLD, respectively [2].

In recent years, emerging evidence has suggested an expanded indication for TIPS including for cirrhotic patients presenting with early ascites. One large multi-center randomized controlled trial found that early TIPS in certain patients requiring frequent paracenteses exhibited a significant transplant free survival benefit when compared with patients undergoing repeated large volume paracenteses with albumin replacement [3].

N. K. Agarwalla (✉)
Department of Anesthesiology, Sidney Kimmel Medical College, Thomas Jefferson University, Philadelphia, PA, USA

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_19

Table 19.1 Indications for placement of a TIPS [2]

Secondary prevention variceal bleeding
Refractory cirrhotic ascites
Refractory acutely bleeding varices
Portal hypertensive gastropathy
Bleeding gastric varices
Gastric antra vascular ectasia
Refractory hepatic hydrothorax
Hepatorenal syndrome (types 1 and 2)
Budd-Chiari syndrome
Veno-occlusive disease
Hepatopulmonary syndrome

Table 19.2 Contraindications to placement of a TIPS [2]

Absolute
Primary prevention of variceal bleeding
Congestive heart failure
Multiple hepatic cysts
Uncontrolled systemic infection or sepsis
Unrelieved biliary obstruction
Severe pulmonary hypertension
Relative
Hepatoma especially if central
Obstruction of all hepatic veins
Portal vein thrombosis
Severe coagulopathy (INR > 5)
Thrombocytopenia of <20,000 cm^3
Moderate pulmonary hypertension

Several groups have examined the role of TIPS as a primary management option in certain patients with cirrhosis who present with acute variceal bleeding. A multi-center randomized controlled trial involving 63 patients with Child-Pugh class B or C disease found that early TIPS (within 72 h of acute variceal bleeding) is associated with reduced failure to control acute bleeding, reduced rebleeding occurrence, and a mortality improvement [4]. Interestingly, this study also demonstrated no increase in the risk of hepatic encephalopathy within the TIPS group. A recent large observational study involving 671 patients corroborated these benefits of preemptive TIPS in high risk cirrhotic patients [5].

In the United States, a TIPS is created by an interventional radiologist with significant experience in the procedure. The goal of the procedure is to create a shunt successfully and achieve a post-operative hepatic venous pressure gradient (HVPG) < 12 mmHg [2]. It remains unclear whether a reduction of the HVPG below an absolute number versus a relative decrease in the HVPG from baseline for a given patient should be the gold standard for the prevention of rebleeding [6, 7].

Procedure

TIPS requires careful preoperative planning by the proceduralist, typically including abdominal ultrasonography and cross-sectional computed tomography (CT) imaging to best evaluate hepatic anatomy. If ascites is present, therapeutic paracentesis is performed with colloid replacement prior to TIPS creation. This can aid in decreasing liver mobility which in turn allows for easier vascular cannulation [8]. The left or right internal jugular vein is accessed with ultrasound guidance, after which one of the hepatic veins is cannulated. Often the right hepatic vein is chosen due to its favorable anatomic position relative to the portal vasculature. Shunt creation via middle or left hepatic veins is possible, however this can be technically more challenging with more passes required by the radiologist to cannulate the portal vein [8].

Wedged hepatic venography is performed to visualize the portal vein. This is often accomplished with carbon dioxide portography as the use of iodinated contrast may increase risk of hepatic parenchymal rupture. A catheter is directed through the portal vein and into the splenic vein to further evaluate portal inflow veins and the presence of mesenteric varices. After balloon dilation of the parenchymal tract, a stent graft is deployed. The proximal and distal ends of the stent graft should reside at the confluence of the hepatic veins with the inferior vena cava and the main portal vein, respectively. The degree to which the graft is expanded is operator dependent, with the patient's underlying pathology dictating the extent of portal decompression desired. Covered stents such as the Viatorr expanded polytetrafluoroethylene (ePTFE) (W. L. Gore & Associates Inc., Newark DE) have largely supplanted bare metal stents due to their improved patency rates.

More recently, adoption of advanced imaging technology such as intravascular ultrasound (IVUS) with intracardiac echocardiography (ICE) has improved on the procedure. ICE has been used to identify hepatic venous anatomy more accurately, especially in patients with anatomic variability or Budd-Chiari syndrome. ICE has also proven helpful in portal venous puncture via hepatic parenchyma, thereby reducing known risks including hepatic capsular injury, hemobilia or hepatic arterial puncture [9].

Use of controlled expansion stents such as the Viatorr CX (Gore, Newark DE) has also helped mitigate several complications associated with TIPS and its associated shunting [9]. While increased shunting may decrease refractory ascites or portal hypertensive bleeding events, it can result in development of de novo hepatic encephalopathy (HE) or worsening of preexisting HE. Additional intrinsic stent dilation post-TIPS can also cause worsening liver failure. Controlled expansion stents offer improved control over the final dilation diameter, thereby taking advantage of the benefits of TIPS without compromising HE symptoms or accelerating hepatic failure [9].

Preoperative Evaluation

A thorough preoperative workup including comprehensive history and physical is essential prior to TIPS. When TIPS is performed as an emergency procedure with the patient in extremis from massive variceal bleeding, complications and mortality rates increase [10, 11]. A multidisciplinary approach (including hepatology, liver transplant surgery, interventional radiology, and anesthesiology) to the management of cirrhotic patients undergoing TIPS can help identify which patients may benefit from the procedure. Consultation with a liver transplant center for a possible inter-facility transfer of care may be appropriate in many cases.

The Model for End-Stage Liver Disease (MELD) scoring system was initially devised to predict 3-month survival in patients following TIPS [12, 13]. Subsequent research also demonstrated the MELD score as a reliable system for measuring the risk of death in patients with end-stage liver disease [14]. As such, it has become the most commonly used scoring system in liver transplant organ allocation. Despite MELD's widespread popularity in liver transplantation, it remains helpful in stratifying patients undergoing TIPS, with scores <18 and non-alcohol-induced disease incurring a more favorable 3-month post-operative survival rate [15].

Neurological Evaluation

The neurological exam will help shape the decision on anesthetic management for those undergoing TIPS as these patients often have underlying neurologic compromise in the setting of advanced liver disease. Degree of HE, while not an absolute contraindication to TIPS, must be evaluated as this will likely worsen post-TIPS. Data have varied widely to the extent of iatrogenic HE post-TIPS, with one study suggesting that 5–35% of patients undergoing TIPS will develop new or worsening HE post-procedure [16].

Additionally, patients with advanced hepatic dysfunction secondary to alcohol use may demonstrate signs and symptoms of acute alcohol withdrawal while hospitalized in the perioperative period. Timing of last alcohol intake should be determined, and consideration should be given that these patients may need additional pharmacologic therapies with sedative agents including benzodiazepines.

Comorbid conditions such as severe electrolyte abnormalities including hyponatremia and hypokalemia may also contribute to altered sensorium in the patient with advanced hepatic disease.

Cardiovascular Evaluation

Many patients presenting for TIPS will present with some form of cardiovascular dysfunction with symptoms consistent with cirrhotic cardiomyopathy (CCM). This may include, but is not limited to systolic dysfunction, abnormal myocardial relaxation, or electrophysiological abnormalities [17].

Cirrhosis is typically characterized by a hyperdynamic state with increased cardiac output in response to chronic arteriolar vasodilatation. These patients present with total body volume overload, but can be intravascularly volume depleted. The expected volume shifts associated with TIPS—secondary to both therapeutic paracentesis and shunt creation—require anesthesiologists to be prepared with necessary colloid therapy and often vasoactive medications.

Shunt creation will increase cardiac output as more venous blood returns to the systemic circulation and symptomatic heart failure, particularly right-sided, can be precipitated. Increased right ventricular preload may also worsen preexisting triscuspid regurgitation, which should be evaluated preoperatively. A transthoracic echocardiogram should be obtained in all patients with close attention given to biventricular function, presence of diastolic dysfunction, degree of pulmonary hypertension if present, and severe valvular disease such as triscuspid regurgitation [18].

Routine electrocardiogram should also be obtained prior to TIPS. Cannulation and guidewire advancement to the inferior vena cava can result in ectopic atrial or ventricular beats as the wire traverses the right atrium [19]. Knowledge of a preexistent left bundle branch block is important as iatrogenic right bundle branch block from guidewire manipulation can result in fatal complete heart block. Ectopy is typically transient with resolution upon guidewire withdrawal however persistent arrhythmias have been reported. For patients at increased risk of this complication, access to immediate pacing support is recommended (e.g. transcutaneous or transvenous pacing).

Respiratory Evaluation

As refractory cirrhotic ascites is an indication for TIPS, many patients exhibit a reduced functional residual capacity secondary to abdominal distension. Severe ascites can make performing this procedure in the supine position under sedation prohibitive, and the vast majority of patients at our institution undergo general anesthesia with endotracheal intubation in part for this reason.

Hepatic hydrothorax may be present, and should be evaluated with thoracic imaging if clinically indicated. The recurrence of pleural effusions should improve post-TIPS with thoracentesis not frequently required during the TIPS procedure.

Chronic hypoxemia can be present in patients with hepatopulmonary syndrome (HPS) and its characteristic intrapulmonary vascular dilatation. The prevalence of HPS has been reported as between 4 and 19% among cirrhotic patients [20]. Limited evidence has also demonstrated a transient improvement in dyspnea symptoms and pulmonary gas exchange in HPS patients after TIPS creation, however long term improvement has yet to be proven [21].

Renal Evaluation

Baseline renal function may be impaired in patients presenting for TIPS. Patients with refractory ascites are often prescribed loop diuretics (e.g. furosemide) and/or aldosterone receptor blocking agents (e.g. spironolactone). Baseline creatinine should be obtained prior to TIPS. Injection of iodinated contrast during TIPS can exacerbate pre-existing renal impairment.

Hepatorenal syndrome (HRS) can occur in chronic liver disease patients presenting for TIPS. Several theories have been proposed on the pathophysiologic mechanisms underlying HRS including renal arteriolar vasoconstriction and a severe systemic pro-inflammatory state [22, 23]. Management typically includes intravascular volume expansion and systemic vasoconstrictor therapy (e.g. terlipressin). HRS has been suggested as an indication for TIPS as renal function can improve with portal decompression, however long term data have not demonstrated a clear clinical benefit [24].

Gastrointestinal Evaluation

Increased abdominal pressure secondary to refractory ascites place these patients at increased risk of aspiration of gastric contents. Additionally, the possible presence of gastro-esophageal vari-

ces must be considered prior to any instrumentation (e.g. esophageal stethoscope, transesophageal echocardiography) [25]. Autonomic dysfunction with associated gastroparesis may be present in patients with chronic liver disease (especially alcoholic liver disease) [26]. Obtaining a thorough history of the patient's gastrointestinal symptoms is warranted prior to determination of the anesthetic plan.

Hematologic Evaluation

Coagulopathy secondary to preexisting liver disease is common among patients presenting for elective TIPS. For the patient in extremis being considered for emergent TIPS due to gastrointestinal bleeding, acute blood loss anemia may be present. Severe coagulopathy and thrombocytopenia are relative contraindications to TIPS placement. All patients should have a coagulation profile and complete blood count performed preoperatively. When able, all underlying coagulopathy should be corrected preoperatively (as time permits in the emergent setting). It is also prudent to have blood products readily available in emergent cases of acute variceal bleeding.

Intracardiac echocardiography has demonstrated clear improvement in procedural bleeding complications such as hepatic capsular perforation [9]. Additional studies are warranted to investigate the impact these results may have on patient outcomes. Decreased needle passes required for portal vein cannulation when using ICE may also translate into decreased hematologic complications [27].

Intraoperative Management

Delivering an anesthetic in a remote location comes with unique and complicated challenges. As with any case taking place outside the operating suite, preparedness and foresight are critical. Anticipation of the complications associated with TIPS, such as intra-peritoneal bleeding or pulmonary aspiration, may be lifesaving for the patient. Conscious sedation is an option in these cases, however general anesthesia with endotracheal intubation is the preferred approach at our institution.

If considering sedation for TIPS, one must be prepared for conversion to general anesthesia without delay. Dilatation of intrahepatic tracts during TIPS is painful, and may be intolerable to patients under sedation. Significant abdominal ascites may not permit a prolonged procedure in the supine position due to patient discomfort.

Large bore intravenous access should be obtained given the risk of clinically significant bleeding. As the radiologist will likely be accessing the right internal jugular vein, alternative sites must be used by the anesthesiologist if central access is desired. In cases of difficult intravenous access, the radiologist can assist with obtaining additional access under fluoroscopy. Typically two large bore peripheral intravenous catheters are sufficient. Arterial cannulation for continuous blood pressure monitoring is recommended in high risk patients. It has been noted that the femoral arterial waveform tracing can be compromised in the setting of massive ascites [28]. Impedance of arterial blood flow from elevated intra-abdominal pressure is easily reversed after the peritoneal drainage catheter is placed at the commencement of the TIPS procedure.

Caution should be exercised when using medications with active metabolites or requiring hepatic metabolism as these drugs may result in excessive or prolonged sedation. Patients presenting with hepatic encephalopathy should have medications dose-adjusted based on clinical effect. In cases where general anesthesia with endotracheal intubation is planned, rapid sequence induction should be considered due to the likelihood of increased abdominal pressure and related aspiration risk. Accordingly, we would not recommend the elective use of supraglottic airways (e.g. laryngeal mask airway) for these procedures. In emergency TIPS for refractory variceal bleeding, the airway must be secured to minimize catastrophic aspiration.

Maintenance of anesthesia can be achieved using inhaled volatile anesthetics or total intravenous anesthesia (TIVA). Employing a TIVA technique has been described as safe and effective for patients undergoing TIPS [29]. In remote procedural areas, access to inhaled anesthetic gas

scavenging systems may be limited, making TIVA preferable in such situations.

Forced air patient warming systems including underbody warming blankets can be used intraoperatively. Maintenance of normothermia should be prioritized in patients with underlying coagulopathy secondary to chronic liver disease, as hypothermia may exacerbate bleeding complications.

Endotracheal extubation may be considered with patients once laryngeal reflexes are restored and hemodynamic stability is achieved. As some patients may have baseline hepatic encephalopathy prior to TIPS, the mental status exam must be carefully performed prior to extubation. The positive impact of TIPS on acute variceal hemorrhage can be seen immediately, however the presence of gastric blood as a pro-emetic should be considered prior to extubation. At our institution, these patients typically remain intubated post-operatively for airway protection and are extubated in the intensive care unit (ICU) once clinically stabilized.

Postoperative Care

Patients should be observed post-procedurally in a monitored setting such as a post-anesthesia care unit (PACU). For patients with acute variceal bleeding, strong consideration should be given to ICU monitoring until stabilized. Hemobilia may be seen and usually resolves spontaneously. As the procedure can be associated with significant abdominal pain due to hepatic tract dilatation, sedating analgesic medications should be used judiciously. Use of a multi-modal strategy for pain control can mitigate some of the respiratory compromise associated with opiates, especially in patients with advanced hepatic and/or renal disease.

Procedural Complications

Complications during the procedure include ventricular arrhythmias with vascular catheterization. Instrumentation of the superior and inferior vena cavae often transiently induce atrial and/or ventricular ectopy that typically self-resolves. Persistent arrhythmias should be managed with expeditious withdrawal of vascular instrumentation and supportive care.

Hypotension is commonly observed during TIPS from multiple causes: splanchnic vasodilatation with decreased arterial pressure, anesthesia induced hypotension, decreased preload with large volume paracentesis, and potentially significant bleeding. Each of these factors must be considered when treating a patient undergoing TIPS. Intraoperative access to vasoactive infusions and colloid fluid therapy (e.g. albumin) should be required of the anesthesiology care team. The immediate availability of blood products has been recommended, however with improved procedural techniques this may be unnecessary for all patients.

Many institutions will prepare blood products for TIPS in the event of clinically significant bleeding. For the patient receiving a TIPS for acute variceal bleeding, the availability of blood products for volume resuscitation is paramount. Portal vein or hepatic capsular rupture can result in devastating blood loss, during which massive transfusion protocols would likely be activated for resuscitation. These complications are extremely rare, especially with growing utilization of ICE. Institutional adoption of practice-based blood allocation strategies such as the maximum surgical blood order schedule (MSBOS) can help reduce unnecessary cross-matching for surgical procedures with low transfusion rates [30]. As institutions continue to perform TIPS with increased frequency, MSBOS will more closely align preoperative blood orders with historically-driven transfusion data.

Venous return is increased post-TIPS which may exacerbate acute heart failure (particularly right-sided symptoms). Aggressive diuresis may therefore be required in the immediate postoperative period. Close attention should be paid to early signs of post-operative infectious complications such as fever, worsening leukocytosis, and hemodynamic instability. Clinicians should have a low threshold for the initiation of antimicrobial therapy, especially those covering enteric gram

negative organisms (e.g. *Escherichia coli, Klebsiella* spp.) and *Streptococcus* spp. In rare instances, shunt revisions may be required for post-operative symptoms such as clinically intolerable encephalopathy or congestive heart failure.

Conclusion

The indications for TIPS continue to expand as further research has consistently demonstrated both short and long term benefit in early TIPS for advanced liver disease. Accordingly, anesthesiologists will increasingly be called upon to assist in the care of these complex patients. As with many procedures taking place in remote procedural areas such as the interventional radiology suite, anesthesiologists must be prepared for the many clinical challenges posed by TIPS. Further research in the perioperative management of TIPS patients is warranted.

Funding and Conflicts of Interest
None.

References

1. Saad WE. The history and future of transjugular intrahepatic portosystemic shunt: food for thought. Semin Intervent Radiol. 2014;31(3):258–61. https://doi.org/10.1055/s-0034-1382794.
2. Boyer TD, Haskal ZJ, American Association for the Study of Liver Diseases. The role of Transjugular Intrahepatic Portosystemic Shunt (TIPS) in the management of portal hypertension: update 2009. Hepatology. 2010;51(1):306. https://doi.org/10.1002/hep.23383.
3. Bureau C, Thabut D, Oberti F, Dharancy S, Carbonell N, Bouvier A, Mathurin P, Otal P, Cabarrou P, Péron JM, Vinel JP. Transjugular intrahepatic portosystemic shunts with covered stents increase transplant-free survival of patients with cirrhosis and recurrent ascites. Gastroenterology. 2017;152(1):157–63. https://doi.org/10.1053/j.gastro.2016.09.016. Erratum in: Gastroenterology. 2017;153(3):870
4. García-Pagán JC, Caca K, Bureau C, Laleman W, Appenrodt B, Luca A, Abraldes JG, Nevens F, Vinel JP, Mössner J, Bosch J, Early TIPS (Transjugular Intrahepatic Portosystemic Shunt) Cooperative Study Group. Early use of TIPS in patients with cirrhosis and variceal bleeding. N Engl J Med. 2010;362(25):2370–9. https://doi.org/10.1056/NEJMoa0910102.
5. Hernández-Gea V, Procopet B, Giráldez Á, Amitrano L, Villanueva C, Thabut D, Ibañez-Samaniego L, Silva-Junior G, Martinez J, Genescà J, Bureau C, Trebicka J, Llop E, Laleman W, Palazon JM, Castellote J, Rodrigues S, Gluud LL, Noronha Ferreira C, Barcelo R, Cañete N, Rodríguez M, Ferlitsch A, Mundi JL, Gronbaek H, Hernández-Guerra M, Sassatelli R, Dell'Era A, Senzolo M, Abraldes JG, Romero-Gómez M, Zipprich A, Casas M, Masnou H, Primignani M, Krag A, Nevens F, Calleja JL, Jansen C, Robic MA, Conejo I, Catalina MV, Albillos A, Rudler M, Alvarado E, Guardascione MA, Tantau M, Bosch J, Torres F, Garcia-Pagán JC, International Variceal Bleeding Observational Study Group and Baveno Cooperation. Preemptive-TIPS improves outcome in high-risk variceal bleeding: an observational study. Hepatology. 2019;69(1):282–93. https://doi.org/10.1002/hep.30182.
6. Rössle M, Siegerstetter V, Olschewski M, Ochs A, Berger E, Haag K. How much reduction in portal pressure is necessary to prevent variceal rebleeding? A longitudinal study in 225 patients with transjugular intrahepatic portosystemic shunts. Am J Gastroenterol. 2001;96(12):3379–83. https://doi.org/10.1111/j.1572-0241.2001.05340.x.
7. Casado M, Bosch J, García-Pagán JC, Bru C, Bañares R, Bandi JC, Escorsell A, Rodríguez-Láiz JM, Gilabert R, Feu F, Schorlemer C, Echenagusia A, Rodés J. Clinical events after transjugular intrahepatic portosystemic shunt: correlation with hemodynamic findings. Gastroenterology. 1998;114(6):1296–303. https://doi.org/10.1016/s0016-5085(98)70436-6.
8. Keller FS, Farsad K, Rösch J. The Transjugular intrahepatic portosystemic shunt: technique and instruments. Tech Vasc Interv Radiol. 2016;19(1):2–9. https://doi.org/10.1053/j.tvir.2016.01.001.
9. RiChard J, Thornburg B. New techniques and devices in transjugular intrahepatic portosystemic shunt placement. Semin Intervent Radiol. 2018;35(3):206–14. https://doi.org/10.1055/s-0038-1660800.
10. Ripamonti R, Ferral H, Alonzo M, Patel NH. Transjugular intrahepatic portosystemic shunt-related complications and practical solutions. Semin Intervent Radiol. 2006;23(2):165–76. https://doi.org/10.1055/s-2006-941447.
11. Bañares R, Casado M, Rodríguez-Láiz JM, Camúñez F, Matilla A, Echenagusía A, Simó G, Piqueras B, Clemente G, Cos E. Urgent transjugular intrahepatic portosystemic shunt for control of acute variceal bleeding. Am J Gastroenterol. 1998;93(1):75–9. https://doi.org/10.1111/j.1572-0241.1998.075_c.x.
12. Malinchoc M, Kamath PS, Gordon FD, Peine CJ, Rank J, ter Borg PC. A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. Hepatology. 2000;31(4):864–71. https://doi.org/10.1053/he.2000.5852.

13. Singal AK, Kamath PS. Model for end-stage liver disease. J Clin Exp Hepatol. 2013;3(1):50–60. https://doi.org/10.1016/j.jceh.2012.11.002.
14. Kamath PS, Wiesner RH, Malinchoc M, Kremers W, Therneau TM, Kosberg CL, D'Amico G, Dickson ER, Kim WR. A model to predict survival in patients with end-stage liver disease. Hepatology. 2001;33(2):464–70. https://doi.org/10.1053/jhep.2001.22172.
15. Ferral H, Gamboa P, Postoak DW, Albernaz VS, Young CR, Speeg KV, McMahan CA. Survival after elective transjugular intrahepatic portosystemic shunt creation: prediction with model for end-stage liver disease score. Radiology. 2004;231(1):231–6. https://doi.org/10.1148/radiol.2311030967.
16. Zuckerman DA, Darcy MD, Bocchini TP, Hildebolt CF. Encephalopathy after transjugular intrahepatic portosystemic shunting: analysis of incidence and potential risk factors. AJR Am J Roentgenol. 1997;169(6):1727–31. https://doi.org/10.2214/ajr.169.6.9393198.
17. Carvalho MVH, Kroll PC, Kroll RTM, Carvalho VN. Cirrhotic cardiomyopathy: the liver affects the heart. Braz J Med Biol Res. 2019;52(2):e7809. https://doi.org/10.1590/1414-431X20187809.
18. Chana A, James M, Veale P. Anaesthesia for transjugular intrahepatic portosystemic shunt insertion. BJA Educ. 2016;16(12):405–9. https://doi.org/10.1093/bjaed/mkw022.
19. Freedman AM, Sanyal AJ, Tisnado J, Cole PE, Shiffman ML, Luketic VA, Purdum PP, Darcy MD, Posner MP. Complications of transjugular intrahepatic portosystemic shunt: a comprehensive review. Radiographics. 1993;13(6):1185–210. https://doi.org/10.1148/radiographics.13.6.8290720.
20. Schenk P, Fuhrmann V, Madl C, Funk G, Lehr S, Kandel O, Müller C. Hepatopulmonary syndrome: prevalence and predictive value of various cut offs for arterial oxygenation and their clinical consequences. Gut. 2002;51(6):853–9. https://doi.org/10.1136/gut.51.6.853.
21. Tsauo J, Zhao H, Zhang X, Ma H, Jiang M, Weng N, Li X. Effect of transjugular intrahepatic portosystemic shunt creation on pulmonary gas exchange in patients with hepatopulmonary syndrome: a prospective study. J Vasc Interv Radiol. 2019;30(2):170–7. https://doi.org/10.1016/j.jvir.2018.09.017.
22. Angeli P, Garcia-Tsao G, Nadim MK, Parikh CR. News in pathophysiology, definition and classification of hepatorenal syndrome: a step beyond the International Club of Ascites (ICA) consensus document. J Hepatol. 2019;71(4):811–22. https://doi.org/10.1016/j.jhep.2019.07.002.
23. Appenrodt B, Lammert F. Renal failure in patients with liver cirrhosis: novel classifications, biomarkers, treatment. Visc Med. 2018;34(4):246–52. https://doi.org/10.1159/000492587.
24. Brensing KA, Textor J, Perz J, Schiedermaier P, Raab P, Strunk H, Klehr HU, Kramer HJ, Spengler U, Schild H, Sauerbruch T. Long term outcome after transjugular intrahepatic portosystemic stent-shunt in non-transplant cirrhotics with hepatorenal syndrome: a phase II study. Gut. 2000;47(2):288–95. https://doi.org/10.1136/gut.47.2.288.
25. Jaffe RA. Transjugular intrahepatic portosystemic shunt (TIPS). In: Anesthesiologist's manual of surgical procedures. 6th ed. Philadelphia, PA: Wolkers Kluwer; 2020. p. 1675–80.
26. Huynh D, Nguyen NQ. Gastrointestinal dysfunction in chronic liver disease. J Gastrointest Dig Syst. 2015;5(1):257.
27. Kao SD, Morshedi MM, Narsinh KH, Kinney TB, Minocha J, Picel AC, Newton I, Rose SC, Roberts AC, Kuo A, Aryafar H. Intravascular ultrasound in the creation of transhepatic portosystemic shunts reduces needle passes, radiation dose, and procedure time: a retrospective study of a single-institution experience. J Vasc Interv Radiol. 2016;27(8):1148–53. https://doi.org/10.1016/j.jvir.2016.01.137.
28. Kreisler NS, Stone DJ, Spiekermann BF. Radial to femoral arterial pressure gradient from massive ascites. Anesthesiology. 2000;92(5):1508. https://doi.org/10.1097/00000542-200005000-00067.
29. DeGasperi A, Corti A, Corso R, Rampoldi A, Roselli E, Mazza E, Fantini G, Prosperi M. Transjugular intrahepatic portosystemic shunt (TIPS): the anesthesiological point of view after 150 procedures managed under total intravenous anesthesia. J Clin Monit Comput. 2009;23(6):341–6. https://doi.org/10.1007/s10877-009-9167-y.
30. Frank SM, Oleyar MJ, Ness PM, Tobian AA. Reducing unnecessary preoperative blood orders and costs by implementing an updated institution-specific maximum surgical blood order schedule and a remote electronic blood release system. Anesthesiology. 2014;121(3):501–9. https://doi.org/10.1097/ALN.0000000000000338.

20 Anesthetic Considerations in Candidates for Lung Volume Reduction Surgery (LVRS)

Raiyah Sheriffdeen, Zahid Iqbal, Nisarg Patel, and Ron L. Leong

Introduction

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of morbidity and mortality throughout the world [1]. Increasing disease burden and failure of medical treatment prompted introduction of various surgical techniques with initial limited success. These early surgical attempts included pneumoperitoneum formation, phrenic nerve paralysis, thoracoplasty, lung denervation, and fixation of trachea [2].

The first lung volume reduction surgery (LVRS) was described by Brantigan and Muller in the 1950s where they performed multiple resections of hyperinflated lung parenchyma through a standard thoracotomy approach combined with hilar stripping for lung denervation [3]. Although they reported 75% of patients having clinical improvement, the lack of positive objective metrics from the procedure and an operative mortality of 18% prevented widespread acceptance of the procedure [2].

Cooper et al. revitalized interest in LVRS by publishing promising results in the 1990s. He utilized a median sternotomy for bilateral 20–30% lung volume resection and a surgical technique of stapled lung resections buttressed by pericardial strips [2, 4, 5]. This small case series of 20 patients demonstrated improvements in lung function after LVRS and no mortality [5]. Subsequently, numerous prospective studies have reported favorable results in selected patients [6–17].

LVRS has prompted many randomized control trials including the large-scale National Emphysema Treatment Trial (NETT) published in 2003 [18]. Moreover, a recent Cochrane review concluded lung volume reduction surgery as an effective treatment option for carefully selected patients with severe emphysema leading to better health status and improved quality of life, especially in patients with predominantly upper lobe emphysema with a baseline low exercise capacity [19].

R. Sheriffdeen
Division of Cardiac Anesthesiology, Department of Anesthesiology, Medstar Washington Hospital Center, Washington, DC, USA
e-mail: Raiyah.Sheriffdeen@medstar.net

Z. Iqbal
Division of Critical Care, Department of Anesthesiology, Washington University School of Medicine, St. Louis, MO, USA
e-mail: ZahidIqbal@wustl.edu

N. Patel
Department of Anesthesiology, Thomas Jefferson University Hospital, Philadelphia, PA, USA
e-mail: Nisarg.Patel@jefferson.edu

R. L. Leong (✉)
Department of Anesthesiology, Thomas Jefferson University Hospital, Philadelphia, PA, USA

Department of Anesthesiology, Sidney Kimmel Medical College, Philadelphia, PA, USA
e-mail: Ron.Leong@jefferson.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_20

The goal of this chapter is to understand the mechanism of clinical improvement after surgical resection, preoperative work-up and anesthetic considerations, intraoperative management, and postoperative complications for lung volume reduction surgery.

Pathophysiology

Chronic obstructive pulmonary disease (COPD) is one of the major causes of disability in the world. It is a disorder with a key defining feature of having limited expiratory airflow by comparison of lung volumes [20]. COPD is a progressive disorder with multiple etiologies. However, the single most important contributing factor is a history of smoking. Other etiologies include Alpha-1 antitrypsin deficiency and other chemical exposures.

COPD describes a spectrum of disease including chronic bronchitis, described as central airway inflammation leading to excessive sputum production, and eventual permanent destruction of distal airways causing emphysema [21]. In patients with emphysema, the loss of normal lung architecture results in a loss of elastic recoil of lung tissue which leads to the collapse of small airways causing expiratory airflow limitations, air trapping, hyperinflation and progressive enlargement of the lungs and thorax [4]. The hyperinflated lungs causes flattening of the diaphragm which shortens the diaphragmatic muscle fibers, and ultimately impairs the ability to forcibly contract. The lung hyperinflation also reduces the effectiveness of intercostal muscles due to changes in rib motion. The combination of these emphysematous changes disrupts normal respiratory mechanics, and the end result is an increased total lung capacity and residual volume, a decreased forced expiratory volume in 1 s (FEV_1) and a significant increase in the work of breathing [4].

LVRS produces marked changes in several parameters leading to overall improvement of respiratory function. The resection of hyperinflated lung tissue, allows for re-expansion of previously viable but compressed areas of normal tissue. The alleviated normal lung tissue results in an improved elastic recoil leading to an increased FEV_1 [14], improved work of breathing, intrinsic positive end-expiratory pressure and pulmonary resistance within 24 h after LVRS [4]. The decrease in intrathoracic volume after LVRS allows for re-doming of the diaphragm. This restoration of the diaphragm's normal anatomy and geometry leads to an improved generation of negative intrathoracic pressure [2]. The hyperinflated alveoli do not participate in effective gas exchange. After LVRS, there is a significant improvement in the homogeneity of ventilation and perfusion, leading to a more efficient gas exchange and better maintenance of appropriate blood gas levels [19]. Lastly, there appears to be an improvement in right ventricular function that arises from the release of the compressive effect on the heart and pulmonary vascular structures caused by lung hyperinflation [2, 22].

Pre-operative Evaluation

Consideration for LVRS should begin with a thorough assessment of severity and distribution of emphysema as well as the patient's cardiopulmonary capacity. Preoperative considerations are a collaborative effort between a patient's thoracic surgeon, pulmonologist and other consultant physicians.

Much of the data and considerations for LVRS are based on the NETT trial in 2003 due to its unmatched size, statistical power, and quality of the study [18]. This was a multicenter, randomized, controlled clinical trial that compared the efficacy of lung volume reduction surgery plus medical management with rehabilitation to solely rehabilitation with medical management in patients with severe emphysema. During the start of the trial, the high-risk subgroup of patients had an observed high 30-day mortality versus medical therapy and thus the decision was made to exclude them. This high-risk subgroup included patients that had homogeneous emphysema, an $FEV_1 < 20\%$ or a diffusing capacity of lung for carbon monoxide (DLCO) <20%. Overall

endpoints of NETT were mortality and maximal exercise capacity at 24 months, and LVRS showed no difference in mortality at 2 years between non-high-risk patients and those with maximal medical therapy. In the NETT subgroup analysis it was shown there was benefit in those with heterogeneous distribution of emphysema with particular attention towards upper lobe disease. Typically, patients eligible for LVRS are based on the inclusion and exclusion criteria for the NETT that showed the most promising outcomes.

Inclusion criteria for LVRS [18]
• <75 years • Severe dyspnea in spite of maximum medical therapy and pulmonary rehabilitation • >6 months of smoking cessation • Advanced COPD • DLCO >20% • Residual volume (RV) >150% predicted, total lung capacity (TLC) > 100% predicted, an increased RV/TLC ratio • Computed tomography (CT) showing hyperinflation, heterogeneous emphysema, predominantly upper lung zone • Post-rehabilitation 6-min walk distance great than 140 m

Exclusion criteria for LVRS [18]
• >75 years • Recent cigarette smoking (6 months) • Significant comorbidities that would increase mortality (coronary artery disease, left ventricular ejection fraction <40%) • Extremes of weight • Inability to complete a pulmonary rehabilitation program • Anatomical challenges (i.e. chest wall deformity, previous pleurodesis, etc.) • DLCO <20%, $PaCO_2$ > 60 mmHg, PaO_2 < 45 mmHg • Pulmonary hypertension

Preoperative testing includes pulmonary function testing, arterial blood gases, electrocardiograms, transthoracic echocardiography (including pulmonary artery pressure measurements), exercise stress test, high resolution computed tomography (HRCT). HRCT is useful in identifying the extent of the disease pertaining to its distribution. Patients are also optimized for their comorbidities as they typically are for surgeries [23].

Intra-operative Management

Surgical Procedure

It is helpful for the anesthesia provider to recognize the surgical approach of LVRS as a key part of the anesthetic planning. There are three main access techniques for LVRS: thoracotomy, median sternotomy, and video-assisted thoracoscopic surgery (VATS). Each surgical approach presents its own unique anesthetic considerations with the shared goal of resecting 20–30% of the diseased lung volume as identified on preoperative imaging.

A median sternotomy involves a vertical incision that extends from just below the sternal notch to the tip of the xiphoid process. At this point ventilation is briefly held for sternotomy with a sternal saw. It is important to ensure the patient is appropriately provided analgesia and paralysis prior to incision and sternotomy. The median sternotomy technique allows exposure to bilateral lungs, and the resection of the more diseased lung is preferentially targeted first if bilateral resection is planned. After resection, the open lung tissue is stapled close. As an adjunct to further decrease the risk of pulmonary air leakage, a common post-operative complication after lung resection, reinforced bovine strips or a pleural tent can be placed [5, 24].

An attractive and less invasive approach is a VATS procedure. The surgeon accesses the lungs through small incisions for the placement of trocars. A camera and surgical instruments are utilized to carry out the lung resections. In addition to the more traditional stapling technique, newer technology with the use of thermal energy and neodymium: yttrium-aluminum-garnet (Nd: YAG) laser can be used to reduce lung volume [17].

Lastly, unilateral or bilateral thoracotomy is the least common of the surgical approach options for LVRS. Median sternotomy and VATS are by far the more preferred techniques as reported through international surveys [25]. The NETT trial found similar mortality and morbidity rates between VATS and median sternotomy,

however, a smaller study found a lower incidence of respiratory failure and mortality with the VATS group [9, 18].

Monitoring

Standard monitoring with pulse oximetry, capnography, blood pressure, heart rate, electrocardiography (EKG), and thermometers (via esophageal or Foley catheter) should be utilized for all LVRS cases. Additionally, continuous hemodynamic monitoring with an invasive arterial catheter is essential given the significant baseline co-morbidities, the potential for rapid changes in blood pressure, and the usefulness of intra-operative laboratory data including arterial blood gas analysis.

Special consideration should be given for the use central venous pressure (CVP) monitoring, pulmonary artery catheter or Swan-Ganz catheter, and/or transesophageal echocardiography (TEE). A central venous catheter not only provides crucial intravenous access for the potential need for volume resuscitation and administration of vasoactive medications, but also offers important insight to the assessment of the right ventricle. LVRS patients are at high risk of right ventricular dysfunction from pulmonary hypertension, chronic hypoxia and hypercarbia, and the compressive effects of hyperinflated lungs on the cardiac and vascular structures. Furthermore, venous return is compromised by increases in intrathoracic pressure and flattening of the diaphragm leading to a reduction in right ventricular filling and stroke volume [22]. Depending on the severity of a patient's underlying pulmonary hypertension or cardiac dysfunction, the pulmonary artery catheter and/or TEE can be invaluable to guide these sick patients safely through the intraoperative and immediate recovery period. However, the routine use of pulmonary artery catheters and TEE in LVRS is not supported [26, 27].

Induction Considerations

Premedication with an anxiolytic such as a benzodiazepine may be helpful for patients with high levels of anxiety about the upcoming surgery, especially if the patient is tachypneic or dyspneic. However, if the patient is calm and cooperative, then the avoidance of a premedication is preferred to lessen the potential risk of delaying extubation at the conclusion of the surgery. Bronchodilator therapy prior to the operating room is a prudent strategy for decreasing the risk of bronchospasm during the induction and intubation process.

Before the induction of anesthesia, the patient may require a longer duration of pre-oxygenation to air trapping from their severe emphysematous disease. Furthermore, pre-oxygenation may need to be done in a semi-recumbent position (head elevated 30–45°) for patient comfort due to dyspnea. The induction of anesthesia can be safely performed with any of the common induction agents [26–29]. After the loss of consciousness and the administration of a neuromuscular blocking agent, the patient can then be properly positioned for the control of ventilation and intubation.

Intubation and lung isolation are typically achieved with a left sided double-lumen endotracheal tube, but bronchial blockers with a single lumen endotracheal tube is also an effective alternative [2, 26, 30]. The use of bronchial blockers can reduce the incidence of post-operative hoarseness and sore throat, however, it requires a longer time to achieve complete lung collapse and limits the anesthetist's ability to suction secretions in the operative lung [30, 31]. Regardless of which lung isolation modality is used, a fiberoptic bronchoscopy is performed to confirm the appropriate positioning [32].

Maintenance of Anesthesia

Several techniques have been described for maintenance of anesthesia during lung volume reduction surgery. Total intravenous anesthesia (TIVA) with propofol is often cited as the preferable method over general inhalational anesthesia during one lung ventilation (OLV) since propofol is not associated with an increase in shunt fraction during OLV, which is of particular importance to this patient population [33, 34]. Additionally, propofol can improve oxygenation during OLV, thought to be due to its lack of inhibition of

hypoxic pulmonary vasoconstriction (HPV) [34]. Moreover, propofol does not depend on pulmonary metabolism and elimination [4]. Short-acting drugs, such as remifentanil, may be used as part of the TIVA regimen, since it is vital that these patients resume spontaneous breathing as early as possible in order to prevent air leakage caused by positive pressure ventilation [2, 31]. TIVA has also been used in conjunction with lumbar and thoracic epidurals intraoperatively [29, 35].

Inhalational agents, such as sevoflurane and isoflurane, may be preferred in patients who are particularly prone to bronchospasm, since these agents cause relaxation of airway smooth muscle via mechanisms that reduce intracellular free calcium [2, 36]. Inhalational agents also have immune-modulating effects, and sevoflurane and desflurane have been reported to attenuate the inflammatory reaction in patients undergoing OLV during thoracic surgery [37, 38]. This benefit, however, will need to be weighed against the potential for delayed awakening due to the large dead space that results from the severity of bullous disease and the associated unpredictability of uptake and distribution of these inhalational agents [4, 31]. While the literature is equivocal regarding specific inhalational agents, the use of nitrous oxide has been avoided in all published series due to the potential for gas trapping [4].

Muscle relaxation during surgery should be maintained by short and intermediate-lasting neuromuscular blocking agents without significant hemodynamic effects, such as cisatracurium besylate and vecuronium bromide [2, 31]. Train-of-four twitch monitoring should be performed intraoperatively, since there is some evidence that these patients may have increased sensitivity to neuromuscular blocking agents [31, 39]. As with opioids and sedatives, dosing of neuromuscular blocking agents should be performed with the goal of early extubation in mind [2, 4, 31].

Ventilation Strategies During One-Lung Ventilation

One-lung ventilation causes a variety of pulmonary derangements in both the ventilated and non-ventilated lung—a situation further exacerbated by the preexisting pathology of this patient population. The dependent, ventilated lung is subject to volutrauma [37], atelectasis [37, 40], and disruption of the capillary and alveolar endothelium secondary to vascular shear stress [37, 41]. The collapsed lung, in turn, faces the prospect of atelectasis [37, 40], mechanical stress and strain from re-expansion maneuvers [37, 42, 43], and ischemia-reperfusion injury [37, 44]. Additionally, the emphysematous lung is more prone to barotrauma and dynamic hyperinflation, or air trapping, due to small airway collapse [4, 31, 37, 45].

The optimal ventilation strategy for lung reduction surgery will provide adequate oxygenation while minimizing air trapping with the potential for development of pneumothorax [2, 31]. Historically, pressure-control ventilation has been touted as superior to volume-control ventilation in OLV, since the former reduces peak airway pressures measured proximally by the ventilator [4, 37]. However, more recent evidence has demonstrated minimal differences between the two modes, particularly since most modern ventilation modes are equipped with pressure limitation capabilities [31, 46]. It is of interest to note, however, that pressure-control ventilation does provide the advantage of improved right ventricular function, although this only applies to right-lung ventilation [46].

There is general consensus that a ventilation strategy combining low tidal volume (V_t) ventilation (i.e. V_t of 6–8 mL/kg of ideal body weight [IBW] for two lung ventilation [46] and less than 5 mL/kg IBW for OLV [2, 31, 37, 46]) with low respiratory frequencies (less than 16 breaths per minute during OLV [2]), and an increased expiration time (e.g. I:E ratio of 1:3 to 1:5 [2, 31]) to prevent dynamic hyperinflation [45], should attain the ventilatory goals listed above [2, 4, 31]. In addition, providers should aim for a plateau pressure less than 30 cm H_2O to minimize barotrauma [2, 45]. PEEP is considered a routine requirement to prevent lung strain [37] and increase expiratory flow rates [45], and the addition of CPAP to the deflated lung may be necessary to maintain oxygenation [46], although this may interfere with identification of the most diseased parts of the lung [29]. Decreasing the FiO_2

to the lowest tolerated fraction should be considered after 20–30 min of OLV when oxygenation has reached its lowest point [37], in order to prevent absorption atelectasis [37, 46]; however, this may not be tolerated in severely emphysematous patients. Periodic reinflation of the lung to improve oxygenation may be beneficial to the surgeon as well, enabling assessment of the extent of surgery as well as identification of air leaks [4, 29].

The patient population undergoing LVRS exhibits certain unique challenges to OLV. First, the time to deflation of the operative lung is prolonged due to decreased elastic recoil, with minimal response to suctioning [31]; this could necessitate an earlier initiation of OLV. Second, the diseased parenchyma often deflates more slowly than less emphysematous lung tissue and may need to be deflated with gentle manual pressure by the surgeon [31]. Finally, the ventilation strategy recommended above will inevitably lead to hypercapnia [2, 4, 31]. Mild hypercapnia ($PaCO_2$ of 40–60 mmHg) is generally well tolerated unless the patient has a history of significant right ventricular dysfunction or pulmonary hypertension [28, 37]. If the pH falls below 7.2, an increase in respiratory rate may be instituted, although the provider should be mindful of the increased risk of auto-PEEP [31]. Most patients, however, reach normal $PaCO_2$ values within 24 h after surgery [2, 29].

In some patients, OLV may not be tolerated, and LVRS may have to completed with low tidal volume ventilation during surgical exposure, with stapling of the diseased lung performed under apneic oxygenation [28, 31]. Bilateral bullectomy can be performed under jet ventilation as a last resort [29]. When tolerated, however, OLV is the preferred technique since it provides the ability to identify target areas in the non-ventilated lung.

Intraoperative Complications

Anesthesia providers caring for patients undergoing LVRS should anticipate the gamut of complications associated with OLV and be prepared to manage causes of hypoxemia as well as the challenges associated with positioning [28, 31]. Due to their preexisting pathology, these patients present with increased potential for the following complications:

Hypotension

Hypotension is most often seen on induction, although it can occur at any point during the surgery [31]. Etiologies include decreased intravascular volume, which may be exacerbated by decreased venous return due to auto-PEEP, both during hand ventilation and conversion to mechanical ventilation [31]. In this case, hypotension can be resolved by temporarily disconnecting the ventilator circuit from the endotracheal tube [31]. Myocardial ischemia is a potential etiology for those patients with significant coronary artery disease. Hypotension due to sympathetic blockade should be considered in patients with a thoracic epidural. The anesthesia provider should also be prepared to treat more severe causes of hypotension, such as pneumothorax (see "Tension Pneumothorax") and anaphylaxis. Treatment of hypotension consists of administration of fluid or vasoconstricting agents. Brister et al. recommends the strategy of conservative fluid management in order to facilitate early extubation [31].

Dynamic Hyperinflation

Due to the presence of increased expiratory airway resistance in COPD patients, the expiratory time available to empty the inspired volume may be insufficient, leading to subsequent inspirations starting before completion of expiration. This leads to a baseline state in which the functional residual capacity (FRC) is greater than the volume of relaxation (V_{rel}), a condition of air-trapping known as dynamic hyperinflation (DHI) [45]. As mentioned above, DHI may present as hypotension, due to decreased venous return and decreased left ventricular compliance secondary to increased intrathoracic pressure as well as increase in right ventricular afterload due to alve-

olar capillary compression [45, 47]. DHI may also lead to barotrauma-associated complications such as pneumothorax, pneumomediastinum, and pneumoperitoneum [45]. Ventilatory strategies that prolong expiratory time can help mitigate the risk of DHI (see "Ventilation Strategies During One-Lung Ventilation").

Tension Pneumothorax

The sudden development of cardiovascular collapse that is unresponsive to vasopressor or fluid administration and cannot be explained by DHI or malposition of the endotracheal tube is likely tension pneumothorax in this patient population, given their increased risk of barotrauma [45]. This is a true emergency, and will have to be treated by aborting the surgery, re-expanding the operative lung, and inserting a chest tube.

Patients with COPD provide several challenges for which the OR team must be prepared. It is imperative that effective lines of communication between the surgical and anesthesia staff be in place, in order to manage these patients safely and effectively.

Strategies for Analgesia

Multiple analgesic strategies have emerged over the past few decades for thoracic surgery, including thoracic epidurals, paravertebral catheters [48], intercostal nerve blocks [48, 49], serratus anterior plane blocks [50, 51], pectoralis blocks [51], and erector spinae catheters [51, 52]. The literature for LVRS, however, strongly favors thoracic epidurals [2, 4, 29, 31], with one author describing thoracic epidurals as "mandatory" for optimal analgesia following LVRS [2]. There does exist one case series that advocates for the use of lumbar epidurals due to their ease of placement and effectiveness for thoracic analgesia [2]; however, most reports describe the use of thoracic epidurals.

There is also variance as to what types of drugs are administered epidurally: one school of thought is the use of epidural diamorphine without local anesthetic due to a more favorable hemodynamic profile and improvement in postoperative respiratory function due to lack of blockade of intercostal muscles [29]. However, other studies have demonstrated that 0.25% bupivacaine administered via thoracic epidural does not affect breathing pattern, gas exchange, or ventilatory mechanics adversely [2, 4, 53]. Additionally, if chest tubes are placed, patients may need supplemental analgesia such as NSAIDs [4, 26].

Regardless of the specific choice of analgesic strategy, the goal for these patients is to facilitate early extubation and resumption of adequate spontaneous ventilation in order to minimize exacerbation of air leaks by positive pressure ventilation [2, 31]. A case series published by Buettner et al. described the need for reintubation of eight patients for respiratory failure, with five of these patients experiencing inadequate epidural analgesia [26], demonstrating the importance of a comprehensive and effective analgesic strategy.

Post-operative Complications

Patients are largely monitored post operatively in an intensive care unit or an equivalent setting. Patients are assessed for anemia, cardiac ischemia, electrolyte abnormalities, hypercapnia, hypoxemia, and lung mechanics. Due to the nature of the surgery, patients are at risk of improper lung expansion secondary to an air leak and malfunctioning chest tubes. The majority of patients are extubated in the operating room provided they are stable in an effort to limit positive pressure ventilation [54]. Respiratory insufficiency after extubation could be related to atelectasis, pneumothorax, bronchoconstriction, or splinting due to pain. Noninvasive positive pressure ventilation is a useful tool to prevent hypercapnic respiratory failure and re-intubation.

Appropriately functioning chest tubes are tremendously important to preventing pneumothorax and the associated tension physiology. Intermittent kinking and obstruction of a chest tube can quickly lead to this issue. Daily chest

radiographs to ensure the lung is fully expanded as well as continuous monitoring for air leaks are important. Chest tubes are removed when the air leakage ceases.

Post-operative pain management is tantamount to successful recovery in this patient population. Patients that splint due to pain from thoracic surgery in general are at risk of atelectasis, hypoxia, and pulmonary infections. Thus, the goals of post-operative recovery focus on the promotion of early mobilization and generating a productive cough [55]. Multimodal and multidisciplinary approaches have largely been developed at tertiary care centers that have the available experts to provide care and follow these patients. Effective regional anesthesia techniques and options are discussed in the "Strategies for Analgesia" for intraoperative anesthetic management section.

The most common major short-term complications of LVRS include arrhythmias, intubation, death, mechanical ventilation for more than 2 days, pneumonia, and persistent chest tube air leak. Overall operative mortality including high risk patients was 6% in the NETT [56]. Among the non-high-risk patients, major cardiovascular morbidity was 20% while major pulmonary morbidity was 30%. [57]. Uncommon complications included intraoperative myocardial infarction, pulmonary embolism, and wound infections [54].

Conclusion

LVRS is an operation performed by a thoracic surgeon under general anesthesia to remove non-functional lung in order to improve the function of the remaining lung. This unique surgery presents the anesthesia provider with patients with significant cardiopulmonary co-morbidities and complex pathophysiology relating to the severe lung disease. A proper anesthetic plan requires an understanding of the surgical approach, the various analgesic strategies, the need for continuous invasive monitoring, intubation with lung isolation, and the prevention and management of intraoperative complications.

Funding and Conflicts of Interest
None.

References

1. Burney PGJ, Patel J, Newson R, Minelli C, Naghavi M. Global and regional trends in COPD mortality, 1990–2010. Eur Respir J. 2015;45(5):1239–47.
2. Tschernko EM. Anesthesia considerations for lung volume reduction surgery. Anesthesiol Clin North Am. 2001;19(3):591–609.
3. Brantigan OC, Mueller E, Kress MB. A surgical approach to pulmonary emphysema. Am Rev Respir Dis. 1959;80(1, Part 2):194–206.
4. Hillier J, Gillbe C. Anaesthesia for lung volume reduction surgery. Anaesthesia. 2003;58(12):1210–9.
5. Cooper JD, Trulock EP, Triantafillou AN, Patterson GA, Pohl MS, Deloney PA, et al. Bilateral pneumectomy (volume reduction) for chronic obstructive pulmonary disease. J Thorac Cardiovasc Surg. 1995;109(1):106–16. discussion 116–119
6. Ciccone AM, Meyers BF, Guthrie TJ, Davis GE, Yusen RD, Lefrak SS, et al. Long-term outcome of bilateral lung volume reduction in 250 consecutive patients with emphysema. J Thorac Cardiovasc Surg. 2003;125(3):513–25.
7. Daniel TM, Chan BB, Bhaskar V, Parekh JS, Walters PE, Reeder J, et al. Lung volume reduction surgery. Case selection, operative technique, and clinical results. Ann Surg. 1996;223(5):526–31. discussion 532–533
8. Keenan RJ, Landreneau RJ, Sciurba FC, Ferson PF, Holbert JM, Brown ML, et al. Unilateral thoracoscopic surgical approach for diffuse emphysema. J Thorac Cardiovasc Surg. 1996;111(2):308–15. discussion 315–316
9. Kotloff RM, Tino G, Bavaria JE, Palevsky HI, Hansen-Flaschen J, Wahl PM, et al. Bilateral lung volume reduction surgery for advanced emphysema. A comparison of median sternotomy and thoracoscopic approaches. Chest. 1996;110(6):1399–406.
10. Little AG, Swain JA, Nino JJ, Prabhu RD, Schlachter MD, Barcia TC. Reduction pneumonoplasty for emphysema. Early results. Ann Surg. 1995;222(3):365–71. discussion 371–374
11. Martinez FJ, de Oca MM, Whyte RI, Stetz J, Gay SE, Celli BR. Lung-volume reduction improves dyspnea, dynamic hyperinflation, and respiratory muscle function. Am J Respir Crit Care Med. 1997;155(6):1984–90.
12. O'Brien GM, Furukawa S, Kuzma AM, Cordova F, Criner GJ. Improvements in lung function, exercise, and quality of life in hypercapnic COPD patients after lung volume reduction surgery. Chest. 1999;115(1):75–84.
13. Pompeo E, Marino M, Nofroni I, Matteucci G, Mineo TC. Reduction pneumoplasty versus respiratory rehabilitation in severe emphysema: a randomized study. Pulmonary Emphysema Research Group. Ann Thorac Surg. 2000;70(3):948–53. discussion 954
14. Sciurba FC, Rogers RM, Keenan RJ, Slivka WA, Gorcsan J, Ferson PF, et al. Improvement in pulmonary function and elastic recoil after lung-reduction

surgery for diffuse emphysema. N Engl J Med. 1996;334(17):1095–9.
15. Tan AL, Unruh HW, Mink SN. Lung volume reduction surgery for the treatment of severe emphysema: a study in a single Canadian institution. Can J Surg. 2000;43(5):369–76.
16. Teschler H, Stamatis G, el-Raouf Farhat AA, Meyer FJ, Costabel U, Konietzko N. Effect of surgical lung volume reduction on respiratory muscle function in pulmonary emphysema. Eur Respir J. 1996;9(9):1779–84.
17. Wakabayashi A. Thoracoscopic laser pneumoplasty in the treatment of diffuse bullous emphysema. Ann Thorac Surg. 1995;60(4):936–42.
18. Fishman A, Martinez F, Naunheim K, Piantadosi S, Wise R, Ries A, et al. A randomized trial comparing lung-volume-reduction surgery with medical therapy for severe emphysema. N Engl J Med. 2003;348(21):2059–73.
19. van Agteren JE, Carson KV, Tiong LU, Smith BJ. Lung volume reduction surgery for diffuse emphysema. Cochrane Database Syst Rev [Internet]. 2016 Oct 14 [cited 2020 Sept 19];2016(10). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6461146/
20. Bates DV. Chronic bronchitis and emphysema. N Engl J Med. 1968;278(11):600–5.
21. Criner GJ, Bourbeau J, Diekemper RL, Ouellette DR, Goodridge D, Hernandez P, et al. Prevention of acute exacerbations of COPD. Chest. 2015;147(4):894–942.
22. Mineo TC, Pompeo E, Rogliani P, Dauri M, Turani F, Bollero P, et al. Effect of lung volume reduction surgery for severe emphysema on right ventricular function. Am J Respir Crit Care Med. 2002;165(4):489–94.
23. DeCamp MM, Lipson D, Krasna M, Minai OA, McKenna RJ, Thomashow BM. The evaluation and preparation of the patient for lung volume reduction surgery. Proc Am Thorac Soc. 2008;5(4):427–31.
24. Venuta F, De Giacomo T, Rendina EA, Ricci C, Coloni GF. Thoracoscopic pleural tent. Ann Thorac Surg. 1998;66(5):1833–4.
25. Hamacher J, Russi EW, Weder W. Lung volume reduction surgery: a survey on the European experience [Internet]. Chest 117. 2000 [cited 2020 Sept 29]. Available from: https://pubmed.ncbi.nlm.nih.gov/10858383/
26. Buettner AU, McRae R, Myles PS, Snell GI, Bujor MA, Silvers A, et al. Anaesthesia and postoperative pain management for bilateral lung volume reduction surgery. Anaesth Intensive Care. 1999;27(5):503–8.
27. Triantafillou AN. Anesthetic management for bilateral volume reduction surgery. Semin Thorac Cardiovasc Surg. 1996;8(1):94–8.
28. Zollinger A, Zaugg M, Weder W, Russi EW, Blumenthal S, Zalunardo MP, et al. Video-assisted thoracoscopic volume reduction surgery in patients with diffuse pulmonary emphysema: gas exchange and anesthesiological management. Anesth Analg. 1997;84(4):845–51.
29. Liu EH, Gillbe CE, Watson AC. Anaesthetic management of patients undergoing lung volume reduction surgery for treatment of severe emphysema. Anaesth Intensive Care. 1999;27(5):459–63.
30. Lu Y, Dai W, Zong Z, Xiao Y, Wu D, Liu X, et al. Bronchial blocker versus left double-lumen endotracheal tube for one-lung ventilation in right video-assisted thoracoscopic surgery. J Cardiothorac Vasc Anesth. 2018;32(1):297–301.
31. Brister NW, Barnette RE, Kim V, Keresztury M. Anesthetic considerations in candidates for lung volume reduction surgery. Proc Am Thorac Soc. 2008;5(4):432–7.
32. Smith GB, Hirsch NP, Ehrenwerth J. Placement of double-lumen endobronchial tubes. Correlation between clinical impressions and bronchoscopic findings. Br J Anaesth. 1986;58(11):1317–20.
33. Kellow NH, Scott AD, White SA, Feneck RO. Comparison of the effects of propofol and isoflurane anaesthesia on right ventricular function and shunt fraction during thoracic surgery. Br J Anaesth. 1995;75(5):578–82.
34. Abe K, Shimizu T, Takashina M, Shiozaki H, Yoshiya I. The effects of propofol, isoflurane, and sevoflurane on oxygenation and shunt fraction during one-lung ventilation. Anesth Analg. 1998;87(5):1164–9.
35. Russi EW, Stammberger U, Weder W. Lung volume reduction surgery for emphysema. Eur Respir J. 1997;10(1):208–18.
36. Mondoñedo JR, McNeil JS, Amin SD, Herrmann J, Simon BA, Kaczka DW. Volatile anesthetics and the treatment of severe bronchospasm: a concept of targeted delivery. Drug Discov Today Dis Models. 2015;15:43–50.
37. Lohser J, Slinger P. Lung injury after one-lung ventilation: a review of the pathophysiologic mechanisms affecting the ventilated and the collapsed lung. Anesth Analg. 2015;121(2):302–18.
38. Slinger P, Kilpatrick B. Perioperative lung protection strategies in cardiothoracic anesthesia: are they useful? Anesthesiol Clin. 2012;30(4):607–28.
39. Criner GJ, Barnette RE, D'Alonzo GE, editors. Critical care study guide: text and review [Internet]. 2nd ed. New York: Springer; 2010 [cited 2020 Sep 19]. Available from: https://www.springer.com/gp/book/9780387773278
40. Tusman G, Böhm SH, Sipmann FS, Maisch S. Lung recruitment improves the efficiency of ventilation and gas exchange during one-lung ventilation anesthesia. Anesth Analg. 2004;98(6):1604–9. Table of contents
41. López-Aguilar J, Piacentini E, Villagrá A, Murias G, Pascotto S, Saenz-Valiente A, et al. Contributions of vascular flow and pulmonary capillary pressure to ventilator-induced lung injury. Crit Care Med. 2006;34(4):1106–12.
42. Gattinoni L, Pesenti A. The concept of "baby lung". Intensive Care Med. 2005;31(6):776–84.
43. Silva PL, Moraes L, Santos RS, Samary C, Ornellas DS, Maron-Gutierrez T, et al. Impact of pressure profile and duration of recruitment maneuvers on morpho-

functional and biochemical variables in experimental lung injury. Crit Care Med. 2011;39(5):1074–81.
44. Tekinbas C, Ulusoy H, Yulug E, Erol MM, Alver A, Yenilmez E, et al. One-lung ventilation: for how long? J Thorac Cardiovasc Surg. 2007;134(2):405–10.
45. Reddy RM, Guntupalli KK. Review of ventilatory techniques to optimize mechanical ventilation in acute exacerbation of chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis. 2007;2(4):441–52.
46. Grande B, Ganter MT. What is the best strategy for one-lung ventilation during thoracic surgery? J Thorac Dis. 2018;10(12):6404–6.
47. Oswald-Mammosser M, Apprill M, Bachez P, Ehrhart M, Weitzenblum E. Pulmonary hemodynamics in chronic obstructive pulmonary disease of the emphysematous type. Respiration. 1991;58(5–6):304–10.
48. Nosotti M, Rosso L, Tosi D, Palleschi A, Mendogni P, Righi I, et al. Preventive analgesia in thoracic surgery: controlled, randomized, double-blinded study. Eur J Cardiothorac Surg. 2015;48(3):428–33. discussion 434
49. Goto T. What is the best pain control after thoracic surgery? J Thorac Dis. 2018;10(3):1335–8.
50. Khalil AE, Abdallah NM, Bashandy GM, Kaddah TA-H. Ultrasound-guided serratus anterior plane block versus thoracic epidural analgesia for thoracotomy pain. J Cardiothorac Vasc Anesth. 2017;31(1):152–8.
51. Chakravarthy M. Regional analgesia in cardiothoracic surgery: a changing paradigm toward opioid-free anesthesia? Ann Card Anaesth. 2018;21(3):225–7.
52. Adhikary SD, Pruett A, Forero M, Thiruvenkatarajan V. Erector spinae plane block as an alternative to epidural analgesia for post-operative analgesia following video-assisted thoracoscopic surgery: a case study and a literature review on the spread of local anaesthetic in the erector spinae plane. Indian J Anaesth. 2018;62(1):75–8.
53. Gruber EM, Tschernko EM, Kritzinger M, Deviatko E, Wisser W, Zurakowski D, et al. The effects of thoracic epidural analgesia with bupivacaine 0.25% on ventilatory mechanics in patients with severe chronic obstructive pulmonary disease. Anesth Analg. 2001;92(4):1015–9.
54. Boasquevisque CHR, Yildirim E, Waddel TK, Keshavjee S. Surgical techniques: lung transplant and lung volume reduction. Proc Am Thorac Soc. 2009;6(1):66–78.
55. Muehling BM, Halter GL, Schelzig H, Meierhenrich R, Steffen P, Sunder-Plassmann L, et al. Reduction of postoperative pulmonary complications after lung surgery using a fast track clinical pathway. Eur J Cardiothorac Surg. 2008;34(1):174–80.
56. Fishman A, et al. A randomized trial comparing lung-volume–reduction surgery with medical therapy for severe emphysema. N Engl J Med. 2003;348(21):2059–73.
57. Naunheim KS, Wood DE, Krasna MJ, DeCamp MM, Ginsburg ME, McKenna RJ, et al. Predictors of operative mortality and cardiopulmonary morbidity in the National Emphysema Treatment Trial. J Thorac Cardiovasc Surg. 2006;131(1):43–53.

21 Anesthetic Challenges in Minimally Invasive Cardiac Surgery

Ahmed S. Awad, Kinjal M. Patel, Ronak G. Desai, and Ludmil Mitrev

Evolution of Minimally Invasive Cardiac Surgery

Interest in minimal-access surgery continues to grow in all surgical fields, including cardiac surgery, with a range of procedures using less invasive methods. A median sternotomy had been the conventional approach for all types of cardiac procedures, but minimally invasive cardiac surgery has proven to be a reliable alternative with short-term and long-term benefits [1–3]. According to the Society of Thoracic Surgeons, minimally invasive cardiac surgery (MICS) is "any procedure not performed with a full sternotomy and cardiopulmonary support" [4, 5].

MICS procedures discussed in this chapter include procedures that are performed via incisions smaller than a full sternotomy (Fig. 21.1) and, in some cases, without cardiopulmonary bypass (CPB), such as operations performed for coronary artery bypass and classic heart valve surgery.

A. S. Awad (✉)
Division Head Cardiothoracic Anesthesia, Department of Anesthesiology and Perioperative Medicine, Cooper University Hospital, Camden, NJ, USA

K. M. Patel · R. G. Desai · L. Mitrev
Department of Anesthesiology and Perioperative Medicine, Cooper University Hospital, Camden, NJ, USA
e-mail: Patel-kinjal@cooperhealth.edu

General Concepts for MICS

1. *Preoperative Challenges and Considerations*

   A thorough patient assessment is required before all cardiac surgery procedures. Additionally, the following assessments are required for those who may be candidates for MICS:

   (a) **Computed tomography (CT) of the thoracic cavity and abdomen with three-dimensional reconstruction**. CT will reveal chest anatomy and chest-wall abnormalities such as scoliosis, pectus carinatum, or pectus excavatum; adhesions from prior lung irradiation or thoracic cavity surgery; and the presence and extent of ascending aortic calcification. CT imaging of the iliofemoral vessels can identify the tortuosity and extent of calcification that may influence the site of arterial cannulation and cannula size, which are details needed for establishing CPB.

   (b) **Pulmonary function tests.** These assessments can identify patients with severe pulmonary disease who might not tolerate single-lung ventilation during surgery.

   (c) **Contraindications for transesophageal echocardiography (TEE).** Esophageal pathology that may contraindicate placement of TEE should be identified since the TEE exam is invaluable in many cardiac surgery cases.

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_21

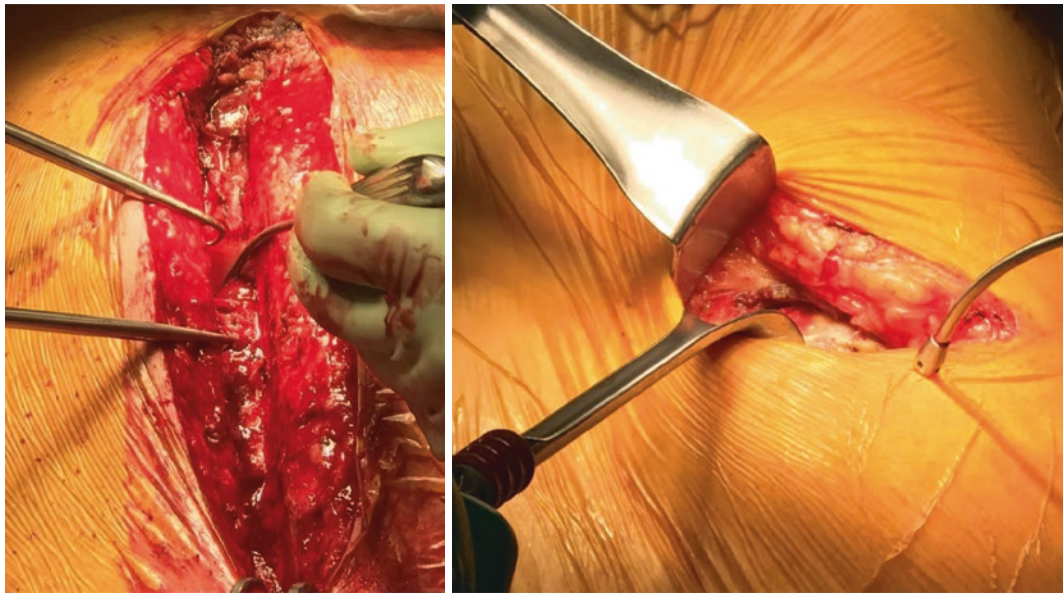


Fig. 21.1 Illustrations from an anesthesiologist's view of Left: traditional midline sternotomy and Right: an anterior mini-thoracotomy

2. *Monitoring*

MICS is conducted with standard American Society of Anesthesiologists (ASA) monitors, which include the five-lead electrocardiogram, capnograph, pulse oximetry, and core temperature, plus other monitoring:

(a) Urine output checked during MICS for volume (to assess adequacy of renal perfusion) and color (to evaluate for hemolysis)

(b) Neuromuscular blockade. Monitoring is vital since appropriate muscle relaxation is essential to avoid sudden patient movement during the procedure while stabilizers are in use or the robot is docked.

(c) Invasive monitoring: intra-arterial (pre-induction) and central venous access

(d) Pulmonary artery catheters with pacing capability. This capability is important in MICS for aortic valve replacement, when the surgeon has limited access to the right ventricle for temporary placement of epicardial wires.

(e) Neurologic monitoring: This includes, near-infrared spectroscopy based cerebral oximetry to monitor cerebral saturation, to provide early detection of a mal-positioned inflated endo-aortic occlusion balloon catheter (EAOBC), and processed electroencephalogram (e.g. bispectral index) for monitoring the depth of anesthesia.

(f) TEE: TEE is especially valuable in MICS because of the inherently limited access to the thorax and mediastinum which obstructs the surgeon's direct view of the heart [6].

(i) A pre-bypass TEE will help confirm the preoperative diagnosis.

(ii) If peripheral CPB is planned, TEE can guide the cannulation of the inferior vena cava, where the guidewire is visualized passing through the femoral vein to the inferior vena cava (IVC) to the right atrium and superior vena cava (SVC). A femoral venous bicaval cannula is inserted over the guidewire, and the distal end is positioned a few centimeters above the SVC- right atrium (RA) junction (Fig. 21.2).

TEE can also help guide the cannulation of the femoral artery: After surgical

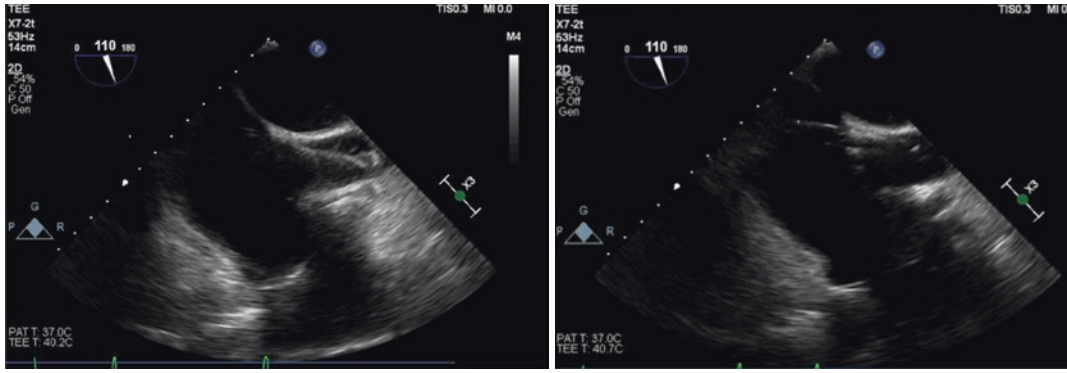


Fig. 21.2 TEE images. Left: midesophageal bicaval view with guide wire in the right atrium and SVC. Right: midesophageal bicaval view with femoral venous bicaval cannula positioned above the SVC-RA junction

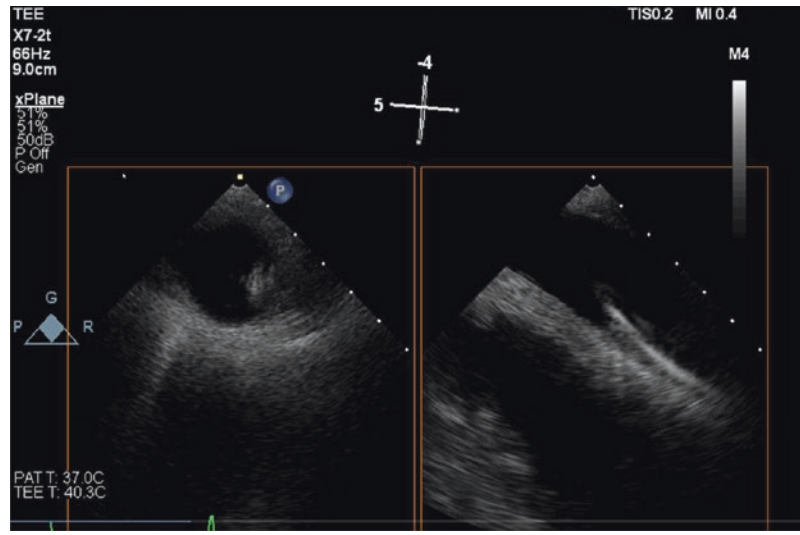


Fig. 21.3 TEE images: X plane of the midesophageal descending aorta in the short and long axis views documenting that the guidewire is in the lumen and not in the wall

exposure of the artery, a guidewire is introduced and passed into the descending aorta. Visual confirmation that the curled J-tip guidewire is in the lumen and not in the wall is needed prior to insertion of the femoral cannula to avoid aortic dissection.

This positioning of the guidewire is seen in short and long axis views of the midesophageal descending aorta (Fig. 21.3).

(g) When required, TEE also guides the placement of a coronary sinus catheter for retrograde delivery of cardioplegia. This is can be seen in the modified midesophageal bicaval view, where the tricuspid valve comes into view at 110–130°.

(h) TEE is used to guide the placement of the EAOBC (if utilized), and to continuously monitor the location of the inflated balloon during CPB and to detect possible migration of the balloon.

(i) TEE is essential for assessing the adequacy of venting and de-airing.

(j) TEE can detect new-onset abnormalities of the left ventricular regional wall motion, which is the basis of diagnosing myocardial ischemia.

(k) TEE also assesses volume status and function of the left and right ventricles, especially during CO2 insufflation.

(l) TEE assesses cardiac and valvular function and confirms a successful surgical procedure at the end of the operation.

(m) TEE is used to guide placement of an intra-aortic balloon pump if it is needed for weaning from CPB.

3. *Preparation for Surgery and Positioning of the Patient*

Most MICS procedures require that the patient be in the supine position, with modifications to maximize exposure of the surgical site. Further information regarding patient positioning will be described later in the chapter.

4. *Various Approaches and Incisions*

Approaches for minimally invasive coronary artery bypass graft surgery are illustrated in Fig. 21.4.

(a) Anterior lateral mini thoracotomy in the left fifth intercostal space. Length of the incision depends on the procedure type.

(b) Anterior lateral mini thoracotomy with smaller incisions for heart positioner and stabilizer

(c) Multiple smaller incisions for a robotic approach

Approaches for mini-aortic valve replacement (AVR): a 5–10-cm incision is usually required [7].

The two most common approaches are:

(a) Partial upper sternotomy with J-shaped extension into the right third or fourth interspace [8]

(b) Right anterior mini-thoracotomy incision in the second or third intercostal space

Less common approaches:

(a) Inverted T-shaped mini-sternotomy

(b) Right parasternal incision

(c) Trans-sternal incision

The most widely used incisions are illustrated in Fig. 21.5.

Approaches for mini-mitral valve replacement (MVR):

(a) Partial lower mini sternotomy

(b) Right parasternal incision

(c) Right mini-thoracotomy through the 3rd or 4th interspace

(d) Multiple smaller incisions for a robotic approach

The most widely used incisions are illustrated in Fig. 21.6.

5. *Anesthesia conduct*

Anesthesia for these procedures follows the same principles as for conventional cardiac anesthesia, but with differences. Distinct considerations are the need to maintain hemodynamic stability and allow for fast emergence from anesthesia with early tracheal extubation. Thus, a tailored balanced anesthesia technique with short-acting medications, rather than the commonly used high-dose opioid regimen, is recommended.

6. *Lung Isolation*

Single-lung ventilation during MICS in cases that involve entry into the thoracic cavity is essential for the surgeons' visualization of cardiac structures. A left-sided double-lumen endotracheal tube (DLT) or a bronchial blocker inserted through a single-lumen endotracheal tube can be used. Left-sided DLT may be the preferred option in cardiac opera-

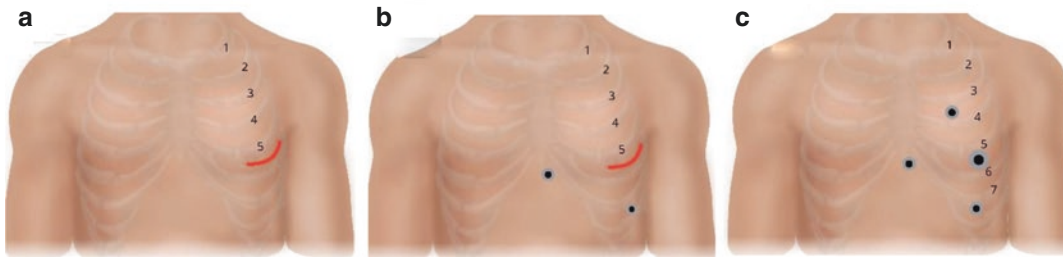


Fig. 21.4 Approaches for minimally invasive coronary artery bypass graft surgery. (**a**) Left anterior mini-thoracotomy. (**b**) Left anterior mini-thoracotomy with stabilizer ports. (**c**) Multiple smaller incisions for robotic ports

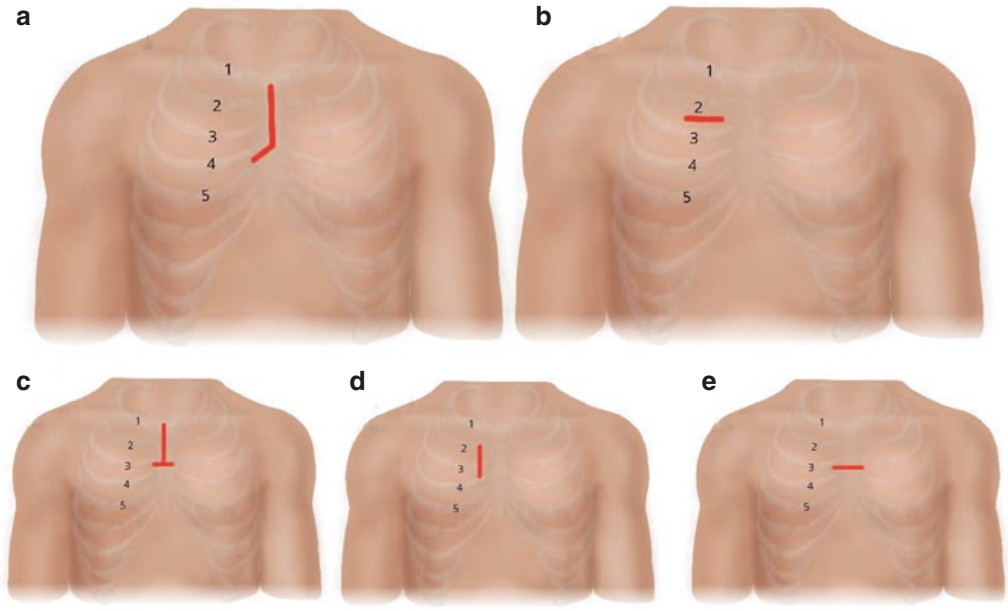


Fig. 21.5 Approaches for minimally invasive aortic valve surgery. The most widely used incisions are (**a**) Upper (J) mini-sternotomy. (**b**) Right anterior mini-thoracotomy. The less common incisions are (**c**) Inverted 'T' incision. (**d**) Right parasternal incision. (**e**) Transverse sternotomy

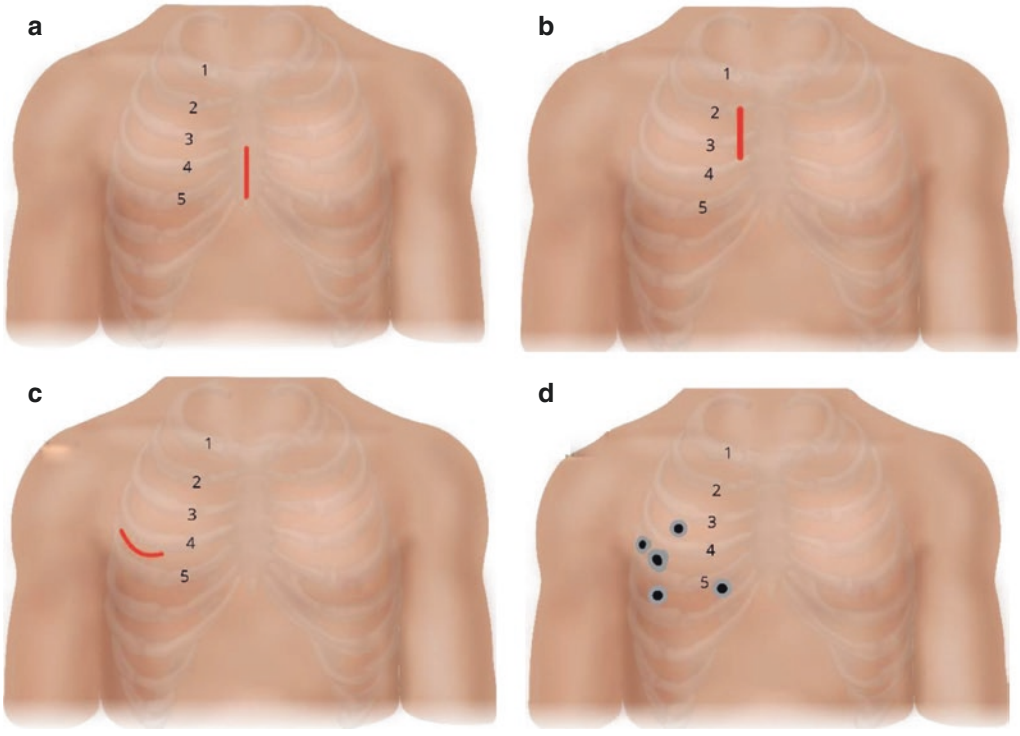


Fig. 21.6 Approaches for minimally invasive mitral valve surgery. The most widely used incisions are (**a**) Lower hemisternotomy. (**b**) Right parasternal incision (**c**) Right lateral mini thoracotomy. (**d**) Multiple smaller incisions for a robotic approach

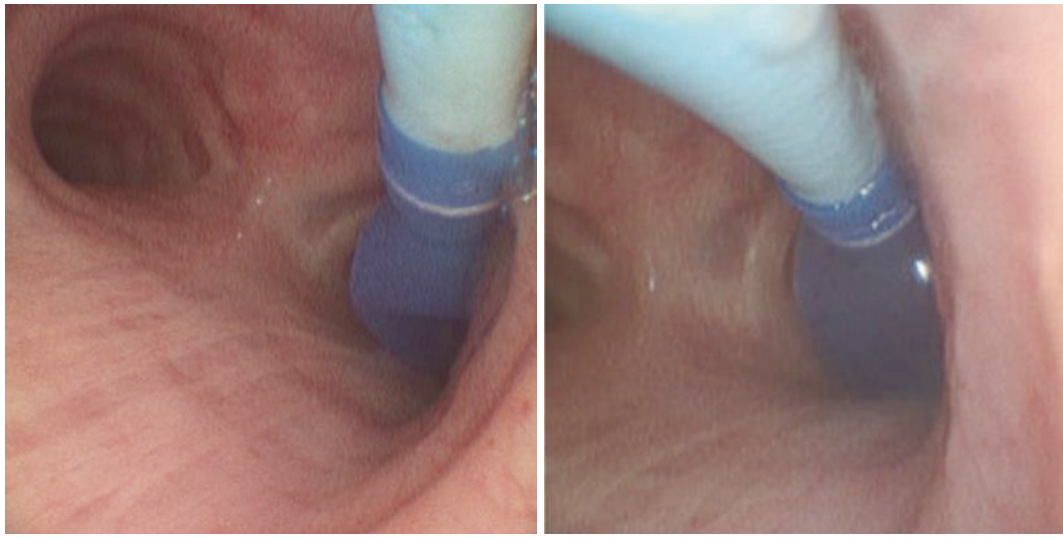


Fig. 21.7 Endobronchial blocker for single-lung ventilation with the balloon in the right main bronchus: Left: balloon not inflated. Right: balloon inflated

tions performed with a left mini-thoracotomy, since these operations tend to be of shorter duration and have less airway edema at the end, and positioning of the bronchial blocker may be more difficult as the left main bronchus is more acutely angulated. On the other hand, for cardiac operations with a right mini-thoracotomy, where right lung deflation is needed, a bronchial blocker may be the choice of preference, as it is easier to position and has a lower incidence of sore throat and vocal cord injuries (Fig. 21.7).

In addition, these right mini-thoracotomy MICS operations tend to be longer and associated with more airway edema, so avoiding tube exchange at the end of the procedure is desirable.

Four types of endobronchial blockers are commercially available: Rusch® EZ-Blocker™, Arndt® wire-guided blocker, Cohen Flexi-tip BB (Cook Critical Care), and Fuji Uni-blocker (Fuji Systems, Tokyo).

7. *Pain Management*

To aid in the early recovery from MICS, the use of opioids should be minimized. As such, regional anesthesia techniques can be used to decrease the need for intraoperative and postoperative opioid consumption:

(a) Single-shot, multilevel intercostal nerve block with long-acting bupivacaine (EXPAREL) injected by the surgeon.
(b) Paravertebral (T2–T3) block is an effective option to aid in early emergence and extubation.
(c) Erector Spinae Plane (ESP) block or continuous catheter can provide excellent analgesia for unilateral chest wall incisions.
(d) Ultrasound-guided serratus anterior plane block (SAPB) can help anesthetize lateral cutaneous branches of intercostal nerves that provide sensation to chest wall incisions.

8. Early Extubation and Fast-Track Management

The invasive nature of cardiac surgery is associated with significant morbidity, especially surgical access-site complications. MICS was developed to minimize these complications and permit early extubation and post-operative fast-track recovery. The potential benefits to a fast-track approach in MICS includes:

(a) fewer ventilator-associated complications (accidental extubation, mucus plugging of the endotracheal tube, pulmonary barotrauma, and ventilator-associated pneumonia)

(b) reduced requirements for sedation in the ICU
(c) early patient mobilization
(d) early ICU discharge
(e) reduced hospital length of stay
(f) lower cost

The Spectrum of Minimally Invasive Techniques

Minimally Invasive Coronary Revascularization Coronary Artery Bypass Graft (CABG)

Various surgical approaches for minimally invasive CABG, which have similar short and long-term postoperative mortality and morbidity, are used. These revascularization strategies include approaches via small thoracotomy incisions (to "preserve sternal integrity") with or without the use of CPB (Fig. 21.8).

Examples of some of the methods are:

- **Off-pump CABG with median sternotomy** [9, 10]. In this approach, CPB and cardioplegic arrest are avoided. Thus, blood elements do not contact the foreign surfaces of the CPB circuit, which could trigger the systemic inflammatory response. Also, deliberate hypothermia while on CPB, and the subsequent risk of post-operative coagulopathy are avoided. Lastly, this approach avoids cannulation of the aorta, which might result in aortic injury (Fig. 21.9).

Anesthetic Challenges of OPCAB

- Off-pump CABG (OPCAB) is a minimally invasive alternative to conventional CABG with CPB, especially for high-risk patients with multiple comorbidities.
- Maintaining myocardial oxygen supply-demand equilibrium to prevent myocar-

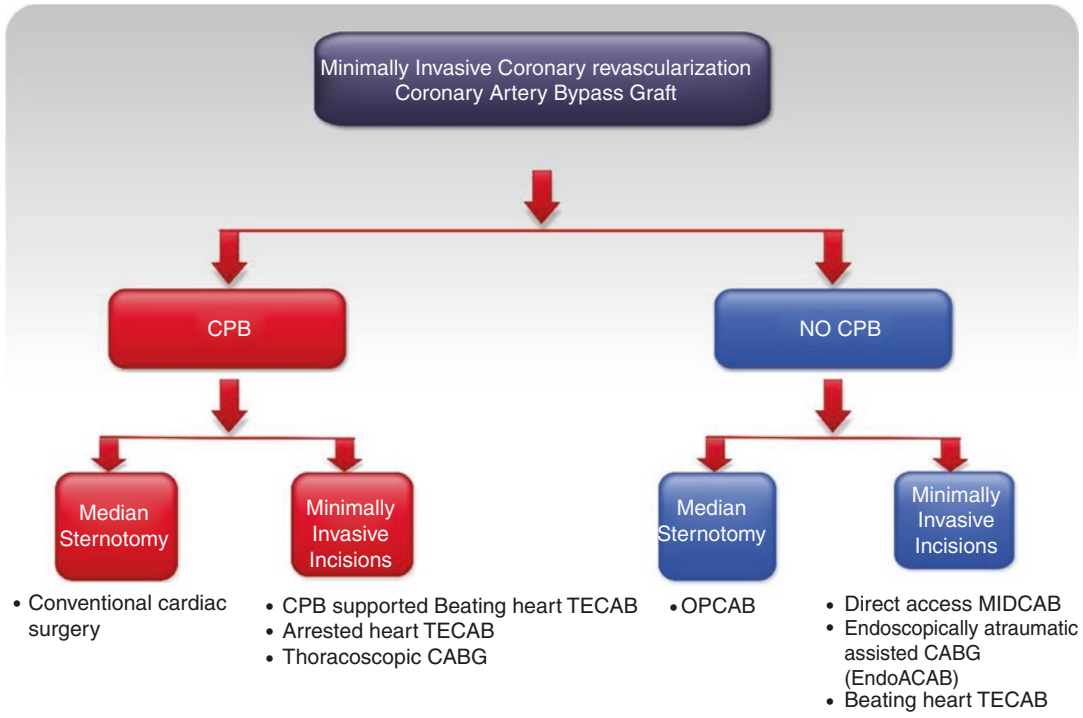


Fig. 21.8 Minimally invasive approaches for coronary revascularization (coronary artery bypass graft [CABG])

dial ischemia during induction of anesthesia and the period prior to revascularization is a priority during these cases.

- The major anesthetic challenge is the maintenance of hemodynamic stability during cardiac manipulation and from ischemia during distal anastomosis. Hemodynamic stability may be achieved with fluid volume administration and, if needed, vasopressor support.
- Diligent ECG monitoring of arrhythmias that may develop as a result of insufflation of air into the distal anastomosis is of paramount importance. Rapid intervention will prevent emergency conversion to an on-pump CPB. Bradycardia often occurs during right coronary artery grafting, which is treatable with ventricular pacing.
- Monitoring for myocardial ischemia during graft anastomosis is essential. Typically, some degree of new onset ST-segment changes (depression or elevation) occurs. Thus, TEE examination for regional wall motion abnormalities is vital; treatment with nitroglycerin may be indicated.
- Ischemia, heart positioning, or both, may lead to worsening mitral regurgitation [11, 12], which may further contribute to hemodynamic instability. Mitral regurgitation is usually easily seen on TEE and is treated by decreasing the stabilizer pressure or adjusting the heart position.
- Maintaining normothermia is a challenge due to the extensive exposure of the body to atmospheric temperature required and the limited body-surface area available for active warming. Preventive or corrective measures include continuous warming of intravenous fluids, raising the operating room temperature, and using an underbody heating blanket.

- **Minimally invasive direct coronary artery bypass (MIDCAB)** [13] is performed through a small left anterolateral mini-thoracotomy without CPB and cardioplegic arrest. The left internal mammary artery is harvested under direct vision (Fig. 21.10). With a stabilizer on the beating heart, this artery is anastomosed to the left anterior descending coronary or diagonal artery. MIDCAB was introduced in the 1990s, but it fell out of favor because of concerns over post-thoracotomy pain from rib-spreading and chest-wall retraction. With newer, improved rib spreaders and chest retractors, interest in MIDCAB is rising again.
- **Thoracoscopic MIDCAB, also referred to as endoscopically atraumatic assisted CABG (EndoACAB)**

  In this approach, thoracoscopy is combined with a mini-thoracotomy to minimize chest-wall retraction and rib-spreading [14]. The procedure was developed as an alternative to robotic- assisted CABG to avoid the high cost of robotics. The left internal mammary artery is harvested using thoracoscopy via a small-access port, and the vessel is anastomosed to the left anterior descending artery of the beating heart through a mini-thoracotomy.
- **Minimally Invasive Multivessel Coronary Artery Bypass Grafting (MICS CABG), also known as Multivessel Small Thoracotomies (MVST)**

  This operation is a multivessel operation that accomplishes complete revascularization, mainly, all-arterial, for the treatment of multivessel disease. The incision for the mini thoracotomy is made more laterally than for MIDCAB, in the left fifth intercostal space, to allow rib spreading without rib injury. This incision allows harvesting of the entire length of the left internal mammary artery and the right internal mammary artery under direct visualization and making multiple proximal aortic anastomoses possible using an anastomotic device, e.g. Heartstring. It also utilizestwo port-site incisions: one access-port incision in the left 7th intercostal space for

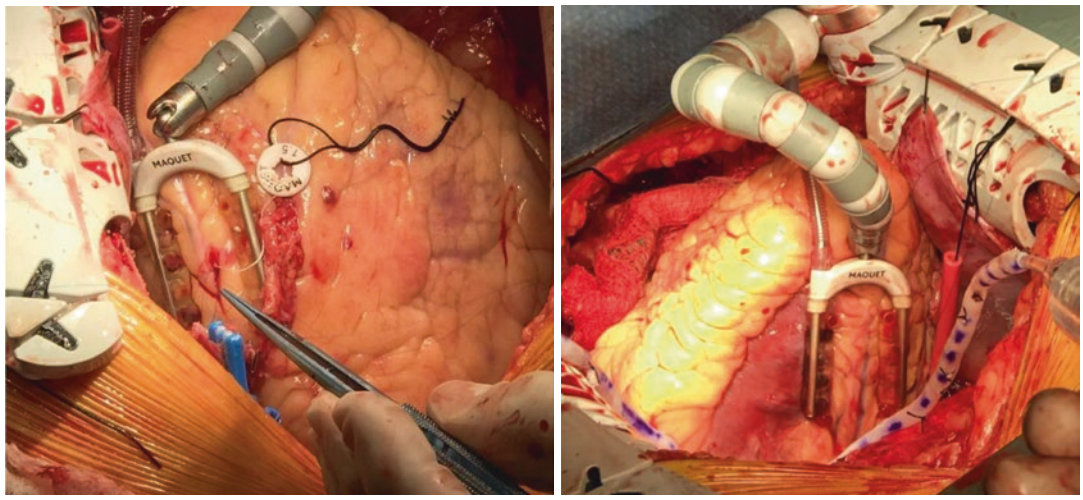


Fig. 21.9 Images of anesthesiologist's view showing distal coronary anastomoses using Octopus stabilization device for off-pump coronary artery bypass

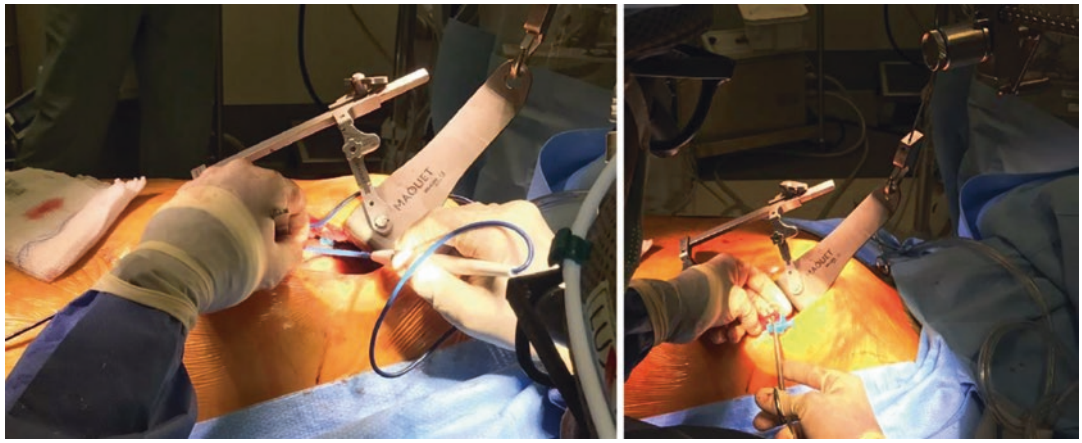


Fig. 21.10 Images of Surgeon's view showing small left anterolateral mini-thoracotomy and the left internal mammary artery is harvested under direct vision

the epicardial stabilizer and another access-port incision for the apical positioner in the subxiphoid (Fig. 21.11). MICS CABG is usually performed on a beating heart [15, 16]. Other variations of multivessel minimally invasive techniques for CABG have been described. An earlier technique to MICS CABG, called the anterolateral thoracotomy/coronary artery bypass (ALT-CAB), used a generous anterolateral thoracotomy incision without the two port-site incisions [17]. Another technique is the bilateral MIDCAB-based approach, which involves bilateral anterior mini-thoracotomies.

- **Totally endoscopic CABG (TECAB) and robotic-assisted CABG.**

  Robotic-assisted CABG is the most technically advanced of these procedures because of the high-quality imaging and magnification afforded by the robot camera, coupled with improved range of motion by the robotic instruments. However, it has significant costs and the longest learning curve. The Da Vinci system (Intuitive Surgical, Mountain View,

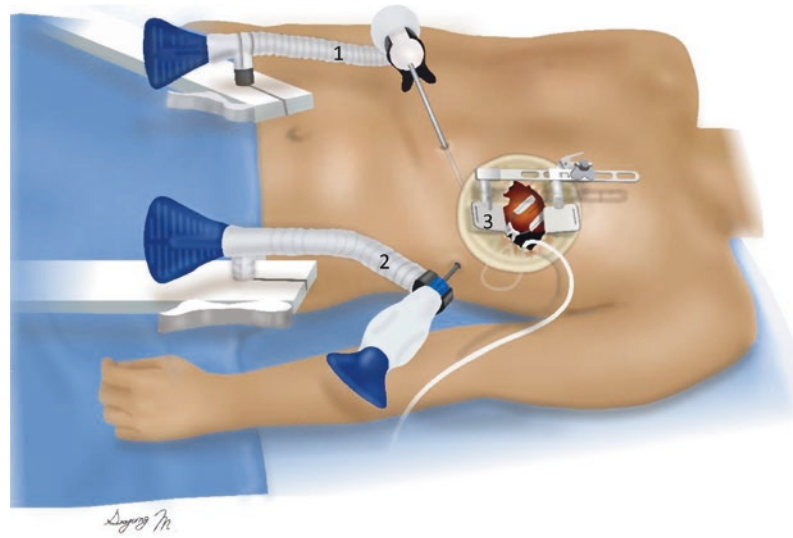


Fig. 21.11 Minimally invasive multivessel CABG with application of minimally invasive stabilizers. (1) Starfish non-sternotomy heart positioner; (2) Octopus Nuvo tissue stabilizer; (3) minimally invasive retractor system

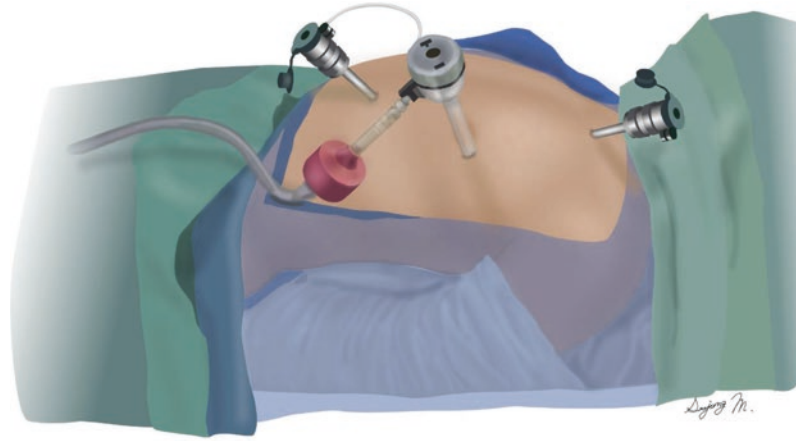


Fig. 21.12 Totally endoscopic CABG with arm positioning and port placement during TECAB

CA) is commercially available and consists of a surgeon console that remotely manipulates micro instruments in a precise fashion. A camera port and two instrument ports are inserted into the patient's left chest to accommodate the robotic arms (Fig. 21.12).

A fourth arm is added to the newer generation da Vinci Surgical System, which can be used to insert endostabilizers, thus facilitating off-pump or on-pump anastomoses. The surgical instruments are attached to the docked robotic arms. Robotic-assisted CABG [18] is performed in various ways, including robotic-assisted MIDCAB, in which the left internal mammary artery is harvested with a robot via a port, and the vessel is anastomosed to the target coronaries through a mini-thoracotomy. Total endoscopic CABG (TECAB) is achieved when the entire coronary revascularization is performed endoscopically, using robotically-enhanced telemanipulation [19, 20]. TECAB can be performed as an arrested heart TECAB, beating heart TECAB with CPB, or beating heart TECAB without CPB.

– *TECAB on the arrested heart (AH-TECAB).*
– Arresting the heart for TECAB provides a bloodless, motionless flaccid heart to facilitate endoscopic suturing of the anastomosis. The innovative endovascular catheter system allows femoral arterial retrograde perfusion with peripheral CPB established in the groin via the common femoral artery and

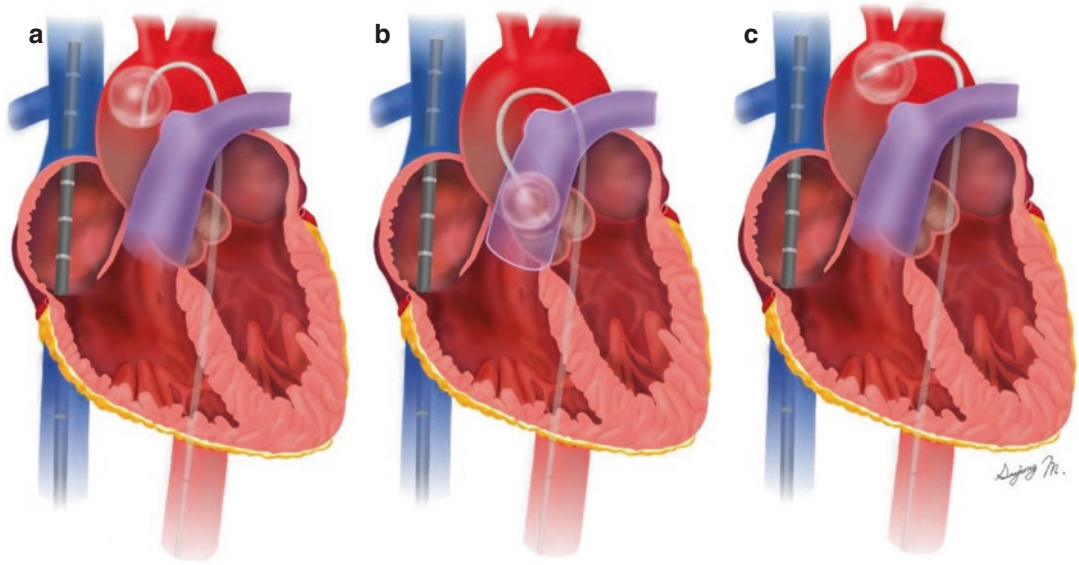


Fig. 21.13 Endoaortic occlusion balloon catheter positioning leading to aortic cross-clamp. (**a**), correct balloon position. (**b**), proximal migration. (**c**), distal migration

vein cannulation. A balloon-tipped catheter, called the endoaortic occlusion balloon clamp, is inserted into the femoral artery and advanced into the ascending aorta distal to the coronaries and proximal to the origin of the arch vessels [21]. The balloon clamp provides aortic occlusion, antegrade perfusion through the distal channel into the aortic root, and venting of the left heart through the same channel (Fig. 21.13).

- TECAB on the beating heart with CPB support (pump-assisted BH-TECAB).
- The advantages of using CPB assist in BH-TECAB is the optimal surgical exposure created by deflation of both lungs. The deflation reduces technical difficulties by unloading the heart, and CPB provides safety in case of the development of ventricular fibrillation when the robot arms are docked, as resuscitation and emergent femoral cannulation are extremely difficult in this situation.
- TECAB on the beating heart without CPB (BH-TECAB).

  Beating heart TECAB should be considered when the transfemoral approach for CPB cannulation is not feasible due to aortoiliac atherosclerosis or small vessel caliber, both of which make insertion of the EAOBC hazardous. The benefits of avoiding CPB are as mentioned earlier. The development of several new technologies have enabled implementation of CBP-free approaches: the addition of a fourth arm to the DaVinci S ™ robotic system; the new endoscopic coronary stabilizer (the Intuitive Endo-wrist™ stabilizer); and the automated distal anastomotic devices that establish anastomosis without disrupting blood flow through the target coronary vessel.

Surgical Technique for Sternal-Sparing Minimally Invasive Coronary Revascularization

The standard anesthesia workflow for sternal sparing minimally invasive coronary revascularization is as follows:

1. Moving the patient to the operating room table; placement of R2 defibrillation pads in a location that avoids the surgical site; place-

ment of all ASA monitors; and placement of an arterial line, if not already placed in the surgical holding area.

2. Induction of anesthesia; securing the airway with DLT or bronchial blocker; and confirmation of proper position of the DLT or bronchial blocker via fiberoptic bronchoscopy.
3. Next, a TEE probe is inserted into the esophagus. A double-lumen central venous catheter is inserted into the right internal jugular vein. If percutaneous CPB and an arrested heart is planned, a second arterial line is inserted into the contralateral radial artery. Also, an EndoVent pulmonary catheter (Edwards Lifesciences, Irvine, CA) and percutaneous retrograde coronary sinus catheter are needed. These catheters are usually inserted and positioned under visualization with TEE and fluoroscopic guidance.
4. The patient is positioned according to the type of approach, usually at 30° right lateral decubitus, with a small roll below the scapula and the left arm either posteriorly placed at the patient's side or elevated over the head with an arm support. The right arm is either tucked or extended for radial artery harvesting.
5. The surgical skin is prepped and draped as for open CABG, in case conversion to an open operation is needed.
6. Then surgery is initiated and single-lung ventilation with CO_2 insufflation is started.

   Depending on the approach, the following steps may be taken:

   (a) A mini thoracotomy incision is made with a retractor placed, and the left internal mammary and, possibly, the right internal mammary artery are harvested. After the grafts are optimized for anastomosis, heparin is administered. The necessary anastomoses are made.

   (b) TECAB. After the camera port is placed, single-lung ventilation and CO2 insufflation (to allow for adequate intra-thoracic space), are initiated. Instrument ports are inserted under camera vision. The robot is docked, and grafts are harvested. Heparin is injected, and the robotic endostabilizers are positioned for distal anastomosis.

   (c) If peripheral CPB is planned, heparin is administered after the grafts are harvested. TEE guides arterial and venous cannulation. CPB is started, and the EAOBC is inflated, serving as an aortic cross clamp. The heart is arrested by infusion of cardioplegia to the aortic root via the distal channel in the EAOBC. The necessary anastomoses are made, and CPB is weaned.
7. The incisions are closed, and in cases utilizing a DLT, the airway is changed to a single-lumen endotracheal tube. In uncomplicated cases where appropriate levels of anesthesia, narcotic and neuromuscular blockers have been utilized, early extubation in the OR may be considered.
8. The patient is brought to the intensive care unit.

Anesthetic Challenges for MIDCAB, EndoACAB, MICS CABG, and TECAB

- Due to the complexity of these operations, communication with the cardiac surgeon is crucial, especially for: timing for one-lung ventilation; level of CO2 insufflation pressure; heparin administration; detecting and correcting malposition of the endoballoon in femoro-femoral CPB; detecting and correcting regional wall-motion abnormalities in the beating-heart approach.
- The major anesthetic challenge is the development of hemodynamic instability after initiation of single-lung ventilation, which is intensified when intrathoracic insufflation of carbon dioxide is used. The instability can result in hypoxia, progressive hypercarbia, pulmonary hypertension, hypoxic pulmonary vasoconstriction, decreased venous return, and increased right ventricular strain, with significant reduction in cardiac index. Positive end expiratory pressure on the ventilated lung, to bring the aorta into surgical view, can further

decrease venous return. Interventions to minimize hemodynamic compromise are prompt administration of intravenous fluid boluses, infusion of vasopressors, and limiting carbon dioxide insufflation pressure to <10 mmHg.

- R2 defibrillation pads are placed on the patient during the pre-induction period. Sterile defibrillator pads are available and may be used after prepping to avoid surgical sites.
- The most common reason for failure of lung isolation with a DLT is failure to recognize the true carina. The true carina can be confirmed with visualization of the trifurcation of the right upper lobe bronchus from the right main bronchus, "the only place that has three orifices." Corrective measures for this problem are withdrawal of the DLT after the tracheal cuff is deflated, guiding the endobronchial lumen of the DLT over the fiberoptic bronchoscope into the left main bronchus, then switching the bronchoscope into the tracheal lumen and observing for inflation of the bronchial cuff at the rim of left main bronchus. The most common reason for failure of lung isolation with a bronchial blocker is dislodgement (herniation) of the balloon; repositioning with the help of the bronchoscope, usually solves the problem. An uncommon reason for failure with a bronchial blocker is origination of the right upper lobe directly from the supracarinal trachea. In this circumstance, using two separate bronchial blockers has isolated the lung successfully [22, 23]
- Unilateral re-expansion pulmonary edema that sometimes develops in single-lung ventilation procedures can be prevented by administering neutrophil elastase inhibitor by intravenous infusion at 0.2–0.25 mg/kg/h from the beginning of anesthesia until the patient is extubated in the postoperative period [24] and by starting two-lung ventilation prior to weaning off CPB.
- Diligent monitoring for ventricular arrhythmias is imperative. Management of ventricular fibrillation in these procedures is challenging: internal defibrillation is not feasible and external defibrillation is less effective, as R2 defibrillation pads are often not placed in an optimal position and insufflated CO_2 attenuates the defibrillation electric current. In addition, chest compressions in BH-TECAB are difficult to perform until the robot is undocked. Lidocaine or amiodarone infusions have been described to lessen the risks of developing VF.
- Bilateral radial arterial lines are required to monitor arterial blood pressure proximal and distal to the EAOBC balloon in on-pump cases where an EAOBC clamp is used. Bilateral arterial lines will help in recognizing dislodgement of the inflated balloon resulting in occlusion of the innominate artery.
- Another challenge for the anesthesia provider in TECAB cases is loss of access to the patient airway after turning the bed to facilitate robot docking.
- Peripheral CPB increases the risk of aortic dissection and cerebral embolization, so confirmation that the guidewire is intraluminal with TEE is critical.
- Accurate placement of the percutaneous retrograde coronary sinus cardioplegia catheter is achieved by using TEE and fluoroscopic guidance.
- For on-pump cases, a bolus of intravenous adenosine will facilitate a rapid cardiac arrest.
- Another challenge for the anesthesiologist in these procedures is changing the DLT to a single lumen endotracheal tube at the end of surgery, when the tongue and upper airway are edematous

and the patient is coagulopathic. The use of video laryngoscopy and two airway exchanger catheters, one in each limb, provides a safe way to change tubes under direct vision.

- Monitoring for myocardial ischemia in these cases is not optimal, given that some of the ECG leads are placed more posteriorly to avoid the operative site of the chest.

Minimally Invasive Mitral Valve Surgery (MIMVS)

1. *Mitral Valve Anatomy* [25]

   The mitral valve apparatus is a complex structure comprising the following:
   (a) Mitral annulus
   (b) Anterior and posterior mitral valve leaflets
   (c) Chordae tendineae
   (d) Papillary muscles
   (e) Wall of the left ventricle
2. *Patient selection and contraindications* [26]

   Patients for MIMVS must be selected judiciously. Suitability is evaluated on an individual basis. Contraindications for MIMVS include:
   (a) Significant aortic root dilation
   (b) Poor lung function or severe pulmonary hypertension that prevent tolerability of single-lung ventilation
   (c) Aortoiliac atherosclerotic disease or a tortuous descending aorta that prevents peripheral arterial cannulation
   (d) Severe aortic valve regurgitation causing difficulties in arresting the heart with antegrade cardioplegia
   (e) Prior pneumonectomy
   (f) Severe circumferential mitral annular calcification
3. *The surgical procedure main events* [27–30] *for MIMVS are these:*
   (a) *Intraoperative Monitoring and Lines:* Moving the patient to the operating room table; placement of R2 defibrillation pads avoid the surgical site; placement of all ASA monitors; and placement of an arterial line, if not already placed in the surgical holding area.
   (b) *Anesthesia Conduct:* Induction of anesthesia; securing the airway with DLT or bronchial blocker; and confirmation of proper position of the DLT or bronchial blocker via fiberoptic bronchoscopy.
   (c) *TEE:* A TEE probe is inserted into the esophagus, and a double-lumen central venous line is inserted into the right internal jugular vein.
   (d) *Positioning:* The patient is positioned supine close to the edge of the right side of the operating table. The right side of the chest is elevated 30°, with a small roll placed inferior to the scapula, and the right arm is slightly flexed and positioned safely behind the posterior axillary line and supported by the table at the side. The left arm is tucked, with pressure points padded. The operating table usually is tilted to the left (Fig. 21.14).
   (e) *Skin prepping and draping:* This should be done in the usual manner, with large

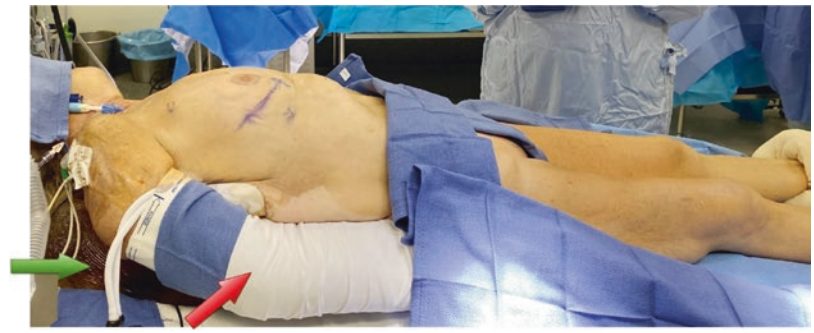


Fig. 21.14 Patient positioned and marked for MIMVS prior to surgery. Notice: a small roll placed inferior to the scapula (green arrow), and the right arm is slightly flexed (red arrow)

exposure to the operating site covering the right side of the chest, sternum, and both groins.

(f) *Incision and exposure:* Types of incisions have been mentioned earlier in the general concepts section. Depending on visualization, there are three different categories:

(i) Direct vision through the mini incision. The current trend is to use a right mini-thoracotomy in the inframammary fold and through the 4th or 5th intercostal space lateral to the anterior axillary line, thus preserving sternal integrity. An example of this exposure and mitral valve repair is shown in Fig. 21.15.

(ii) Direct vision with 2D endoscopic video-assistance. This includes the right mini-thoracotomy and three small incisions: one for insertion of the thoracoscope via the second intercostal space; one entry site for the left atrial retractor; and one for insertion of a Chitwood transthoracic aortic cross-clamp (Scanlan International, Minneapolis, MN) in the third intercostal space. An external flexible aortic cross-clamp can be used instead of the transthoracic clamp (Fig. 21.16).

(iii) 3D Robot-assisted MIMVS through multiple smaller port incisions. A camera port is placed in the 4th inter-

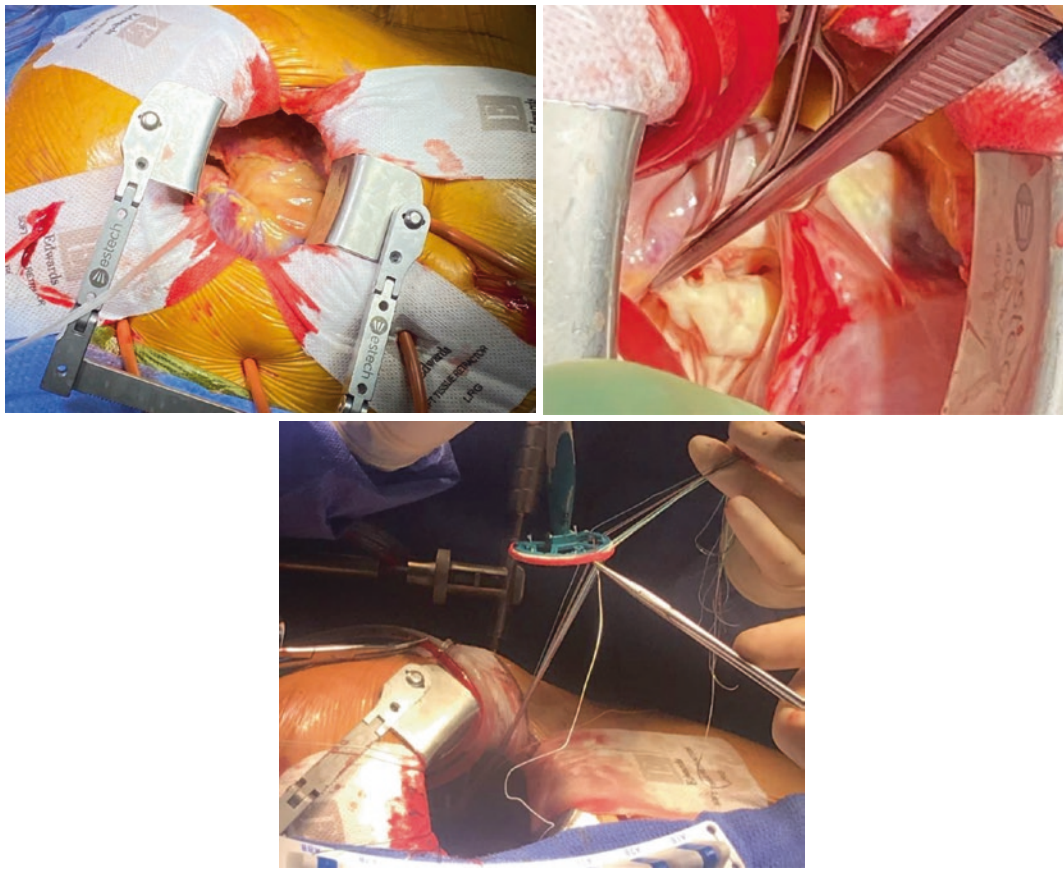


Fig. 21.15 Surgeon's view. Top Left: right mini-thoracotomy incision with soft-tissue retractor and metal retractor system in place, exposing the right atrium. Top Right: mitral valve exposed, showing two rupture chordae of the posterior leaflet (forceps). Bottom: suturing annuloplasty mitral ring

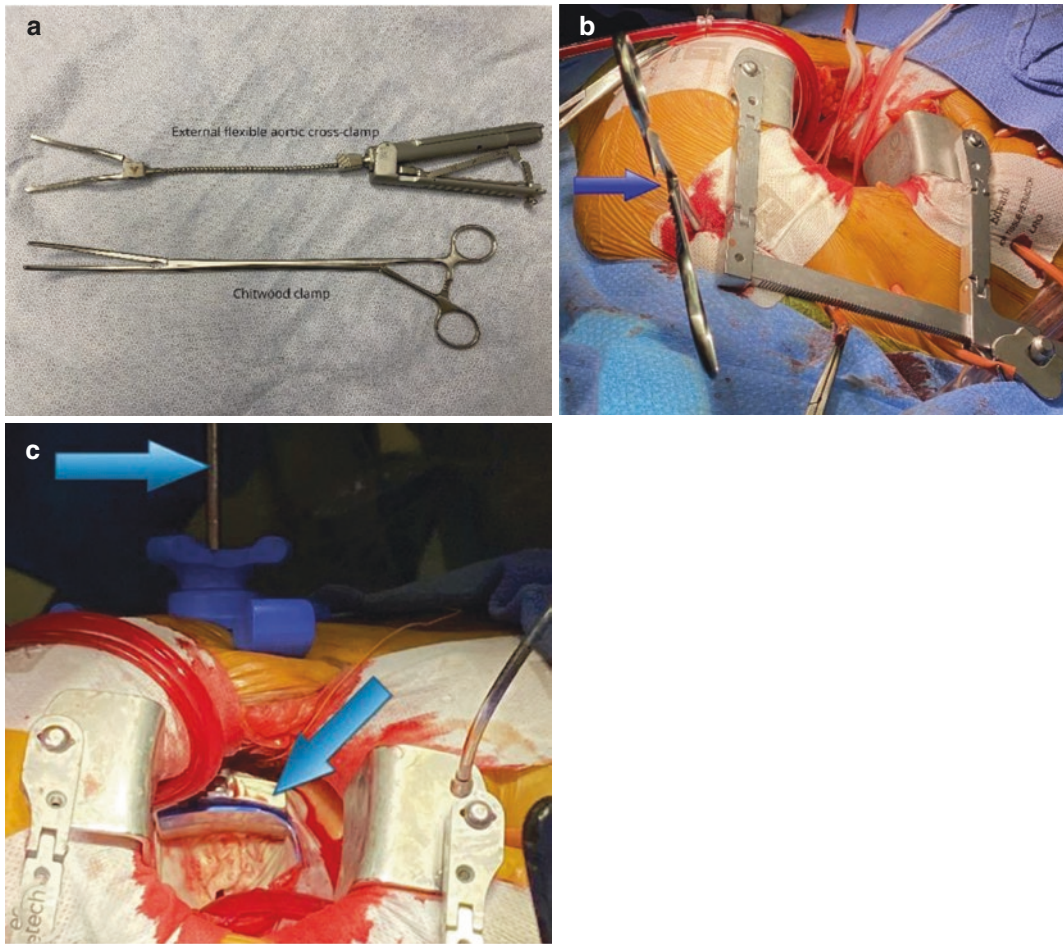


Fig. 21.16 (**a**) Top: External flexible aortic cross-clamp. Bottom: Chitwood transthoracic aortic cross-clamp (**b**) Surgeon's view Chitwood transthoracic aortic cross-clamp in place (blue arrow) with a different stab, (**c**) left atria retractor (blue arrows) through a separate stab incision for placement

costal space at the anterior axillary line; a left atrial retractor arm is placed in the 5th intercostal space medial to the midclavicular line; the left robotic arm is in the 3rd intercostal space at the midaxillary line; the working port in the 4th intercostal space lateral to the camera port; and the right robotic arm in the 5th intercostal space lateral to the anterior axillary line. If use of an aortic endoballoon is contraindicated, a Chitwood transthoracic aortic cross-clamp is inserted via an entry-site incision in the third intercostal space (Fig. 21.17).

(g) *Cardiopulmonary Perfusion:* Several cannulation approaches are available, ranging from standard aorto-bicaval cannulation directly through the surgical incision to complete peripheral femoro-femoral cannulation [31, 32]. Central aortic cannulation may be accomplished after the surgical field is exposed. Following systemic heparinization, the distal ascending aorta is cannulated with a flexible non-kinking aortic cannula. A bicaval venous cannula and antegrade cardioplegia catheter are also inserted through the mini thoracotomy incision (Fig. 21.18). Peripheral cardiopulmonary perfusion is established to avoid placing

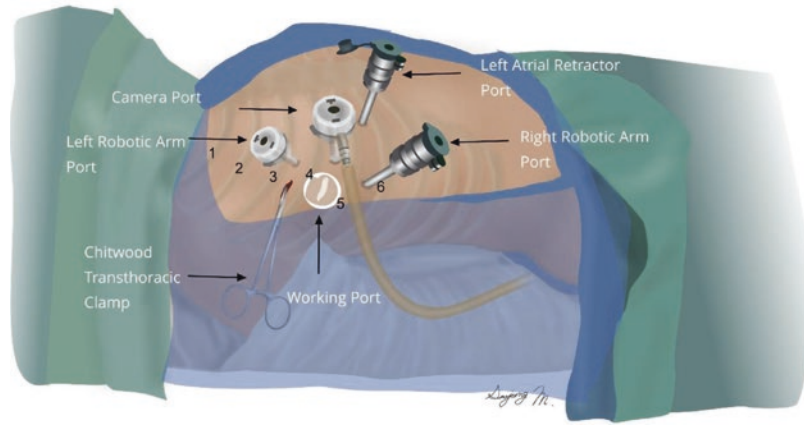


Fig. 21.17 Robotic mitral valve port placement

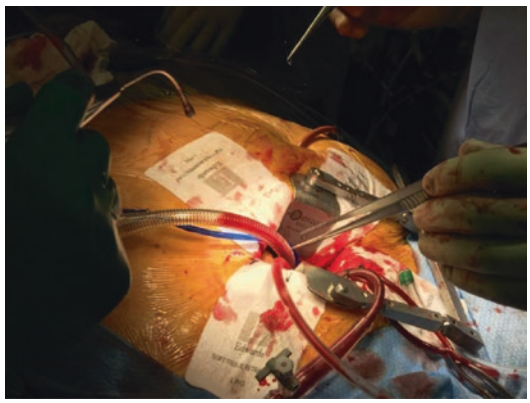


Fig. 21.18 Anesthesiologist's view of a centrally cannulating CPB circuit through mini thoracotomy incision

cannulas through a small incision, which could compromise working space and limit visibility. Perfusion is accomplished via retrograde femoral arterial perfusion through a small incision in the groin. Venous drainage is accomplished with a long multiport femoral venous cannula with vacuum assistance of −40 mmHg, which enables adequate venous drainage through a small cannula. Modern wire-reinforced cannulae tend to have excellent flow properties, since their inner diameter is larger relative to their outer diameter. The femoral venous cannula is inserted through the same groin incision and positioned into the SVC. An open peripheral femoro-femoral cannulation is the most-often used technique for CPB in MIMVS (Fig. 21.19).

(h) *Aortic Cross-Clamping:* Multiple options are available for aortic cross-clamping, including an endoaortic occlusion balloon catheter (Edwards Lifesciences, Irvine, CA) or by direct aortic clamping. The aorta can be directly clamped with a Chitwood transthoracic aortic cross-clamp, applied through a separate small third intercostal space incision, or with an external flexible aortic cross-clamp applied through a mini-thoracotomy incision (Fig. 21.16).

(i) *Myocardial Protection and cardioplegia administration:* Several techniques for myocardial protection have been described [33]. Antegrade cardioplegia can be achieved in the usual fashion with a combined Y-shape cardioplegia/aortic vent long catheter placed into the ascending aorta through the mini incision, or through a separate stab wound into the second or third intercostal space. Single-shot antegrade cardioplegia can be administered via a long needle directly in the aortic root. Antegrade cardioplegia can be also delivered through the EAOBC. In the case of aortic regurgitation, retrograde cardioplegia can be delivered through a percutaneous coronary sinus catheter via the internal jugular vein placed by the anesthesiologist or directly into the right atrium by the surgeon.

(j) *Mitral Valve Exposure:* The mitral valve is exposed by a left atriotomy through a transseptal incision and then applying a

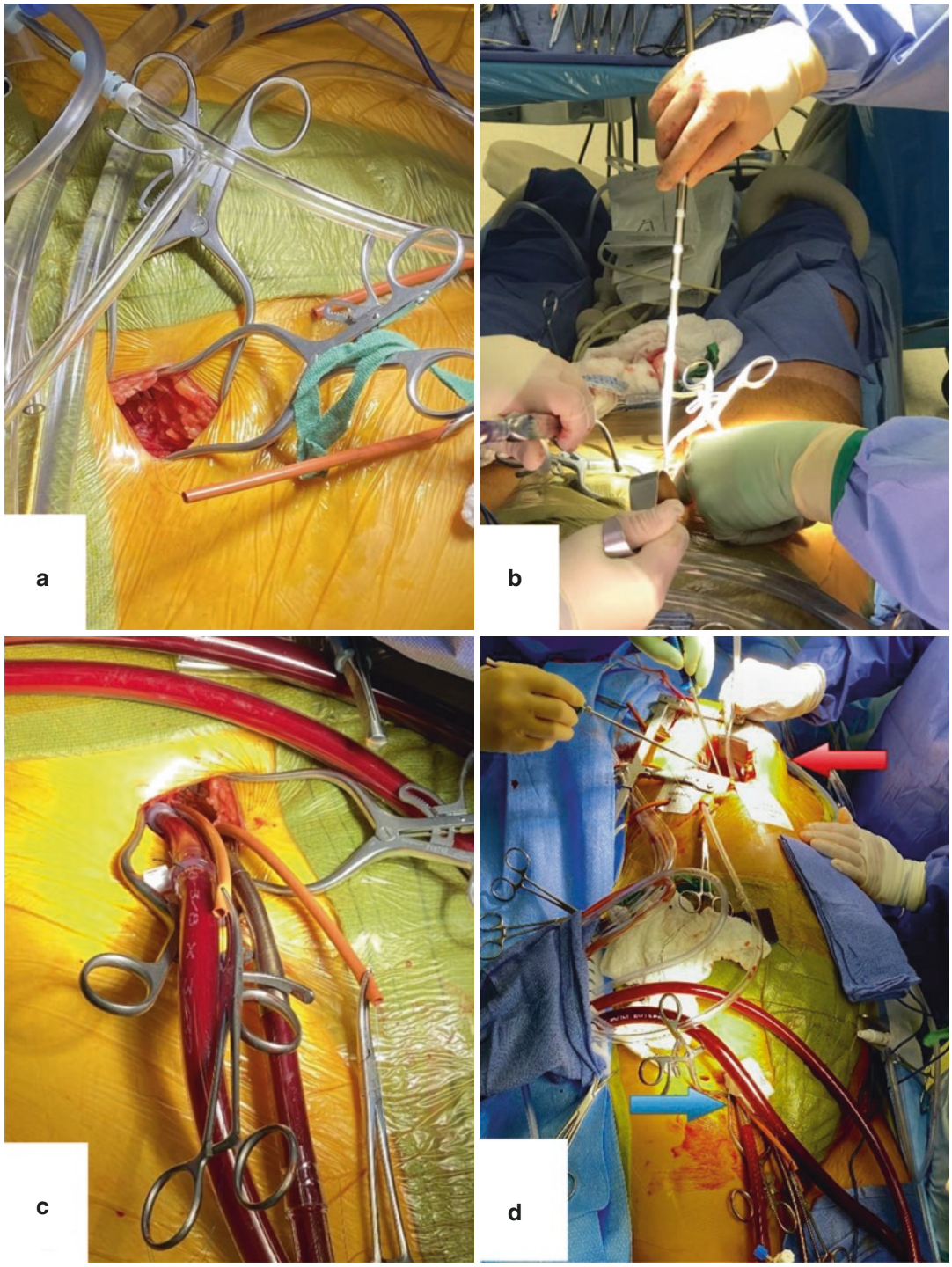


Fig. 21.19 Steps for achieving peripheral CPB circuit. (**a**) A small groin incision exposes the femoral artery and vein. (**b**) Femoral venous cannula is advanced over a guidewire in the right groin. (**c**) The right femoral artery and vein are cannulated. (**d**) Femoro-femoral bypass (blue arrow) and mini thoracotomy incision for MIMVS (red arrow)

self-retaining left atrial retractor to pull in the anterior wall of left atrium and the septum. The retractor is manually adjusted to ensure an unobstructed view of the mitral valve. Thereafter, traditional mitral valve replacement or repair techniques are used.

(k) *De-airing, Decannulation, and Closure:* After the mitral valve procedure is completed, the atrial wall and septum are closed. A temporary epicardial pacing wire is then placed on the right ventricle, followed by placing the patient in the Trendelenburg position and removing the aortic cross-clamp. De-airing of the heart is achieved by applying suction in the aortic root vent, insufflating CO_2 throughout the operation, initiating antegrade cardioplegia, and filling the left ventricle. TEE guides the de-airing process. Next, the patient is weaned from CPB. TEE is performed to check adequacy of the mitral valve procedure, absence of iatrogenic aortic regurgitation, and for assessment of ventricular function. Decannulation and protamine administration are conducted in a standard fashion.

Minimally Invasive Aortic Valve Replacement (MIAVR) [34–37]

1. *Aortic Valve Anatomy*

   The aortic valve apparatus is a complex structure composed of:
   (a) Aortic annulus at ventriculoaortic junction
   (b) The aortic root, which is made up of
      (i) three semilunar cusps, the left coronary, right coronary and non-coronary cusps
      (ii) the sinuses of Valsalva
      (iii) left and right coronary ostia
   (c) Sinotubular junction
2. *Patient selection and contraindications*

   Aortic valve surgery is performed most often to treat severe aortic valve stenosis (Fig. 21.20) or regurgitation. Patient selection for minimally invasive aortic valve surgery is key for a successful operation. Besides the considerations discussed in the preoperative assessment section, these contraindications are specific for MIAVR:
   (a) Small aortic annulus requiring reconstruction
   (b) Significant aortic root dilation

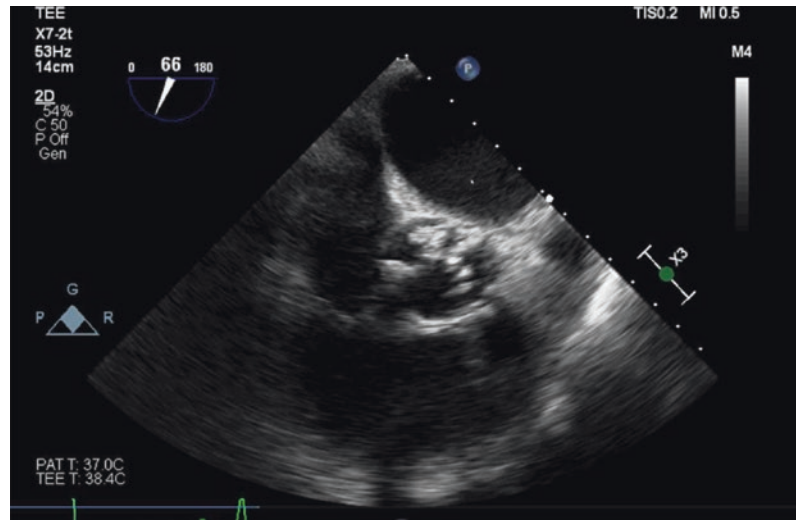


Fig. 21.20 TEE image in the midesophageal aortic valve short-axis view revealing severe stenotic aortic valve

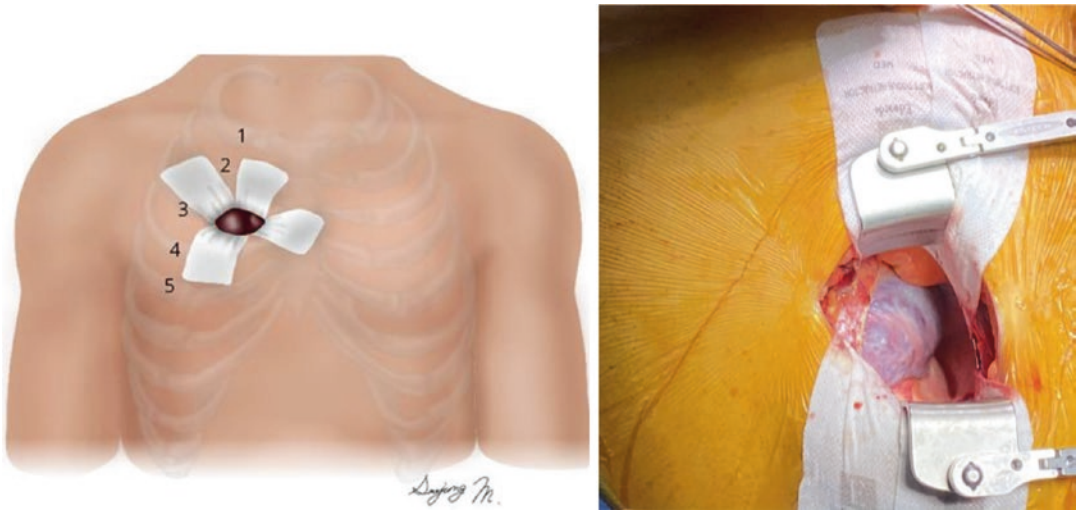


Fig. 21.21 Left: Right anterior mini-thoracotomy incision. Right: Anesthesiologist's view of right anterior mini-thoracotomy incision for mini AVR

(c) Aortoiliac atherosclerotic disease that prevents peripheral arterial cannulation
(d) Severe ascending calcification ("porcelain aorta") or presence of mobile atheroma
(e) Poor left ventricular function
(f) Significant coronary artery disease

3. *The main procedural events for MIAVR are as follows:*
   (a) *Intraoperative monitoring, lines, anesthesia conduct, and TEE:* The actions are the same as for MIMVS.
   (b) *Positioning:* The patient is positioned supine close to the edge of the right side of the operating table with both arms tucked.
   (c) *Skin prepping and draping:* This should be carried out in the same manner as for MIMVS.
   (d) *Incision and Exposure:* Types of incisions have been mentioned earlier in the general concepts section. The two most common operative approaches used are the upper (J) mini-sternotomy approach and the right anterior mini-thoracotomy approach (Fig. 21.5a, b). The limited upper mini-sternotomy incision is followed by a right anterior mini-thoracotomy at the level of the third or fourth intercostal space. The right anterior mini-thoracotomy approach is performed through a 4–6-cm transverse skin incision at the level of the second or third intercostal space (Fig. 21.21). After the intercostal space is entered, single-lung ventilation is initiated, and a soft tissue retractor is placed to allow visualization of the intrathoracic structures. Then, an intercoastal metal retractor is placed to improve exposure. Afterwards, the pericardium is opened to expose the aorta.
   (e) *Cardiopulmonary Perfusion:* Depending on the type of incision, CPB is accomplished either centrally or peripherally. Central CPB is initiated by aorto-right atrial cannulation under direct vision through the incision. Arterial outflow can be achieved by central cannulation of the distal ascending aorta, and venous drainage is achieved by cannulation of the right atrium. Peripheral CPB can be achieved through arterial cannulation of the axillary or femoral artery. For venous cannu-

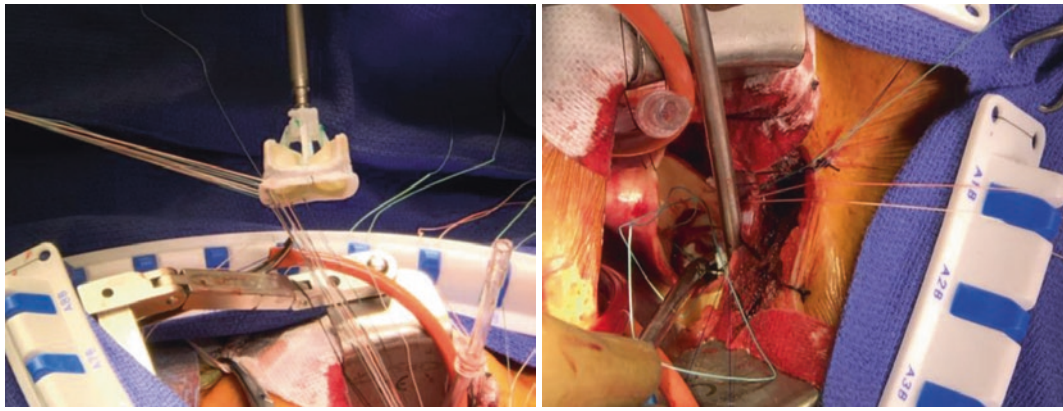


Fig. 21.22 Anesthesiologist's view of mini AVR through right thoracotomy. Left: sewing anchoring sutures of the bioprosthetic aortic valve. Right: inserting the bioprosthetic aortic valve in the aortic root

lation, bicaval-cannulation accessed through the femoral vein is usually adequate with or without vacuum-assisted drainage.

(f) *Aortic cross-clamping, myocardial protection and cardioplegia administration:* Myocardial protection and aortic cross-clamping are identical to those for MIMVS.

(g) *Aortic Valve Exposure:* After the aorta is cross-clamped and the heart is arrested, the aorta is opened, and the valve is exposed. The aortic leaflets are resected and the annulus is debrided, leaving the annulus free of calcification. The prosthetic aortic valve is then sutured with interrupted sutures in the sewing ring, then implanted with a long knotting device (Fig. 21.22).

(h) *Sutureless aortic valve replacement:* The two types of sutureless aortic prostheses that are currently available are the Intuity (Edwards Lifesciences) sutureless valve and the Perceval sutureless valve (Sorin, Saluggia, Italy). These valves can be rapidly deployed. For the Intuity valve, the annulus is sized, and three annular stitches from the nadir of each sinus are stitched to the valve sewing ring. The valve is then deployed with balloon expansion.

(i) *De-airing, Decannulation, and Closure:* After the aortotomy is closed, de-airing is done under TEE guidance with CO_2 continuously insufflated in the field and the aortic cross-clamp removed. With the patient still on CPB and before filling the heart, atrial and ventricular epicardial pacing wires are placed. The patient is then weaned from CPB. The aortic valve is evaluated with TEE before decannulation and protamine administration. Once drains are placed, local anesthetics [e.g. bupivacaine and/or liposomal bupivacaine (EXPAREL) can be administrated via intercostal nerve block and infiltration along the entire surgical field. Finally, the incisions are closed (Fig. 21.23).

Anesthetic Challenges for Minimally Invasive Valve Surgery

- The anesthetic challenges for minimally invasive valve surgery are similar to those for other minimally-invasive heart operations discussed earlier (page 22).
- The unique anesthetic challenge for minimally invasive valve surgery is the ability to de-air the heart, since it is difficult for the surgeon to access the left ventricle.
- De-airing is achieved by a variety of techniques discussed in the text.

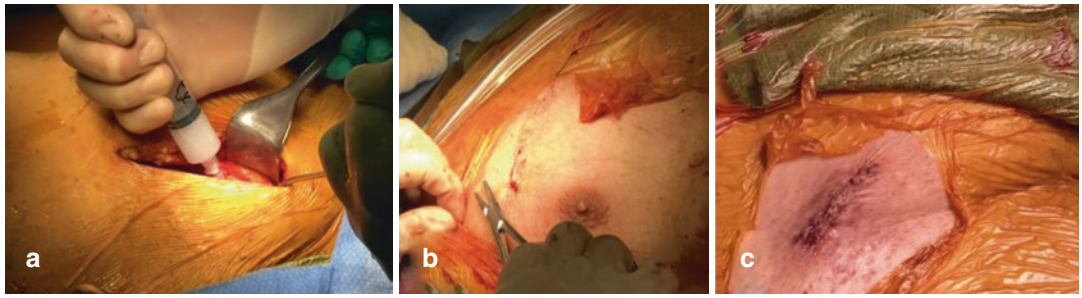


Fig. 21.23 Illustrations of the closure process for minimally invasive aortic valve surgery. (**a**) Injection of liposomal bupivacaine (EXPAREL) for post-operative analgesia. (**b**) Skin closure of the right anterior mini-thoracotomy incision. (**c**) Groin incision after closure

References

1. Attia RQ, Hickey GL, Grant SW, et al. Minimally invasive versus conventional aortic valve replacement: a propensity-matched study from the UK national data. Innovations (Phila). 2016;11(1):15–23. https://doi.org/10.1097/IMI.0000000000000236.
2. Yamada T, Ochiai R, Takeda J, Shin H, Yozu R. Comparison of early postoperative quality of life in minimally invasive versus conventional valve surgery. J Anesth. 2003;17(3):171–6. https://doi.org/10.1007/s00540-003-0176-6.
3. Grossi EA, Zakow PK, Ribakove G, et al. Comparison of post-operative pain, stress response, and quality of life in port access vs. standard sternotomy coronary bypass patients. Eur J Cardiothorac Surg. 1999;16(Suppl 2):S39–42.
4. Schmitto JD, Mokashi SA, Cohn LH. Minimally-invasive valve surgery. J Am Coll Cardiol. 2010;56(6):455–62. https://doi.org/10.1016/j.jacc.2010.03.053.
5. STS National Database Spring 2003. Executive summary. Durham, NC: Duke Clinical Research Institute; 2003.
6. Schulze CJ, Wildhirt SM, Boehm DH, et al. Continuous transesophageal echocardiographic (TEE) monitoring during port-access cardiac surgery. Heart Surg Forum. 1999;2(1):54–9.
7. Malaisrie SC, Barnhart GR, Farivar RS, et al. Current era minimally invasive aortic valve replacement: techniques and practice. J Thorac Cardiovasc Surg. 2014;147(1):6–14. https://doi.org/10.1016/j.jtcvs.2013.08.086.
8. Svensson LG. Minimal-access "J" or "j" sternotomy for valvular, aortic, and coronary operations or reoperations. Ann Thorac Surg. 1997;64(5):1501–3. https://doi.org/10.1016/S0003-4975(97)00927-2.
9. Hoff SJ. Off-pump coronary artery bypass: techniques, pitfalls, and results. Semin Thorac Cardiovasc Surg. 2009;21(3):213–23. https://doi.org/10.1053/j.semtcvs.2009.09.002.
10. Puskas JD, Mack MJ, Smith CR. On-pump versus off-pump CABG. N Engl J Med. 2010;362(9):851–4. https://doi.org/10.1056/NEJMc0912190.
11. George SJ, Al-Ruzzeh S, Amrani M. Mitral annulus distortion during beating heart surgery: a potential cause for hemodynamic disturbance—a three-dimensional echocardiography reconstruction study. Ann Thorac Surg. 2002;73(5):1424–30. https://doi.org/10.1016/s0003-4975(02)03406-9.
12. Kinjo S, Tokumine J, Sugahara K, et al. Unexpected hemodynamic deterioration and mitral regurgitation due to a tissue stabilizer during left anterior descending coronary anastomosis in off-pump coronary artery bypass graft surgery. Ann Thorac Cardiovasc Surg. 2005;11(5):324–8.
13. Reddy RC. Minimally invasive direct coronary artery bypass: technical considerations. Semin Thorac Cardiovasc Surg. 2011;23(3):216–9. https://doi.org/10.1053/j.semtcvs.2011.08.011.
14. Hrapkowicz T, Bisleri G. Endoscopic harvesting of the left internal mammary artery. Ann Cardiothorac Surg. 2013;2(4):565–9. https://doi.org/10.3978/j.issn.2225-319X.2013.07.11.
15. McGinn JT Jr, Usman S, Lapierre H, Pothula VR, Mesana TG, Ruel M. Minimally invasive coronary artery bypass grafting: dual-center experience in 450 consecutive patients. Circulation. 2009;120(11 Suppl):S78–84. https://doi.org/10.1161/CIRCULATIONAHA.108.840041.
16. Guida MC, Pecora G, Bacalao A, Muñoz G, Mendoza P, Rodríguez L. Multivessel revascularization on the beating heart by anterolateral left thoracotomy. Ann Thorac Surg. 2006;81(6):2142–6. https://doi.org/10.1016/j.athoracsur.2006.01.054.
17. Vassiliades TA Jr, Reddy VS, Puskas JD, Guyton RA. Long-term results of the endoscopic atraumatic coronary artery bypass. Ann Thorac Surg. 2007;83(3):979–85. https://doi.org/10.1016/j.athoracsur.2006.10.031.

18. Gong W, Cai J, Wang Z, et al. Robot-assisted coronary artery bypass grafting improves short-term outcomes compared with minimally invasive direct coronary artery bypass grafting. J Thorac Dis. 2016;8(3):459–68. https://doi.org/10.21037/jtd.2016.02.67.
19. Bonaros N, Schachner T, Lehr E, et al. Five hundred cases of robotic totally endoscopic coronary artery bypass grafting: predictors of success and safety. Ann Thorac Surg. 2013;95(3):803–12. https://doi.org/10.1016/j.athoracsur.2012.09.071.
20. Argenziano M, Katz M, Bonatti J, et al. Results of the prospective multicenter trial of robotically assisted totally endoscopic coronary artery bypass grafting. Ann Thorac Surg. 2006;81(5):1666–75. https://doi.org/10.1016/j.athoracsur.2005.11.007.
21. Deshpande SP, Lehr E, Odonkor P, et al. Anesthetic management of robotically assisted totally endoscopic coronary artery bypass surgery (TECAB). J Cardiothorac Vasc Anesth. 2013;27(3):586–99. https://doi.org/10.1053/j.jvca.2013.01.005.
22. Campos JH. Current techniques for perioperative lung isolation in adults. Anesthesiology. 2002;97(5):1295–301. https://doi.org/10.1097/00000542-200211000-00036.
23. Lee DK, Kim YM, Kim HZ, Lim SH. Right upper lobe tracheal bronchus: anesthetic challenge in one-lung ventilated patients—a report of three cases. Korean J Anesthesiol. 2013;64(5):448–50. https://doi.org/10.4097/kjae.2013.64.5.448.
24. Yamashiro S, Arakaki R, Kise Y, Kuniyoshi Y. Prevention of pulmonary edema after minimally invasive cardiac surgery with mini-thoracotomy using neutrophil elastase inhibitor. Ann Thorac Cardiovasc Surg. 2018;24(1):32–9. https://doi.org/10.5761/atcs.oa.17-00102.
25. Dal-Bianco JP, Levine RA. Anatomy of the mitral valve apparatus: role of 2D and 3D echocardiography. Cardiol Clin. 2013;31(2):151–64. https://doi.org/10.1016/j.ccl.2013.03.001.
26. Ailawadi G, Agnihotri AK, Mehall JR, et al. Minimally invasive mitral valve surgery I: patient selection, evaluation, and planning. Innovations (Phila). 2016;11(4):243–50. https://doi.org/10.1097/IMI.0000000000000301.
27. Van Praet KM, Stamm C, Sündermann SH, et al. Minimally invasive surgical mitral valve repair: state of the art review [published correction appears in Interv Cardiol. 2018;13(2):99]. Interv Cardiol. 2018;13(1):14–9. https://doi.org/10.15420/icr.2017:30:1.
28. Goldstone AB, Woo YJ. Is minimally invasive thoracoscopic surgery the new benchmark for treating mitral valve disease? Ann Cardiothorac Surg. 2016;5(6):567–72. https://doi.org/10.21037/acs.2016.03.18.
29. Pope NH, Ailawadi G. Minimally invasive valve surgery. J Cardiovasc Transl Res. 2014;7(4):387–94. https://doi.org/10.1007/s12265-014-9569-1.
30. Goldstone AB, Joseph Woo Y. Minimally invasive surgical treatment of valvular heart disease. Semin Thorac Cardiovasc Surg. 2014;26(1):36–43. https://doi.org/10.1053/j.semtcvs.2014.02.001.
31. Badhwar V. Are we going backwards or forwards in minimally invasive mitral valve surgery? Three eras of perfusion strategy. Semin Thorac Cardiovasc Surg. 2015;27(2):104–5. https://doi.org/10.1053/j.semtcvs.2015.09.002.
32. Grossi EA, Loulmet DF, Schwartz CF, et al. Evolution of operative techniques and perfusion strategies for minimally invasive mitral valve repair. J Thorac Cardiovasc Surg. 2012;143(4 Suppl):S68–70. https://doi.org/10.1016/j.jtcvs.2012.01.011.
33. Garbade J, Davierwala P, Seeburger J, et al. Myocardial protection during minimally invasive mitral valve surgery: strategies and cardioplegic solutions. Ann Cardiothorac Surg. 2013;2(6):803–8. https://doi.org/10.3978/j.issn.2225-319X.2013.09.04.
34. Fudulu D, Lewis H, Benedetto U, Caputo M, Angelini G, Vohra HA. Minimally invasive aortic valve replacement in high risk patient groups. J Thorac Dis. 2017;9(6):1672–96. https://doi.org/10.21037/jtd.2017.05.21.
35. Mihaljevic T, Cohn LH, Unic D, Aranki SF, Couper GS, Byrne JG. One thousand minimally invasive valve operations: early and late results. Ann Surg. 2004;240(3):529–34. https://doi.org/10.1097/01.sla.0000137141.55267.47.
36. Marullo AG, Irace FG, Vitulli P, et al. Recent developments in minimally invasive cardiac surgery: evolution or revolution? Biomed Res Int. 2015;2015:483025. https://doi.org/10.1155/2015/483025.
37. Spadaccio C, Alkhamees K, Al-Attar N. Recent advances in aortic valve replacement. F1000Res. 2019;8:F1000 Faculty Rev-1159. Published 2019 Jul 22. https://doi.org/10.12688/f1000research.17995.1.

22

Surgical Treatment of Infective Endocarditis (IE): Anesthesia Considerations

Kent Berg, Lucas Giunta, Jordan E. Goldhammer, and Ron L. Leong

Introduction

Infected endocarditis (IE) is defined as an infection of the endocardium, which comprises the inner lining of the heart muscle and valves. These infections are often associated with prolonged hospital courses and the need for major surgical procedures. IE provides a unique challenge to clinicians as they attempt to form treatment plans that are mindful of the disease's complex nature. Data from the years 2000–2011 showed over 400,000 reported cases of IE in the United States with the incidence increasing steadily year-to-year [1]. Recent advancements in the diagnosis and management of IE have aided in the improvement of patient prognosis. Even with these developments, in-hospital mortality from IE remains as high as 20–25% [2].

K. Berg
Department of Anesthesiology, Sidney Kimmel Medical College and Thomas Jefferson University Hospital, Philadelphia, PA, USA
e-mail: Kent.Berg@jefferson.edu

J. E. Goldhammer · R. L. Leong (✉)
Department of Anesthesiology, Sidney Kimmel Medical College, Philadelphia, PA, USA

Thomas Jefferson University Hospital, Philadelphia, PA, USA
e-mail: Jordan.Goldhammer@jefferson.edu; Ron.Leong@jefferson.edu

L. Giunta
Department of Anesthesiology, Thomas Jefferson University Hospital, Philadelphia, PA, USA
e-mail: Lucas.Giunta@jefferson.edu

Work up for suspected IE includes physical exam, microbiology cultures, laboratory studies, and imaging. The mainstay of treatment is predicated on early initiation of antimicrobial agents, possible surgical intervention, and prompt removal of infected implantable devices [3]. Generally, antibiotic management is directed towards the most commonly suspected organisms (staphylococcus, streptococcus and enterococcus) with initiation of treatment starting after two positive cultures and continuing for approximately 4–6 weeks [4]. Repeat echocardiograms are often obtained to evaluate for treatment failure and presence of complicating features.

The management of patients with IE continue to present unique concerns for the anesthesiologist and require careful deliberations to guide them safely through their hospital course. The evaluation and treatment of IE requires a multispecialty approach that includes infectious disease specialists, cardiologists, and cardiothoracic surgeons. The purpose of this chapter is to review the preoperative anesthetic considerations, anesthetic management in the operating room, intraoperative complications, and postoperative challenges of IE.

Pathophysiology

IE is caused by bacteria or fungus that are exposed to the blood stream and allowed to seed on at-risk portions of the endocardium.

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_22

Staphylococcus (31%) and Streptococci (17%) represent the largest proportion of causative organisms, with a smaller proportion coming from fungi and other bacterium (ex. HACEK, enterococci and gram-negative bacilli) [5]. Cardiac factors that put patients at risk for IE include congenital heart defects, rheumatic heart disease, other valvular pathologies, hypertrophic cardiomyopathy, and prior endocarditis infections. Male sex, age > 65, IV drug abuse, immunocompromised states and intracardiac hardware also place patients at increased risk of infection [6].

During the process of IE, bacteria or fungi invade an often times damaged endocardium through a mixture of direct invasion, release of liquefactive enzymes and elevated inflammation in the affected tissues, and production of biofilm that enable the bacteria to resist antimicrobial treatment [7, 8]. This process is particularly pronounced when the invasive species is *Staphylococcus aureus*, and especially in the aortic valve (AV) position. When complicated by sudden-onset congestive heart failure (CHF), either by rupture of a papillary muscle or cord, a newly created shunt, or perforation in either a native or prosthetic valve leaflet, the acute volume overload can create significant symptoms for the patient. The degree of CHF symptoms has the greatest prognostic value for patients treated either surgically or medically [9]. Studies dating back to the late 1970s have compared outcomes in IE patients complicated by CHF, which show a substantial benefit of surgical treatment over medical therapy (mortality rates of 23% with surgery versus 71% with antibiotic treatment) [10–12]. Moreover, as IE deteriorates with CHF, both American and European medical societies consider this a Class I indication for surgical intervention [4, 13, 14].

In addition to CHF, other critical events may complicate IE before, during or after surgical repair. Perivalvular extension can be a devastating invasion of the structures supporting the valve annulus, creating potential for complete dehiscence or formation of abscesses or fistulas. Perivalvular extension is most frequently caused by necrotizing bacteria, especially when they affect the AV. The prevalence of perivalvular extension in infected native valves is up to 40%, and in infected prosthetic valves, as high as 100% [15]. Embolization of vegetation or infected tissue, most commonly with mitral valve (MV) lesions, may also cause damage to downstream organs. According to a 2000 study conducted in Finland [16], 65% of embolizations can affect the brain, while 90% of these can target the middle cerebral artery territory. The vascular beds of the kidneys and spleen are also frequently involved. Lastly, organisms that cause less local invasion still cause an immune system response. Glomerulonephritis, septic emboli, other causes of acute renal failure may affect up to 30% of patients suffering from IE [17].

Pre-operative Evaluation of Infective Endocarditis

Physical Exam Findings

Fever and cardiac murmur are the most common clinical manifestations of IE. Physical exam may reveal subtle findings suggestive of severe IE or embolic sequella. Uncommon but highly suggestive physical exam findings include Janeway lesions, Osler nodes, and Roth spots. Janeway lesions, erythematous macules, and Osler nodes, tender subcutaneous nodules, may be evident on upper or lower extremities. Janeway lesions are attributed to small, peripheral abscesses. Osler nodes occur secondary to microemboli, vascular occlusion, and resulting localized vasculitis. Roth spots, due to microemboli mediated vasculitis, occur on the retina and manifest as hemorrhagic lesions on ocular exam. Complications from IE emboli may occur in the central nervous system, gastrointestinal tract, and musculoskeletal tissue. Septic emboli may cause stroke or brain abscess; infarction of the kidneys, liver, or spleen; osteomyelitis, arthritis, or muscular abscess. End organ dysfunction in suspected IE indicates severe disease and requires thorough pre-operative evaluation to define timing, scope, and risk associated with cardiovascular surgery.

Diagnostic Work-Up

Diagnosis of IE relies on the combination of blood culture data, ultrasound imaging evidence and clinical assessment. The "Duke Criteria" for diagnosis of IE remains the standard for ascertaining the possibility of endocardial infection. The criteria relies on both pathology and clinical components for securing a diagnosis. Pathological diagnosis can be made by histological or culture evidence of infection following tissue biopsy. Clinical diagnosis relies on combinations of major and minor criteria outlined in Table 22.1 [18].

Laboratory findings in IE are relatively non-specific and are broadly indicative of an underlying infection or inflammatory process. Phlebotomy results may show increased c-reactive protein (CRP) or erythrocyte sedimentation rate (ESR). EKG is non-specific for IE, but may reflect new conduction abnormalities suggestive of perivalvular disease [19]. For example, when an IE patient develops new onset heart block, abscess formation must be suspected and may accelerate the decision to proceed to the operating room (OR).

Table 22.1 Duke criteria for diagnosis of infective endocarditis [18]

Duke's criteria
Diagnosis made with the following criteria: Two major criteria One major and three minor criteria Five minor criteria
Major criteria
Two separate blood cultures positive for typical microorganism
Blood cultures persistently positive for typical microorganism – Two cultures drawn 12 h apart – Three or a majority of four or more blood cultures – One blood culture positive for Coxiella Burnetii
Evidence of endocardial involvement on echocardiogram – Intracardiac mass present on valve, supporting structure or implanted material – Evidence of abscess formation – New valvular regurgitation or prosthetic valve dehiscence
Minor criteria
Known cardiac lesion or IV drug use
Febrile > 38 ° C
Vascular phenomena – Emboli, pulmonary infarcts, Janeway lesions, conjunctival hemorrhages
Immunological phenomena – Glomerulonephritis, Osler's nodes, Roth spots, rheumatoid factor
Positive blood culture that does not meet major criteria

Echocardiography is the imaging modality best suited for diagnosis. Transthoracic echocardiography (TTE) is the initial study of choice for suspected IE. TTE has a negative predicative value of >90% and can be improved to 97.1% using strict criteria for a negative exam [20, 21]. If TTE is non-diagnostic, transesophageal echocardiography (TEE) should be completed. Vegetation is the classic finding of IE and is identified as a hyperechoic oscillating mass that moves independently of leaflet motion. Vegetation is most commonly attached to low-pressure side of valve leaflets, but can be adherent to valve annular structure [22]. Vegetations adherent to atrial or ventricular septum are less common, but may occur in the setting of congenital heart disease. Size reduction in vegetation may occur during the course of antibiotic therapy [23]. Of note, non-infective vegetations cannot be differentiated from IE with echocardiography alone, however, they may be suspected if the mass is small and fixed without concomitant regurgitant valve pathology [22]. Perivalvular extension of IE may cause abscess, pseudoaneurysm, or fistula. An abscess is identified by a thickened hyperechoic, tissue plane which abuts the valve annular structure. A hypoechoic space may be identified without evidence of color flow into the abscess cavity. Pseudoaneurysm may have a similar hypoechoic appearance on TEE, however, pulsatile blood flow will be apparent in the hypoechoic cavity. The sensitivity of TTE is 50% for abscess and pseudoaneurysm compared with 90% for TEE [24]. Therefore, if TEE is not completed in the preoperative evaluation, intraoperative TEE must carefully assess for complex IE pathology.

Surgical Indication

When a patient presents with IE, antimicrobial therapy is started immediately to treat the invading organisms, and the goals of surgical treatment are to restore cardiac structures and treat hemodynamic instability. As many as 50% of IE patients will require surgical intervention due to persistent bacteremia, emboli, or heart failure [25]. Indications for surgery include: heart failure, refractory pulmonary edema, persistent infection, IE due to drug resistant organism or fungi, heart block, annular abscess, severe valvular regurgitation or stenosis, left sided mobile vegetations >10 mm, or prosthetic valve endocarditis [4, 13].

An important objective in the preoperative evaluation of IE is the determination of the need for early surgery, prior to completion of antibiotic therapy, or late surgery. Early surgery (i.e. within 24 h) is recommended for cardiogenic shock, progressive heart failure, prevention of embolic events or in those with complex IE due to either perivalvular extension, including abscess, pseudoaneurysm, or fistula formation, or IE in the setting of congenital heart disease [26]. Heart failure due to valve dysfunction is the most common indication for surgery; however, the timing of surgical intervention is based largely on observational studies and differs between major European and US guidelines [4, 13]. In general, patients with device related endocarditis (e.g., infected defibrillator or pacemakers wires) and prosthetic valve endocarditis (PVE) often proceed to surgery faster than patients with native valve endocarditis (NVE) or right-sided lesions.

Intra-operative Anesthesia Management

Surgical Procedure

While the exact surgical technique needed to repair all types of IE lesions is beyond the scope of this text, in general, anesthesia staff members should review all images available from prior echocardiographic and radiologic studies and discuss the proposed intervention directly with the cardiac surgeon. Evidence of perivalvular extension, abscesses or fistulas may require repair of the valve annulus and/or remodeling techniques with pericardial patch material. For IE involving the aortic annulus, thorough TEE examination of the aortic root should be performed to rule out potential for abscess invasion into the adjacent structures, as this would likely change the procedure from an aortic valve replacement (AVR) to a homograft root replacement with reimplantation of the coronary arteries. For IE involving the MV or tricuspid valve (TV), annular rupture, abscess or fistula formation are all possible, which require significant architectural repair. If the MV, AV and adjoining aorto-mitral curtain are involved, a complex replacement of all structures may be required (e.g., "Commando" or "hemi-Commando" procedure). One must be careful when planning the induction technique, intraoperative monitoring and be prepared for potential complications during surgery.

Induction Considerations

Hemodynamic instability is common in IE patients who present for cardiac surgery. Overall, the goals of anesthesia induction should include treating the acute effects of aortic regurgitation (AR), mitral regurgitation (MR) and tricuspid regurgitation (TR), as well as special circumstances.

Aortic Regurgitation

The adage for treating patients with AR is to keep them "full, fast and forward." Normal to slightly higher intravascular volume (preload) will promote better cardiac output. Since the main hemodynamic effect of acute AR occurs during diastole, maintaining a high (or high normal) heart rate shortens the time spent in the diastolic phase of the cardiac cycle and minimizes backward flow through the AV. Decreasing afterload (e.g., us of arterial vasodilators) is beneficial to promote increased cardiac output (CO).

Mitral Regurgitation

The most important goal during induction of the patient with MR is to decrease afterload. Systemic hypertension will worsen the regurgitant fraction across the MV and reduce CO. In the setting of MR, however, bradycardia can increase diastolic filling time, thus increasing left ventricular end diastolic pressure (LVEDP) and expanding the MV annular dimension. It is recommended to avoid bradycardia in MR patients to avoid further distension of the MV annulus and worsening of MR. Maintaining preload or normal intravascular volume is also beneficial.

Tricuspid Regurgitation

When inducing a patient with TR, it is important to avoid causes of increased pulmonary vasoconstriction, such as hypoxemia, hypercarbia, high airway pressures or excessively high tidal volumes. In addition, it is recommended to maintain normal to high preload and heart rate in order to promote RV function. If the RV is already showing signs of volume overload, adding medications to decrease pulmonary pressures (e.g., intravenous (IV) Milrinone or inhaled Epoprostenol/Nitric Oxide) may be necessary if MR is not significant.

Special Circumstances

If the baseline systolic function of the LV or RV is poor, one should consider adding inotropes or vasopressors prior to administering induction medications. In addition, if a shunt exists between the left and right sides of the heart, one must take caution to avoid introducing air into IV lines to prevent air embolus. If more than one valvular lesion coexists in the same patient, consider defining hemodynamic goals based on the most critical lesion.

Monitoring

According to the intraoperative monitoring guideline updated by the American Society of Anesthesiologists (ASA) in 2015, qualified anesthesia staff should continuously evaluate the patient's oxygenation, ventilation, circulation, and temperature during the delivery of all anesthetic agents. As such, pulse oximetry, capnography, blood pressure, heart rate, electrocardiography (EKG), and thermometers (via esophageal or Foley catheter) are standard practice for patients undergoing any type of surgery with anesthesia staff involvement.

For cardiac patients specifically, anesthesia staff use additional devices for intraoperative management. Arterial lines are utilized for real-time blood pressure monitoring and drawing blood samples. Arterial blood gas analysis, paying particular attention to glucose, hemoglobin, and potassium levels, is routine in caring for the cardiac surgery patient, as well as monitoring the activated clotting time (ACT) for systemic anticoagulation with heparin. At most institutions where cardiac surgery is performed, a target ACT of 480 s is required for full anticoagulation on cardiopulmonary bypass (CPB), although this exact value may change slightly based on the type of CPB circuit used by perfusion staff. Central venous lines (CVLs) are used to administer vasoactive drugs and monitor central venous pressure (CVP). The trend of CVP over time is an indication of intravascular volume status. Depending on which type of lesion is involved with IE, pulmonary artery catheters (PACs) may also be used. PACs are frequently avoided in the presence of right heart lesions (e.g., TR) or intracardiac shunts to avoid embolizing infected material into the lungs or across shunts to the left side of the heart.

Optimizing patient physiologic parameters and surgical techniques are also critical to preserving renal function during cardiac surgery. A Foley catheter is usually placed to measure urine output (UOP) and to observe the quality of the urine produced. Low UOP and blood-tinged urine may be markers of acute kidney injury (AKI), and it is important to communicate this information to intensive care unit (ICU) staff during handoffs postoperatively. Of note, depending on how one defines AKI and which procedure is performed, AKI may occur in 20–70% of cardiovascular procedures [27–31]. In cases of IE, blood tinged urine may raise suspicion of kidney insult, possibly from infarction due embolic

material, hypoperfusion or local hypoxia. According to an international consensus on cardiovascular surgery and AKI published in 2018 [32], several intraoperative strategies are recommended to prevent AKI. The task force recommended use of volatile anesthetics, avoidance of hyperthermia (temp greater than 37 °C), and avoidance of hemodilution (hematocrit less than 24%). Unfortunately, current ultrafiltration methods do not appear efficacious in preventing AKI due to the hemodilution caused by CPB.

Lastly, perioperative neurologic injury can be an unfortunate complication during cardiac and non-cardiac surgery, and the reasons for cerebrovascular accident (CVA) and neurocognitive dysfunction may be classified into ischemic or embolic groups. In a 2003 study of more than 11,000 patients who underwent coronary artery bypass graft (CABG) surgery, researchers reported a stroke incidence of 1.5% and found that 75% of CVAs occurred in the 90% of low-medium risk patients. Of note, an acute CVA puts additional brain tissue at risk, and low blood pressure or systemic anticoagulation may further worsen ischemic insult or introduce a hemorrhagic component while on CPB [33]. Cerebral oximetry (COx) uses sensors placed on the patient's forehead to measure regional oxygen saturations of the frontal cortex, an area of the brain that is highly susceptible to changes in oxygen supply and demand. Although COx measures primarily venous blood (75%), this technology has been validated with non-pulsatile flow, which makes it particularly attractive for use during CPB. COx has been available commercially in the US for nearly 20 years, and is frequently used as an early detector of changes in cerebral perfusion during cardiac surgery [34]. Specific to valve surgery in IE patients, COx is used as a monitor of potential injury to the brain due to embolism or hypoperfusion.

Intra-operative TEE

According to a clinical guideline published by the European Society of Cardiology in 2015 [13], intraoperative TEE is recommended during surgical intervention of valvular structures due to IE. The primary goals of TEE in this setting are to confirm the extent of infected valves and surrounding tissues, to inspect function of the repair or newly placed prosthetic valve, to exclude intra-cardiac air prior to separation from CPB, and to provide a basis of comparison for the early recovery phase in the ICU. Intraoperative TEE is recommended if intracardiac leads are also present. At the start of the operative procedure, TEE is used to evaluate if valvular repair is sufficient to remove all infected tissue and restore normal function, especially if it is an isolated MV or TV lesion without significant invasion into or beyond the annulus. As with any cardiac surgery where TEE is indicated, however, it is critical to perform an entire comprehensive TEE exam as IE can affect multiple cardiac structures. Missing a coexisting infected structure during an initial operative procedure may require re-exploration and be potentially life-threatening.

The exact views that allow for critical examination of specific structures are well described in the 2013 TEE exam guideline published by the American Society of Echocardiography (ASE) and the Society of Cardiovascular Anesthesiologists (SCA) [35].

In summary, the AV and aortic root are well interrogated by the mid-esophageal (ME) AV long-axis view (120°–140°), ME AV short-axis view (45°–60°), deep transgastric (TG) view, and the ME ascending aorta long-axis view. The MV and subvalvular apparatus are well examined by the ME four-chamber view, ME mitral commissural view, ME long-axis view, and the TG basal short-axis view. The TV and caval structures are well inspected by the ME RV inflow-outflow view (50°–70°), and the ME modified bicaval TV view. In addition, multiplane, 3-dimensional TEE and color flow doppler (CFD) modalities allow for even greater detail during examination of potentially infected cardiac tissues. After valve repair or replacement, the use of CFD is particularly important to evaluate for paravalvular leaks or residual shunt flow.

Intra-operative Complications

During a valve replacement or repair in a patient with IE, similar intraoperative complications may occur as with valve surgery in a non-IE patient. Risk of paravalvular leaks, stroke, post-operative cognitive dysfunction, and AKI still exist. Specific to patients with IE, however, showering of septic emboli, pulmonary embolism, mycotic aneurysm with or without aortic dissection, acute coronary syndrome, coagulopathy, systemic inflammatory response syndrome (SIRS) or frank sepsis may occur in the OR or immediate ICU setting. Failure to resect all infected tissue may risk incomplete clearance of infection and require a return trip to the OR. Rarely, if the infection involves the MV, AV and the aorto-mitral curtain, this may require a complex procedure called a "Commando" or "hemi-Commando" procedure, which may increase the duration on CPB and increase the risk of bleeding, vasoplegia, ventricular dysfunction, conduction disturbances, and neurologic events [36]. These technically challenging operations are only performed at a select number of institutions.

Post-operative Considerations

The post cardiac surgical management of the patient with IE presents unique considerations for the intensive care unit. The pre-existing comorbidities, cardiac involvement of IE with its corresponding surgical intervention, and potential complications are significant factors in determining the patient's hospital course. Moreover, the social issues in certain populations (i.e. patients with a history of IV drug abuse) contribute to a prolonged post-operative length of stay, higher recurrence of IE, and reoperation rates compared to those who undergo adult cardiac surgery for traditional indications such as CABG or valvular surgery for valve degeneration [33, 37–39]. Continued multidisciplinary care in addition to a vigilant intensive care unit staff are paramount to effective management.

Typically, the post cardiac surgical IE patient will have the aid of invasive continuous monitoring including the use of an arterial catheter, CVL and PAC to optimize post-operative management. The measurement of central venous pressure, pulmonary artery pressure, pulmonary artery wedge pressure, cardiac output and mixed venous oxygen saturation may be of tremendous value to unravel the complex underlying mechanism of an unstable IE patient. In addition, TTE or TEE is a useful adjunctive tool to assess volume status, cardiac function, adequacy of valve repair or replacement, and pathologies including pericardial effusion with tamponade or regional cardiac dysfunction suggestive of myocardial ischemia.

The IE patient who meet the indication for surgical treatment is by definition more critically ill and generally require ICU admission with mortality rates ranging as high as 45% [40, 41]. A Simplified Acute Physiology Score (SAPS) II score > 35, Sepsis-related Organ Failure Assessment (SOFA) score > 8, septic shock, *S. aureus* IE, neurologic failure, immunosuppression, and prosthetic valve IE are recognized as independent prognostic factors for mortality [40–42]. Furthermore, depending on the complexity and duration of the surgical procedure, significant coagulopathy, conduction abnormalities and refractory vasoplegia may pose life threatening issues post-operatively. Lastly, it is crucial to follow up with the cultures of the operative specimen for definitive sensitivity of the appropriate antimicrobial or antifungal treatment. Standard duration for antimicrobial therapy is 6 weeks and lifelong suppressive therapy for fungal IE.

Conclusions

The surgical treatment of IE is an operation performed by a cardiac surgeon under general anesthesia and with the assistance of CPB to radically debride infected tissue, repair or replace infected valve(s), and repair or reconstruct perivalvular invasive disease. The anesthesia provider should be familiar of the pathophysiology of IE and its unique complications. Expertise in the monitor-

ing of hemodynamics and the use of TEE are necessary to guide surgical management and ensure a successful perioperative course.

Funding and Conflicts of Interest
None.

References

1. Pant S, Patel NJ, Deshmukh A, et al. Trends in infective endocarditis incidence, microbiology, and valve replacement in the United States from 2000 to 2011. J Am Coll Cardiol. 2015;65(19):2070–6. https://doi.org/10.1016/j.jacc.2015.03.518.
2. Ambrosioni J, Hernandez-Meneses M, Téllez A, et al. The changing epidemiology of infective endocarditis in the twenty-first century. Curr Infect Dis Rep. 2017;19(5):21. https://doi.org/10.1007/s11908-017-0574-9.
3. Wang A, Gaca JG, Chu VH. Management considerations in infective endocarditis: a review. JAMA. 2018;320(1):72–83. https://doi.org/10.1001/jama.2018.7596.
4. Baddour Larry M, Wilson Walter R, Bayer Arnold S, et al. Infective endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications. Circulation. 2015;132(15):1435–86. https://doi.org/10.1161/CIR.0000000000000296.
5. Murdoch DR, Corey GR, Hoen B, et al. Clinical presentation, etiology, and outcome of infective endocarditis in the 21st century: the international collaboration on endocarditis-prospective cohort study. Arch Intern Med. 2009;169(5):463–73. https://doi.org/10.1001/archinternmed.2008.603.
6. Strom Brian L, Abrutyn E, Berlin Jesse A, et al. Risk factors for infective endocarditis. Circulation. 2000;102(23):2842–8. https://doi.org/10.1161/01.CIR.102.23.2842.
7. Bedeir K, Reardon M, Ramlawi B. Infective endocarditis: perioperative management and surgical principles. J Thorac Cardiovasc Surg. 2014;147(4):1133–41. https://doi.org/10.1016/j.jtcvs.2013.11.022.
8. Elgharably H, Hussain ST, Shrestha NK, Blackstone EH, Pettersson GB. Current hypotheses in cardiac surgery: biofilm in infective endocarditis. Semin Thorac Cardiovasc Surg. 2016;28(1):56–9. https://doi.org/10.1053/j.semtcvs.2015.12.005.
9. Hasbun R, Vikram HR, Barakat LA, Buenconsejo J, Quagliarello VJ. Complicated left-sided native valve endocarditis in adults: risk classification for mortality. JAMA. 2003;289(15):1933–40. https://doi.org/10.1001/jama.289.15.1933.
10. Aksoy O, Sexton DJ, Wang A, et al. Early surgery in patients with infective endocarditis: a propensity score analysis. Clin Infect Dis. 2007;44(3):364–72. https://doi.org/10.1086/510583.
11. Croft CH, Woodward W, Elliott A, Commerford PJ, Barnard CN, Beck W. Analysis of surgical versus medical therapy in active complicated native valve infective endocarditis. Am J Cardiol. 1983;51(10):1650–5. https://doi.org/10.1016/0002-9149(83)90203-5.
12. Richardson JV, Karp RB, Kirklin JW, Dismukes WE. Treatment of infective endocarditis: a 10-year comparative analysis. Circulation. 1978;58(4):589–97. https://doi.org/10.1161/01.cir.58.4.589.
13. Habib G, Lancellotti P, Antunes MJ, et al. 2015 ESC guidelines for the management of infective endocarditis: the Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). Eur Heart J. 2015;36(44):3075–128. https://doi.org/10.1093/eurheartj/ehv319.
14. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014;129(23):2440–92. https://doi.org/10.1161/CIR.0000000000000029.
15. Fernicola DJ, Roberts WC. Frequency of ring abscess and cuspal infection in active infective endocarditis involving bioprosthetic valves. Am J Cardiol. 1993;72(3):314–23. https://doi.org/10.1016/0002-9149(93)90679-7.
16. Heiro M, Nikoskelainen J, Engblom E, Kotilainen E, Marttila R, Kotilainen P. Neurologic manifestations of infective endocarditis: a 17-year experience in a teaching Hospital in Finland. Arch Intern Med. 2000;160(18):2781–7. https://doi.org/10.1001/archinte.160.18.2781.
17. Conlon PJ, Jefferies F, Krigman HR, Corey GR, Sexton DJ, Abramson MA. Predictors of prognosis and risk of acute renal failure in bacterial endocarditis. Clin Nephrol. 1998;49(2):96–101.
18. Li JS, Sexton DJ, Mick N, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis. 2000;30(4):633–8. https://doi.org/10.1086/313753.
19. Meine TJ, Nettles RE, Anderson DJ, et al. Cardiac conduction abnormalities in endocarditis defined by the Duke criteria. Am Heart J. 2001;142(2):280–5. https://doi.org/10.1067/mhj.2001.116964.
20. McDermott BP, Cunha BA, Choi D, Cohen J, Hage J. Transthoracic echocardiography (TTE): sufficiently sensitive screening test for native valve infective endocarditis (IE). Heart Lung. 2011;40(4):358–60. https://doi.org/10.1016/j.hrtlng.2010.07.007.
21. Sivak JA, Vora AN, Navar AM, et al. An approach to improve the negative predictive value and clinical utility of transthoracic echocardiography in suspected native valve infective endocarditis. J Am Soc Echocardiogr. 2016;29(4):315–22. https://doi.org/10.1016/j.echo.2015.12.009.

22. Vilacosta I, Olmos C, de Agustín A, et al. The diagnostic ability of echocardiography for infective endocarditis and its associated complications. Expert Rev Cardiovasc Ther. 2015;13(11):1225–36. https://doi.org/10.1586/14779072.2015.1096780.
23. Manzano C, Vilacosta I, Fernández C, et al. Evolution of vegetation size in left-sided endocarditis. Is it a prognostic factor during hospitalization? Rev Esp Cardiol. 2011;64(8):714–7. https://doi.org/10.1016/j.recesp.2010.10.027.
24. Daniel WG, Mügge A, Martin RP, et al. Improvement in the diagnosis of abscesses associated with endocarditis by transesophageal echocardiography. N Engl J Med. 1991;324(12):795–800. https://doi.org/10.1056/NEJM199103213241203.
25. Tornos P, Iung B, Permanyer-Miralda G, et al. Infective endocarditis in Europe: lessons from the Euro heart survey. Heart. 2005;91(5):571–5. https://doi.org/10.1136/hrt.2003.032128.
26. Kang D-H. Timing of surgery in infective endocarditis. Heart. 2015;101(22):1786–91. https://doi.org/10.1136/heartjnl-2015-307878.
27. Quan S, Pannu N, Wilson T, et al. Prognostic implications of adding urine output to serum creatinine measurements for staging of acute kidney injury after major surgery: a cohort study. Nephrol Dial Transplant. 2016;31(12):2049–56. https://doi.org/10.1093/ndt/gfw374.
28. Englberger L, Suri RM, Li Z, et al. Clinical accuracy of RIFLE and acute kidney injury network (AKIN) criteria for acute kidney injury in patients undergoing cardiac surgery. Crit Care. 2011;15(1):R16. https://doi.org/10.1186/cc9960.
29. Bastin AJ, Ostermann M, Slack AJ, Diller G-P, Finney SJ, Evans TW. Acute kidney injury after cardiac surgery according to risk/injury/failure/loss/end-stage, acute kidney injury network, and kidney disease: improving global outcomes classifications. J Crit Care. 2013;28(4):389–96. https://doi.org/10.1016/j.jcrc.2012.12.008.
30. Machado MN, Nakazone MA, Maia LN. Prognostic value of acute kidney injury after cardiac surgery according to kidney disease: improving global outcomes definition and staging (KDIGO) criteria. PLoS One. 2014;9(5):e98028. https://doi.org/10.1371/journal.pone.0098028.
31. James MT, Dixon E, Roberts DJ, et al. Improving prevention, early recognition and management of acute kidney injury after major surgery: results of a planning meeting with multidisciplinary stakeholders. Can J Kidney Health Dis. 2014;1:20. https://doi.org/10.1186/s40697-014-0020-y.
32. Nadim MK, Forni LG, Bihorac A, et al. Cardiac and vascular surgery-associated acute kidney injury: the 20th international consensus conference of the ADQI (acute disease quality initiative) group. J Am Heart Assoc. 2018;7(11):e008834. https://doi.org/10.1161/JAHA.118.008834.
33. Jamil M, Sultan I, Gleason TG, et al. Infective endocarditis: trends, surgical outcomes, and controversies. J Thorac Dis. 2019;11(11):4875–85. https://doi.org/10.21037/jtd.2019.10.45.
34. Vretzakis G, Georgopoulou S, Stamoulis K, et al. Cerebral oximetry in cardiac anesthesia. J Thorac Dis. 2014;6(Suppl 1):S60–9. https://doi.org/10.3978/j.issn.2072-1439.2013.10.22.
35. Hahn RT, Abraham T, Adams MS, et al. Guidelines for performing a comprehensive transesophageal echocardiographic examination: recommendations from the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists. J Am Soc Echocardiogr. 2013;26(9):921–64. https://doi.org/10.1016/j.echo.2013.07.009.
36. Navia JL, Elgharably H, Hakim AH, et al. Long-term outcomes of surgery for invasive valvular endocarditis involving the aortomitral fibrosa. Ann Thorac Surg. 2019;108(5):1314–23. https://doi.org/10.1016/j.athoracsur.2019.04.119.
37. Volk L, Verghis N, Chiricolo A, Ikegami H, Lee LY, Lemaire A. Early and intermediate outcomes for surgical management of infective endocarditis. J Cardiothorac Surg. 2019;14(1):211. https://doi.org/10.1186/s13019-019-1029-1.
38. Kim JB, Ejiofor JI, Yammine M, et al. Surgical outcomes of infective endocarditis among intravenous drug users. J Thorac Cardiovasc Surg. 2016;152(3):832–841.e1. https://doi.org/10.1016/j.jtcvs.2016.02.072.
39. Rabkin DG, Mokadam NA, Miller DW, Goetz RR, Verrier ED, Aldea GS. Long-term outcome for the surgical treatment of infective endocarditis with a focus on intravenous drug users. Ann Thorac Surg. 2012;93(1):51–7. https://doi.org/10.1016/j.athoracsur.2011.08.016.
40. Mourvillier B, Trouillet J-L, Timsit J-F, et al. Infective endocarditis in the intensive care unit: clinical spectrum and prognostic factors in 228 consecutive patients. Intensive Care Med. 2004;30(11):2046–52. https://doi.org/10.1007/s00134-004-2436-9.
41. Leroy O, Georges H, Devos P, et al. Infective endocarditis requiring ICU admission: epidemiology and prognosis. Ann Intensive Care. 2015;5:45. https://doi.org/10.1186/s13613-015-0091-7.
42. Samol A, Kaese S, Bloch J, et al. Infective endocarditis on ICU: risk factors, outcome and long-term follow-up. Infection. 2015;43:287–95. https://doi.org/10.1007/s15010-014-0715-0.

23 Anesthetic Management for Atrial Fibrillation Procedures in the Electrophysiology Lab

Keyur Trivedi, Gilbert Esselfie, Kinjal M. Patel, and Ronak G. Desai

Learning Points

The electrophysiology lab presents difficulties for the anesthesia team including a confined work space, difficulty accessing the patient and obtaining emergency supplies, and an ancillary staff that is unfamiliar with the practice of anesthesiology.

Patients with atrial fibrillation often have multiple comorbidities that must be managed perioperatively and impact the choice of anesthetic technique.

Pulmonary vein isolation is the most frequent **invasive** procedure for managing atrial fibrillation. This procedure requires the patient to be motionless during the ablation.

The anesthetic plan for the Watchman procedure should provide for absence of patient movement during deployment, including periods of apnea.

K. Trivedi (✉) · K. M. Patel · R. G. Desai
Department of Anesthesiology, Cooper Medical School of Rowan University, Cooper University Hospital, Camden, NJ, USA
e-mail: trivedi-keyur@cooperhealth.edu; patel-kinjal@cooperhealth.edu; desai-ronak@cooperhealth.edu

G. Esselfie
Fellow, Clinical Cardiac Electrophysiology, Department of Cardiology, Cooper University Hospital, Camden, NJ, USA
e-mail: essilfie-gilbert@cooperhealth.edu

Introduction

An estimated 33 million people globally are living with atrial fibrillation (AF) [1]. The incidence of AF increases with age; fewer than 1% of patients are under 60 years old and more than 33% of patients are over 80 years old. AF is categorized according to the durations of each episode (Table 23.1). The number of patients living with AF is increasing and they are presenting to electrophysiology (EP) labs in increasing numbers [1, 3]. The care of this patient population in the EP lab requires careful planning as the anesthesia provider has to work in a remote environment managing not only the patient's AF but also the many comorbidities found in this group (Table 23.2). This chapter will review the considerations of working in the EP lab and managing these complex patients for EP procedures involving the left atrium [pulmonary vein isolation (PVI) and implantation of left atrial appendage (LAA) occlusion devices] as well as atrioventricular (AV) node ablations for permanent AF.

Table 23.1 Describing atrial fibrillation [1, 2]

Paroxysmal	Terminates within 7 days of onset
Persistent	Lasts greater than 7 days
Long Standing Persistent	Lasts greater than 12 months
Permanent	Irreversible

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_23

Table 23.2 Chronic comorbid conditions in medicare beneficiaries with AF > 65 years old [2]

Comorbid condition	Incidence (%)
Hypertension	83.0
Ischemic heart disease	63.8
Hyperlipidemia	62.1
Heart failure	51.4
Anemia	42.3
Arthritis	39.8
Diabetes mellitus	36.5
Chronic kidney disease	32.3
Chronic obstructive pulmonary disorder	22.5

Working in the Electrophysiology Lab

Providing anesthesia care in the EP lab can be challenging. The workspace is often designed without the anesthesia provider in mind. Space for the anesthesia machine, medication cart and even the anesthesia provider may be limited. There may be a scarcity of power outlets or the location of the outlets may be inconvenient. Access to the patient is also limited once the procedure starts. The patient's arms are secured under sterile drapes. The equipment for the procedure, such as the fluoroscopy machine, lead shield, EP monitors and possibly transesophageal echo (TEE) machine acts as an obstacle between the anesthesia provider and the patient. The entrance to the EP lab may be across the room from the anesthesia provider, making access to additional equipment and emergency help difficult. In addition, the anesthesia provider may position themselves farther away from the patient to minimize their radiation exposure. For these reasons it becomes imperative to ensure adequate oxygenation and ventilation, sufficient intravenous (IV) line placement, arterial access if needed, access to ports for delivery of medication and drawing of blood samples prior to the start of the procedure. Additionally, the entire EP lab team should develop a plan for emergency management including the provision of supplies and equipment for the anesthesia team.

Another consideration when providing care in the EP lab is the remote location of the lab. The ancillary staff is often unfamiliar with the anesthesia equipment and the practice of anesthesiology. Oftentimes, the lab is on a separate floor relative to the operating room and anesthesia workroom. This distance makes access to anesthesia supplies difficult. Requests for additional drugs, equipment and provider help may be met with delays due to geography.

Preoperative Considerations

All patients presenting to the EP lab should have a thorough history and physical exam prior to their procedure. Identifying comorbid conditions and ensuring medical optimization are important preoperative goals. Preoperative testing generally consists of an electrocardiogram and echocardiogram, the latter of which is used to detect intracardiac thrombus and/or valvulopathies that may alter the planned anesthetic induction and maintenance. Cardiac stress testing may also be warranted in patients with poor functional status. Additional laboratory studies will be predicated on the medical history. A type and screen should be obtained given the potential for intraoperative bleeding.

Procedures in the Electrophysiology Lab and Anesthetic Considerations

Pulmonary Vein Isolation

The high prevalence of AF is well recognized and pulmonary vein isolation is the most frequently performed ablation procedure for managing AF [4].

The conventional method for AF ablation employs catheter-based radiofrequency (RF) energy for PVI and ablation of ectopic triggers of AF. In a randomized control trial—CASTLE-AF (Catheter Ablation vs. Standard Conventional Treatment in Patients With LV Dysfunction and AF), patients with heart failure with reduced ejection fraction (HFrEF) and paroxysmal or persistent AF and an implanted cardioverter-defibrillator who did not respond to or could not take antiarrhythmic drugs were randomized to

receive RF catheter ablation versus medical therapy in addition to guideline directed management for HFrEF. Patients in the ablation group had significantly lower mortality, reduced rate of hospitalization for HF and improved left ventricular systolic function [5]. Other ablation methods include cryoablation which applies cryoenergy from a balloon-tip catheter to freeze tissue at the pulmonary vein ostia and laser-ablation which uses laser energy in a balloon-tip catheter to achieve pulmonary vein isolation.

For RF ablation, bilateral femoral veins are cannulated, and venous sheaths are placed for access. An intracardiac echocardiography probe is advanced into the right atrium and used to create a live echocardiographic image of cardiac anatomy including the right and left pulmonary veins, left atrial appendage, superior vena-cava and interatrial septum. Heparin is infused and activated clotting time (ACT) is maintained above 300 s. Under ultrasound and fluoroscopic guidance, a trans-septal needle is advanced via a long sheath onto the interatrial septum and transseptal puncture is achieved in a posterior orientation. The sheath is advanced across the septum and the needle is withdrawn. An electroanatomic mapping catheter is advanced into the left atrium and used to generate an anatomic map of the posterior wall and pulmonary veins. Using the electroanatomic map, sequential contiguous lesions are delivered with an RF ablation catheter around the left and right pulmonary veins to electrically isolate the veins. During this part of the procedure, catheter stability is of prime importance to ensure adequate focal ablation and avoid gaps in the circumferential lesions around the pulmonary veins. The anesthetic management at this point of the procedure is critical for success. The ablation catheter is sequentially placed in each pulmonary vein and pacing pulses are delivered while monitoring electrical activity in the heart to confirm successful pulmonary vein isolation. At the end of the case, catheters are removed from the heart, sheaths are removed from the groin and hemostasis is achieved. Procedural complications include left atrial flutter/atrial tachycardia, cardiac perforation, pericarditis, cardiac tamponade, vascular access complications (bleeding, hematoma, pseudoaneurysms), thromboembolism, left atrium-esophageal fistulae, phrenic nerve injury and pulmonary vein stenosis.

Atrioventricular Junction/Node Ablation

Among patients with permanent AF, some present with recurrent symptomatic rapid ventricular rates that have failed attempts at maintaining rate control with several medications. Often these patients have failed attempts at rhythm control with prior ablation procedures, antiarrhythmic medications and cardioversions. These patients are evaluated by electrophysiologists and offered the option of pacemaker implantation and ablation of the AV junction to achieve rate control of AF.

Patients who are scheduled to have AV node ablation as a strategy for rate control usually undergo placement of a pacemaker prior to ablation. For AV node ablation, the right or left femoral vein is cannulated and venous sheaths are placed for access. A quadripolar catheter is advanced via the femoral vein into the right ventricle under fluoroscopic guidance and the His bundle anatomic location is identified using intracardiac electrograms and an electroanatomic mapping system. An ablation catheter is advanced into the right ventricle and is gradually withdrawn to the location of the compact AV node using fluoroscopy and intracardiac electrograms for guidance. RF lesions are delivered while monitoring intracardiac electrograms for junctional beats and evidence of complete heart block with a stable junctional escape rhythm. Patients are monitored and AV junction ablation is confirmed by demonstrating complete heart block on intracardiac electrograms. At the end of the case, catheters are removed from the heart, sheaths are removed from the groin and hemostasis is achieved. Procedural complications are rare, but these include vascular access complications (bleeding, hematoma, pseudoaneurysms) and myocardial injury or perforation.

Anesthetic Considerations

Both monitored anesthesia care (MAC) and general anesthesia (GA) are employed for the management of patients undergoing PVI procedures and AV node ablations. Each technique has its advantages and disadvantages. MAC is often performed with supplemental local anesthesia at the femoral cannulation site. Patient's receiving MAC usually receive less anesthetic drugs and are more hemodynamically stable during the procedure. MAC is usually sufficient for AV node ablations as the requirements for sedation and keeping patients still during this procedure are generally not as stringent because of the limited ablation required. GA has been described with both an endotracheal tube and laryngeal mask airway [6]. GA allows for controlled respiration (including periods of apnea) thus minimizing patient movement. In the absence of movement, the RF ablation catheter is more stable, and the PVI is more successful [7–9]. The choice of anesthetic technique is often determined by the patient's comorbidities, duration of the procedure, the electrophysiologist's needs for the procedure and the patient's preference. Additionally, the use of TEE may require the use of GA to provide a safer anesthetic.

Regardless of the type of anesthesia chosen, the intraoperative care of the patient should be consistent with the American Society of Anesthesia providers (ASA) standards for patient care in the operating room with additional considerations for the procedure and potential complications [10]. Prior to the start of the procedure, transcutaneous defibrillation pads should be placed on the patient [11]. Placing an arterial line may also be necessary, depending on the patient's comorbidities and hemodynamic changes expected during the procedure. Large bore IV access allows for rapid delivery of drugs and fluids should the patient need hemodynamic support or emergency management of a procedure related complication.

PVI requires specific anesthetic considerations, beyond those for AV node ablation, to address procedure-specific complications (Table 23.3). The amount of intravenous fluid given to a patient must be carefully managed, particularly the volume of fluid the patient receives via the RF ablation catheter which may total several liters during the case [11]. An atrial-esophageal fistula is a devastating complication with high mortality [13]. For patients receiving GA, an esophageal temperature probe is the preferred way to monitor temperature. An increase in the temperature greater than 38 °C may alert the team of an esophageal injury secondary to the RF ablation catheter. The risk of thromboembolic stroke can be reduced with heparin administration to prevent the formation of clots on the transseptal catheter [11]. Phrenic nerve injury is a known complication of the procedure (especially cryoablation) and the integrity of the nerve may be monitored during the procedure by the electrophysiologist. The use of muscle relaxants may prevent this monitoring and may mask a potential injury [12].

Table 23.3 Procedural complications during pulmonary vein isolation [11, 12]

Complication	Incidence
Myocardial perforation/cardiac tamponade	1.3%
Phrenic nerve injury	0.3–0.5% Up to 7% with cryoablation
Left atrium—esophageal fistula	0.04–0.2%
Stroke	0.4–1%
Esophageal ulcer	Up to 12%
Retroperitoneal bleed	0.07%

At the conclusion of the procedure patients are taken to the post anesthesia recovery area for further monitoring. Post anesthesia patients that are hemodynamically stable can usually be recovered in the standard recovery area. Patients remaining intubated or having hemodynamic instability may require an escalation of care to the intensive care unit for recovery. Regardless of the post-operative location, patients undergo routine post anesthetic recovery with special attention given to identifying signs and symptoms of procedure related complications. A retroperitoneal bleed may manifest as hypovolemia and may require further surgical intervention [11]. Patient monitoring should also focus on the possibility of thromboembolic ischemia. The patient

may not receive anticoagulation for several hours after the procedure. Despite a successful procedure, the atria might be stunned immediately after the ablation and may be prone to thrombus formation [11].

Left Atrial Appendage Occlusion: Watchman Implant

The Watchman device is an occlusion device implanted in the LAA of AF patients in whom long term anticoagulation is contraindicated. A meta-analysis combining data from the PROTECT AF (WATCHMAN Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation) and the PREVAIL (Evaluation of the WATCHMAN LAA Closure Device in Patients With Atrial Fibrillation) trials demonstrated that patients who received the device had significantly fewer hemorrhagic strokes than those receiving Warfarin [14].

The procedural flow for Watchman implantation is similar to that for PVI in many aspects. A TEE is performed to evaluate the left atrial appendage for thrombus as a pre-requisite for implantation. TEE is also used to size the LAA and determine the appropriate Watchman device size to facilitate optimal occlusion of the appendage. A venous sheath is placed in the femoral vein. Heparin infusion is started and ACT is maintained above 300 s. Using fluoroscopic and ultrasound guidance, trans-septal access is achieved. The sheath is advanced across the septum and a wire is advanced into the left superior pulmonary vein. The sheath is removed and a pig-tail catheter and Watchman access sheath are advanced over the wire and positioned into the left atrial appendage. Once the optimal position for the Watchman device is determined the pig-tail catheter is removed while the Watchman access sheath is kept in the LAA. A Watchman delivery sheath with a pre-loaded Watchman device is advanced into the LAA. The positioning, anchoring, size and seal are confirmed and the device is deployed under TEE and fluoroscopic guidance. During deployment, some electrophysiologists require a period of apnea (2–4 min) for stability and precise placement of the Watchman device. Once the positioning of the device is confirmed, catheters are removed from the heart, sheaths are removed from femoral access sites, and hemostasis is achieved.

Anesthetic Considerations

Patients presenting for LAA occlusion devices require special considerations for preoperative management beyond those mentioned above. A critical assessment of preoperative medications should also be completed, paying specific attention to antiarrhythmic and anticoagulation therapy. Because of the risk of bleeding during percutaneous LAA occlusion procedures, any anticoagulation beyond aspirin should be ceased prior to the day of surgery with laboratory evidence of complete reversal. However, institutional experience will ultimately determine the timing for discontinuation of anticoagulants [15].

Risks of LAA occlusion device procedures include cardiac rupture, pericardial effusion and tamponade, dysrhythmias, vascular access complications including abrupt and/or concealed hemorrhage, and device embolization requiring surgical exploration. (See Table 23.4 for incidence of major complications) As such, large bore intravenous access is paramount. Standard ASA monitoring for general anesthesia will suffice, but the medical history may necessitate continuous arterial blood pressure monitoring (e.g. low ejection fraction, valvular heart disease). Placement of ECG leads should not interfere

Table 23.4 Incidence of major complications associated with LAA occlusion device procedures [16]

Complication	Incidence (%)
Pericardial effusion requiring intervention	1.39
Major bleeding	1.25
Cardiac arrest	0.24
Death	0.19
Major vascular complication	0.15
Ischemic stroke	0.12
Device embolization	0.07

with fluoroscopy. Transcutaneous defibrillation pads should also be applied prior to the onset of the anesthetic. It may be prudent to have blood products available in the procedure room as well prior to commencement.

In the United States, general endotracheal anesthesia is the preferred anesthetic of choice given the necessity of continuous TEE monitoring for the WATCHMAN procedure. More recently, reports describe using intracardiac echocardiography (ICE) under moderate sedation as a means to eliminate TEE and the need for GA. Benefits with this approach have included shorter in-room time (by 18%), room turnover time (by 45%) and total fluoroscopy time (by 33%). Furthermore, potential improvements to the patient experience include reducing the risks associated with endotracheal intubation and esophageal instrumentation (e.g. tooth–lip injuries, esophageal tears, aspiration pneumonia, and ventilator dependence) [17, 18]. Although MAC anesthesia may seem favorable, the patient must tolerate the presence of the TEE probe, maintain the supine position for the duration of the procedure and lay motionless during key intraoperative events such as trans-septal puncture and device deployment. Institutional and proceduralist experience should be a consideration in the development of the anesthetic plan.

General anesthesia induction techniques in these patients may vary amongst anesthesia providers, but the overarching theme is that of hemodynamic stability and swift management of the airway. Benzodiazepines should be used judiciously especially in the aging population as it may contribute to prolonged emergence and/or postoperative cognitive dysfunction or delirium [19]. Nonopioids will generally be adequate for the procedure; however, opioids may be considered in patients taking opioids preoperatively or those who report incisional pain. The limited use of short-acting muscle relaxants can help facilitate early tracheal extubation at the end of the procedure. Short acting anesthetic agents should be used to permit a prompt neurologic exam to exclude peri-procedural neurologic events.

Intraoperative fluid management is governed by the patient's comorbidities, overall cardiac function and intraoperative blood loss. Generally, a conservative approach is used. However, arrhythmias and hypovolemia on TEE may necessitate larger fluid boluses. Crystalloids and colloids may be used at the discretion of the anesthesia team.

Additional intraoperative considerations include systemic anticoagulation with heparin immediately prior to trans-septal puncture. Initial heparin bolus is typically 100 units/kg to achieve a goal activated clotting time (ACT) of at least 300 s. Hemodynamics must be carefully monitored as the WATCHMAN device is advanced into the LAA, as there is an increased risk of dysrhythmias and LAA rupture during device expansion. After device deployment and the conclusion of the procedure, residual heparin may be left unreversed with a gradual normalization of the ACT or protamine may be administered to inactivate heparin. An ACT should be measured to confirm reversal.

Postoperatively, the patient should be monitored overnight for complications such as pericardial effusion, cardiac tamponade and groin hematoma. A transthoracic echocardiogram may be performed if clinical suspicion warrants and to confirm appropriate device position. Lastly, anticoagulation will be maintained for 45–90 days postoperatively, depending on practitioner experience [20, 21].

Conclusion

As the incidence of AF increases, EP procedures requiring anesthesia will also increase. The remote work environment in the EP lab requires special considerations. Patients can present complex anesthetic challenges and different procedures have specific anesthetic requirements. A well-developed anesthetic plan accounts for the challenges of the physical environment, the management of the patient's medical problems and knowledge of the procedure and its potential complications.

References

1. Chugh SS, Havmoeller R, Narayanan K, et al. Worldwide epidemiology of atrial fibrillation: a global burden of disease 2010 study. Circulation. 2014;129(8):837–47.
2. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. Circulation. 2014;130(23):e199–267.
3. Kece F, Zeppenfeld K, Trines SA, et al. The impact of advances in atrial fibrillation ablation devices on the incidence and prevention of complications. Arrhythmia Electrophysiol Rev. 2018;7(3):169–80.
4. Calkins H, Kuck KH, Cappato R, et al. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints and research trial design: a report of the Heart Rhythm Society (HRS) Task Force on Catheter and Surgical Ablation of Atrial Fibrillation. EP Eur. 2012;14(4):528–606.
5. Marrouche NF, Brachmann J, Andresen D, et al. Catheter ablation for atrial fibrillation with heart failure. N Engl J Med. 2018;378:417–27.
6. Koyama T, Kobayashi M, Ichikawa T, et al. Laryngeal mask versus facemask in the respiratory management during catheter ablation. BMC Anesthesiol. 2020;20:9.
7. DiBiase L, et al. General anesthesia reduces the prevalence of pulmonary vein reconnection during repeat ablation when compared with conscious sedation: results from a randomized study. Heart Rhythm. 2011;8(3):368–72.
8. Chikata A, Kato T, Yaegashi T, et al. General anesthesia improves contact force and reduces gap formation in pulmonary vein isolation: a comparison with conscious sedation. Heart Vessel. 2017;32:997–1005.
9. Martin CA, Curtain JP, Gajendragadkar PR, et al. Improved outcome and cost effectiveness in ablation of persistent atrial fibrillation under general anaesthetic. Europace. 2018;20:935–42.
10. The American Society of Anesthesia Providers. Standards for basic anesthetic monitoring. Committee on Standards and Practice Parameters. https://www.asahq.org/standards-and-guidelines/standards-for-basic-anesthetic-monitoring. Accessed March 24, 2020.
11. Malladi V, Naeini PS, Razavi M, et al. Endovascular ablation of atrial fibrillation. Anesthesiology. 2014;120(6):1513–9.
12. Price A, Santucci P. Electrophysiology procedures: weighing the factors affecting choice of anesthesia. Semin Cardiothorac Vasc Anesth. 2013;17(3):203–11.
13. Singh A, Whisenant TE, Peiris AN. Cardiac catheter ablation for heart rhythm abnormalities. JAMA. 2019;321(11):1128.
14. Holmes DR Jr, Doshi SK, Kar S, et al. Left atrial appendage closure as an alternative to warfarin for stroke Prevention in atrial fibrillation: a patient-level meta-analysis. J Am Coll Cardiol. 2015;65:2614–23.
15. Lee RJ, Lakkireddy D, Mittal S, et al. Percutaneous alternative to the Maze procedure for the treatment of persistent or long-standing persistent atrial fibrillation (aMAZE trial): rationale and design. Am Heart J. 2015;170:1184–94.
16. Freeman JV, Varosy P, Price MJ, Slotwiner D, Kusumoto FM, Rammohan C, Kavinsky CJ, Turi ZG, Akar J, Koutras C, Curtis JP, Masoudi FA. The NCDR left atrial appendage occlusion registry. J Am Coll Cardiol. 2020;75(13):1503–18.
17. Hemam ME, Kuroki K, Schurmann PA, Dave AS, Rodríguez DA, Sáenz LC, Reddy VY, Valderrábano M. Left atrial appendage closure with the Watchman device using intracardiac vs transesophageal echocardiography: procedural and cost considerations. Heart Rhythm. 2019;16:334–42.
18. Frangieh AH, Alibegovic J, Templin C, et al. Intracardiac versus transesophageal echocardiography for left atrial appendage occlusion with WATCHMAN. Catheter Cardiovasc Interv. 2017;90:331–8.
19. Maurice-Szamburski A, Auquier P, Viarre-Oreal V, Cuvillon P, Carles M, Ripart J, Honore S, Triglia T, Loundou A, Leone M, Bruder N, PremedX Study Investigators. Effect of sedative premedication on patient experience after general anesthesia: a randomized clinical trial. JAMA. 2015;313(9):916–25.
20. Holmes DR, Kar S, Price MJ. Prospective randomized evaluation of the WATCHMAN left atrial appendage closure device in patients with atrial fibrillation versus long-term warfarin therapy: the PREVAIL trial. J Am Coll Cardiol. 2014;64:1–12.
21. Baker MS, Mounsey JP, Gehi AK, Chung EH. Left atrial thrombus after appendage ligation with LARIAT. Heart Rhythm. 2014;11:1489.

24

Hypertrophic Cardiomyopathy-Anesthesia Considerations for Septal Myectomy

Regina E. Linganna, Ron L. Leong, and Eric T. Feduska

Introduction

The earliest documented association between enlarged hearts and sudden cardiac death was made through a collection of post mortem examinations by Swiss physician Théophile Bonet and Italian anatomist John Baptiste Morgagni in the late seventeenth and early eighteenth century, respectively [1]. However, British pathologist Robert Donald Teare is often credited with the modern discovery of what is now referred to as hypertrophic cardiomyopathy (HCM) in 1958. Remarkably, in a case series of eight patients, Dr. Teare characterized the hallmarks of HCM as an asymmetric LV hypertrophy, an abnormal myocardial appearance on histology, and a familial pattern of inheritance [2].

Since then, the terminology to describe this disease has evolved over time which is reflective of our improved understanding. Initially, Dr. Eugene Braunwald and colleagues put forth a comprehensive review of 64 patients highlighting the obstructive form of this condition and, consequently, coined the diagnosis of idiopathic hypertrophic subaortic stenosis (IHSS) [3]. IHSS, hypertrophic obstructive cardiomyopathy and as many as 75 different names have been attributed to this disease entity [4]. Nonetheless, HCM is the preferred terminology for primary non-dilated left ventricular hypertrophy in the absence of a secondary cause such as cardiac, systemic or metabolic etiology.

Epidemiology

HCM is the most common genetic cardiovascular disease with a reported prevalence of 1 case per 200–500 persons in the general population based on epidemiologic studies [5, 6]. Based on conservative estimates of the most current census data, the possible number of affected people with HCM in the United States extrapolates out to approximately 660,000 persons. However, as progress has been made in understanding HCM, it is increasingly clearer that the overall disease burden is underrecognized and far-reaching. HCM is a global disorder that affects men and women equally in 122 countries and 90% of the world's population [7].

Pathophysiology

There is considerable heterogeneity in the genotypic and phenotypic presentation of HCM. Although suggested by Dr. Teare over 60 years ago, the familial pattern of inheritance was not confirmed until 1990 with the discovery of a mutation in a cardiac beta-myosin heavy

R. E. Linganna (✉) · R. L. Leong · E. T. Feduska
Thomas Jefferson University, Philadelphia, PA, USA
e-mail: Regina.linganna@jefferson.edu; Ron.leong@jefferson.edu; Eric.feduska@jefferson.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_24

chain [8]. Since then, we have learned that HCM has an autosomal dominant pattern of inheritance with over 2000 mutations identified in 11 or more genes encoding cardiac sarcomere proteins with varying degrees of pathogenicity [9–11]. As such, a gene positive person can present phenotypically with a clinical spectrum that ranges widely from asymptomatic to symptomatic with any combination of the absence or presence of left ventricular hypertrophy, left ventricular outflow tract (LVOT) obstruction, heart failure, and arrhythmias.

The root cause of HCM begins with a disorganized arrangement of the cardiac sarcomere. The mutations cause a disarray of the myocardial architecture with myocytes aligned at perpendicular and oblique angles rather than the normal parallel pattern. These nucleotide sequence variants most commonly affect the beta-myosin heavy chain and myosin-binding protein C genes that are vital for encoding sarcomeric contractile proteins [12]. The disrupted myocardial structure then leads to hypertrophy and interstitial fibrosis. This can affect any anatomic region of the left ventricle (basal, mid-ventricular, apical) with varying patterns (diffuse, segmental, focal) and may even extend to the right ventricle [13, 14]. A completely concentric or symmetric pattern is rare for HCM and would suggest a secondary cause of hypertrophy.

As the myocardium enlarges, the coronary microvasculature becomes compromised and predisposes the heart to myocardial ischemia, fibrosis, conduction abnormalities, and heart failure [15]. The increased wall to vessel lumen ratio and the tunneling of the coronary vasculature within the hypertrophied myocardium leads to decreased circulatory flow in the setting of increased oxygen demand. Moreover, the compensatory remodeling of the heart in response to ongoing ischemia and fibrosis further exacerbates this detrimental progression with worsening impairment of left ventricular relaxation, left ventricular and left atrial pressures, wall tension, LVOT obstruction, and arrhythmias.

Arrhythmias

HCM is known to cause both atrial and ventricular arrhythmias. Atrial fibrillation is the most common arrhythmia seen, and it occurs in 22–32% of patients with HCM [16]. The elevated left atrial pressures and left atrial enlargement commonly seen in this population are predisposing factors to the development of paroxysmal or chronic atrial fibrillation. Atrial fibrillation can be particularly harmful in HCM patients due to the loss of the atrial kick to ventricular filling in the setting of significant diastolic dysfunction and left ventricular hypertrophy. Furthermore, there is an increased risk of worsening heart failure and embolic stroke [17]. However, the majority of patients with atrial fibrillation and HCM are asymptomatic and the atrial fibrillation is discovered incidentally. There is debate regarding how atrial fibrillation affects mortality ranging the gamut from increasing mortality significantly to not affecting overall mortality [18].

The risk of arrhythmias ranges from this relatively common occurrence of atrial fibrillation to the infrequent occurrence of lethal ventricular tachyarrhythmias. HCM is the most common cause of sudden death in young people and is invariably the most devastating [19]. Often times there are no warning signs or symptoms; however, it is frequently associated with strenuous physical exertion [20]. Reviews of electrocardiograms from HCM patients suffering sudden cardiac deaths showed that a primary ventricular tachycardia or ventricular fibrillation were the main causes of death [21]. The degree of cellular disarray and fibrosis correlate to a higher arrhythmogenicity and risk of sudden death [22]. Ischemia is thought to also play a role in the development of ventricular arrhythmias, as the coronary arteries narrow over time as they transverse the hypertrophied myocardium [23]. There are also electrophysiological abnormalities that result in conduction delay and block, which is consistent with the regions of scarred myocardium [24]. Interestingly, Maron et al. reports that HCM patients who live

into their seventh decade and beyond have their risk of sudden cardiac death normalized to general population rates [25].

Left Ventricular Outflow Tract Obstruction and Systolic Anterior Motion of the Anterior Mitral Valve Leaflet

The pathophysiology of LVOT obstruction in HCM is multifactorial. Anatomically, the abnormalities of the mitral valve apparatus in addition to an asymmetrical LV hypertrophy increase susceptibility for LVOT obstruction. The potential anomalies of the mitral valve apparatus include anterior displacement of the mitral valve, anterior leaflet elongation, intrinsic valve dysplasia, chordal laxity, accessory papillary heads, papillary muscle hypertrophy, and an anteriorly displaced papillary muscle with anomalous attachment directly to the valve [26]. Of the numerous phenotypic expressions of LV hypertrophy in HCM, septal involvement is most associated with LVOT obstruction and of this subset, the catenoid and neutral septal morphologies have been identified to have the highest resting gradients [27].

Another important contributing factor to LVOT obstruction in HCM is the systolic anterior motion (SAM) of the mitral valve. Historically, it was initially thought that high velocity in the LVOT pulled the anterior mitral leaflet perpendicularly into the LVOT by Venturi effect [28]. However, several studies have shown that drag forces are responsible for linearly displacing an abnormally positioned mitral valve apparatus into the LVOT [29]. Additionally, there is a dynamic component to the LVOT obstruction that is related to variable loading conditions (decreased preload, decreased afterload), contractility, and heart rate that alter the size of the ventricular cavity relative to the size and location of the mitral valve apparatus and worsen subaortic pressure gradients. Likely, SAM is resultant of a mixture both the Venturi effect and drag forces [30–32].

SAM and LVOT obstruction occur in approximately 70% of patients with HCM. This anterior motion of the mitral valve results in left ventricular outflow tract obstruction either at rest with or exercise. Peak gradients across the LVOT are typically >30 mmHg [33]. These gradients are often referred to as subaortic gradients as that is where the highest flow velocities typically occur. These gradients are dynamic and very responsive to a change in loading conditions, as is often experienced with general anesthesia.

Significant mitral regurgitation (MR) results from SAM of the mitral valve and native abnormalities of the mitral valve apparatus. SAM related MR leads to a restricted anterior leaflet motion and a subsequent malcoaptation of the leaflets. Unrelated to SAM, MR can develop from primary degenerative MV disease. Coupled with these potential etiologies of MR is the presence of increased intracavitary LV pressures that exacerbates the MR.

Clinical Course

Patients can be diagnosed with hypertrophic cardiomyopathy at any point in life, from the neonatal period to geriatric patients in their final decade of life. The clinical course of the disease tends to fall into one of three categories [34]. The first category is that of sudden cardiac death. These are often the cases that are publicized in the news media when a young athlete dies suddenly on the playing field. The second course is a more indolent one, in which the patient exhibits progressive symptoms of exertional dyspnea and chest pain. These patients will have normal systolic function, and the symptomatology is secondary to diastolic heart failure. A subset of these patients will present with progressive heart failure and left ventricular remodeling. The third category contains those patients who show complications related to atrial fibrillation such as embolic stroke or right heart failure.

Heart failure with preserved ejection fraction or diastolic dysfunction is common with HCM. This can occur with or without LVOT

obstruction and can eventually progress to systolic compromise. The disarray of the cellular structure and microvascular dysfunction causes increased myocardial interstitial fibrosis, ventricular stiffness and decreased compliance. In addition, LVOT obstruction and increased left ventricular pressures present a systolic mechanical impedance to outflow which potentiates diastolic dysfunction. Worsening impairment of left ventricular relaxation causes a rise in left atrial pressures, left atrial enlargement, and pulmonary hypertension [35]. A subset of HCM patients with heart failure with preserved ejection fraction will progress to end-stage heart failure with reduced ejection fraction [36]. There is a conversion of the conventional HCM presentation from hypertrophic hearts with reduced end-diastolic volumes to an end stage presentation with dilated cardiomyopathy attributed to diffuse, irreversible myocardial scarring [37].

Medical Management

As the primary goal of treatment is to relieve symptoms of heart failure, many of the treatment options for hypertrophic cardiomyopathy overlap with those of heart failure. Beta-adrenergic blocking agents (atenolol, metoprolol, and propranolol) and calcium-channel blockers (verapamil and diltiazem) are often first-line agents given their atrioventricular nodal blocking. They are also able to inhibit the sympathetic surge that occurs with exercise [38].

Surgical Management

When patients remain symptomatic, despite medical therapy, alcohol septal ablation or septal myectomy is indicated [39]. In alcohol septal ablations, the first septal branch of the left anterior descending coronary artery is injected with ethanol, which results in myocardial infarction and subsequently decreased muscle mass of the interventricular septum. This is a percutaneous procedure is most commonly performed in a cardiac catheterization lab. In a septal myectomy, the interventricular septum is excised from just below the aortic annulus to the level of the papillary muscles [40]. This procedure is performed in the operating room on cardio-pulmonary bypass. Patients with LVOT obstruction who undergo surgical myectomy have been shown to have long-term survival equivalent to the general population [41]. Surgical myectomy has been shown to decrease the number of lethal arrhythmias, regardless of the resulting gradient across the LVOT [42].

For patients with persistent symptoms despite pharmacologic therapy, both alcohol septal ablation and surgical myectomy have been shown to reduce LVOT obstruction and improve NYHA class in HCM. Choosing the appropriate non-pharmacologic intervention is a challenge. In addition to patient preferences, the decision must consider the pathophysiology of the LVOT obstruction, concomitant cardiac problems, as well as medical comorbidities. Irrespective of the intervention selected, the procedure should be performed at an experienced center, as the rates of morbidity, mortality, and procedural complications are all significantly better at experienced centers [43–47].

Alcohol Septal Ablation

Alcohol septal ablation induces circumscribed infarction of the hypertrophied myocardium with the injection of alcohol into septal branches of the left anterior descending coronary artery. The resulting septal thinning, widens the left ventricular outflow tract and relieves the obstructive pathophysiology. Although complete remodeling can take weeks to months to occur, the initial myocardial stunning can result in immediate improvements in gradients [5, 34, 43, 48–51]. Patients deemed poor surgical candidates or who wish to avoid open heart surgery can undergo, alcohol septal ablation as an alternative to septal myectomy [5, 43, 48, 49, 51].

Complications from alcohol septal ablation include: complete heart block, coronary artery dissection, pericardial effusion, and ventricular fibrillation [52]. Transient conduction abnormali-

ties after the injection of ethanol are common. Permanent conduction abnormalities are the result of the long-term effects of myocardial scarring and remodeling [52]. The development of malignant arrhythmias, including ventricular fibrillation and ventricular tachycardia, is also attributable to the intentional infarction of myocardium.

Septal Myectomy

For patients with severe symptoms or significant gradients, surgical septal myectomy is a class I indication [5, 34, 43, 48–50]. Surgical myectomy relieves the left ventricular outflow tract obstruction by direct removal of the hypertrophied musculature.

The surgical approach occurs through a median sternotomy with the support of cardiopulmonary bypass. Since a variety of HCM variants exist, the surgical technique will vary depending on the location of the ventricular hypertrophy and the obstruction. Asymmetric hypertrophy of the basal septum is the most common and best described phenotype. In cases of basal septal hypertrophy, the hypertrophied septum is excised via a transaortic approach [53, 54]. Midventricular obstruction, results from the apposition of the midventricle septum and the lateral wall or papillary muscles during systole. Given its anatomical location in the midventricular a transapical approach is favored for adequate surgical exposure [53, 55–57]. Resections for apical HCM are also approached transapically [53, 57, 58].

In general, there is no significant difference in survival when comparing surgical myomectomy versus alcohol ablation for the treatment of HCM. Both procedures effectively relieve obstruction and improve patient symptoms. The advantages of alcohol ablation revolve around its less invasive nature. A major disadvantage of alcohol septal ablation, is its inability to address concomitant abnormalities of the mitral valve, papillary muscles, or coronaries [5, 34, 48–50]. Compared to surgical myomectomy, alcohol septal ablation is associated with a higher risk of need for permanent pacemaker placement [38]. Additionally, the use of alcohol septal ablation in cases of massive LV hypertrophy and severe gradients, may have little benefit [59]. Proper procedure selection is best based on the individual patient [44, 60–67].

Preoperative Evaluation

One should obtain a thorough history and physical from the patient. This should include a history of atrial and ventricular arrhythmias as described previously, as well as if the patient has a personal history of SAM with or without LVOT obstruction.

Physical Exam

On physical exam, patients with LVOT obstruction will demonstrate a loud apical systolic ejection murmur [68].

Echo Findings

Two-dimensional echocardiography has been used to diagnosis hypertrophic cardiomyopathy [69]. One will see asymmetric left ventricular hypertrophy, not associated with a dilated left ventricle, in the absence of other cause of hypertrophy, such as chronic hypertension or aortic stenosis [68]. The LVOT is usually >15 mm thick. While echocardiography was formerly the primary means of diagnosis, cardiac magnetic resonance imagining is coming to the forefront in the modern era of cardiac imaging [70].

AICD Placement

Automatic implantable cardioverter-defibrillator (AICD) has been shown to be very effective in primary and secondary prevention of sudden cardiac death (SCD) from HCM. Maron et al. showed that when placed for primary prevention, the AICD discharged appropriately for life-

threatening ventricular arrhythmias in 20% of the approximately 500 high-risk patients they enrolled [71]. This study paved the way for placement of an AICD in patients with one high-risk factor for SCD in the HCM population. If an AICD has been placed, it should be interrogated prior to surgery.

Anesthetic Management for Septal Myectomy

Induction

Septal myectomy is a procedure that is performed via median sternotomy on cardio-pulmonary bypass (CPB). As such the induction of general anesthesia is necessary.

The volume status of the patient is of paramount importance. With decreased intravascular volume, the left ventricular cavity also has less volume, predisposing the patient to SAM and LVOT obstruction. Therefore, the patient should be euvolemic prior to induction of general anesthesia. These patients should be scheduled for the first case of the day in order to limit the time that they need to remain nil per os. The patient should be permitted to drink clear liquids until 2 h prior to surgery.

Great care should be taken to avoid a sympathetic surge associated with patient anxiety preoperatively as well as with laryngoscopy. This can be accomplished with opioids and benzodiazepines. While judicious administration of these are useful in preventing sympathetic stimulation at the beginning of the case, it is important to be planning for emergence as well. This group of patients tend to be younger and with minimal other comorbidities, making them great candidates for early extubation, either in the intensive care unit or the operating room.

Neuromuscular blocking drugs should utilized during induction and throughout the case to optimize the surgical conditions. The patient should not be ventilated during sternotomy as to allow the lungs to collapse to prevent injury.

A post-induction arterial catheter should be placed in order to facilitate transition on and off CPB. As mentioned previously, these patients tend to have few other comorbidities, making the placement of a pre-induction arterial catheter unnecessary in most instances.

Central venous access is typically obtained during these cases. While inotropic drugs are not often necessary, given that they will put the patient at an increased risk of SAM and LVOT obstruction, vasopressor support is often needed to maintain afterload. A pulmonary artery catheter is not typically placed in these patients. As mentioned, these patients tend to be without other major comorbidities, making a pulmonary artery catheter superfluous in hemodynamic management.

Blood products should be available for the patient; however, it is unlikely that this procedure will require the patient to be transfused.

Maintenance

As alluded to previously, the patient should be deeply anesthetized. Light anesthesia will result in sympathetic stimulation. This will result in an increased inotropic state, which will increase the patient's risk of SAM and LVOT obstruction. Euvolemia should be maintained as hypovolemia will predispose the patient to SAM and LVOT obstruction. This will best be monitored with intraoperative transesophageal echocardiography (TEE). Neuromuscular blocking drug should be used to maintain an ideal surgical field.

Intraoperative Transesophageal Echocardiography

Intraoperative TEE in an invaluable tool in this procedure. The TEE will be used to confirm the preoperative diagnosis of HCM. The cardiac anesthesiologist will measure the thickness of the interventricular septum to guide the surgeon in his or her decision of how much of the septum to "shave off." It will allow the team to evaluate for the gradients across the LVOT, as well as assess the degree of LVOT obstruction and SAM.

After the aortic cross clamp is removed, TEE will allow for the team to evaluate the resolution of the interventricular septal thickness, often described as the septal knuckle. Here one can also assess the resolution of SAM and LVOT obstruction if there was obstruction prior to CPB. After aortic cross-clamp removal, myocardial irritability is common and arrhythmias should be anticipated and addressed with either electrical or pharmacologic conversion. Post bypass reductions in systemic vascular resistance and vasoplegia can be treated with phenylephrine or vasopressin. With time, post procedural hypotension will improve. One will also assess for the critical complication of a septal myectomy, the iatrogenic ventricular septal defect (VSD).

Emergence and Extubation

As these patients tend to have few comorbidities, they make excellent candidates for early extubation, whether that be in the operating room or the intensive care unit. Opioids should be titrated to facilitate this. These patient are also ideal candidates for multimodal analgesia and an Enhanced Recovery After Surgery (ERAS) if one exists at the institution in which surgery is being performed.

Procedural Complications

Surgical complications after myomectomy include complete heart block, a membranous ventricular septal defect, or injury to the mitral or aortic valves [53, 54]. A left bundle branch block and partial left bundle branch block are common postoperatively, and in the setting of a preoperative right bundle branch block, there is an increased likelihood of complete heart block [53, 54]. TEE can be used to assess the degree of residual mitral regurgitation and evidence of continued SAM and LVOT obstruction. Because of the potential for an iatrogenic VSD, the ventricular septum should be closely inspected for shunting. Small shunts resulting from the transection of septal perforating coronaries arteries are not uncommon. These clinically insignificant shunts must be distinguished from true iatrogenic VSDs. If an iatrogenic VSD is present, the resulting shunt is expected to occur from the left ventricle to right ventricle—shunts due to transected septal perforators occur in the opposite direction. The timing of the shunt during the cardiac cycle can also be used to differentiate the type of shunt that is present. Shunting that occurs during systole is most consistent with iatrogenic VSDs whereas shunting seen during diastole, a time of coronary filling, is most consistent with exposed septal perforators.

Conclusions

Septal myectomy for HCM is a procedure that is performed under general anesthesia with the assistance of cardio-pulmonary bypass. It is critical that the anesthesiologist be familiar with the pathophysiology of HCM and its complications in order to ensure that the patient undergo a safe anesthetic. Familiarity with transesophageal echocardiography is essential in guiding surgical management and confirming a successful procedure. Hemodynamics must also be optimized throughout the procedure in order to maintain an adequate cardiac output, and decreased the incidence of left ventricular outflow tract obstruction.

References

1. Coats CJ, Hollman A. Hypertrophic cardiomyopathy: lessons from history. Heart. 2008;94(10):1258–63. https://doi.org/10.1136/hrt.2008.153452.
2. Teare D. Asymmetrical hypertrophy of the heart in young adults. Br Heart J. 1958;20(1):1–8.
3. Braunwald E, Lambrew CT, Rockoff SD, Ross J, Morrow AG. Idiopathic hypertrophic subaortic stenosis: I. A description of the disease based upon an analysis of 64 patients. Circulation. 1964;30:3–119. https://doi.org/10.1161/01.CIR.29.5S4.IV-3.
4. Maron BJ, Seidman CE, Ackerman MJ, et al. How should hypertrophic cardiomyopathy be classified? What's in a name? Dilemmas in nomenclature characterizing hypertrophic Cardiomyopathy and left ventricular hypertrophy. Circ Cardiovasc

Genet. 2009;2(1):81–6. https://doi.org/10.1161/CIRCGENETICS.108.788703.
5. Maron BJ, Ommen SR, Semsarian C, Spirito P, Olivotto I, Maron MS. Hypertrophic cardiomyopathy: Present and future, with translation into contemporary cardiovascular medicine. J Am Coll Cardiol. 2014;64(1):83–99. https://doi.org/10.1016/j.jacc.2014.05.003.
6. Semsarian C, Ingles J, Maron MS, Maron BJ. New perspectives on the prevalence of hypertrophic cardiomyopathy. J Am Coll Cardiol. 2015;65(12):1249–54. https://doi.org/10.1016/j.jacc.2015.01.019.
7. Maron BJ, Rowin EJ, Maron MS. Global burden of hypertrophic cardiomyopathy. JACC Heart Fail. 2018;6(5):376–8. https://doi.org/10.1016/j.jchf.2018.03.004.
8. Geisterfer-Lowrance AAT, Kass S, Tanigawa G, et al. A molecular basis for familial hypertrophic cardiomyopathy: a β cardiac myosin heavy chain gene missense mutation. Cell. 1990;62(5):999–1006. https://doi.org/10.1016/0092-8674(90)90274-I.
9. Burke MA, Cook SA, Seidman JG, Seidman CE. Clinical and mechanistic insights into the genetics of cardiomyopathy. J Am Coll Cardiol. 2016;68(25):2871–86. https://doi.org/10.1016/j.jacc.2016.08.079.
10. Maron BJ, Maron MS, Semsarian C. Genetics of hypertrophic cardiomyopathy after 20 years: clinical perspectives. J Am Coll Cardiol. 2012;60(8):705–15. https://doi.org/10.1016/j.jacc.2012.02.068.
11. Biagini E, Olivotto I, Iascone M, et al. Significance of sarcomere gene mutations analysis in the end-stage phase of hypertrophic cardiomyopathy. Am J Cardiol. 2014;114(5):769–76. https://doi.org/10.1016/j.amjcard.2014.05.065.
12. Maron BJ. Clinical course and management of hypertrophic cardiomyopathy. In: Longo DL, editor. N Engl J Med. 2018;379(7):655–68. https://doi.org/10.1056/NEJMra1710575.
13. Maron BJ, Maron MS. The remarkable 50 years of imaging in HCM and how it has changed diagnosis and management: from M-mode echocardiography to CMR. JACC Cardiovasc Imaging. 2016;9(7):858–72. https://doi.org/10.1016/j.jcmg.2016.05.003.
14. Maron MS, Hauser TH, Dubrow E, et al. Right ventricular involvement in hypertrophic cardiomyopathy. Am J Cardiol. 2007;100(8):1293–8. https://doi.org/10.1016/j.amjcard.2007.05.061.
15. Camici PG, Olivotto I, Rimoldi OE. The coronary circulation and blood flow in left ventricular hypertrophy. J Mol Cell Cardiol. 2012;52(4):857–64. https://doi.org/10.1016/j.yjmcc.2011.08.028.
16. Patten M, Pecha S, Aydin A. Atrial fibrillation in hypertrophic cardiomyopathy: diagnosis and considerations for management. J Atr Fibrillation. 2018;10(5):1556. https://doi.org/10.4022/jafib.1556.
17. Olivotto I, Cecchi F, Casey SA, Dolara A, Traverse JH, Maron BJ. Impact of atrial fibrillation on the clinical course of hypertrophic cardiomyopathy. Circulation. 2001;104(21):2517–24.
18. Elliott PM, Anastasakis A, Borger MA, et al. 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy: the Task Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC). Eur Heart J. 2014;35(39):2733–79. https://doi.org/10.1093/eurheartj/ehu284.
19. Maron BJ, Doerer JJ, Haas TS, Tierney DM, Mueller FO. Sudden deaths in young competitive athletes: analysis of 1866 deaths in the United States, 1980–2006. Circulation. 2009;119(8):1085–92. https://doi.org/10.1161/CIRCULATIONAHA.108.804617.
20. Maron BJ, Maron MS, Lesser JR, et al. Sudden cardiac arrest in hypertrophic Cardiomyopathy in the absence of conventional criteria for high risk status. Am J Cardiol. 2008;101(4):544–7. https://doi.org/10.1016/j.amjcard.2007.09.101.
21. Maron BJ. Contemporary insights and strategies for risk stratification and prevention of sudden death in hypertrophic cardiomyopathy. Circulation. 2010;121(3):445–56. https://doi.org/10.1161/CIRCULATIONAHA.109.878579.
22. Chan RH, Maron BJ, Olivotto I, et al. Prognostic value of quantitative contrast-enhanced cardiovascular magnetic resonance for the evaluation of sudden death risk in patients with hypertrophic cardiomyopathy. Circulation. 2014;130(6):484–95. https://doi.org/10.1161/CIRCULATIONAHA.113.007094.
23. Moore B, Semsarian C, Chan KH, Sy RW. Sudden cardiac death and ventricular arrhythmias in hypertrophic cardiomyopathy. Heart Lung Circ. 2019;28(1):146–54. https://doi.org/10.1016/j.hlc.2018.07.019.
24. Schumacher B, Gietzen FH, Neuser H, et al. Electrophysiological characteristics of septal hypertrophy in patients with hypertrophic obstructive Cardiomyopathy and moderate to severe symptoms. Circulation. 2005;112(14):2096–101. https://doi.org/10.1161/CIRCULATIONAHA.104.515643.
25. Maron BJ, Rowin EJ, Casey SA, et al. Risk stratification and outcome of patients with hypertrophic cardiomyopathy ≥60 years of age. Circulation. 2013;127(5):585–93. https://doi.org/10.1161/CIRCULATIONAHA.112.136085.
26. Maron MS, Olivotto I, Harrigan C, et al. Mitral valve abnormalities identified by cardiovascular magnetic resonance represent a primary phenotypic expression of hypertrophic Cardiomyopathy. Circulation. 2011;124(1):40–7. https://doi.org/10.1161/CIRCULATIONAHA.110.985812.
27. Turer AT, Samad Z, Valente AM, et al. Anatomic and clinical correlates of septal morphology in hypertrophic cardiomyopathy. Eur J Echocardiogr. 2011;12(2):131–9. https://doi.org/10.1093/ejechocard/jeq163.
28. Henry WL, Clark CE, Griffith JM, Epstein SE. Mechanism of left ventricular outflow obstruction in patients with obstructive asymmetric septal hypertrophy (idiopathic hypertrophic subaortic stenosis). Am J Cardiol. 1975;35(3):337–45. https://doi.org/10.1016/0002-9149(75)90025-9.

29. Sherrid MV, Gunsburg DZ, Moldenhauer S, Pearle G. Systolic anterior motion begins at low left ventricular outflow tract velocity in obstructive hypertrophic cardiomyopathy. J Am Coll Cardiol. 2000;36(4):1344–54. https://doi.org/10.1016/S0735-1097(00)00830-5.
30. Shah PM, Kramer DAH, et al. Circulation. 1969;40:9.
31. Maslow AD, Regan MM, Haering JM, Johnson RG, Levine RA. Echocardiographic predictors of left ventricular outflow tract obstruction and systolic anterior motion of the mitral valve after mitral valve reconstruction for myxomatous valve disease. J Am Coll Cardiol. 1999;34(7):2096–104. https://doi.org/10.1016/S0735-1097(99)00464-7.
32. Jiang L, Levine RA, King ME, Weyman AE. An integrated mechanism for systolic anterior motion of the mitral valve in hypertrophic cardiomyopathy based on echocardiographic observations. Am Heart J. 1987;113(3):633–44. https://doi.org/10.1016/0002-8703(87)90701-0.
33. Maron MS, Olivotto I, Zenovich AG, et al. Hypertrophic cardiomyopathy is predominantly a disease of left ventricular outflow tract obstruction. Circulation. 2006;114(21):2232–9. https://doi.org/10.1161/CIRCULATIONAHA.106.644682.
34. Gersh BJ, Maron BJ, Bonow RO, et al. 2011 ACCF/AHA guideline for the diagnosis and treatment of hypertrophic cardiomyopathy: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2011;124(24):e783–831. https://doi.org/10.1161/CIR.0b013e318223e2bd.
35. Maron MS, Olivotto I, Betocchi S, et al. Effect of left ventricular outflow tract obstruction on clinical outcome in hypertrophic cardiomyopathy. N Engl J Med. 2003;348(4):295–303. https://doi.org/10.1056/NEJMoa021332.
36. Maron BJ, Rowin EJ, Udelson JE, Maron MS. Clinical spectrum and management of heart failure in hypertrophic cardiomyopathy. JACC Heart Fail. 2018;6(5):353–63. https://doi.org/10.1016/j.jchf.2017.09.011.
37. Rowin EJ, Maron BJ, Abt P, et al. Impact of advanced therapies for improving survival to heart transplant in patients with hypertrophic Cardiomyopathy. Am J Cardiol. 2018;121(8):986–96. https://doi.org/10.1016/j.amjcard.2017.12.044.
38. Kaplan J. Kaplan's cardiac anesthesia. 7th ed. Philadelphia, PA: Elsevier; 2017.
39. Solomon Z, Breton C, Rowin EJ, et al. Surgical approaches to hypertrophic obstructive Cardiomyopathy. Semin Thorac Cardiovasc Surg. 2018;30(2):125–8. https://doi.org/10.1053/j.semtcvs.2018.02.034.
40. Excision of anomalous muscle bundles as an important addition to extended septal myectomy for treatment of left ventricular outflow tract obstruction. Elsevier Enhanced Reader. https://doi.org/10.1016/j.jtcvs.2016.01.051
41. Ommen SR, Maron BJ, Olivotto I, et al. Long-term effects of surgical septal myectomy on survival in patients with obstructive hypertrophic cardiomyopathy. J Am Coll Cardiol. 2005;46(3):470–6. https://doi.org/10.1016/j.jacc.2005.02.090.
42. McLeod CJ, Ommen SR, Ackerman MJ, et al. Surgical septal myectomy decreases the risk for appropriate implantable cardioverter defibrillator discharge in obstructive hypertrophic cardiomyopathy. Eur Heart J. 2007;28(21):2583–8. https://doi.org/10.1093/eurheartj/ehm117.
43. Maron BJ, Nishimura RA. Surgical septal myectomy versus alcohol septal ablation: assessing the status of the controversy in 2014. Circulation. 2014;130(18):1617–24. https://doi.org/10.1161/CIRCULATIONAHA.114.011580.
44. Alam M, Dokainish H, Lakkis NM. Hypertrophic obstructive cardiomyopathy-alcohol septal ablation vs. myectomy: a meta-analysis. Eur Heart J. 2009;30(9):1080–7. https://doi.org/10.1093/eurheartj/ehp016.
45. Kim LK, Swaminathan RV, Looser P, et al. Hospital volume outcomes after septal myectomy and alcohol septal ablation for treatment of obstructive hypertrophic cardiomyopathy: US nationwide inpatient database, 2003–2011. JAMA Cardiol. 2016;1(3):324–32. https://doi.org/10.1001/jamacardio.2016.0252.
46. Bonow RO, Yancy CW. Procedural volumes, outcomes, and quality in hypertrophic cardiomyopathy. JAMA Cardiol. 2016;1(3):334. https://doi.org/10.1001/jamacardio.2016.0711.
47. Ommen SR, Nishimura RA. Hypertrophic Cardiomyopathy—one case per year? A clarion call to do what is right. JAMA Cardiol. 2016;1(3):333–4. https://doi.org/10.1001/jamacardio.2016.0277.
48. Maron BJ, Maron MS. Hypertrophic cardiomyopathy. Lancet. 2013;381(9862):242–55. https://doi.org/10.1016/S0140-6736(12)60397-3.
49. Maron BJO. Hypertrophic cardiomyopathy. In: Braunwald's heart disease: a textbook of cardiovascular medicine. 10th ed. Philadelphia, PA: Elsevier/Saunders; 2014.
50. Maron BJ, McKenna WJ, Danielson GK, et al. American College of Cardiology/European Society of Cardiology clinical expert consensus document on hypertrophic cardiomyopathy. A report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents and the European Society of Cardiology Committee for Practice Guidelines. J Am Coll Cardiol. 2003;42(9):1687–713. https://doi.org/10.1016/s0735-1097(03)00941-0.
51. Sigwart U. Non-surgical myocardial reduction for hypertrophic obstructive cardiomyopathy. Lancet. 1995;346(8969):211–4. https://doi.org/10.1016/s0140-6736(95)91267-3.
52. Alam M, Dokainish H, Lakkis N. Alcohol septal ablation for hypertrophic obstructive cardiomyopathy: a systematic review of published studies. J Interv Cardiol. 2006;19(4):319–27. https://doi.org/10.1111/j.1540-8183.2006.00153.x.

53. Said SM, Schaff HV. Surgical treatment of hypertrophic cardiomyopathy. Semin Thorac Cardiovasc Surg. 2013;25(4):300–9. https://doi.org/10.1053/j.semtcvs.2014.01.001.
54. Schaff HV, Said SM. Transaortic extended septal myectomy for hypertrophic cardiomyopathy. Oper Tech Thorac Cardiovasc Surg. 2012;17(4):238–50. https://doi.org/10.1053/j.optechstcvs.2012.04.002.
55. Kunkala MR, Schaff HV, Nishimura RA, et al. Transapical approach to myectomy for midventricular obstruction in hypertrophic cardiomyopathy. Ann Thorac Surg. 2013;96(2):564–70. https://doi.org/10.1016/j.athoracsur.2013.04.073.
56. Ong KC, Geske JB, Schaff HV, Nishimura RA. Transapical myectomy for severe mid-ventricular obstructive hypertrophic cardiomyopathy. Eur Heart J. 2014;35(39):2713. https://doi.org/10.1093/eurheartj/ehu146.
57. Said SM, Schaff HV, Abel MD, Dearani JA. Transapical approach for apical myectomy and relief of midventricular obstruction in hypertrophic cardiomyopathy. J Card Surg. 2012;27(4):443–8. https://doi.org/10.1111/j.1540-8191.2012.01475.x.
58. Schaff HV, Brown ML, Dearani JA, et al. Apical myectomy: a new surgical technique for management of severely symptomatic patients with apical hypertrophic cardiomyopathy. J Thorac Cardiovasc Surg. 2010;139(3):634–40. https://doi.org/10.1016/j.jtcvs.2009.07.079.
59. ten Cate FJ, Soliman OII, Michels M, et al. Long-term outcome of alcohol septal ablation in patients with obstructive hypertrophic cardiomyopathy: a word of caution. Circ Heart Fail. 2010;3(3):362–9. https://doi.org/10.1161/CIRCHEARTFAILURE.109.862359.
60. Valeti US, Nishimura RA, Holmes DR, et al. Comparison of surgical septal myectomy and alcohol septal ablation with cardiac magnetic resonance imaging in patients with hypertrophic obstructive cardiomyopathy. J Am Coll Cardiol. 2007;49(3):350–7. https://doi.org/10.1016/j.jacc.2006.08.055.
61. Maron BJ. Is septal ablation preferable to surgical myomectomy for obstructive hypertrophic cardiomyopathy? Circulation. 2007;116:196. https://doi.org/10.1161/CIRCULATIONAHA.107.691378.
62. Liebregts M, Vriesendorp PA, Mahmoodi BK, Schinkel AFL, Michels M, ten Berg JM. A systematic review and meta-analysis of long-term outcomes after septal reduction therapy in patients with hypertrophic cardiomyopathy. JACC Heart Fail. 2015;3(11):896–905. https://doi.org/10.1016/j.jchf.2015.06.011.
63. Sorajja P, Ommen SR, Holmes DR, et al. Survival after alcohol septal ablation for obstructive hypertrophic cardiomyopathy. Circulation. 2012;126(20):2374–80. https://doi.org/10.1161/CIRCULATIONAHA.111.076257.
64. Vriesendorp PA, Liebregts M, Steggerda RC, et al. Long-term outcomes after medical and invasive treatment in patients with hypertrophic cardiomyopathy. JACC Heart Fail. 2014;2(6):630–6. https://doi.org/10.1016/j.jchf.2014.06.012.
65. Steggerda RC, Damman K, Balt JC, Liebregts M, ten Berg JM, van den Berg MP. Periprocedural complications and long-term outcome after alcohol septal ablation versus surgical myectomy in hypertrophic obstructive cardiomyopathy: a single-center experience. JACC Cardiovasc Interv. 2014;7(11):1227–34. https://doi.org/10.1016/j.jcin.2014.05.023.
66. Nguyen A, Schaff HV, Hang D, et al. Surgical myectomy versus alcohol septal ablation for obstructive hypertrophic cardiomyopathy: a propensity score–matched cohort. J Thorac Cardiovasc Surg. 2019;157(1):306–315.e3. https://doi.org/10.1016/j.jtcvs.2018.08.062.
67. Kimmelstiel C, Zisa DC, Kuttab JS, et al. Guideline-based referral for septal reduction therapy in obstructive hypertrophic cardiomyopathy is associated with excellent clinical outcomes. Circ Cardiovasc Interv. 2019;12(7):e007673. https://doi.org/10.1161/CIRCINTERVENTIONS.118.007673.
68. American College of Cardiology/European Society of Cardiology Clinical Expert Consensus Document on Hypertrophic cardiomyopathy. Elsevier Enhanced Reader. https://doi.org/10.1016/S0735-1097(03)00941-0
69. Klues HG, Schiffers A, Maron BJ. Phenotypic spectrum and patterns of left ventricular hypertrophy in hypertrophic cardiomyopathy: morphologic observations and significance as assessed by two-dimensional echocardiography in 600 patients. J Am Coll Cardiol. 1995;26(7):1699–708. https://doi.org/10.1016/0735-1097(95)00390-8.
70. Maron MS, Maron BJ, Harrigan C, et al. Hypertrophic cardiomyopathy phenotype revisited after 50 years with cardiovascular magnetic resonance. J Am Coll Cardiol. 2009;54(3):220–8. https://doi.org/10.1016/j.jacc.2009.05.006.
71. Maron BJ, Spirito P, Shen W-K, et al. Implantable cardioverter-defibrillators and prevention of sudden cardiac death in hypertrophic cardiomyopathy. JAMA. 2007;298(4):405–12. https://doi.org/10.1001/jama.298.4.405.

Surgical Ventricular Remodeling (SVR): Anesthesia Considerations

25

Lucas Giunta, Daniel Katz, and Ron L. Leong

Introduction

Heart failure affects around 6.5 million people in the United States and remains one of the leading causes of death each year [1]. Approximately two thirds of those with heart failure are caused by coronary artery disease and ischemic cardiomyopathy [2]. The overall prognosis is poor for patients with advanced congestive heart failure (CHF) as the 5 year survival rate is less than 50% and even more grim when ischemia is the cause for CHF [3, 4]. In these ischemic areas, cardiac myocytes undergo necrosis and heart function becomes compromised regardless of timing or effectiveness of revascularization. There is a natural injurious process that occurs thereby leading to left ventricular (LV) dilatation, increased wall stress and further worsening of heart failure.

Medical therapy targeting the neurohormonal activation with angiotensin-converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARB), beta blockers, and aldosterone antagonists have shown the ability to improve the survival and quality of life in this patient population [5]. However, when the size of the LV or extent of myocardial necrosis has increased beyond a recoverable threshold, heart failure progresses despite optimal medical management. Surgical ventricular remodeling or reconstruction (SVR) is a procedure that was introduced to directly address the deleterious post-myocardial infarction (MI) ventricular remodeling by restoring the size and shape of the left ventricle and, in turn, reduce myocardial wall tension and improve heart function.

The goals for this chapter are to understand the pre-operative concerns, intra-operative anesthetic management, and perioperative complications related to SVR. The patient presenting for SVR are among the most challenging anesthetic cases for the cardiac anesthesia provider due to the critical pre-existing co-morbidities associated with advanced heart failure.

Pathophysiology

Following myocardial infarction, the patient's heart experiences changes in structure and configuration that adversely affect its ability to function [6]. As the damaged heart fails to meet the demands of the body, pressure rises in the ventricles and wall tension increases. Living heart

L. Giunta · D. Katz
Department of Anesthesiology, Thomas Jefferson University Hospital, Philadelphia, PA, USA
e-mail: Lucas.Giunta@jefferson.edu; Daniel.Katz4@jefferson.edu

R. L. Leong (✉)
Department of Anesthesiology, Thomas Jefferson University Hospital, Philadelphia, PA, USA

Department of Anesthesiology, Sidney Kimmel Medical College, Philadelphia, PA, USA
e-mail: Ron.Leong@jefferson.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_25

tissue responds by increasing sarcomere number and myocyte size leading to an increased ventricular cavity size. Meanwhile, damaged tissue responds with fibrosis and scar tissue formation. The increase in the ventricular cavity size and pressure without a compensatory increase in wall thickness, or hypertrophy, results in a rise in wall stress as dictated by Laplace's Law (LV wall stress is proportional to the LV radius and pressure within the LV, and inversely proportional to LV wall thickness). This process causes a change in the heart's shape and composition leading to an increase in myocardial oxygen demand, reduction in subendocardial perfusion and in the percentage of blood pumped per contraction [7, 8]. It is this functional reduction that leads to the characteristic symptomatology of congestive heart failure. Prognostically, a post-infarction left ventricular end-systolic volume (LVESV) greater than 60 ml/m^2 leads to a fivefold increase in mortality compared to a normal LVESV of 30 ml/m^2 or less [9].

The alterations in the geometric shape of the LV also plays a crucial role in the post-infarcted remodeling process. The normal LV has an elliptical structure with rapid torsional deformations for ventricular ejection and filling [10]. The diseased heart undergoes a shape transformation to a more spherical architecture that greatly compromises LV torsion and function. The loss of the uniform twisting contraction contributes to an inefficient and reduced ventricular work [11]. In addition, mitral regurgitation (MR) commonly occurs through dilatation of the mitral annulus and displacement of the posterior papillary muscle. The severity of the MR is independently associated with a worse prognosis regardless of LV function [12].

An altered and fibrotic myocardial architecture leads to an electrical remodeling and an increased risk of life-threatening ventricular arrhythmias such as ventricular tachycardia (VT) and ventricular fibrillation (VF). The risk of mortality due to ventricular arrhythmia is reported to be as high as 50% [13]. During the remodeling process, there is decreased electrical conduction through intercalated disks, decreased gap junctions, inactivation of sodium, calcium, and potassium ion channels in the myocytes, and increases in collagen content [14]. These detrimental changes cause disruption to normal cardiac conduction and promote an arrhythmogenic prolonged QT interval and reentry arrhythmias [14]. Furthermore, an elevated LVESV index is associated with an increased ventricular arrhythmia potential [15]. The ventricular conduction delay and dyssynchrony also compromises LV systolic and diastolic performance through uneven contraction, relaxation, and filling [16].

Evidence for Surgical Ventricular Remodeling

There is considerable ongoing debate regarding the clinical effectiveness of SVR. The pathophysiological reasoning behind the surgical procedure is logical and convincing. However, the insights from the existing literature paint an unclear picture for the role of ventricular reconstruction.

Hypothesis II of the STICH (Surgical Treatment for Ischemic Heart failure) trial is the best data available as it is the only prospective, randomized, controlled trial to specifically compare coronary artery bypass grafting (CABG) with or without SVR [17]. This large multicenter study comprised of 1000 patients with an inclusion criteria that involved patients with CAD requiring CABG, an LV ejection fraction (LV EF) of 35% or less, and an anterior akinetic or dyskinetic region of myocardium amenable to ventricular reconstruction. There was no significant difference seen in the primary outcome, a composite of death from any cause or cardiac related hospitalization, when compared at 48 months. Although the data demonstrated a reduction in LVESV in the "CABG with SVR" group, the results were unimpressive for the routine use of the SVR procedure in patients with systolic heart failure with CABG.

The proponents of SVR point to the relatively small percentage reduction in LVESV after SVR that left a still dilated LV (greater than 60 ml/m^2) as a significant reason for the STICH trial's failure to show mortality benefit [18, 19]. A STICH trial post hoc analysis demonstrated that a

post-operative LVESV of 70 ml/m^2 or less resulted in a survival benefit of the "CABG with SVR" group compared to CABG alone [20]. Moreover, the STICH trial does not mention any myocardial viability testing to confirm the appropriate operative indication of non-viable myocardium for SVR [18]. The design of STICH trial protocol was also completed at a time when the use of cardiac magnetic resonance imaging (cMRI) with late gadolinium enhancement (LGE), the gold standard imaging modality for cardiac viability, was not widespread which further complements the concern for proper patient selection for SVR.

Despite the numerous observational studies with consistent results suggesting reduced LV size, improved LV shape, improved LV function, improved symptoms and high survival rates with ventricular reconstruction [21–24], the results from the STICH trial continue to cloud the picture for the standard use of SVR with CABG for post-infarction patients with substantial systolic LV dysfunction. Further research with prospective, randomized, controlled studies are needed to assess SVR's role in certain clinical subtypes.

Pre-operative Evaluation

Diagnostic Work-Up

Additional testing should include a complete blood count, coagulation studies, electrolyte panel, baseline electrocardiogram (ECG) and an echocardiographic examination. Typically, a complete, comprehensive transthoracic echocardiogram (TTE) exam is performed with an added focus on LV function, LV dimensions, regional wall motion abnormalities, right ventricular (RV) function, degree of MR, presence of left atrial appendage (LAA) or LV thrombus, and presence of an LV aneurysm. Echocardiography can be limited in its ability to completely visualize the heart's apex and endocardial borders when large cardiac volumes are present [19]. Nonetheless, echocardiography provides a quick, noninvasive and inexpensive test to evaluate the feasibility and aptness of the procedure.

Cardiac magnetic resonance imaging (cMRI) with late gadolinium enhancement (LGE) has become an important imaging modality when evaluating heart anatomy, function and scar extension [25]. Gadolinium is a contrast agent that gets taken up into the extracellular compartment. Unlike normal myocardium where the tissue is densely packed with myocytes, infarcted areas of the heart have an expanded extracellular space and will appear bright on cMRI with LGE. In terms of surgical planning, cMRI with LGE provides a roadmap outlining viable myocardium from endoventricular scar that can be surgically excluded. This imaging technique is currently the gold standard assessment for quantification of myocardial fibrosis, viability, and LV volumes [26]. When cMRI is not able to be performed due to the presence of metal in the body (i.e. automated implantable cardioverter defibrillator [AICD] or pacemaker), then a cardiac computed tomography (CT), positron emission tomography (PET) or nuclear scanning may be considered.

Surgical ventricular remodeling is still largely done in combination with coronary artery revascularization. In preparation for a possible surgical coronary revascularization, left sided heart catheterization is necessary for operative planning. Coronary angiography provides useful metrics for defining ischemic burden and CAD territories. In addition, ventriculography allows for accurate quantification of left ventricular function. A right sided heart catheterization may also be helpful in diagnosing pre-existing pulmonary hypertension and to measure the patient's cardiac output.

Physical Exam Findings

Physical examination findings can provide valuable insight into the extent of a patient's volume status, ventricular size, filling pressures, and cardiac output. Patients with volume overload show evidence of lower extremity swelling, jugular venous distention and rales consistent with pulmonary congestion. Cardiomegaly causes displacement of the api-

cal impulse upon palpation of the lateral chest wall. Subsequent elevation of left sided filling pressures results in the presence of an S3 heart gallop. The finding of an S3 heart gallop is highly specific for the clinical diagnosis of heart failure in studied populations [27]. Signs of poor tissue perfusion include tachycardia, narrow pulse pressure, delayed capillary refill and peripheral vasoconstriction. Alternating strong and weak peripheral pulses, also known as "pulsus alternans," is also highly suggestive of left ventricular systolic dysfunction.

Medications

Heart failure patients will often be prescribed a host of cardiovascular medications designed to medically manage their symptoms and lower their risk of disease progression. The decision to continue or discontinue these medications prior to surgery can pose a challenge to the anesthesia team and alter the intra-operative anesthetic plan. The medical management of heart failure with CAD will generally include, at a minimum, the use of aspirin, statins, beta-blockers, ACE inhibitors, ARBs, and diuretics.

The continuation of aspirin pre-operatively warrants discussions at a multidisciplinary level. Some observational data has suggested a reduction in hospital mortality following CABG in patients that have continued aspirin pre-operatively [28]. Likewise, Statins and beta-blockers are also recommended for continuation prior to surgical procedures. Statins provide few intra-operative concerns and studies suggest a reduction in cardiovascular events following surgery [29]. Beta-blockers have similarly shown reduction in perioperative ventricular arrhythmias and post-operative atrial arrythmias [30]. Conversely, the continuation of ACE inhibitors and ARBs and diuretics before surgery is still being debated. It is hypothesized that the blockage of the renin-angiotensin compensatory responses from ACE inhibitors and ARBs can cause unnecessary hypotension intra-operatively. It is reasonable to discontinue all ACE inhibitors and ARBs prior to the day of surgery for this reason. Diuretics can also cause gratuitous drops in blood pressure and continuation should be based on the volume status of the patient.

SVR Indications

The severity of the patient's heart failure symptoms, the functional appearance of the patient's myocardium, and the extent to which there is myocardial scarring are important considerations for SVR [19]. The indications for SVR are currently not well defined and procedural planning must account for patient specific factors on a case by case basis. Patients that are suggested to benefit from SVR procedures generally have had a previous MI with regional wall motion abnormality, evidence of an eccentric dilated cardiomyopathy, and heart failure symptoms refractory to heart failure medical treatment. A patient's functional status as it relates to heart failure severity is often described using the New York Heart Association (NYHA) functional class designations. SVR patients should meet NYHA class III or IV where symptoms occur with minor activities or at rest. Additionally, patients with recurrent angina or ventricular dysrhythmias who meet the other conditions for SVR surgery may be considered to prevent unfavorable ventricular evolution.

SVR Contraindications

Diligent and comprehensive operative planning are the pillars for a successful SVR procedure. The diagnostic work-up should confirm there is non-viable myocardium that can be surgically excluded. In addition, patients with a small pre-operative ventricular size should be avoided due to the higher likelihood of worse diastolic function with SVR [31]. Similarly, patients with a restrictive pattern of diastolic dysfunction with MR and a high functional status (NYHA greater than class II) had a higher operative risk of mortality with SVR and should be avoided [22]. Lastly, patients with severe RV dysfunction and severe pulmonary hyperten-

sion not secondary to MR should not be operative candidates due to worsened long-term outcomes after SVR [32].

Intra-operative Anesthesia Management

Surgical Procedure

The procedure was first developed by Vincent Dor, a French cardiac surgeon, in 1985. Although there are several accepted techniques for SVR, the "Dor procedure" remains the most popular. His technique involves replacing scarred heart tissue with surgical patching to bypass the damaged sections and provide an attachment point for healthy endocardial muscle [23]. This excludes non-contractile cardiac muscle and restores function. The procedure has been modified from its original form to include the placement of an intraventricular balloon prior to suturing the patch to provide structure to the unfilled ventricle. This balloon provides assurance that the heart retains a more physiologic elliptical shape. The balloon is then removed prior to complete surgical closure of the heart. SVR is performed under total cardiac arrest and is frequently done after myocardial revascularization with CABG and, if indicated, before mitral valve (MV) repair or replacement [19, 23].

Induction Considerations

The primary concern for the anesthesia provider taking care of a patient presenting for SVR is the poor myocardial reserve and the risk for significant hemodynamic decompensation during induction of anesthesia. Occasionally, these patients arrive to the operating room with an intra-aortic balloon pump (IABP) in place to augment cardiac output and coronary perfusion pressure. A pre-induction arterial catheter placement is highly advisable for real-time blood pressure monitoring. If an IABP is in place, then invasive blood pressure monitoring can be achieved through slaving of the central aortic pressures from the IABP. A careful induction of general anesthesia with a high dose opioid technique is recommended to avoid dramatic hemodynamic changes. Generally, these patients are not fast track extubation candidates. The goal is to avoid increases in myocardial oxygen demand through blunting of the sympathetic effects of laryngoscopy and intubation while sustaining coronary perfusion pressure with optimization of preload and afterload. Inotropes and vasopressors should be readily available for hemodynamic support as needed.

Other considerations include avoiding excessive afterload and bradycardia if significant MR (moderate to severe) is present in order to reduce the regurgitant fraction of the stroke volume. Moreover, a normal sinus rhythm should be maintained, if possible, to preserve atrial contribution to the stroke volume. In scenarios when multiple pathologies are present, especially in the setting of low cardiac reserve, there is a fine balance for the optimal hemodynamics making the anesthetic management even more challenging.

Monitoring

In addition to the standard American Society of Anesthesia providers (ASA) intra-operative monitors, it is preferable for patients to have invasive hemodynamic monitoring with an arterial catheter, central venous catheter (CVC), pulmonary artery catheter (PAC) or also known as a Swan-Ganz catheter, and transesophageal echocardiography (TEE). As mentioned earlier, arterial catheters are necessary for second-by-second blood pressure monitoring during cardiac surgery where profound blood pressure changes occur frequently and acutely. Arterial catheters also allow for drawing blood to monitor intra-operative and post-operative arterial blood gases, electrolytes, glucoses, hemoglobin levels, and coagulation studies.

Central venous access is needed for the anticipated administration of vasoactive medications and the potential for large volume resuscitation. Furthermore, the monitoring of central venous pressures (CVP) through the CVC, and the moni-

toring of pulmonary artery pressures (PAP), pulmonary capillary wedge pressures (PCWP), mixed venous oxygen saturation (SvO_2), and cardiac outputs through the PAC provide vital information about how the heart is performing. These invasive monitors serve to unravel the complex underlying mechanism of an unstable heart failure patient.

Maintenance

Muscle relaxation is maintained throughout the surgical procedure with intermittent dosing of neuromuscular blocking agents. To ensure an adequate anesthetic depth, an inhaled anesthetic is typically used to supplement the opioid anesthetic and to reduce the risk of intra-operative awareness. A working temporary pulse generator for epicardial pacing, external cardiac defibrillator with electrode pads, and blood products should be available at hand in the operating room.

Intra-operative TEE

The utilization of TEE is an invaluable imaging modality during the SVR operation. The intra-operative TEE goals can be categorized as pre cardiopulmonary bypass (CPB) and post CPB findings. The pre CPB assessment is vital in confirming the operative plan with or without a combined procedure. The post CPB assessment focuses on a successful transition off CPB and to evaluate for any surgical complications.

Prior to CPB initiation, a comprehensive exam should be completed with similar emphases as the pre-operative echocardiographic assessment. The exam should include a comparison to the pre-operative findings and assessment of preload, LV size dimensions during systole and diastole, LV function, regional wall motion abnormalities, RV function, presence of intracavitary LV thrombus, spontaneous echo contrast, LV aneurysm, and LAA thrombus. A thorough assessment of the MV is necessary to aid the cardiac surgeon's decision for a possible concomitant MV repair or replacement. Often times, the severe functional MR is present due to the dilatation of the MV annulus resulting in malcoaptation of the MV leaflets. Inferior territory infarcts can cause posterior wall motion abnormalities and posterior papillary muscle displacement thereby contributing to the MR [33]. If an IABP is present, the tip of the IABP should be confirmed to be approximately 1 cm distal to the aortic arch to ensure proper positioning.

When the patient is ready for separation from CPB, the TEE is used to exclude the presence of intra-cardiac air, iatrogenic aortic dissection, and critical surgical complications. The echocardiographer should assess the previously dysfunctional LV wall segment for any improvement, the integrity of the ventricular patch repair with its accompanying suture lines, and the adequacy of any valvular intervention. Meanwhile continuous attention to the ventricular preload and contractility is required during operative care until the end of the case.

Procedural Complications

In the setting of severe, pre-existing CAD, the potential for hemodynamic changes throughout the operation results in an increased risk for exacerbating myocardial ischemia and infarction. A sympathetic surge can occur during laryngoscopy, intubation, surgical incision, or median sternotomy. An adequate anesthetic depth attenuates this sympathetic response and maintains an optimal myocardial oxygen demand to supply ratio. Alternatively, the induction and maintenance of general anesthesia may cause an afterload reduction and hypotension that could compromise coronary perfusion. A cautious approach to the patient's volume status is paramount to avoid excessive fluid administration that may lead to the detrimental cycle of increased LV size, wall tension, and ischemia. Likewise, the concurrent increase in the MV annulus size can worsen MR and precipitate pulmonary edema.

A low cardiac output state is not uncommonly seen in this patient population. Inotropes such as epinephrine, dobutamine, or milrinone are gener-

ally needed in the immediate post bypass and operative period. The placement or continuation of an IABP may be needed and slowly weaned post-operatively. Atrioventricular synchrony with atrial pacing or biventricular pacing may assist with augmenting cardiac output at heart rates of 90–100 beats per minute.

Intraoperative arrhythmias are frequently experienced during cardiac surgery. Arrhythmias can occur when the aortic cross clamp is removed due to myocardial electrochemical irritability. It is important to monitor and correct electrolytes throughout the perioperative period. The patients presenting for SVR have an inherent susceptibility to developing life-threatening arrhythmias as discussed earlier in this chapter. Up to 30–40% of patients undergoing SVR encountered intraoperative arrhythmias, with a higher incidence of atrial fibrillation (AF) than VT or VF [34, 35].

When an accompanying MV repair or replacement is performed, there is a potential for an inadequate valvular intervention with resultant mitral stenosis, paravalvular leaks, or improper leaflet motion. Additionally, there is a rare risk of unintentional suture placement into the left circumflex coronary artery as it courses adjacent to the MV and can cause an associated vascular territory cardiac dysfunction. It is essential to evaluate and rule out these complications on TEE exam.

Post-operative bleeding requiring blood transfusions from a SVR procedure has been reported to be as high as 20%, however, the rate of surgical re-exploration was low [34]. In a separate cohort of patients, there was a higher risk of bleeding after CABG with SVR than without SVR [36]. In addition to ensuring normothermia and correcting laboratory coagulopathy, bleeding from the ventriculotomy or patch repair site must be suspected as a cause for ongoing bleeding.

Conclusion

SVR is a procedure that may benefit a specific subgroup of heart failure patients. The proper perioperative management of the patient requires coordination with the cardiac surgeon, heart failure cardiologist, and the cardiac anesthesia provider. It is important for anesthesia providers to understand the complex pathophysiology of ischemic dilated cardiomyopathy to supplement their anesthetic management and to be prepared for the possible intra-operative complications that can arise.

Funding and Conflicts of Interest

None.

References

1. Benjamin EJ, Muntner P, Alonso A, et al. Heart disease and stroke statistics-2019 update: a report from the American Heart Association. Circulation. 2019;139(10):e56–e528. https://doi.org/10.1161/CIR.0000000000000659.
2. Gheorghiade M, Bonow RO. Chronic heart failure in the United States: a manifestation of coronary artery disease. Circulation. 1998;97(3):282–9. https://doi.org/10.1161/01.cir.97.3.282.
3. Engelfriet PM, Hoogenveen RT, Boshuizen HC, van Baal PHM. To die with or from heart failure: a difference that counts: is heart failure underrepresented in national mortality statistics? Eur J Heart Fail. 2011;13(4):377–83. https://doi.org/10.1093/eurjhf/hfq223.
4. Felker GM, Shaw LK, O'Connor CM. A standardized definition of ischemic cardiomyopathy for use in clinical research. J Am Coll Cardiol. 2002;39(2):210–8. https://doi.org/10.1016/s0735-1097(01)01738-7.
5. Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. Circulation. 2017;136(6):e137–61. https://doi.org/10.1161/CIR.0000000000000509.
6. Cohn JN, Ferrari R, Sharpe N. Cardiac remodeling—concepts and clinical implications: a consensus paper from an international forum on cardiac remodeling. Behalf of an international forum on cardiac remodeling. J Am Coll Cardiol. 2000;35(3):569–82. https://doi.org/10.1016/s0735-1097(99)00630-0.
7. McKay RG, Pfeffer MA, Pasternak RC, et al. Left ventricular remodeling after myocardial infarction: a corollary to infarct expansion. Circulation. 1986;74(4):693–702. https://doi.org/10.1161/01.cir.74.4.693.
8. Olivetti G, Capasso JM, Meggs LG, Sonnenblick EH, Anversa P. Cellular basis of chronic ventricular remodeling after myocardial infarction in rats. Circ

Res. 1991;68(3):856–69. https://doi.org/10.1161/01.res.68.3.856.
9. White HD, Norris RM, Brown MA, Brandt PW, Whitlock RM, Wild CJ. Left ventricular end-systolic volume as the major determinant of survival after recovery from myocardial infarction. Circulation. 1987;76(1):44–51. https://doi.org/10.1161/01.cir.76.1.44.
10. Shapiro EP, Rademakers FE. Importance of oblique fiber orientation for left ventricular wall deformation. Technol Health Care. 1997;5(1–2):21–8.
11. Sasayama S, Nonogi H, Fujita M, et al. Analysis of asynchronous wall motion by regional pressure-length loops in patients with coronary artery disease. J Am Coll Cardiol. 1984;4(2):259–67. https://doi.org/10.1016/s0735-1097(84)80211-9.
12. Rossi A, Dini FL, Faggiano P, et al. Independent prognostic value of functional mitral regurgitation in patients with heart failure. A quantitative analysis of 1256 patients with ischaemic and non-ischaemic dilated cardiomyopathy. Heart. 2011;97(20):1675–80. https://doi.org/10.1136/hrt.2011.225789.
13. St John Sutton M, Lee D, Rouleau JL, et al. Left ventricular remodeling and ventricular arrhythmias after myocardial infarction. Circulation. 2003;107(20):2577–82. https://doi.org/10.1161/01.CIR.0000070420.51787.A8.
14. Azevedo PS, Polegato BF, Minicucci MF, Paiva SAR, Zornoff LAM. Cardiac remodeling: concepts, clinical impact, pathophysiological mechanisms and pharmacologic treatment. Arq Bras Cardiol. 2016;106(1):62–9. https://doi.org/10.5935/abc.20160005.
15. DiDonato M, Sabatier M, Dor V, Buckberg G, RESTORE Group. Ventricular arrhythmias after LV remodelling: surgical ventricular restoration or ICD? Heart Fail Rev. 2004;9(4):299–306.; discussion 347–351. https://doi.org/10.1007/s10741-005-6806-3.
16. Shanmugam G, Ali IS. Surgical ventricular restoration: an operation to reverse remodeling—the basic science (part I). Curr Cardiol Rev. 2009;5(4):343–9. https://doi.org/10.2174/157340309789317878.
17. Jones RH, Velazquez EJ, Michler RE, et al. Coronary bypass surgery with or without surgical ventricular reconstruction. N Engl J Med. 2009;360(17):1705–17. https://doi.org/10.1056/NEJMoa0900559.
18. Conte J. An indictment of the STICH trial: "true, true, and unrelated". J Heart Lung Transplant. 2010;29(5):491–6. https://doi.org/10.1016/j.healun.2009.12.010.
19. Castelvecchio S, Garatti A, Gagliardotto PV, Menicanti L. Surgical ventricular reconstruction for ischaemic heart failure: state of the art. Eur Heart J Suppl. 2016;18(Suppl E):E8–E14. https://doi.org/10.1093/eurheartj/suw028.
20. Michler RE, Rouleau JL, Al-Khalidi HR, et al. Insights from the STICH trial: change in left ventricular size after coronary artery bypass grafting with and without surgical ventricular reconstruction. J Thorac Cardiovasc Surg. 2013;146(5):1139–1145.e6. https://doi.org/10.1016/j.jtcvs.2012.09.007.
21. Athanasuleas CL, Buckberg GD, Stanley AWH, et al. Surgical ventricular restoration in the treatment of congestive heart failure due to post-infarction ventricular dilation. J Am Coll Cardiol. 2004;44(7):1439–45. https://doi.org/10.1016/j.jacc.2004.07.017.
22. Menicanti L, Castelvecchio S, Ranucci M, et al. Surgical therapy for ischemic heart failure: single-center experience with surgical anterior ventricular restoration. J Thorac Cardiovasc Surg. 2007;134(2):433–41. https://doi.org/10.1016/j.jtcvs.2006.12.027.
23. Castelvecchio S, Menicanti L, Donato MD. Surgical ventricular restoration to reverse left ventricular remodeling. Curr Cardiol Rev. 2010;6(1):15–23. https://doi.org/10.2174/157340310790231626.
24. Dor V, Civaia F, Alexandrescu C, Sabatier M, Montiglio F. Favorable effects of left ventricular reconstruction in patients excluded from the Surgical Treatments for Ischemic Heart Failure (STICH) trial. J Thorac Cardiovasc Surg. 2011;141(4):905–916, 916.e1–4. https://doi.org/10.1016/j.jtcvs.2010.10.026.
25. Schuster A, Morton G, Chiribiri A, Perera D, Vanoverschelde J-L, Nagel E. Imaging in the management of ischemic cardiomyopathy: special focus on magnetic resonance. J Am Coll Cardiol. 2012;59(4):359–70. https://doi.org/10.1016/j.jacc.2011.08.076.
26. Pennell DJ, Sechtem UP, Higgins CB, et al. Clinical indications for cardiovascular magnetic resonance (CMR): consensus panel report. Eur Heart J. 2004;25(21):1940–65. https://doi.org/10.1016/j.ehj.2004.06.040.
27. Mant J, Doust J, Roalfe A, et al. Systematic review and individual patient data meta-analysis of diagnosis of heart failure, with modelling of implications of different diagnostic strategies in primary care. Health Technol Assess Winch Engl. 2009;13(32):1–207, iii. https://doi.org/10.3310/hta13320.
28. Bybee KA, Powell BD, Valeti U, et al. Preoperative aspirin therapy is associated with improved postoperative outcomes in patients undergoing coronary artery bypass grafting. Circulation. 2005;112(9 Suppl):I286–92. https://doi.org/10.1161/CIRCULATIONAHA.104.522805.
29. Durazzo AES, Machado FS, Ikeoka DT, et al. Reduction in cardiovascular events after vascular surgery with atorvastatin: a randomized trial. J Vasc Surg. 2004;39(5):967–75.; discussion 975–976. https://doi.org/10.1016/j.jvs.2004.01.004.
30. Blessberger H, Lewis SR, Pritchard MW, et al. Perioperative beta-blockers for preventing surgery-related mortality and morbidity in adults undergoing non-cardiac surgery. Cochrane Database Syst Rev. 2019;9:CD013438. https://doi.org/10.1002/14651858.CD013438.
31. Castelvecchio S, Menicanti L, Ranucci M, Di Donato M. Impact of surgical ventricular restoration on diastolic function: implications of shape and residual ventricular size. Ann Thorac Surg.

2008;86(6):1849–54. https://doi.org/10.1016/j.athoracsur.2008.08.010.
32. Garatti A, Castelvecchio S, Di Mauro M, Bandera F, Guazzi M, Menicanti L. Impact of right ventricular dysfunction on the outcome of heart failure patients undergoing surgical ventricular reconstruction†. Eur J Cardiothorac Surg. 2015;47(2):333–40.; discussion 340. https://doi.org/10.1093/ejcts/ezu152.
33. Garatti A, Castelvecchio S, Bandera F, Guazzi M, Menicanti L. Surgical ventricular restoration: is there any difference in outcome between anterior and posterior remodeling? Ann Thorac Surg. 2015;99(2):552–9. https://doi.org/10.1016/j.athoracsur.2014.07.076.
34. Di Donato M, Frigiola A, Benhamouda M, Menicanti L. Safety and efficacy of surgical ventricular restoration in unstable patients with recent anterior myocardial infarction. Circulation. 2004;110(11 Suppl 1):II169–73. https://doi.org/10.1161/01.CIR.0000138220.68543.e8.
35. Patel ND, Barreiro CJ, Williams JA, et al. Surgical ventricular remodeling for patients with clinically advanced congestive heart failure and severe left ventricular dysfunction. J Heart Lung Transplant. 2005;24(12):2202–10. https://doi.org/10.1016/j.healun.2005.06.024.
36. Dzemali O, Risteski P, Bakhtiary F, et al. Surgical left ventricular remodeling leads to better long-term survival and exercise tolerance than coronary artery bypass grafting alone in patients with moderate ischemic cardiomyopathy. J Thorac Cardiovasc Surg. 2009;138(3):663–8. https://doi.org/10.1016/j.jtcvs.2009.02.012.

Pediatric Cardiac Transplantation and Anesthesia

26

Andres Bacigalupo Landa, Meagan E. King, and Jennifer E. Lam

Learning Points

- Orthotopic Heart Transplant is currently the standard of care for end-stage heart disease in children. Congenital heart disease is the most common cause in infants, whereas dilated cardiomyopathy is the most common cause in older children.
- The average waiting time for heart transplant depends on age, ABO group, UNOS status and ethnicity.
- The preoperative assessment is of paramount importance, especially in patients with a complex surgical history, those with hemodynamic instability, and those requiring mechanical circulatory support.
- Intraoperative hemodynamic goals include maintaining an adequate preload, keeping the heart rate normal or slightly elevated, preserving myocardial contractility, avoiding an increase in SVR, and maintaining a low PVR.
- The main characteristics of the transplanted heart include cardiac denervation and consequent increased resting heart rate (the cardiac output is dependent on preload and circulating catecholamines), diastolic dysfunction, elevated filling pressures, temporary sinus node dysfunction, and decreased exercise capacity.
- Post-transplant morbidities include rejection, infections, cardiac allograft vasculopathy, progressive graft failure, renal failure, risk for malignancies, and behavioral and adjustment difficulties. Immunosuppressive therapy and routine surveillance have improved the long-term survival in this patient population.

Introduction

After the first pediatric heart transplant was performed on December 1967 by Adrian Kantrowitz on an 18-day-old neonate with tricuspid atresia [1], the number of transplants has dramatically increased through the years. According to the International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation (ISHLT), over 14,000 transplants have been reported in children so far. The annual number of transplants reported to the registry has increased from 414 reported in the year 2000 to 684 reported in 2015 and has been stable over the past 5 years [2].

The anesthesiologist will encounter these children in the pre- and post-transplantation period, for both cardiac and non-cardiac procedures. This patient population is complex with unique issues to consider during anesthetic care.

A. Bacigalupo Landa (✉) · M. E. King · J. E. Lam
Department of Anesthesia, Cincinnati Children's Hospital Medical Center, University of Cincinnati, Cincinnati, OH, USA
e-mail: meagan.king@cchmc.org; jennifer.lam@cchmc.org

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_26

Indications for Cardiac Transplantation

Orthotopic heart transplant (OHT) is currently the standard of care for end-stage heart disease in children. The indication for transplant varies with the age of the patient; the most common cause being congenital heart disease (CHD) in infants and dilated cardiomyopathy (DCM) in adolescents (idiopathic, myocarditis, neuromuscular or genetic) [3]. Restrictive and hypertrophic cardiomyopathy, cardiac tumors, and Kawasaki's disease are less common indications. Retransplantation represents 3–7% of all pediatric heart transplants performed, with most of them occurring in older children with an inter-transplant interval of >60 months [2].

Pediatric heart failure is classified by the American Heart Association (AHA) using the same guidelines as adults and is staged A through D based on cardiac function and physical symptoms (Table 26.1) [4, 5]. This heart failure staging is the basis for the indications for pediatric heart transplantation (Table 26.2) [6].

Once the patients have met the indication for heart transplantation, the United Network for Organ Sharing (UNOS) will list these children as Status 1A, 1B or 2 based on medical urgency (Table 26.3), with status 1A having the highest priority [7]. According to the Organ Procurement and Transplantation Network (OPTN) data as of March 2020, the average waiting time will vary according to age (longest for patients 1–5 years old: 188 days; shortest for patients 11–17 years old: 72 days), blood type (AB: 70 days, O: 535 days), UNOS status (1A: 87 days, 1B: 253 days, 2: 726 days) and ethnicity (shortest for Asians and longest for African Americans) [8].

Table 26.1 American Heart Association pediatric heart failure classification

Stage	Description
A	At risk for developing heart failure
B	Abnormal cardiac structure and/or function with no past or present symptoms
C	Abnormal cardiac structure and/or function with past or present symptoms
D	End-stage heart failure

Adapted from Rosenthal D, Chrisant MR, Edens E, Mahony L, Canter C, Colan S, et al. International Society for Heart and Lung Transplantation: Practice guidelines for management of heart failure in children. J Heart Lung Transplant. 2004;23(12):1313–1333 [5]

Table 26.2 Indications for cardiac transplantation in children

Class I recommendations	
Heart failure stage	Associated with
D	Systemic ventricular dysfunction
C	Severe limitation of exercise and activity
C	Systemic ventricular dysfunction associated with significant growth failure
C	Near sudden death and/or life-threatening arrythmias untreatable with medications or implantable defibrillator
C	Restrictive cardiomyopathy associated with reactive pulmonary hypertension
In patients with other indications for heart transplantation, if they have a PVR > 6 woods units/m^2 or a TPG > 15 mmHg, but administration of inotropic support or pulmonary vasodilators can decrease the PVR to <6 woods units/m^2 or the TPG to <1 5 mmHg, heart transplant is feasible	
Retransplantation is indicated in children with abnormal ventricular function and at least moderate graft vasculopathy	

PVR pulmonary vascular resistance, *TPG* transpulmonary pressure gradient. Adapted from Thrush PT, Hoffman TM. Pediatric heart transplantation-indications and outcomes in the current era. J Thorac Dis. 2014;6(8):1080–1096 [6]

Bridge to Transplantation

While on the wait list, patients may be medically managed for heart failure with medications such as diuretics, angiotensin-converting enzyme inhibitors, pulmonary hypertension agents or continuous inotropic therapy. However, some

Table 26.3 UNOS pediatric heart allocation

Status 1A *Require at least one of the following, while admitted to the transplant hospital where the candidate is registered*
• Need for continuous mechanical ventilation • Need for intra-aortic balloon pump • Presence of ductal-dependent systemic or pulmonary circulation requiring a prostaglandin infusion or stent for maintaining ductal patency • Has a hemodynamically significant congenital heart disease requiring high-dose of one or multiple intravenous inotrope infusions • Need for mechanical circulatory support
Status 1B *Require at least one of the following*
• Requires one or more intravenous inotrope infusions not qualifying for status 1A • <1 year old at the time of registration with restrictive or hypertrophic cardiomyopathy
Status 2 All other pediatric patients with an indication for heart transplantation not meeting the criteria for status 1A or 1B

Adapted from (https://unos.org) [7]

patients require mechanical circulatory support (MCS) either with ventricular assist device (VAD) or extra-corporeal membrane oxygenation (ECMO) as a bridge to transplantation. According to the ISHLT, from January 2009 to June 2017, 30% of patients required bridging therapy. Most patients over 1 year old with DCM require MCS (most commonly VAD), whereas only 13% of infants with CHD require MCS (mostly with ECMO) [2]. Adverse events associated to MCS include stroke, bleeding and sensitization. Post-transplant complications for patients that required MCS include stroke, rehospitalization, kidney failure and infection [9]. Patients who required ECMO as bridging therapy have shown to have a lower post-transplant survival rate compared to those who were treated with a VAD or medical therapy. Conversely, the post-transplant survival rate is similar among patients bridged to transplant with a VAD compared with medical therapy alone [2]. Notably, the increase in use of VAD has led to an overall decrease in mortality of pediatric patients in the heart transplant waitlist by 50% [9].

Preoperative Assessment

The preoperative assessment of patients scheduled for cardiac transplantation should include a complete history with an emphasis on background cardiac disease, surgical procedures/interventions received, interval history, current functional status, medications (especially any anticoagulation agents), and associated comorbidities. Physical exam should note current access lines as well as potential vascular access points, as repeat hospitalizations and procedures may make access difficult. Imaging and laboratory data, including chest x-rays, echocardiography exams, ABO type, and hepatic, renal and coagulation panels should be reviewed. Ensure the availability of blood products. Due to previous blood transfusions, patients may be allosensitized (defined as a panel reactive antibody level (PRA) > 10% [2]) and may require exchange transfusions or plasmapheresis prior to surgery [10, 11].

Special attention has to be given to patients with history of single-ventricle physiology, specifically the ones who had undergone palliative surgery. Their chronic low cardiac output state may predispose them to malnourishment, feeding difficulties, anemia, electrolyte imbalances, coagulopathy and protein-losing enteropathy. They have the potential for massive bleeding from multiple redo sternotomies, post-surgical adhesions, aortopulmonary collaterals and the need to reconstruct the pulmonary artery [12]. This makes the preoperative evaluation, adequate planning and multidisciplinary coordination extremely important.

Additionally, although not always available, it is important to inquire about the donated organ: ABO compatibility, weight of the organ (ideal donor: recipient weight ratio is 0.8–2.0), organ function assessment, as well as donor infectious screening [13]. Additionally, longer allograft ischemic time (ideally <3.5 h from aortic cross-clamp performed during procurement to coronary artery reperfusion during transplant surgery [14]) has been independently associated with increased 1-year and 5-year mortality [15].

Intraoperative Management

The nature of patients listed for cardiac transplantation makes their intraoperative management challenging. Factors such as decreased left and/or right ventricular function (hence decreased cardiopulmonary reserve), hemodynamic instability, pulmonary hypertension, hepatic and/or renal insufficiency, potential difficult access and bleeding require the anesthesia provider to have an adequate plan for pre-medication, monitoring, induction and maintenance of anesthesia [16, 17].

1. *Pre-medication*

   The need for pre-medication in this patient population must be carefully evaluated. Due to multiple hospitalization and/or long-standing hospitalizations these patients may have higher levels of perioperative anxiety as well as tolerance to the recommended sedation dosages. However, potential consequences from over-sedation, such us hypoxemia, hypercarbia and respiratory acidosis, in patients with underlying pulmonary hypertension and/or right ventricular heart failure, must be considered. For this reason, standard non-invasive monitoring should be established beforehand, supplemental oxygen should be readily available and medications should be slowly titrated (intravenous midazolam 0.03–0.05 mg/kg in divided doses or intravenous ketamine 0.5–1.0 mg/kg) [18, 19].

2. *Monitoring*

   As referred above, standard non-invasive monitors should be established before premedication is administered. An invasive arterial catheter may be indicated prior to induction of anesthesia in cases of severe ventricular disfunction. A central venous catheter (CVC) and a transesophageal echocardiogram (TEE) should be placed after induction of general anesthesia. Finally, near-infrared spectroscopy monitors may be used as well.

   When considering vascular access sites (venous and arterial), it is important to keep in mind that patients undergoing OHT will be having routine endomyocardial biopsies in the future. These procedures are typically done via the femoral vessels in infants and young children, and via the right internal jugular vein in older children and adults. For this reason, some centers prefer to preserve these sites for future access [10]. Additionally, careful review of the anatomy of the patient is paramount, as the presence of an aberrant subclavian artery or a previously created Blalock-Taussig shunt would preclude the placement of an arterial catheter in a particular limb.

3. *Hemodynamic Goals*

   The hemodynamic goals in patients undergoing OHT are as follows [11]:

   (a) **Preload**. Because the diseased myocardium has limited ability to increase stroke volume by increasing contractility, the cardiac output in patients with cardiac failure is largely preload dependent. Because of this, it is important to consider the current volume status of the patient: many are on diuretic therapy and may present relatively hypovolemic. Judicious fluid replacement will augment cardiac output in these patients. Conversely, patients with end-stage disease or inadequate diuretic therapy may present with fluid overload: administration of additional fluids will worsen myocardial performance. Irrespective of the volume status of the patient, it is prudent to avoid acute pre-load changes by carefully titrating induction medications.

   (b) **Heart rate and rhythm**. Similar to preload, cardiac output is also heart-rate dependent in this patient population. It is important to maintain a normal-slightly elevated heart rate. Additionally, maintaining a sinus rhythm will also preserve atrial systole (often referred to as “atrial kick”), helping maximize stroke volume.

   (c) **Contractility**. It is important to maintain cardiac contractility in an already diseased myocardium. In that sense, avoiding myocardial depressants and having inotropic support readily available (in

some cases started before induction of general anesthesia) is crucial.

(d) **Systemic vascular resistance (SVR)**. Maintaining SVR while avoiding either hyper- or hypotension is important with the failing heart. A low SVR will favor forward flow but excessive hypotension will reduce coronary artery perfusion. An increase in SVR may, on the other hand, decrease the stroke volume of a diseased ventricle.

(e) **Pulmonary vascular resistance (PVR)**. In patients with right ventricular failure and/or pulmonary hypertension, avoiding increase in PVR (triggered by hypoxia, hypercarbia, acidosis, increase in sympathetic response and hypothermia) is paramount. Additionally, care must be taken when transitioning from negative to positive pressure ventilation, which may also increase PVR.

Considering the previously discussed hemodynamic goals, induction of general anesthesia will depend on the patient's cardiac function. In patients with significantly decreased function, agents such as high-dose volatile anesthetics (myocardial depressants), nitrous oxide (a myocardial depressant and pulmonary vasoconstrictive agent), propofol (significantly reduces SVR) and high-dose ketamine (although it has indirect sympathomimetic properties, the direct cardiac depressant effects may prevail in patients with chronic heart failure) should be best avoided. There is no absolute correct combination of intravenous medications for induction; midazolam, fentanyl or etomidate, along with a muscle relaxant will have a minimal direct effect on preload, heart rate, myocardial function and SVR. Furthermore, avoiding hypoxemia and hypercarbia, as well as assuring a deep plane of anesthesia before intubating the trachea are key in order to prevent an increase in PVR. Additionally, inotropes should be readily available (or continued) as they will help preserve contractility and SVR. Finally, anesthetic maintenance can be achieved by using a balanced technique with low-dose inhalational anesthetics (0.5–0.75 minimum alveolar concentration (MAC)) combined with additional narcotics and benzodiazepines, as needed [19].

4. *Mechanical Ventilation Goals*

As referred above, PPV will increase PVR and hence can compromise right ventricular function. With this in mind, many authors recommend a pressure-control mode using the minimal pressure required to obtain adequate tidal volumes with minimum or no positive end-expiratory pressure (PEEP $\leq$ 5 mmHg), a normal respiratory rate and a prolonged expiratory time (inspiratory: expiratory ratio of 1:3) [18].

5. *Cardio-pulmonary Bypass (CPB)*

In general, CPB maintenance is similar to other pediatric patients undergoing cardiac surgery with a few caveats. For patients who are currently on anticoagulation (as is the case on patients with MCS or with a mechanical valve), fresh-frozen plasma may be added to the bypass prime. Patients with aorto-pulmonary collaterals may have a risk for systemic hypoperfusion and low cerebral blood flow. In these cases, measures like moderate hypothermia (25–30 °C) with a pH-stat blood management system, higher pump flows and a higher hematocrit level may be beneficial during CPB [18].

Weaning from CPB, as in the general pediatric population, is one of the most critical parts of the procedure. In this particular case, special attention should be directed to the management of a denervated donor heart (see following section), arrhythmias, and elevated PVR with consequent right ventricular failure. Inotropic support and maintaining a low PVR may be necessary to ensure an adequate coronary artery perfusion pressure [19].

Finally, persistent bleeding after adequate heparin reversal often represents a challenge in the management of these patients, especially on the ones who had been bridged with MCS. Thromboelastography may be useful in

guiding therapy in order to correct the coagulopathy while preventing volume overload and precipitating right ventricular failure.

Management of the Transplanted Heart

The physiology of a transplanted heart is characterized by restrictive physiology, with increased filling pressures and low-normal left ventricular ejection fraction. Sinus node dysfunction is not uncommon in the immediate postoperative period. Loss of sympathetic and parasympathetic innervation causes an increased resting heart rate (due to loss of vagal input) as well as loss of cardiac baroreceptor and mechanoreceptor reflexes. Without these reflexes, cardiac output becomes dependent on the Frank-Starling mechanism (increased preload as a way to increase contractility) and circulating catecholamines. These changes also result in a decrease exercise capacity in OHT recipients [16].

Certain medications may have an altered effect on the denervated heart [16, 19–22]:

- Indirect-acting sympathomimetics (ephedrine and dopamine) may have a decreased effect due to depleted norepinephrine in the cardiac nerve endings.
- Direct-acting sympathomimetics (epinephrine and norepinephrine) may have an exaggerated response due to the lack of presynaptic reuptake.
- Parasympatholytic agents such as atropine and glycopyrrolate may have no chronotropic effects.
- Acetylcholinesterase inhibitors should be used cautiously, as there are case reports of bradycardia and cardiac arrest after reversal of neuromuscular blockade with neostigmine. It is still unclear if this is due to an indirect effect secondary to its anti-cholinesterase activity on a partially reinnervated heart, or due to a direct effect on the muscarinic acetylcholine receptor. It should be mentioned that most of the patients reported were actively experiencing transplant-related complications (sinus node dysfunction, rejection and cardiac allograft vasculopathy (CAV)). On the other hand, sugammadex, although has no cholinergic effects and hence its use for neuromuscular blockade reversal has been favored in patients post-OHT, has been reported to cause bradycardia and cardiac arrest on patients with and without underlying cardiac disease. Even though the mechanism by which it decreases heart rate is still unclear, just as with anticholinesterase inhibitors, caution should be taken with its use.
- Direct vasodilators (sodium nitroprusside, nitroglycerine and hydralazine) may cause profound hypotension due to the lack of reflex tachycardia.
- Increased sensitivity to calcium channel blockers, beta blockers and adenosine. It is recommended to reduce the initial dose by 50%.

The above described effects of certain medications on the transplanted heart should help guide the management of these patients. Hypotension is best managed by intravenous fluids and small doses of direct-acting sympathomimetics. Atropine and glycopyrrolate should not be used for treatment of bradycardia; carefully titrated direct sympathomimetics should be used instead. The need for neuromuscular blockade during procedures should be carefully evaluated. Direct agonists such as epinephrine should be readily available when planning to use neostigmine or sugammadex for reversal of neuromuscular blockade.

Although cardiac denervation occurs immediately and universally after OHT, cardiac reinnervation has been shown to occur postoperatively in 40–70% of recipients. Reinnervation is partial and regionally heterogeneous: the sympathetic and parasympathetic pathways may occur in different areas of the heart, at different times, and this imbalance may affect the resting heart rate and its response to stimuli. Sympathetic reinnervation can be seen as early as 5–6 months post-transplant, although it is more likely to be present after 18 months. On the contrary, parasympathetic reinnervation can occur as early as 3–6 months,

although it usually occurs 2 years post-transplant. It is important to mention that sympathetic reinnervation may occur without parasympathetic reinnervation; however, parasympathetic reinnervation appears to be present only in sympathetically reinnervated patients [23]. This is a continuous process but may not be complete even after 15 years post-transplantation [24].

Clinical indicators of cardiac reinnervation include increase in heart rate variability, exercise tolerance and oxygen consumption during exercise. Additionally, echocardiography and scintigraphy imaging, biochemical and hormonal levels, as well as histopathologic and immunohistochemistry studies may also help in determining the presence and degree of reinnervation [23].

The Role and Consequences of Immunosuppression

According to the ISHLT registry, approximately 70% of patients transplanted from January 2004 to June 2017 received induction immunosuppressive therapy intraoperatively (the exact timing is institution-specific). This is accomplished with either polyclonal antithymocyte globulin or and interleukin-2 receptor antagonist. The use of induction therapy is associated with a decrease in CAV [2]. However, it is important to keep in mind the potential systemic inflammatory effects secondary to massive cytokine release caused by immunosuppressive drugs (often referred to as "cytokine release syndrome"). In severe cases, the inflammatory response may cause fever, hypotension, vasodilatory shock, disseminated intravascular coagulation and multi-organ system failure [25].

Tacrolimus, mycophenolate mofetil (MMF) and prednisone are the most common maintenance immunosuppression agents [2]. It is important to consider the side effects of such medications: tacrolimus causes nephrotoxicity, hyperglycemia and hepatotoxicity, MMF causes bone marrow suppression, and prednisone causes adrenocortical suppression, hypertension and osteoporosis [26].

Post-transplant Morbidities

The long-term morbidities and limitations of patient post-OHT has improved over time. At 1, 2, and 3 years post-transplant, between 84 and 87% of patients have no or only minor physical limitations in strenuous activities [2]. However, there is evidence that these patients may develop significant behavioral and adjustment difficulties which could result in poor compliance [27, 28]. When it comes to rehospitalization, infections are the most common cause at 1 and 3 years post-transplant, becoming much less common after 5 years post-transplant [2].

CAV is a limiting factor for long-term graft survival. According to the ISHLT registry, CAV will affect >50% of recipients within 15 years post-transplant. Its prevalence, though, has decreased with the use of induction therapy. Additionally, age at time of transplant has also been shown to be related to CAV development: infants have a lower occurrence than older children [2]. Treatment options include medical (antiplatelet) therapy and angioplasty, although eventually it may require re-transplant [29].

Progressive graft (heart) failure is the most common cause of death across all age groups, and is usually due to chronic ischemia caused by progressive coronary artery disease or by episodes of acute or chronic rejection [2].

Severe renal failure (defined as a serum creatinine level of >2.5 mg/dl, dialysis, or renal transplant) will affect less than 10% of patients at 10 years post-transplant. This complication also depends on the age at the time of transplant, being less common in infants than older children/adolescents [2].

Finally, an increased risk for malignancy development has been shown in this patient population. Lymphoma (usually B-cell type and located in the gastrointestinal tract) is the most common malignancy observed and may occur in up to 10% of patients at 10 years post-transplant [2]. More than 80% of the cases have been shown to be Epstein-Barr virus positive, and treatment is usually with rituximab [30].

Long-Term Survival

The overall survival rate for pediatric patients post-OHT is 37% at 25 years post-transplant [2]. The median survival is highest (22 years) among patients who underwent transplantation in infancy and lowest (13 years) for those who received their transplant at age 11–17 years. Additionally, it is important to consider that survival rate is also affected by the indication for heart transplantation: overall, patients with CHD had decreased survival rates compared to those with DCM [2].

In order to increase survival rate, early detection of rejection or CAV by continuous surveillance is key. The current standard of care is serial endomyocardial biopsies (EMB) and annual coronary angiographies (CA). Depending on the age/maturity of the patient, these procedures can be done either under sedation or general anesthesia. Complications from EMB include cardiac perforation of heart block from sampling from the RV septum. On the other hand, reported CA complications include left main coronary dissection, air embolus and ST-T wave changes. As with every cardiac catheterization, bleeding (from vascular access sites) and hemothorax or pneumothorax may also occur [31].

Conclusion

Pediatric patients undergoing OHT represent a unique challenge to anesthesia providers due to decreased cardiopulmonary reserve, as well as the complexity of the procedure itself. For this reason, a thorough preoperative evaluation is of outmost importance. Additionally, preoperative coordination between the anesthesia, organ procurement, surgical, perfusion, blood bank and intensive care teams is paramount to optimize the intraoperative management of the patient. The understanding of the restrictive physiology and denervated state of the newly transplanted heart is key for maintaining intra and postoperative hemodynamic stability. During each subsequent surveillance encounter, a complete patient evaluation including current physical status, signs or symptoms of organ rejection or CAV, current immunosuppressive medications and possible side effects, and signs of cardiac reinnervation should be performed. This will not only allow anticipation and prevention of perioperative complications, but also help improve long-term survival.

Funding and Conflicts of Interest None.

References

1. Kantrowitz A, Haller JD, Joos H, Cerruti MM, Carstensen HE. Transplantation of the heart in an infant and an adult. Am J Cardiol. 1968;22(6):782–90.
2. Rossano JW, Cherikh WS, Chambers DC, Goldfarb S, Hayes DJ, Khush KK, et al. The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: twenty-first pediatric heart transplantation report-2018; focus theme: multiorgan transplantation. J Heart Lung Transplant. 2018;37(10):1184–95. https://doi.org/10.1016/j.healun.2018.07.018.
3. Thrush PT, Hoffman TM. Pediatric heart transplantation-indications and outcomes in the current era. J Thorac Dis. 2014;6(8):1080–96. https://doi.org/10.3978/j.issn.2072-1439.2014.06.16.
4. Hunt SA, Baker DW, Chin MH, Cinquegrani MP, Feldman AM, Francis GS, et al. ACC/AHA guidelines for the evaluation and management of chronic heart failure in the adult: executive summary a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to revise the 1995 guidelines for the evaluation and management of heart failure): developed in collaboration with the International Society for Heart and Lung Transplantation; endorsed by the Heart Failure Society of America. Circulation. 2001;104(24):2996–3007. https://doi.org/10.1161/hc4901.102568.
5. Rosenthal D, Chrisant MR, Edens E, Mahony L, Canter C, Colan S, et al. International Society for Heart and Lung Transplantation: practice guidelines for management of heart failure in children. J Heart Lung Transplant. 2004;23(12):1313–33. https://doi.org/10.1016/j.healun.2004.03.018.
6. Canter CE, Shaddy RE, Bernstein D, Hsu DT, Chrisant MRK, Kirklin JK, et al. Indications for heart transplantation in pediatric heart disease: a scientific statement from the American Heart Association Council on cardiovascular disease in the young; the councils

on clinical cardiology, cardiovascular nursing, and cardiovascular surgery and anesthesia; and the quality of care and outcomes research interdisciplinary working group. Circulation. 2007;115(5):658–76. https://doi.org/10.1161/CIRCULATIONAHA.106.180449.
7. UNOS. United Network for Organ Sharing. Pediatric heart allocation. https://unos.org. Accessed 23 March 2020.
8. OPTN. Organ Procurement and Transplantation Network. Current U.S. waiting list. 2020. http://optn.transplant.hrsa.gov/latestData/rptData.asp. Accessed 23 March 2020.
9. Lorts A, Blume ED. Pediatric mechanical circulatory support: available devices and outcomes as bridge-to-transplant therapy. Curr Opin Organ Transplant. 2015;20(5):557–61. https://doi.org/10.1097/MOT.0000000000000226.
10. Schure AY, Kussman BD. Pediatric heart transplantation: demographics, outcomes, and anesthetic implications. Paediatr Anaesth. 2011;21(5):594–603. https://doi.org/10.1111/j.1460-9592.2010.03418.x.
11. Williams GD, Ramamoorthy C, Sharma A. Anesthesia for cardiac and pulmonary transplantation. In: Andropoulos DB, Stayer SA, Mossad EB, Miller-Hance WC, editors. Anesthesia for congenital heart disease. 3rd ed. Hoboken, NJ: Wiley-Blackwell; 2015. p. 636–60.
12. Jayakumar KA, Addonizio LJ, Kichuk-Chrisant MR, Galantowicz ME, Lamour JM, Quaegebeur JM, et al. Cardiac transplantation after the Fontan or Glenn procedure. J Am Coll Cardiol. 2004;44(10):2065–72. https://doi.org/10.1016/j.jacc.2004.08.031.
13. Morrissey PE, Monaco AP. Donation after circulatory death: current practices, ongoing challenges, and potential improvements. Transplantation. 2014;97(3):258–64. https://doi.org/10.1097/01.TP.0000437178.48174.db.
14. Ford MA, Almond CS, Gauvreau K, Piercey G, Blume ED, Smoot LB, et al. Association of graft ischemic time with survival after heart transplant among children in the United States. J Heart Lung Transplant. 2011;30(11):1244–9. https://doi.org/10.1016/j.healun.2011.05.001.
15. Rossano JW, Cherikh WS, Chambers DC, Goldfarb S, Khush K, Kucheryavaya AY, et al. The registry of the International Society for Heart and Lung Transplantation: twentieth pediatric heart transplantation report-2017; focus theme: allograft ischemic time. J Heart Lung Transplant. 2017;36(10):1060–9. https://doi.org/10.1016/j.healun.2017.07.018.
16. Ashary N, Kaye AD, Hegazi AR, M Frost EA. Anesthetic considerations in the patient with a heart transplant. Heart Dis. 2002;4(3):191–8. https://doi.org/10.1097/00132580-200205000-00010.
17. Eltzschig HK, Zwissler B, Felbinger TW. Perioperative implications of heart transplant. Anaesthesist. 2003;52(8):678–89. https://doi.org/10.1007/s00101-003-0556-1.
18. Burbano-Vera N, Schure AY. Pediatric heart transplantation. In: Lalwani K, Cohen IT, Choi EY, Raman VT, editors. Pediatric anesthesia: a problem-based learning approach. New York, NY: Oxford University Press; 2018. p. 111–24.
19. Nasr VG, DiNardo JA, Transplantation H. In: Nasr VG, Dinardo JA, editors. The pediatric cardiac anesthesia handbook. Hoboken, NJ: Wiley; 2017. p. 199–215.
20. Bertolizio G, Yuki K, Odegard K, Collard V, Dinardo J. Cardiac arrest and neuromuscular blockade reversal agents in the transplanted heart. J Cardiothorac Vasc Anesth. 2013;27(6):1374–8. https://doi.org/10.1053/j.jvca.2012.09.009.
21. Barbara DW, Christensen JM, Mauermann WJ, Dearani JA, Hyder JA. The safety of neuromuscular blockade reversal in patients with cardiac Transplantation. Transplantation. 2016;100(12):2723–8. https://doi.org/10.1097/TP.0000000000001060.
22. Yuki K, Scholl R. Should we routinely reverse neuromuscular blockade with sugammadex in patients with a history of heart Transplantation? Transl Perioper Pain Med. 2020;7(2):185–9.
23. Awad M, Czer LS, Hou M, Golshani SS, Goltche M, De Robertis M, et al. Early denervation and later reinnervation of the heart following cardiac transplantation: a review. J Am Heart Assoc. 2016;5(11):e004070. Published 2016 Nov 1. https://doi.org/10.1161/JAHA.116.004070.
24. Bengel FM, Ueberfuhr P, Ziegler SI, Nekolla S, Reichart B, Schwaiger M. Serial assessment of sympathetic reinnervation after orthotopic heart transplantation. A longitudinal study using PET and C-11 hydroxyephedrine. Circulation. 1999;99(14):1866–71. https://doi.org/10.1161/01.cir.99.14.1866.
25. Shimabukuro-Vornhagen A, Gödel P, Subklewe M, Stemmler HJ, Schlöber HA, Schlaak M, et al. Cytokine release syndrome. J Immunother Cancer. 2018;6:56. https://doi.org/10.1186/s40425-018-0343-9.
26. Singh RK, Humlicek T, Jeewa A, Fester K. Pediatric Cardiac Intensive Care Society 2014 consensus statement: pharmacotherapies in cardiac critical care immune therapy. Pediatr Crit Care Med. 2016;17(3 Suppl 1):S69–76. https://doi.org/10.1097/PCC.0000000000000626.
27. Brosig C, Pai A, Fairey E, Krempien J, McBride M, Lefkowitz DS. Child and family adjustment following pediatric solid organ transplantation: factors to consider during the early years post-transplant. Pediatr Transplant. 2014;18(6):559–67. https://doi.org/10.1111/petr.12286.
28. Fredericks EM, Zelikovsky N, Aujoulat I, Hames A, Wray J. Post-transplant adjustment—the later years. Pediatr Transplant. 2014;18(7):675–88. https://doi.org/10.1111/petr.12366.
29. Kindel SJ, Pahl E. Current therapies for cardiac allograft vasculopathy in children. Congenit

Heart Dis. 2012;7(4):324–35. https://doi.org/10.1111/j.1747-0803.2012.00666.x.
30. Haynes SE, Saini S, Schowengerdt KO. Post-transplant lymphoproliferative disease and other malignancies after pediatric cardiac transplantation: an evolving landscape. Curr Opin Organ Transplant. 2015;20(5):562–9. https://doi.org/10.1097/MOT.0000000000000227.
31. Daly KP, Marshall AC, Vincent JA, Zuckerman WA, Hoffman TM, Canter CE, et al. Endomyocardial biopsy and selective coronary angiography are low-risk procedures in pediatric heart transplant recipients: results of a multicenter experience. J Heart Lung Transplant. 2012;31(4):398–409. https://doi.org/10.1016/j.healun.2011.11.019.

Pediatric Lung Transplantation and Anesthesia

27

Premal M. Trivedi

Learning Points

- Pediatric lung transplantation is an accepted therapy for select children with end-stage lung or pulmonary vascular disease.
- The age group most commonly transplanted is 11–17 years old for whom cystic fibrosis is the most common indication. This may change in the coming years, however, as the introduction of cystic fibrosis transmembrane regulator (CFTR) modulators has led to decreased symptomatology in this patient population.
- Pre-transplant, patients can range from critically ill inpatients on mechanical circulatory support to stable outpatients presenting from home.
- Pre-transplant evaluation focuses on baseline pulmonary function, extra-pulmonary manifestations of the disease process, prior anesthetics, cardiac function including concerns for pulmonary hypertension, and history of vascular access.
- A clear plan for the immunosuppressants and antibiotics to be administered intraoperatively should be conveyed.
- Double-lung transplant with the assistance of cardiopulmonary bypass is most commonly performed in children.
- Post-bypass, attention is given to optimizing V/Q matching while minimizing the peak inspiratory pressures and FiO_2 needed.
- Unique features of the transplanted lungs include the absence of (1) afferent and efferent innervation and (2) lymphatic drainage. These predispose to an impairment of the cough reflex and mucus clearance, and pulmonary edema, respectively.
- Post-transplant anesthetics require an assessment of allograft function and common co-morbidities in the post-transplant period, including immunosuppressant-related side effects.
- Survival following lung transplant is lower than that for other solid organ transplants, mainly due to the issues of infection, rejection, and chronic lung allograft dysfunction (of which bronchiolitis obliterans is the major contributor).

Introduction

The first pediatric lung transplant was performed in 1987 at the University of Toronto in a 15-year-old adolescent with familial pulmonary fibrosis [1]. Since that time, over 2500 children have received lung transplants worldwide, with an annual number ranging between 97 and 136 children over the past decade (Fig. 27.1). Most recently, a total of 101 pediatric lung transplants were reported from 37 centers in the year 2017 [2]. The majority of these institutions were

P. M. Trivedi (✉)
Division of Pediatric Cardiovascular Anesthesiology, Department of Anesthesiology, Perioperative, and Pain Medicine, Texas Children's Hospital, Baylor College of Medicine, Houston, TX, USA
e-mail: ptrivedi@bcm.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_27

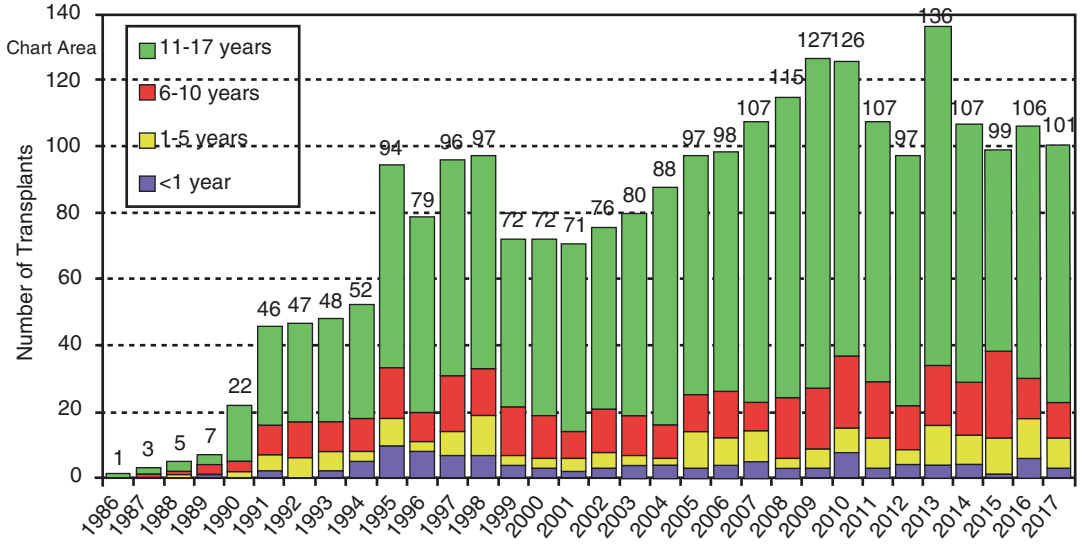


Fig. 27.1 Annual pediatric transplant volume by year and recipient age. (Reproduced with permission from Hayes et al. [2])

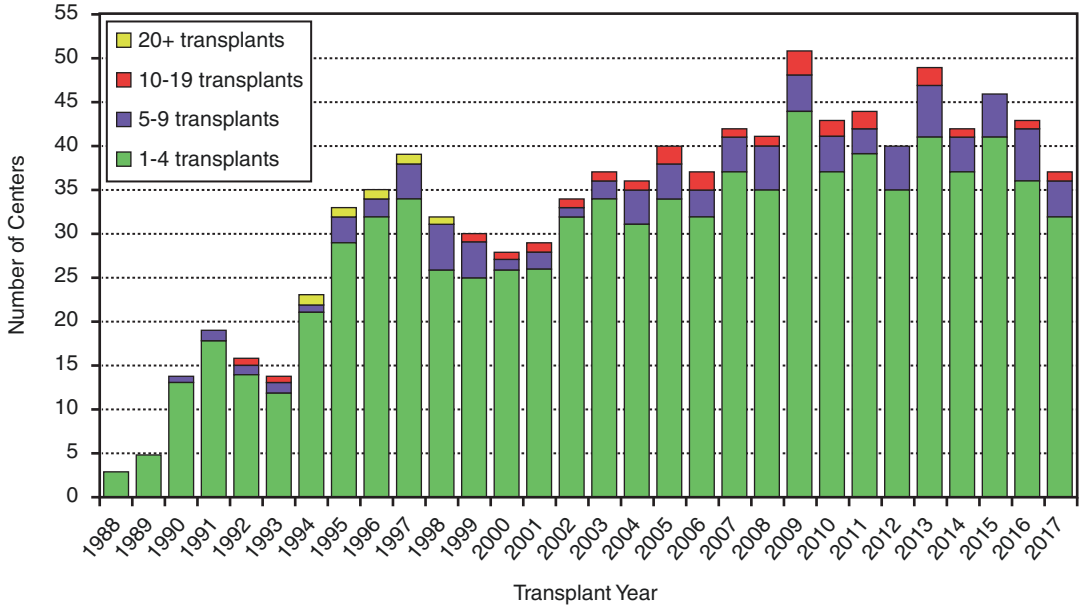


Fig. 27.2 Centers reporting pediatric lung transplants worldwide by year and volume. (Reproduced with permission from Hayes et al. [2])

located in Europe and North America and performed 1–4 transplants (Fig. 27.2). Only a single center reported greater than 10.

While these numbers reflect the consistency in the need for this procedure, they also highlight its relative infrequency. Pediatric lung transplants have accounted for only 5.5% of all lung transplants since 1988, and represent an equally small percentage of all pediatric solid organ transplants [3, 4]. This lag has been attributed to a lower prevalence of end-stage lung disease in children, a relative scarcity of donors, an improved sur-

vival among patients with cystic fibrosis and pulmonary hypertension, and to a lesser extent, the modest long-term survival associated with this therapy [5–7].

Children who receive lung transplants are thus among the most rare of all pediatric transplant recipients. At those centers performing these transplants, however, it is not uncommon to provide an anesthetic either in the period leading up to or following transplantation. And as these patients return to their home communities, the anesthesiologist may be needed to provide care for procedures unrelated to transplantation. Care for these unique patients focuses on an understanding of the common disease processes that led to transplant, the process of transplantation itself, the unique physiology of the transplanted lungs, and the common complications that can occur in the post-transplant period.

Common Indications for Pediatric Lung Transplantation

In general, children with end-stage or progressive pulmonary disease who have exhausted medical therapy are candidates for lung transplant evaluation. Specific indications largely correlate with age (Table 27.1). For those greater than 6 years, cystic fibrosis (CF) is the dominant diagnosis leading to transplantation. In those less than 6, pulmonary hypertension (both idiopathic and associated with congenital heart disease or other pulmonary vascular abnormalities), disorders of surfactant metabolism, and interstitial lung disease are the leading indications.

Contraindications vary among institutions, but generally include those conditions associated with poor post-transplant outcome. These may include medical concerns such as systemic infection, severe multi-organ dysfunction, and recent active malignancy, or anatomic ones, such as severe chest wall abnormalities, a history of talc pleurodesis, or severe aorta-pulmonary collaterals [5, 8].

Characteristics of Transplant Recipients

Transplant recipients between 1988 and 2008 had a mean age of 12 ± 5.6 years and a mean weight of 33.6 ± 16.3 kg [9]. This trend has continued in the recent era in which older children (aged > 11 years) are most commonly transplanted, followed by those between 1 and 10 years (Fig. 27.1). Infants are the group least commonly transplanted, representing only 1–3% of the total recipients in any given year. When listed, infants tend to be in intensive care and either mechanically ventilated or on extracorporeal membrane oxygenation (ECMO). Some may even have a tracheostomy pre-transplant. This is in contrast to older children, many of whom wait at home while listed and are able to oxygenate and ventilate with either no support or non-invasive assistance.

Table 27.1 Common indications for pediatric lung transplantation by age groups, 2002–2018

	Age			
Diagnosis	<1 year (%)	1–5 years (%)	6–10 years (%)	11–17 years (%)
Cystic fibrosis	–	3.4	48.1	65.4
Idiopathic pulmonary hypertension	11.3	26.7	10	8.9
Pulmonary hypertension—not idiopathic	25.8	21.6	2.9	2.1
Interstitial lung disease	17.8	13.8	10.8	7.8
Surfactant protein B deficiency	22.6	3.4	0.4	–
ABCA3 transporter mutation	7	4	0.5	0.1
Bronchopulmonary dysplasia	4.8	3.4	1.2	0.2
Obliterative bronchiolitis (non-retransplant)	–	8.6	13.3	4.8
Retransplant	–	7.7	5.8	6.2

Adapted with permission from The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: Twenty-second Pediatric Lung and Heart-Lung Transplantation Report (Hayes et al. [2])

Pre-operative Evaluation for Lung Transplantation

Pre-operative assessment focuses on the patient's indication for transplantation, the disease process's current effect on oxygenation and ventilation, and any other end-organ dysfunction that may be present (Table 27.2).

Of particular concern regarding co-morbidities are those patients with cystic fibrosis (CF). Given that the mutated gene, the cystic fibrosis transmembrane regulator (CFTR), is expressed in multiple organs, patients with CF can also present with diverse manifestations including diabetes, pancreatic exocrine insufficiency, and hepatic dysfunction (Table 27.3). Hypo- or hyperglycemia are both possible, and insulin is often needed intraoperatively to manage hyperglycemia. The presence of multi-drug resistant bacteria is another concern in patients with end-stage cystic fibrosis. This has implications not only for antibiotic management during the transplant, but also for possible hemodynamic lability associated with bacteremia. The antibiotic plan should therefore be clear and vasopressors should be available to treat hypotension associated with a septic-like picture.

Table 27.2 Pre-operative evaluation for lung transplantation

Age, indication, and pre-operative location	• Indicative of the child's clinical status and potential for extrapulmonary comorbidities
Respiratory support	• Current oxygen saturations • Type of support: non-invasive, ventilator dependent, or ECMO • If mechanically ventilated: baseline ventilatory settings
Prior anesthetics	• History of difficult mask ventilation or intubation • Post-intubation difficulties with oxygenation, ventilation or hemodynamics • Ventilatory settings with anesthesia
Echocardiography	• Evidence of PH • Ventricular function • Atrial septal defect or PFO (requiring cross clamp to address)
Vascular access history	• Prior history of ECMO or vascular thromboses • Current central access (PICC or port-a-cath)
Immunosuppressant and antibiotic plan	• To be clearly communicated prior to proceeding

ECMO extracorporeal membrane oxygenation, *PH* pulmonary hypertension, *PFO* patent foramen ovale, *PICC* peripherally-inserted central catheter

Table 27.3 Extra-pulmonary manifestations of cystic fibrosis

Upper airway	• Chronic sinusitis • Nasal polyps
Cardiovascular	• Right ventricular dysfunction (cor pulmonale)
Gastrointestinal	• Gastroesophageal reflux • Meconium ileus in the neonate • Distal intestinal obstruction in adults • Intussusception • Fibrosing colonopathy
Hepatobiliary	• Gallstones • Cirrhotic liver disease • Hepatic steatosis
Exocrine pancreas	• Malnutrition • Steatorrhea • Fat-soluble vitamin deficiency
Endocrine pancreas	• CF-related diabetes mellitus
Bone and joints	• Fractures • Arthritis • Osteopenia • Osteoporosis

Other general data to review include prior anesthetics and echocardiograms, and history of vascular access. Prior anesthetics can reveal information regarding the airway, baseline ventilatory settings and oxygen requirements once anesthetized, and any respiratory or hemodynamic events to anticipate. Of note, a portion of infants and children less than 3 years of age are likely to have tracheostomies pre-transplant. As the tracheostomy is removed for the transplant (and generally reinserted 24–48 h afterwards), specific attention should be paid to the size of the airway and any anticipated difficulties with the placement of an oral or nasal endotracheal tube.

Critical features to assess on prior echocardiograms include (1) right ventricular (RV) function,

(2) tricuspid regurgitation (TR) velocity, (3) displacement of the interventricular septum (IVS), and (4) left ventricular (LV) function. Because patients undergoing lung transplantation may either have or be at risk for pulmonary hypertension, this information can help risk-stratify the patient and assist with planning. Findings concerning for significant pulmonary hypertension would include depressed RV function, flattening or bowing of the IVS into the LV, and a TR velocity greater than 2.8 m/s. Due to ventricular interdependence, RV dysfunction may also cause LV dysfunction. Any pulmonary hypertension medications should be continued pre-operatively.

Information regarding prior and current vascular access should focus on any history of venous or arterial occlusions that may affect access options intraoperatively. In a patient with a prior history of ECMO, the vessels at the site of cannulation can be evaluated with ultrasound for patency prior to surgery. If an indwelling port-a-cath or peripherally-inserted central catheter (PICC) is present, one should clarify whether those will be removed at the end of surgery so that alternate central venous access can be obtained.

Lastly, in reviewing previous surgeries, particular attention should be given to prior thoracic procedures. Their presence may suggest an increased risk of bleeding and/or a lengthy dissection period due to adhesions.

Intraoperative Course and Considerations During Transplantation

Airway Management

Our practice at Texas Children's Hospital is to orally intubate children and adolescents and nasally intubate infants. The nasal endotracheal tube provides a more secure airway relative to an oral one, and may be better tolerated post-operatively if extubation is not planned in the first 24 h. In the event the patient has a tracheostomy, we remove the tube for the procedure and intubate orally. Care is taken to maintain the tracheostomy tract with packing, and suture closure may be necessary to prevent an air leak. Within 24–48 h post-transplant, most have their tracheostomy tubes reinserted.

Vascular Access

A thorough review of prior invasive lines and history of vascular occlusions may guide which vessels to access.

Arterial access is often obtained at the femoral artery due to the observation that radial arterial lines can fail in this population. This may be due, in part, to the clamshell incision that can lead to compression of the subclavian artery, or as is the case in patients with cystic fibrosis, the decrease in systemic vascular resistance that can occur with dissection-induced bacteremia. In infants and small children, the accuracy of blood pressure monitoring has to be weighed against the higher risk of arterial thrombosis with a femoral arterial line.

Central venous access is routinely obtained, often even if a patient has an indwelling PICC or port-a-cath. Multiple venous access points may be necessary to give the many antibiotics that can be required, and any previous central lines may also be removed post-procedure. Given the potential for intraoperative bleeding, adequate large-bore peripheral access should also be placed if possible.

Analgesia: Is There a Role for a Thoracic Epidural?

While a thoracic epidural would offer the potential advantages of improved analgesia, earlier mobilization, and earlier extubation, unique risks are present in the setting of lung transplantation that warrant discussion. Because pediatric lung transplantation is performed using cardiopulmonary bypass (CPB), and thus involves systemic heparinization, the possibility of an associated neuraxial hematoma is theoretically increased. Moreover, delaying the surgery in the

event of a bloody insertion would be detrimental to the donor lungs by prolonging their ischemic time [10].

The age of the patient at the time of transplantation and the presence of other co-morbidities may also influence the decision on whether or not to place an epidural. On average, infants require 24 ± 19 days of postoperative mechanical ventilation because of their accompanying medical issues [11], which would make epidural placement less advantageous; older patients with cystic fibrosis, on the other hand, are commonly weaned from mechanical ventilation within 1–3 days [12].

Consideration, then, needs to be given to the risks and benefits of an epidural as well as to the timing of placement should it be part of institutional practice. At our institution, we no longer place epidurals due to the potential risk of a bloody tap and the observation that time to extubation and respiratory function do not appear compromised when using intravenous analgesics alone.

Pre-bypass Concerns

Hemodynamic volatility as well as challenges in oxygenation and ventilation are the foremost concerns in the pre-bypass period. Equally important are the timing of immunosuppression and antibiotics, and the padding of bony prominences to mitigate the risk of pressure injury or nerve palsy.

Hypotension during dissection can be multifactorial. Common etiologies include increases in pulmonary vascular resistance (PVR) that can cause RV dysfunction and decreased LV preload, decreased systemic vascular resistance (SVR), and hypovolemia if bleeding is significant. The usual maneuvers to manipulate PVR (adjusting ventilation, oxygenation, and pH), can be challenging in lung transplant patients due to their intrinsic lung abnormality. Particularly in patients with pulmonary hypertension, inhaled nitric oxide (iNO) or an inhaled prostacyclin may be needed. The risk for hypotension can be compounded in patients with cystic fibrosis. Nearly half of these patients develop low SVR associated with bacteremia, and 25% have positive blood cultures for their dominant respiratory pathogen upon arrival to the ICU. Inotropes and pressors can help maintain coronary and other end-organ perfusion in these settings. For those patients who require high ventilatory parameters in order to maintain a reasonable pH, the use of an ICU ventilator can be considered.

Protocols for immunosuppression and antibiotics are guided by the transplant and infectious disease teams. A common regimen for immunosuppression includes a pre-operative cell cycle inhibitor (mycophenolate) and calcineurin inhibitor (tacrolimus), and intraoperative corticosteroids (methylprednisolone) and induction immunotherapy (anti-thymocyte globulin or basiliximab) [5]. Regimens for antibiotics are highly variable due to individual tailoring to the patient's and donor's microbial history.

Less obvious concerns include the risks of pressure ulcers and nerve palsies, hypothermia, and hyperglycemia (specifically in patients with cystic fibrosis). The increased caloric consumption and depressed growth associated with end-stage lung disease can leave the pre-transplant patient frail and cachectic. This, combined with an average anesthetic time of 10–12 h, places the patient at an increased risk of position-related injuries. Care should be taken to ensure that all bony prominences are padded along with the head, elbows, knees, and heels. Hypothermia, particularly in the period while awaiting visualization of the donor lungs, can be avoided with the use of a forced-air warming blanket and/or a warm operating room. Hyperglycemia is to be expected in patients with cystic fibrosis, and an insulin infusion can be titrated to keep blood glucose <300 mg/dl.

Surgical Approach

In contrast to the adult population, the use of cardiopulmonary bypass (CPB) in pediatric lung transplantation is routine. Often times the child's airway size makes one-lung-ventilation with sequential single lung transplantation impracti-

cal; other times the child's clinical status mandates the use of CPB to ensure a hemodynamically stable dissection and implantation. Disadvantages to CPB include an increased risk of coagulopathy and need for transfusion, and activation of the systemic inflammatory response with potential for allograft injury on reperfusion [13].

The surgical approach can be through a median sternotomy, but more often is through a clamshell incision, or bilateral thoracosternotomy (Fig. 27.3). Cardiopulmonary bypass is established via aortobicaval cannulation and bilateral pneumonectomies are performed sequentially. If an intracardiac procedure is needed, such as closure of a patent foramen ovale or atrial septal defect (ASD), then cardioplegic arrest is applied.

Techniques for transplantation include en bloc, implying a tracheal anastomosis, or the more commonly performed bilateral sequential transplantation, implying bilateral bronchial anastomoses (Fig. 27.3). En bloc lung transplantation offers the advantage of fewer anastomoses, and when combined with bronchial artery revascularization, may decrease the incidence of airway ischemia and its related complications

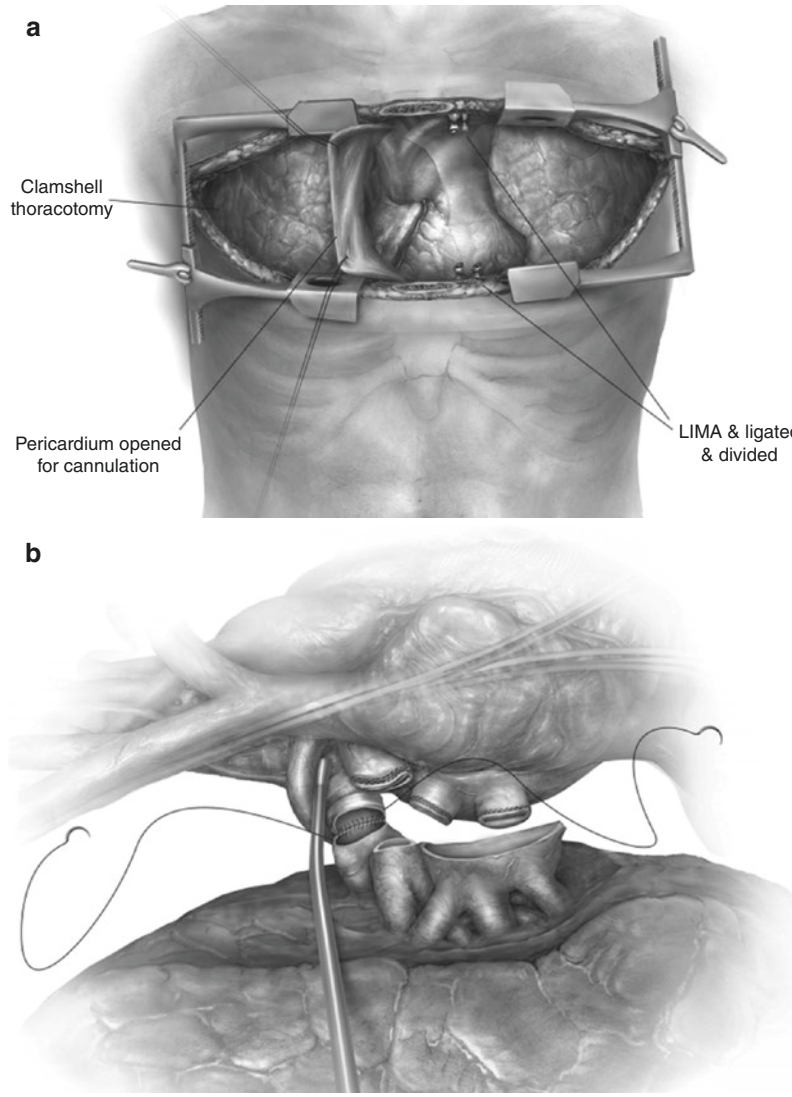


Fig. 27.3 (**a**) Bilateral thoracosternotomy, or clamshell incision, commonly used for pediatric lung transplantation; (**b**) Right bronchial anastomosis as part of bilateral sequential lung transplantation. The typical sequence for the implantation of each donor lung is first the bronchial anastomosis, followed by the pulmonary venous and lastly the pulmonary artery anastomoses. (Reproduced with permission from Aigner C, Klepetko W. Operative Techniques in Thoracic and Cardiovascular Surgery. 17:181–193, 2012.)

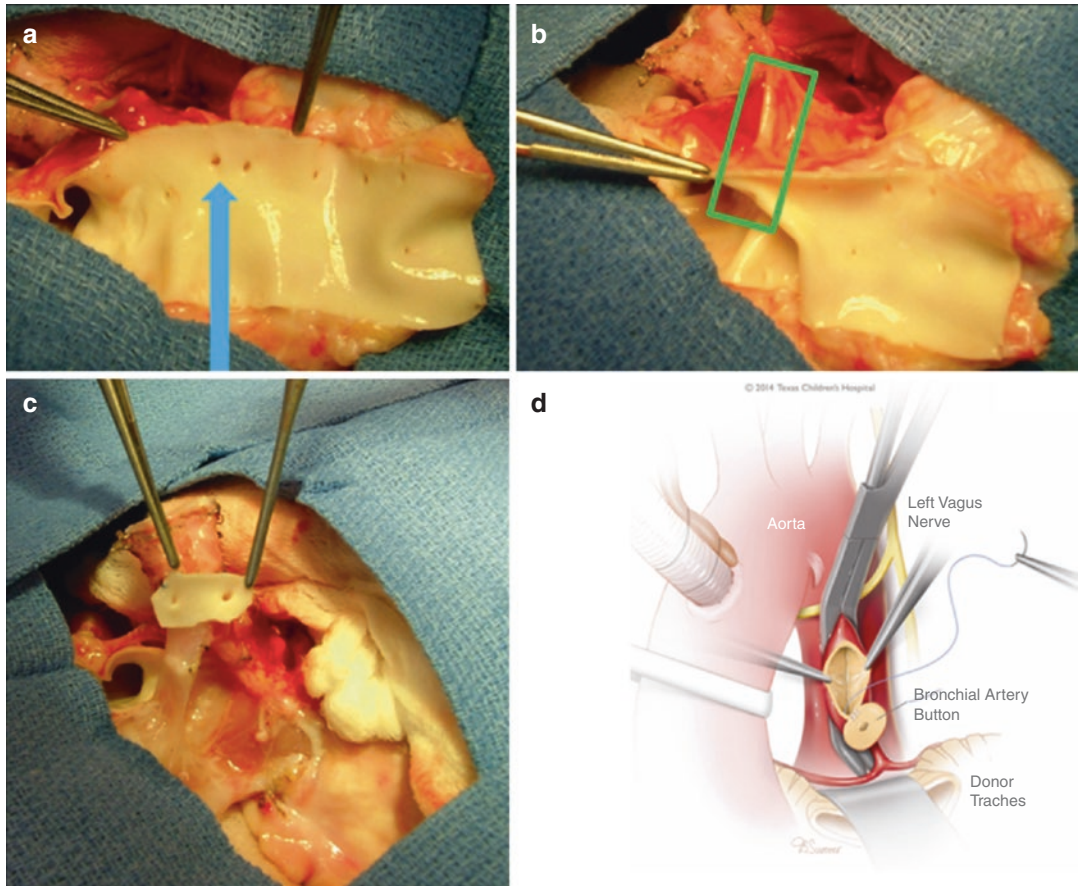


Fig. 27.4 Bronchial artery revascularization. (**a**) the descending donor thoracic aorta is opened longitudinally; (**b**) the bronchial artery is identified arising from the aorta; (**c**) aortic button containing the origin of the two bronchial arteries; (**d**) suturing the bronchial arteries to the recipient aorta. (Reproduced with permission from Guzman-Pruneda A., Orr Y, Trost JG et al. J Heart Lung Transplant. 35: 122–29, 2016.)

post-transplant (Fig. 27.4). Following completion of the airway anastomosis(-es), the donor pulmonary veins are directed to the recipient left atrium and the donor and recipient pulmonary arteries are anastomosed. Of note, if the en bloc technique is used, a brief period of cross clamp is necessary for the left atrial cuff anastomosis.

Weaning from Bypass

Once the tracheal or bilateral bronchial anastomoses are complete, bronchoscopy is used to clear the airway of bloody secretions. This process is repeated prior to weaning from bypass when perfusion to the airways can also be assessed (the airway around the anastomotic site(s) should appear pink).

The process of ventilating the transplanted lungs begins with gentle recruitment breaths and non-toxic levels of oxygen supplementation. Knowledge of the donor size can help in judging what tidal volumes to use. To start, no more than 10 cc/kg tidal volumes are selected (Table 27.4). Fractional inspired oxygen (FiO_2) is set between 40 and 50%.

Based on the patient's anticipated physiology, inotropic and/or pressor support can be initiated. We commonly wean on low-dose epinephrine and add vasopressin as indicated. To assist with PVR and ventilation/perfusion matching, we routinely start prostaglandin E_1 (PGE_1) and iNO.

Table 27.4 Texas Children's protocol for allograft ventilation post-bypass

Recruitment maneuvers	<30 cm H_2O
Ventilatory mode	Pressure control ventilation
Peak inspiratory pressure (PIP)	<25 cm H_2O
Positive end expiratory pressure (PEEP)	5
Tidal volumes	Donor-appropriate, <10 cc/kg
FiO_2	0.4–0.5, goal $SpO_2 > 90\%$

Post-bypass Concerns

The adequacy of the transplanted lungs is the chief concern in the post-bypass period. An assessment of PaO_2:FiO_2, $PaCO_2$, and lung compliance in the first few minutes after bypass can give a sense of the trajectory to anticipate. If marginal, maneuvers to improve lung function can include recruitment, suctioning, and optimizing ventilator settings. An alternative if escalating measures fail to produce improvement is veno-venous ECMO.

Of note, even in circumstances when allograft function is initially adequate, acute changes can occur due to a re-accumulation of secretions or the onset of pulmonary edema. Consequently, meticulous attention to the peak inspiratory pressures needed to generate the desired tidal volumes and to the trends in PaO_2 and $PaCO_2$ is essential. Bronchoscopy can be used to diagnose and suction secretions, whereas pulmonary edema may be more difficult to manage acutely. Because the transplanted lungs lack an intact lymphatic system, they are prone to pulmonary congestion in the setting of volume administration (Table 27.5). This is relevant in that another major concern in the post-bypass period is hemostasis. Long bypass runs are associated with deficiencies in platelets, fibrinogen, and factors which must be restored in order to control bleeding. The process of achieving hemostasis, then, may also negatively affect graft function. To help guide transfusion and minimize the volume of blood products necessary, point-of-care testing can be used. Alternatively, consideration can be given to administering hemostatic agents such as a prothrombin complex concentrate or fibrinogen concentrate as an adjunct, that may be of a lower volume compared to standard blood product therapy.

Table 27.5 Physiologic changes affecting lung function following transplantation

Anticipated changes influencing lung function	End results
Vagal denervation and loss of afferent stimuli	• Less effective cough • Decreased clearance of secretions • Transient decrease in response to hypercapnea • Potential for bronchial hyperreactivity
Absence of lymphatic drainage	• Decreased lung compliance • Potential for worsening pulmonary edema with volume administration • Impaired immune cell trafficking

Chest closure represents the next hurdle after weaning from bypass and achieving hemostasis. Changes in gas exchange, lung compliance, and cardiac output may all occur. If significant and not amenable to the usual interventions (suctioning/recruitment), the chest may be left open with a plan to close in the subsequent 24–48 h.

Myocardial function post-transplant should either be unchanged or improved assuming adequate allograft function. The right ventricle, in fact, may become hyperdynamic due to a normalization in right ventricular afterload compared to the pre-transplant state.

Post-transplant Complications

Post-transplant complications can be categorized into three phases: the immediate phase, representing the first week after transplantation; the early phase, including the first 3 months; and the late phase, entailing the time beyond 3 months.

Immediate and Early Phase Complications

Primary Graft Dysfunction

The most common complication in the first week post-transplant is primary graft dysfunction (PGD) [14, 15]. Characterized by a decrease in oxygenation and the development of diffuse infiltrates on x-ray, PGD can range from mild hypoxemia to severe respiratory distress syndrome requiring ECMO support. Its incidence is related to donor lung ischemic time and may be a consequence of pro-inflammatory mediators that accumulate in this setting [16–18].

Rejection

Hyperacute rejection is rare as it represents a previous exposure to donor human leukocyte antigen. Acute rejection, however, is common in the first 3 months post-transplant. Presentation can mimic infection and include cough, tachypnea, dyspnea, hypoxia, and fever [5]. But more often symptoms are subtle or altogether absent. For this reason, surveillance bronchoscopies, transbronchial biopsies, and pulmonary function testing are performed at regular intervals. One paradigm is to assess patients at 2 weeks post-transplant, then every 3 months during the first year, and then every 6 months thereafter [5]. For young patients unable to perform spirometry, radiographic imaging in the form of computed tomography (CT) or ventilation perfusion scanning is used.

Infection

Infection, always a concern following any transplantation, is of greater risk in the lung transplant recipient. Beyond the effects of immunosuppression, the lungs are directly exposed to the external environment, are colonized with donor bacteria, and have a decreased ability to clear pathogens due to reduced cough and mucociliary clearance (Table 27.5). Complicating diagnosis is the often similar presentation of rejection and infection. Of all age groups, infants and young children are particularly susceptible to severe viral infections [5, 19]. These have impact not only on short-term survival, but also on long-term graft function.

Surgical Complications

Complications involving the airway or vascular anastomoses are infrequent but significant. Strictures can develop in the airway requiring balloon dilation or placement of biodegradable stents. Tracheo- or bronchomalacia can also result as a consequence of poor healing. Respiratory function can be further compromised due to phrenic or recurrent laryngeal nerve injury.

Pulmonary artery or pulmonary venous stenoses are uncommon and can usually be discerned by echocardiography post-transplant (if not used intraoperatively). More common are transient supraventricular arrhythmias like atrial flutter or fibrillation associated with left atrial suture lines.

Late Phase Complications

Major issues in the late phase include bronchiolitis obliterans (BO), malignancy, and immunosuppressant-related side effects.

Bronchiolitis Obliterans

BO is the major cause of death and need for retransplantation in those who survive 1 year post-transplant. BO is a histologic diagnosis marked by fibroproliferative obliteration of the small airways, complete or partial luminal occlusion, and destruction of the airway walls [5]. Clinically, this presents as airway obstruction with decreased forced expiratory volume (FEV_1), and is termed bronchiolitis obliterans syndrome. In the absence of a tissue diagnosis, BO can thus be described using the surrogate of decreases in FEV_1 over time. The age group at highest risk for rejection and BO are those who receive their transplants between the ages of 11–17 years [20]. Those at lowest risk are infants. Nonetheless, concern for BO should be raised with each additional year following transplantation as <50% of patients are free from this entity at 5 years post-transplant [20].

Malignancy

The overall incidence of malignancy after lung transplantation is 5–10%, of which post-transplant lymphoproliferative disease (PTLD) is a major contributor [21]. Primary Epstein-Barr virus (EBV) is a risk factor for PTLD [22]. Children may be more susceptible to this complication because they are often seronegative for EBV at the time of transplantation, and can thus acquire a primary EBV infection thereafter. Manifestations are often pulmonary in the first year, and extrapulmonary thereafter.

Immunosuppressant-Related Side Effects

Due to concerns over the high risk of rejection in lung transplant recipients, immunosuppression regimens are aggressive with resulting side-effects [5, 23]. Common side effects include hypertension, diabetes, renal dysfunction, and seizures. Within 1 year of transplant, the prevalence of hypertension is 40.9%, diabetes 20.3%, renal dysfunction 9.7%, and hyperlipidemia 5%; these numbers increase with time (Table 27.6) [20, 24]. Headaches, sleep disturbance, and posterior reversible encephalopathy syndrome may also develop in response to calcineurin inhibitors [25, 26]. Cell-cycle inhibitors can cause leukopenia. And steroids, which are used in nearly all patients 1- and 5-years post-transplant, can lead to myopathies, adrenal suppression, cataracts, insulin-resistance, and osteoporosis [5].

Table 27.6 Pediatric lung transplants: cumulative morbidity in survivors within 1- and 5-years post-transplant (1994–2013)

Outcome	Within 1 year (%)	Within 5 years (%)
Hypertension	40.9	69
Diabetes	22.2	35.7
Bronchiolitis obliterans syndrome	12.9	35.5
Renal dysfunction	9.4	31.3
Abnormal creatinine ≤2.5 mg/dl	6.3	24.1
Creatinine > 2.5 mg/dl	2.0	4.5
Chronic dialysis	0.8	1.8
Renal transplant	0.3	0.9
Malignancy	5.3	10.7
Hyperlipidemia	5	17.8

Adapted with permission from The Registry of the International Society for Heart and Lung Transplantation: Seventeenth Pediatric Lung and Heart-Lung Transplantation Report (Benden et al. [24])

Anesthetic Management of the Post-transplant Patient

An assessment of graft function and post-transplant complications are central to developing an appropriate anesthetic plan (Table 27.7). While these patients can generally tolerate any anesthetic technique or airway manipulation given adequate graft function, consideration

Table 27.7 Anesthetic considerations following lung transplantation

Assessment of graft function	Concerning signs/symptoms • New history of fever, dyspnea, cough, or fatigue • Exam revealing desaturation, tachypnea, crackles, or wheezes Spirometry and Imaging • Decline in FEV_1 or FVC over time? – >10% decline in FEV_1 is significant • Air-trapping on CT? History of rejection or respiratory infection? Years since transplant • Risk of BO increases with time Baseline respiratory support
Evaluation of other end-organs affected	Immunosuppressant-related adverse effects Need for stress dose steroids? Surgical sequelae • Airway strictures or malacia • Phrenic or laryngeal nerve injury • Gastroparesis or dysmotility • GERD • Atrial arrhythmias Sleep-disordered breathing PTLD

FEV_1 forced expiratory volume in 1 s, *FVC* forced vital capacity, *CT* computed tomography, *BO* bronchiolitis obliterans, *GERD* gastroesophageal reflux, *PTLD* post-transplant lymphoproliferative disease

should be given to using regional or neuraxial anesthesia to supplement analgesia when safe, and ensuring sufficient anesthetic depth if tracheal intubation is needed. Ventilatory strategy should take into account the age and location of the anastomosis so as to avoid injury to a relatively fresh surgical site. If delivering positive pressure ventilation, typical lung-protective parameters would entail tidal volumes of 5–7 cc/kg, a plateau inspiratory pressure of <30 cm H_2O, and an inspired oxygen concentration of less than 60% to maintain an arterial saturation of 94% or greater [27, 28]. Further, a humidifier should be used to lessen the burden of dried secretions in patients who already have limited cough and mucociliary clearance. Because of the lungs' increased susceptibility to pulmonary edema, particularly in the early phase following transplantation, fluids should be administered cautiously.

Those at highest risk for perioperative deterioration are patients with acute rejection, pulmonary infection, or bronchiolitis obliterans [29]. In these settings, lung compliance may be significantly decreased while airway reactivity may be accentuated. Acute rejection may also impair hypoxic pulmonary vasoconstriction [30]. As such, additional invasive monitoring may be indicated intraoperatively, and postoperative intensive care admission should be considered. Other post-transplant complications of note include anastomotic airway strictures, renal dysfunction, gastroparesis with reflux, diabetes, and steroid-induced adrenal suppression and myopathy. The latter findings may impact airway management, drug choice and dosing, aspiration risk, perioperative glucose management, and the risk of adrenal insufficiency and post-operative weakness, respectively.

Anesthesiologists caring for these children often encounter them in the setting of lung surveillance or those procedures common to the general pediatric population. The most common of these anesthetics is for bronchoscopy and transtracheal lung biopsy. Anesthetic considerations unique to these cases include the use of a laryngeal mask airway (LMA) to accommodate the placement of a larger bronchoscope when clinically feasible, and the potential for pneumothorax or hemorrhage with lung biopsy. Spontaneous ventilation and avoidance of nitrous oxide may help limit the risk of pneumothorax. And while clinically significant hemorrhage has a reported incidence of 1–5%, risk can be mitigated by the use of instilled hemostatic agents and treatment of pre-existing uremia or thrombocytopenia [31]. Other common procedures in this population include Nissen fundoplication due to the high incidence of post-transplant reflux, and endoscopic sinus surgery in children with cystic fibrosis.

Outcomes Following Lung Transplantation

Survival has increased over the years due to advances in surgical technique, immunosuppressive regimens, patient selection, and post-transplant care [9]. But morbidity and mortality remain high, particularly within the first year due to infection and rejection, and overall in comparison to other solid organ transplants. Long-term survival is limited by the development of chronic graft failure, of which BO is a major cause.

Across all eras, median survival in children undergoing lung transplantation is 5.7 years (1992–2017) [2]. This compares favorably to adults who have a median survival of 6.2 years. For those surviving 1 year post-transplant, median survival increases to 9.1 years in children and 8.3 years in adults.

Survival is similar across age groups in pediatric lung transplant recipients. When considering the impact of diagnosis on survival, pulmonary hypertension (not idiopathic) is associated with the worst outcomes. Children with cystic fibrosis, on the other hand, had survival comparable to those with other diagnoses. Factors predictive of 10-year mortality after transplant are donor age (>50 years), recipient estimated glomerular filtration rate, and a female donor-to-female recipient combination [2].

Children undergoing lung transplantation can be expected to have marked improvement in their functional status. Most are fully active or have

only minor restrictions in physically strenuous activity through 3 years post-transplant [2].

Conclusions

Pediatric lung transplantation has become an accepted therapy for select patients with otherwise untreatable pulmonary parenchymal or vascular disease. Ongoing areas to address include the limited availability of suitable donor organs and the increased incidence of rejection, infection, and chronic graft failure following transplantation in this population.

Anesthesiologists can contribute greatly to the care of these patients in their intraoperative management during the transplantation itself or in the post-transplant period when the patient returns for biopsies, bronchoscopies, or unrelated procedures. Care during the transplantation can be divided into the pre-bypass and post-bypass periods. Pre-bypass considerations include delivery of the scheduled immunosuppressants and antibiotics, along with optimization of oxygenation, ventilation, and hemodynamics. Post-bypass concerns focus on maintaining or improving allograft function. Post-transplant anesthetics, beyond an assessment of the transplanted lungs, should direct attention to the immunosuppressant-induced comorbidities and other common post-transplant complications that may be present.

Funding and Conflicts of Interest None.

References

1. Grossman RF, Frost A, Zamel N, et al. Results of single-lung transplantation for bilateral pulmonary fibrosis. N Engl J Med. 1990;322:727–33.
2. Hayes D, Wida SC, Chambers DC, et al. The registry of the International Society for Heart and Lung Transplantation: twenty-second pediatric lung and heart-lung transplantation report—2019. J Heart Lung Transplant. 2019;38:1015–27.
3. Organ Procurement and Transplantation Network; 2020. https://optn.transplant.hrsa.gov/data/view-data-reports/national-data. Accessed July 10 2020.
4. Mallory GB, Spray TL. Paediatric lung transplantation. Eur Respir J. 2004;24:839–45.
5. Sweet SC. Pediatric lung transplantation. Respir Care. 2017;62(6):776–98.
6. Benza RL, Miller DP, Barst RJ, et al. An evaluation of long-term survival from time of diagnosis in pulmonary arterial hypertension from the REVEAL registry. Chest. 2012;142(2):448–56.
7. Cystic Fibrosis Foundation Patient Registry 2019 annual data report. Bethesda, MD: Cystic Fibrosis Foundation; 2019. https://www.cff.org/Research/Researcher-Resources/Patient-Registry/Cystic-Fibrosis-Foundation-Patient-Registry-Highlights.pdf. Accessed July 10 2020.
8. Bryant RB, Morales D, Schecter M. Pediatric lung transplantation. Semin Pediatr Surg. 2017;26:213–6.
9. Zafar F, Heinle JS, Schecter MG, et al. Two decades of pediatric lung transplant in the United States: have we improved? J Thorac Cardiovasc Surg. 2011;141:828–32.
10. Williams GD, Ramamoorthy C. Anesthesia considerations for pediatric thoracic solid organ transplant. Anesthesiol Clin North Am. 2005;23:709–31.
11. Huddleston CB, Sweet SC, Mallory GB, et al. Lung transplant in very young infants. J Thorac Cardiovasc Surg. 1999;118:796–804.
12. Meneloff EN, Huddleston CB, Mallory GB, et al. Pediatric and adult lung transplantation for cystic fibrosis. J Thorac Cardiovasc Surg. 1998;115:404–13.
13. Solomon M, Grasemann H, Keshavjee S. Pediatric lung transplantation. Pediatr Clin North Am. 2010;57:375–91.
14. Christie JD, Van Raemdonck D, de Perrot M, et al. Report of the ISHLT Working Group on Primary Lung Graft Dysfunction part I: introduction and methods. J Heart Lung Transplant. 2005;24(10):1451–3.
15. Christie JD, Carby M, Bag R, et al. Report of the ISHLT Working Group on Primary Lung Graft Dysfunction part II: definition: a consensus statement of the International Society for Heart and Lung Transplantation. J Heart Lung Transplant. 2005;24(10):1454–9.
16. De Perrot M, Bonser RS, Dark J, et al. Report of the ISHLT Working Group on Primary Lung Graft Dysfunction part III: donor-related risk factors and markers. J Heart Lung Transplant. 2005;24(10):1460–7.
17. Barr ML, Kawut SM, Whelan TP, et al. Report of the ISHLT Working Group on Primary Lung Graft Dysfunction part IV: recipient-related risk factors and markers. J Heart Lung Transplant. 2005;24(10):1468–82.
18. Areasoy SM, Fisher A, Hachem RR, et al. Report of the ISHLT Working Group on Primary Lung Dysfunction part V: predictors and outcomes. J Heart Lung Transplant. 2005;24(10):1483–8.
19. Khalifah AP, Hachem RR, Chakinala MM, et al. Respiratory viral infections are a distinct risk for

bronchiolitis obliterans syndrome and death. Am J Respir Crit Care Med. 2004;170(2):181–7.
20. Goldfarb SB, et al. Registry of the International Society for Heart and Lung Transplantation: twentieth pediatric lung and heart-lung transplantation report-2017; focus theme: allograft ischemic time. J Heart Lung Transplant. 2017;36(10):1070–9.
21. Huddleston CB. Pediatric lung transplantation. Curr Treat Options Cardiovasc Med. 2011;13:68–78.
22. Walker RC, Paya CV, Marshall WF, et al. Pretransplantation sero-negative Epstein–Barr virus status is the primary risk factor for post-transplantation lymphoproliferative disease in adult heart, lung and other solid organ transplantation. J Heart Lung Transplant. 1995;14:214–21.
23. Mendeloff EN. Pediatric lung transplantation. Chest Surg Clin North Am. 2003;13(3):485–504.
24. Benden C, et al. The registry of the International Society for Heart and Lung Transplantation: seventeenth official pediatric lung and heart-lung transplantation report—2014; focus theme: retransplantation. J Heart Lung Transplant. 2014;33(10):1025–33.
25. Wong M, et al. Neurologic complications of pediatric lung transplantation. Neurology. 1999;53(7):1542–9.
26. Bartynski WS, et al. Posterior reversible encephalopathy syndrome after solid organ transplantation. AJNR Am J Neuroradiol. 2008;29(5):924–30.
27. Conrad C, Cornfield DN. Pediatric lung transplantation: promise being realized. Curr Opin Pediatr. 2014;26(3):334–42.
28. Seo M, Kim WJ, Choi IC. Anesthesia for nonpulmonary surgical intervention following lung transplantation: two cases report. Korean J Anesthesiol. 2014;66(4):322–6.
29. Feltracco P, et al. Anesthetic considerations for nontransplant procedures in lung transplant patients. J Clin Anesth. 2011;23(6):508–16.
30. Aarnio P, et al. Effects of acute rejection and antirejection therapy on arteries and veins from canine single lung allografts. J Thorac Cardiovasc Surg. 1996;111(6):1219–29.
31. Wong JY, Westall GP, Snell GI. Bronchoscopic procedures and lung biopsies in pediatric lung transplant recipients. Pediatr Pulmonol. 2015;50(12):1406–19.

Anaesthesic Considerations in Fetal Therapy

28

Ritu Gupta, Ruwan Wimalasundera, and Phil Moore

Learning Points

1. Fetal therapy is a rapidly developing speciality
2. It is carried out in a few specialist centres, requiring a multidisciplinary approach.
3. The anesthesia provider needs to consider both the mother and fetus, prioritising maternal well-being
4. Effective analgesia/anaesthesia, antibiotic prophylaxis and tocolysis is required to optimise maternal and fetal outcome

Introduction

The standard treatment of congenital malformations has traditionally been planned delivery at a tertiary centre, with attempted post-natal repair. Advances in prenatal diagnostic ultrasonography, and improved prenatal diagnosis of anomalies has led to the development of fetal therapy. Such therapies can include surgical interventions as well as treatments which can optimise fetal survival until delivery at an appropriate gestation when more definitive therapies can be provided postnatally e.g. intrauterine transfusion, antiarrhythmic medication and shunt insertion.

Fetal intervention is considered for those with life threatening conditions (e.g. congenital diaphragmatic hernia, twin-twin transfusion syndrome and selective growth restriction/severe fetal anomalies in monochorionic twins) and for those who will suffer serious developmental consequences (e.g. myelomeningocele). If these anomalies are not treated, they can lead to significant long-term morbidity and mortality.

Antenatal diagnosis of such differences allows time for appropriate multidisciplinary care incorporating specialists such as consultants in obstetrics, fetal medicine & therapy, neonatologists, anesthesia providers, electrical physicists, radiologists, pediatric surgeons, paediatric neurologist and geneticists to be coordinated for pre and postnatal care, including transfer to an appropriate specialist tertiary centre.

Although open fetal surgery for procedures such as in utero spina bifida repair are now established treatments, due to risks associated with open interventions such as preterm labour, and preterm rupture of membranes, minimal access surgical techniques are being developed.

There are specific requirements before fetal surgery can be considered. These are that an accurate diagnosis of the lesion needs to be made,

R. Gupta (✉)
Hillingdon Hospital, Uxbridge, UK
e-mail: Ritu.gupta@nhs.net

R. Wimalasundera
Fetal Medicine Unit, University College London Hospital, London, UK
e-mail: ruwan.wimalasundera@nhs.net

P. Moore
Birmingham Women's Hospital, Birmingham, UK
e-mail: phil.moore@nhs.net

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_28

the maternal risks need to be acceptable, a neonatal outcome needs to be better with in utero surgery rather than post delivery and fully informed maternal consent is needed. The key role for the anesthesia provider in leading the team in fetal intervention is to minimise maternal risk and provide the safest form of anaesthesia for the mother while attempting to optimise conditions for the interventionalist.

Fetal therapeutic interventions can be divided into three groups:

1. Open surgical procedures such as myelomeningocele repair or surgical resection of sacrococcygeal tumours, require a maternal laparotomy and hysterotomy. These open procedures involve higher risks to the mother than with minimally invasive techniques. Risks include preterm premature rupture of membranes (PPROM), preterm labour, uterine dehiscence, haemorrhage, infection and pulmonary oedema. However, fetal outcomes appear to be better than the more recently developed fetoscopic techniques such as for myelomeningocele repair.
2. Minimally invasive techniques such as percutaneous insertion of pleural or bladder shunts, intrauterine blood transfusions, fetoscopic laser ablation of placental vessels and selective reduction using cord-occlusion or radiofrequency ablation in monochorionic twins with discordant anomalies, twin-reversed arterial perfusion sequence or severe selective growth restriction, involve percutaneous insertion of needles, trocars and fetoscopes into the uterine cavity to access the fetus. These involve lower maternal risks with improved fetal outcome.
3. Intrapartum procedures such as Ex utero intrapartum therapy (EXIT) involve the continued placental perfusion of the partially exteriorised fetus until a definitive airway is established. The technique is used to allow time to intubate and ventilate fetuses with an upper airway obstruction (e.g. cystic hygroma, lymphangioma, cervical teratoma) to prevent hypoxia in the neonate during a difficult intubation.

The broad challenges for the anesthesia provider are:

1. Prior review of the patient for assessment of pre-operative anaesthetic risk and ordering of necessary investigations where relevant;
2. liaison with the multi-disciplinary team including ensuring completion of the World Health Organization (WHO) checklist which may be customised for fetal procedures;
3. obtaining adequate intravenous access and obtaining a blood group and storage as well as baseline maternal haemoglobin;
4. Insertion of arterial lines as necessary
5. optimal positioning of the patient, particularly in instances of raised body mass index and to limit aorto-caval compression;
6. Maintenance of maternal homeostasis—overseeing optimal maternal physiology, airway and anaesthesia;
7. safe transfer of the patient to and from a specialist centre
8. steps to limit venous thromboembolism where relevant.
9. Techniques to prevent preterm labour and infection.
10. Providing fetal anaesthesia.

The most frequently occurring fetal condition requiring fetal surgery is twin-to twin transfusion syndrome (TTTS).

Twin-Twin Transfusion Syndrome (TTTS)

Is a serious complication of a monochorionic twin pregnancy in which there is a shared placental circulation. It complicates 15% of monochorionic twin pregnancies [1] and can manifest at any gestation although treatment is typically provided from 16 up until 26 weeks gestation [1]. The disease pathology is typically secondary to arteriovenous anastomoses on the placental surface with an imbalance of compensatory arterioarterial anastomoses. The physiology of TTTS can overlap with other pathologies such as Twin

Anaemia Polycythemia Sequence (TAPS) and selective growth restriction.

TTTS is due to unequal blood flow across vascular anastomoses between the two fetal circulations with the larger "recipient" twin exhibiting volume overload with polyhydramnios and right-heart strain. The smaller "donor" twin is hypo-perfused and anaemic leading to growth restriction and severe oligohydramnios with a non-visible bladder due to oliguria resulting in a stuck twin. Both twins are at risk of severe haemodynamic compromise, brain injury, death and premature delivery.

Diagnosis is made using ultrasound which facilitates diagnosis based upon the Quintero staging system with; (1) amniotic fluid discordancy; (2) differences in bladder size and visualisation; (3) abnormal Doppler waveforms; (4) hydrops or; (5) co-twin demise (Table 28.1) [1]. With stage II and beyond, perinatal mortality is >90% without intervention [3].

As well as fetal complications, mothers with untreated severe TTTS may rarely develop "mirror syndrome" where the mother "mirrors" the oedema present in the fetus [4]. It is characterised by a pre-eclampsia like pathology with hypertension, generalised oedema, proteinuria and in severe cases pulmonary oedema, stroke, renal and hepatic dysfunction or eclampsia.

Treatment options for TTTS include:

1. Amnioreduction—This involves percutaneous insertion of a 18 g needle into the recipient amniotic sac under local anaesthetic applied to the maternal skin. Amniotic fluid is drained either using 50 ml syringes or a redivac, until the amniotic fluid is returned to normal (i.e. a deepest vertical pool of 5 cm) or a maximum of 3000 ml at any one time. The procedure can improve outcomes in approximately 20% by reducing the intrauterine pressure caused by the polyhydramnios and therefore improving placental blood flow. However, as it does not alter the pathophysiology of the unbalanced blood flow through the placental anastomosis, it will usually require serial procedures until delivery, with the inherent risk of miscarriage with each procedure. It is therefore, now only reserved for when the more definitive fetoscopic laser ablation is not possible either because the polyhydramnios is too severe to risk transfer to a tertiary unit for the laser or the TTTS presents after 26-weeks gestation when laser cannot be performed.
2. Selective fetocide of either the donor or recipient depending on which one is the most compromised, to allow the other fetus to survive. This is considered in cases of severe disease where there may be overlapping severe selective fetal growth restriction of the donor, or when there is severe TTTS occurring before 16 weeks gestation and laser cannot be performed. This is typically performed using Bipolar Cord Occlusion or radiofrequency ablation under ultrasound guidance.
3. Fetoscopic laser ablation (FLA) using the Solomon technique where unidirectional arteriovenous vascular anastomoses on the surface of the twin placenta distal to the intertwin membrane are selectively ablated and then the entire vascular equator is coagulated [5]. This technique is the first line treatment with stage II TTTS or beyond, and significantly improves both double and single twin-survival [6]. Rates of at least one twin surviving were sig-

Table 28.1 Quintero staging of TTTS using ultrasound and doppler results

Stage	Abnormal Liquor volume	Bladder absent in donor	Abnormal doppler present	Fetal Hydrops	Demise of either twin
I	Yes	–	–	–	–
II	Yes	Yes	–	–	–
III	Yes	Yes	Yes	–	–
IV	Yes	Yes	Yes	Yes	–
V	Yes	Yes	Yes	Yes	Yes

Adapted from Quintero et al. [2]

nificantly higher in the laser treatment group at both 28 days (76 vs. 56%) and 6 months (76 vs. 51%, $p < 0.01$) compared with serial amnioreduction. Neurological outcomes were also better in the laser treatment group. A Cochrane review of TTTS treatment showed similar findings [7].

Initially the placental position, fetal position and placental cord insertions are mapped using ultrasound to decide on the optimal position for the fetoscope insertion into the recipient amniotic sac to be able to see the vascular equator most clearly. Then local anaesthetic (20 ml of 1% lidocaine) is inserted into the maternal skin and a 10F catheter is inserted under ultrasound guidance into the recipient amniotic sac. A 2-3 mm fetoscope with a laser channel is then inserted into the uterine cavity to visualise the placental equator. An anterior placenta can be technically more challenging. Selection of a curved or straight scope, modifying the patients position, and creating a "window" using amnioinfusion can help with optimal trocar placement. Vascular anastomoses crossing the dividing membrane which separate the amniotic sac are visualised, and abnormal vessel connections are coagulated with a diode laser. Failure to ablate all disease causing anastomoses can lead to complications such as TAPS or recurrence of TTTS [6]. Following anastomotic laser coagulation, amnioreduction is performed to reduce the degree of polyhydramnios and hence reduce the risk of preterm labour. Following the procedure, patients are usually monitored weekly for continued TTTS, TAPS, selective growth restriction or single/double fetal demise.

Other complications of this procedure include PPROM, preterm labour, infection, placing the trocar through the placenta leading to placental abruption/haemorrhage, and possible membrane perforation resulting in limb entrapment and ischaemia. A tocolytic (Table 28.2) and intravenous antibiotic are also typically administered pre-induction.

Table 28.2 Summarises the main tocolytics that can be used [8]

Tocolytic drug	Examples	Possible side-effects
β adrenergic agonists	Ritodrine, terbutaline, salbutamol	Cardiac arrhythmias, ↓ blood pressure (BP), ↑ glucose, ↓ potassium, pulmonary oedema
MgSO4 (loading dose followed by an infusion)		Flushing, respiratory depression, ↓ BP, pulmonary oedema Potentiates neuromuscular blockade Added advantage of fetal neuroprotection
Halogenated volatile agents (as part of GA for a fetal procedure)	Sevoflurane	
Nitric oxide donors	Glyceryl trinitrate (GTN)	Headache, flushing, ↓ BP, ↑heart rate, pulmonary oedema Can cause asthma in aspirin sensitive patients
Non steroidal anti-inflammatory drugs (NSAIDs)	Indomethacin per rectum	Premature closure ductus arteriosus
Calcium channel blockers	Nifedipine	Maternal ↓ BP, dizziness
Oxytocin receptor blockers	Atosiban	GI upset Administration is complex (different bolus and infusion rates), expensive

Poor neurodevelopmental outcomes are associated with severe TTTS, delayed therapeutic interventions, and preterm delivery [2].

Although some centres still perform this procedure under maternal neuraxial blockade (spinal, epidural or combined spinal/epidural anaesthesia), most experienced units will perform the procedure under local anaesthetic (LA) infiltration with 1% lignocaine from the skin to the myometrium.

Maternal sedation is also helpful for both the mother and fetal immobilisation. An RCT showed that maternal sedation using remifentanil is better than diazepam [9]. Ultimately the mode of anaesthesia will be at the discretion of the anesthesia provider but liaison with the operating team is vital. The advantages of regional anaesthesia or local without sedation versus sedation are; (1) patient stays awake, (2) early contact with the family, (3) early food intake post procedure, (4) cardiovascular and respiratory stability, (5) rapid post-operative recovery, (6) airway reflexes are preserved [10].

Sedation can be used as a continuum ranging from minimal sedation (e.g. as an anxiolytic) through to general anaesthesia. Verbal contact is usually maintained. The aim of sedation is; (1) patient comfort, (2) some amnesia from the surgical procedure, (3) patient preference [10] (4) using sedation has been shown to have improved patient satisfaction during regional anaesthesia [11].

Critical Fetal Aortic Stenosis

The most commonly performed closed fetal cardiac intervention for a congenital heart defect is percutaneous aortic valvuloplasty for critical aortic stenosis with evolving hypoplastic left heart syndrome. Many fetuses with critical aortic stenosis will survive until birth but with significant risk of adverse neonatal outcome and significant morbidity. At birth, neonates with critical aortic stenosis may not be able to have biventricular repair and 50% die within the first year of life [12]. In babies with adequate biventricular function, postnatal balloon valvuloplasty followed with a valve replacement can be performed. For those fetuses with a high risk of compromise in utero, and high postnatal morbidity and mortality, in utero valvuloplasty can be performed, typically at 21–32 weeks' gestation. NICE (National Institute for Clinical Excellence) has produced interventional procedure guidance for fetal percutaneous balloon valvuloplasty for aortic stenosis [12]. Currently there is insufficient evidence on the safety and efficacy of this technique. Any cases done should be entered onto the intention to treat registry developed by the Association for European Paediatric Cardiology.

In most centres, this procedure is performed under local anaesthesia (with/without maternal sedation such as lorazepam and morphine with the mother in a fasted state) using real time ultrasound. A needle is inserted through the maternal abdominal wall into the fetal left ventricular outflow tract. Fetal analgesia (fentanyl 10 μg/kg i.m. or via the cord) is used before the needle is advanced through the fetal chest wall and then into the ventricle [12]. A guidewire is inserted through the needle, across the aortic valve. A balloon catheter is then inserted and inflated across the stenotic valve.

Arzt et al. [13] have described 24 cases under maternal GA. Using maternal remifentanil also provided fetal analgesia.

Congenital Diaphragmatic Hernia (CDH)

The incidence of CDH is 1:2500–5000 [14]. Diagnosis is made using ultrasound with fetal magnetic resonance imaging augmenting the diagnosis. The diagnosis is typically made at the time of the mid trimester fetal anatomy scan with fetal cardiac deviation and visualisation of the stomach in the fetal thorax. It is important to exclude other associated anomalies and fetal aneuploidy, which can be present in 40% cases, and <15% will survive [14]. Left sided CDH occurs more commonly than right sided CDH. Without fetal intervention, CDH causes significant mortality from pulmonary hypoplasia and pulmonary hypertension [15]. Overall survival rates are approximately 70% in centres using standardised postnatal treatment protocols and gentle ventilation strategies, planned delivery and post-natal therapy [16] and is dependent on the presence of (1) additional anomalies; (2) gestation at delivery; (3) presence of aneuploidy and copy number variation and; (4) liver involvement.

Negative prognostic predictors for CHD include liver in the fetal chest and lung-head ratio (LHR) of <1.2 (survival of 0–38%) [17]. Intervention to reverse the development of pulmonary hypoplasia before delivery can be considered [14]. FETO (Fetoscopic Endoluminal Tracheal Occlusion) has shown promising results for the treatment of severe CDH. Following tracheal occlusion, accumulated lung fluid creates positive pressure, and is levelled by fetal breathing movements. This has the effect of stimulating lung growth. It is carried out at 27–29 weeks [16]. The balloon is then decompressed by ultrasound guided needle aspiration or fetoscopic removal at approximately 34 weeks gestation.

European studies have shown an increased survival in left CDH from 24 to 49% when compared to historical controls [18].

TOTAL (Tracheal Occlusion to Accelerate Lung Growth) is a multi-centre randomised trial in Europe and North America comparing FETO to standard post-natal care. They are currently awaiting publication of the results (SEVERE trial) (http://totaltrial.eu/).

Anaesthesia for this procedure was initially performed under epidural anaesthesia. In many centres, it is now performed under local anaesthetic at 27–29 weeks' gestation with/without maternal sedation (remifentanyl).

Prophylactic tocolysis (atosiban, indomethacin or nifedipine) are required to limit the risk of preterm delivery, and prophylactic antibiotics (cefazolin 2 g i.v. 8 hourly) are used until 24 h after the procedure [16].

The patient is placed in a dorsal supine position with left lateral tilt (to prevent caval compression). External manipulation of the fetal position may be required so that there is direct access to the fetal mouth. Once in the correct position, fetal muscle relaxant (pancuronium 0.2 mg/kg), atropine (20 μg/kg), fentanyl (15 μg/kg) is given imtramuscularly to the fetus percutaneously under ultrasound guidance to provide fetal analgesia, immobilisation, and prophylaxis against bradycardia [16].

After sterile draping, the insertion site in infiltrated with LA (1% lignocaine 10–20 ml). The 10F trocar is then inserted through the maternal abdomen into the amniotic sac and the fetoscope inserted. The scope is then directed into the fetal mouth under direct vision and the use of ultrasound. The scope is then guided under direct vision past the uvula and through the vocal cords with the entotracheal balloon being deployed and inflated below the cords.

The procedure usually lasts between 10 and 60 min depending on fetal position, but is usually abandoned if not competed by 60 min. The length of the procedure is proportional to the risk of PPROM and uterine stimulation.

By far the most important aspect of neonatal survival is removal of the balloon before birth. Ideally the balloon is electively removed at 34 weeks gestation. This is done either by balloon rupture percutaneously under ultrasound guidance or if this is not possible it can be removed fetoscopically in the same way as insertion, using the same drugs. In 28% cases, balloon removal will be indicated earlier because of impending delivery [19]. If the patient is in established labour before the balloon can be removed then an EXIT procedure (as below) can be performed with the fetal head being delivered at caesarean and whilst the baby is still on the placental circulation the same fetoscope can be used as a tracheoscope and the balloon ruptured under direct vision. This therefore needs experienced operators to be available, and oncall, to perform an emergency balloon removal in case of preterm labour before elective removal at 34 weeks.

Lower Urinary Tract Obstruction (LUTO)

LUTO occurs in approximately 0.1% of pregnancies [20]. Congenital bilateral hydronephrosis occurs due to fetal urethral obstruction at the bladder outlet, usually by posterior urethral valves in males or urethral atresia in female fetuses. Other causes include obstruction at the uretopelvic or vesicoureteric junction. These anomalies are typically detected on ultrasound. Reduced fetal urine output causes oligohydramnios. Severe obstruction can lead to megacystis, renal dysplasia and dysfunction,

oligohydramnios and developmental problems (e.g. limb/facial deformities, pulmonary hypoplasia). This is associated with increased perinatal mortality.

Obstruction results in increased bladder pressure causing changes to the bladder structure and function, vesicoureteric reflux, hydroureter and hydronephrosis, leading to increased risk of chronic renal failure. There is limited evidence to support fetal interventions in LUTO. Open surgery (nephrostomy) carries a high mortality rate, and a third of these patients will still require a renal transplant later in life. Other options for antenatal treatment include percutaneous drainage of the urinary bladder (vesicocentesis) under real time ultrasound to relieve the pressure within the urinary tract and facilitating investigations such as urinary electrolytes. Dependent upon the underlying pathology megacystis will typically recur at which point vesicoamniotic shunting can be considered to minimise compression damage to the renal tissue and reduce the risk of pulmonary hypoplasia. This involves placing a catheter, using a percutaneous needle via a Rocket KCH™ Fetal Bladder Catheter with real time ultrasound, into the fetal bladder. A study by Coplen et al. [21] reported the survival rate as 47%, but the rate of end stage renal disease was 40% in survivors. PLUTO (percutaneous vesicoamniotic shunting vs. conservative management for fetal lower urinary tract obstruction), an international multicentre randomised trial suggests that vesicoamniotic shunting improves overall perinatal survival, but the long-term outlook for these babies is poor, with high mortality and morbidity, primarily due to renal failure [22]. However, PLUTO was limited by small number of participants who were recruited. Hence parents must be counselled appropriately as to the risks and benefits of the procedure.

Specific assessment and treatment for urethral obstruction using fetal cystoscopy has also been described. This technique allowed normal bladder dynamics to be restored as opposed to chronic bladder decompression, but has only been assessed in small cohorts [23]. Its use is limited due to complications including bleeding, preterm labour, PPROM, infection, and intrauterine death.

This procedure is usually performed under LA infiltration, with/without maternal sedation.

Congenital Lung Malformations (CLM's)

This includes CCAM (congenital cystic adenomatoid malformations), Bronchopulmonary sequestrations (BPS) and hybrid lesions.

These lesions grow unpredictably, especially during mid-gestation [24]. Serial ultrasound scanning allows monitoring of growth and associated fetal compromise with complications such as cardiac failure and hydrops fetalis [24]. Small lesions do not tend to cause respiratory symptoms at birth, and infants usually have conservative management or rarely postnatal resection at 2–6 months of age [25]. Large lesions can cause a significant mass effect in the chest with cardiomediastinal shift, and compression of the normal lung. Fetal hydrops occurs with very severe lesions with high mortality [25].

Fetuses with large lesions can be considered for fetal intervention. Ultrasound is used to determine the cystic adenomatoid malformation volume ratio (CVR), to identify fetuses who will require in utero treatment. Fetuses with CVR >1.6 have an 80% risk of developing hydrops [26]. Maternal betamethasone can be used to arrest lesion growth in these high risk cases, although outcomes are variable [27].

Thoracoamniotic shunts can be used to treat lesions CCAM with a dominant macrocyst and associated hydrops. This can result in sustained decompression and resolution of hydrops [28], and liaison with thoracic surgeons and neonatologists is vital as such fetuses will require postnatal surgery. Prior needle decompression using percutaneous drainage may be beneficial in the first instance to determine if the lesion is compressible, if cysts are connected and if a therapeutic effect can be seen with this less complex intervention.

Not all lesions can be decompressed because the cysts are not always contiguous (i.e. in communication with each other) and can rapidly refill.

Risks of thoracoamniotic shunt placements include malfunction, displacement, fetal haemorrhage, chorioamnionitis, intrauterine death and preterm delivery [29].

Microcystic/solid lesions not responding to maternal steroid treatment may require open fetal resection although this is not commonly performed due to risks associated with maternal morbidity [30].

In the future, minimally invasive techniques using fetoscopic radiofrequency thermal ablation may be possible [31].

This procedure is performed under LA infiltration with/without maternal sedation.

Ex Utero Intrapartum Treatment (EXIT) Procedure

An EXIT procedure is used to establish a patent airway in fetuses who have potential prenatally diagnosed airway obstruction. It allows the airway to be established, whilst placental perfusion continues. It is used for:

(a) Upper airway obstruction (e.g. cystic hygroma, large cervical mass)
(b) Congenital high airway obstruction syndrome (CHAOS)—this spectrum consists of laryngeal web atresia, or cyst, and tracheal atresia or stenosis.
(c) Thoracic abnormalities (e.g. CLM's, tumours)
(d) Assisting transition to ECMO [24]
(e) Removal of Tracheal Balloon for Congenital Diaphragmatic Hernia in preterm labour.

This procedure requires a coordinated, multidisciplinary approach involving paediatric anesthesia providers, ear-nose and throat surgeons, fetal medicine subspecialists, obstetricians, and neonatologists are all present during the procedure. Anesthesia providers are required to minimise uterine tone at the time of caesarean section without compromising maternal blood pressure and hence placental blood flow. Maternal safety is paramount throughout the procedure.

The patient is prepared as for a general anaesthetic for Caesarean section. A systematic review found that both GA and regional anaesthesia were successfully described for EXIT procedures, but GA was performed in majority of cases [32]. The mother is positioned in a slight lateral decubitus position and prepared in case of major haemorrhage. Two wide bore intravenous canulae are recommended, and the placement of an arterial line and central venous pressure (CVP) line should be considered. Cross matched blood should be made available. A maternal epidural can be considered for post-operative analgesia (if there are no contraindications). A rapid sequence induction is performed with left lateral displacement of the uterus (to reduce aorto caval compression). Aim for a minimum alveolar concentration (MAC) of two to three for uterine relaxation. Other tociolytics may be required if uterine relaxation is inadequate (e.g. GTN) (Table 28.2). Vasopressors may be required for the consequent maternal hypotension, and maintaining uterine blood flow.

The mother is placed in a slight left lateral tilt with the legs in a flattened lithotomy position. A Pfannenstiel incision is used to gain access to the uterus. Real time ultrasound is used to locate the placenta, and perform a lower segment incision avoiding the placenta. Only the fetal head and shoulders are delivered to preserve umbilical blood flow, and to prevent evaporative heat loss and fluid loss. On occasion, manipulation of the uterus aided by tocolytics may be required prior to commencing the procedure to ensure cephalic delivery (Table 28.2).

Fetal anaesthesia occurs via placental transfer of volatile agents. Fetal immobilisation may require the use of muscle relaxants (e.g. pancuronium 0.3 mg/kg i.m. or via the umbilical cord). Additional fetal anaesthesia can be given such as fentanyl 10 μg/kg i.m. or via the cord [33].

The fetal airway is then secured (intubation, tracheostomy, or even resection of the lesion whilst the infant has placental support), *before* the umbilical cord is clamped. Continued uteroplacental circulation has been maintained for up

to an hour without fetal compromise [34]. Once the airway is established, the fetus is delivered and the umbilical cord is cut [35]. Agents to contract the uterus (e.g. oxytocin infusion) will be required once the fetal airway is secured and if a tocolytic infusion is being used this should be ceased. The MAC is also reduced. Post operatively, high-dependency care may be required to monitor cardiovascular parameters, and assess for signs of haemorrhage.

Most procedures require less than 1 h, but the anaesthetic technique should be capable of providing maternal, fetal and uteroplacental stability over several hours [35, 36].

In two studies [35, 37] there were no maternal deaths. One study showed that 51 of 52 (98%) EXIT procedures had patients born alive, and 52% were alive at long term follow up [35].

Reasons to Consider Fetal Analgesia

Fetal analgesia is a controversial subject of great debate. Some studies have shown that several intrauterine endocrine neuroinhibitors (ENIn) anaesthetise the fetus, keeping it in a constant state of sleep, and making pharmacological fetal anaesthesia useless for fetal surgery. However, other studies argue that fetal pain is possible and should be prevented with fetal anaesthesia [38]. Fetal pain is important as fetal surgery becomes more frequent [39].

Analgesia is recommended from the second trimester onwards as neuroadaptive phenomenon appear, and pain becomes more significant to the fetus [39]. The presence of ENIn in the amniotic fluid does not inhibit fetal pain perception [39]. It is used for:

1. Endoscopic, intrauterine surgery on the placenta, cord and membranes.
2. Late termination of pregnancy
3. Direct surgical trauma to the fetus.

The nociceptive stimulation of the fetus can have long term effects (including abnormal behavioural patterns, or altered sensory processing), hence there is a need for fetal analgesia [33]. Evidence supporting the need for fetal analgesia has been shown by Anand 1998 [40].

Fetal Stress Response

Preterm neonates have hormonal stress response following invasive uterine interventions. This is shown by an increase in cortisol and beta endorphin levels, increased fetal movements and breathing. There is no correlation between maternal and fetal hormone levels, indicating that there is no placental transfer of these hormones.

Fetal anaesthesia is required to prevent fetal movements, and to reduce the fetal physiological response to pain [33].

For open surgery, where a general anaesthetic is used (with or without neuraxial blockade) the fetus is anaesthetised via the placenta. Direct fetal administration of anaesthesia (i.m. or via the umbilical cord) can also be used [33].

Neural Development

For pain to be experienced, pathways must exist from peripheral receptors to the cerebral cortex. Peripheral receptors develop from 7 weeks gestation. From 20 weeks gestation, there are peripheral receptors on the whole body. The spinothalamic tract begins developing from 14 weeks gestation, and is complete at 20 weeks gestation. Thalamocortical connections are present from 17 weeks gestation, and are completely developed at 26–30 weeks gestation. From 16 weeks gestation, pain transmission from a peripheral receptor to the cortex is possible [33].

Haemodynamic Response

The fetus is able to redistribute blood in response to acute stressors (e.g. heamorrhage, pain, hypoxia). Fisk et al. [41] have shown that acute painful stimuli to the fetus is associated with haemodynamic changes which is consistent with redistribution of blood supply to the brain.

Maternal and Fetal Analgesia

Fetal fetoscopic procedures are usually performed under LA infiltration and/or neuraxial blockade which can be supplemented with maternal sedation. Maternal sedation is helpful for both the mother and fetal immobilisation. LA, used in clinical doses, have not been shown to be associated with teratogenicity. There is usually considerable maternal anxiety, and these local techniques do not immobilise the fetus. A mobile fetus may displace the fetoscope, resulting in bleeding, fetal trauma or a compromised umbilical circulation causing fetal death. Opioids have been shown to be devoid of teratogenic effects [42]. An RCT showed that maternal sedation using remifentanil rather than diazepam [43] is better as it is easy to titrate and crosses the placenta readily immobilising the fetus. Using a continuous remifentanil infusion rate of 0.1–0.2 μg/kg/min produces good effect [33].

Benzodiazepines were initially thought to be associated with cleft lip and palate, but subsequent studies have not confirmed this. A single dose of benzodiazepine can be used safely for maternal anxiolysis [33].

Table 28.3 summarises both maternal and fetal anaesthesia required for the various fetal surgeries carried out.

Tocolysis

Tocolysis may be required during fetal surgery and post procedure, as fetal interventions are associated with preterm labour. Uterine incisions or manipulation can impair uterine blood flow, which in turn affects placental blood flow and the fetus. Even minor uterine interventions (e.g. needle insertion for a blood transfusion) can cause uterine contractions. Tocolysis is also required post procedure as preterm uterine contractions may still occur. The choice of tocolytic depends on maternal side effects.

Atosiban resulted in identical short term uterine outcome without any serious maternal complications when compared with magnesium sulphate [44].

Table 28.3 Overview of fetal procedure and type of anaesthesia

	Maternal anaesthesia	Fetal anaesthesia
Open surgery (e.g. myelomeningocele)	GA (± epidural)	Fetus anaesthetised through placental passage. *Additional* fetal anaesthesia can be given i.m. or via umbilical cord (e.g. fentanyl 10 μ/kg) and muscle relaxants (e.g. pancuronium 0.3 mg/kg) if fetus is moving
Fetoscopic fetal surgery (e.g. obstructive uropathy)	Usually performed under LA ± i.v. remifentanil Can use regional anaesthesia (spinal, epidural or CSE) if complex	Fetal (i.m. or cord) opioids (e.g. fentanyl 10 μ/kg) and muscle relaxants (e.g. pancuroinum 0.3 mg/kg), or maternal i.v. remifentanil 0.1–0.2 μg/kg/min
Fetoscopic surgery on placenta and cord (e.g. TTTS)	Usually under LA ± i.v. remifentanil. Can use regional anaesthesia (spinal, epidural or CSE) if complex	Maternal i.v. remifentanil 0.1–0.2 μg/kg/min
Late termination of pregnancy via intracardiac puncture	LA or regional anaesthesia	Fetal intracardiac opioids (e.g. fentanyl 10 μg/kg) or anaesthesia (Alcuronium), followed by drugs to perform fetocide (potassium or lidocaine)
EXIT procedure	GA ± regional anaesthesia (CSE) with additional uterine relaxation	Fetal (i.m. or cord) opioids (e.g. fentanyl 10 μg/kg) and muscle relaxants (e.g. pancuronium 0.3 mg/kg),or maternal i.v. remifentanil 0.1–0.2 mg/kg/min. This is needed if EXIT procedure is performed under regional anaesthesia

Table adapted from Van de Velde [33]

Conclusion

Fetal therapy requires a well organised, multidisciplinary teamwork. Continued collaborative clinical research and investigation will allow this sub-speciality to evolve. As imaging and interventional techniques improve, so does the number and complexity of fetal anomalies treated in utero. We need to ensure we use good quality evidence before implementing them in clinical practice, and use informed maternal consent. There are also complex ethical, social and legal issues to consider. Central to the provision of fetal therapy is the preservation of maternal well-being.

References

1. Chalouhi GE, Essaoui M, Stimemann J, Quibel T, Deloison B, Salomon L, et al. Laser therapy for twin-to- twin transfusion syndrome (TTTS). Prenat Diagn. 2011;31:637–46.
2. Quintero RA, Morales WJ, Allen WJ, Allen MH, Bornick PW, Johnson PK, et al. Staging of twin-twin transfusion syndrome. J Perinatol. 1999;19:550–5.
3. Yamamoto M, El Murr L, El Murr L, Robyr R, Leleu F, Takahashi Y, et al. Incidence and impact of perioperative complications in 175 fetoscopy-guided laser coagulations of chorionic plate anastomoses in fetofetal transfusion syndrome before 26 weeks gestation. Am J Obstet Gynaecol. 2005;193:1110–6.
4. Chimenea A, Garcia-Diaz L, Calderón AM, Moreno-De Las Heras M, Antiñolo G. Resolution of maternal mirror syndrome after successful fetal intrauterine therapy: a case series. BMC Pregnancy Childbirth. 2018;18:85.
5. Slaghekke F, Oepkes D. Solomon technique versus selective coagulation for twin-twin transfusion syndrome. Twin Res Hum Genet. 2016;19(3):217–21.
6. Senat MV, Deprest J, Boulvain M, Paupe A, Winer N, Ville Y. Endoscopic laser surgery versus serial amnioreduction for severe twin-to-twin transfusion syndrome. N Engl J Med. 2004;351:136–44.
7. Roberts D, Gates S, Kilby M, Neilson JP. Interventions for twin-twin transfusion syndrome: a Cochrane review. Ultrasound Obstet Gynecol. 2008;31:701–11.
8. https://www.nice.org.uk/guidance/ng25?unlid=92910360720162132012 57 and guideline central https://www.guidelinecentral.com/summaries/tocolysis-for-women-in-preterm-labour/#section-date
9. Missant C, Van Schoubroeck D, Deprest J, et al. Outcomes of different anesthetic techniques in fetoscopic laser ablation for TT transfusion syndrome. Acta Anaesthesiol Belg. 2004;55:239–44.
10. Höhener D, Blimenthal S. Sedation and regional anaesthesia in the adult patient. BJA. 2008;100:8–16.
11. Wu CL, Naqibuddin M. Measurement of patient satisfaction as an outcome of regional anaesthesia and analgesia: a systematic review. Reg Anesth Pain Med. 2001;26:196–208.
12. https://www.nice.org.uk/guidance/ipg613/chapter/1-Recommendations NICE IPG613
13. Artz W, Wertaschnigg D, et al. Intrauterine aortic valuloplasty in fetuses with critical aortic stenosis: experience and results of 24 procedures. Ultrasound Obstet Gynaecol. 2011;37(6):689–95.
14. Morris RK, Chan BC, Kilby MD. Advances in fetal therapy. Obstet Gynaecol. 2010;12:94–102.
15. Metkus AP, Filly RA, Stringer MD, Harrison MR, Adzick NS. Sonographic predictors of survival in fetal diaphragmatic hernia. J Pediatr Surg. 1996;31:148–51.
16. Van der Veeken L, Maria Russo F, De Catte L, Gratacos E, Benachi A, Ville Y, et al. Fetoscopic endoluminal tracheal occlusion and reestablishment of fetal airways for congenital diaphragmatic hernia. Gynecol Surg. 2018;15(1):9.
17. Lipshutz GS, Albanese CT, Feldstein VA, Jennings RW, Housley HT, Beech R, et al. Prospective analysis of lung-to-head ratio predicts survival for patients with prenatally diagnosed congenital diaphragmatic hernia. J Pediatr Surg. 1997;32:1634–6.
18. Deprest J, Jani J, Lewi L, Ochsenbein-Kölble N, Cannie M, Doné E, et al. Fetoscopic surgery: encouraged by clinical experience and boosted by instrument innovation. Semin Fetal Neonatal Med. 2006;11:398–412.
19. Jimenez JA, Eixarch E, DeKoninck P, Bennini JR, Devlieger R, Peralta CF, et al. Balloon removal after fetoscopic endoluminal tracheal occlusion for congenital diaphragmatic hernia. Am J Obstet Gynecol. 2017;217:78.
20. Estes JM, MacGilliuray TE, Hedrick MH, et al. Fetoscopic surgery for the treatment of congenital anomalies. J Pediatr Surg. 1992;27:950–4.
21. Coplen DE. Prenatal intervention for hydronephrosis. J Urol. 1997;157:2270–7.
22. Morris RK, Malin GL, Quinlan-Jones E, Middleton LJ, Hemming K, Burke D, et al. Percutaneous vesicoamniotic shunting versus conservative management for fetal lower urinary tract obstruction (PLUTO): a randomised trial. Lancet. 2013;382(9903):1496–506.
23. Agarwal S, Fisk N. In utero therapy for lower urinary tract obstruction. Prenat Diagn. 2001;21:970–6.
24. Maselli KM, Badillo A. Advances in fetal surgery. Ann Transl Med. 2016;4(20):394.
25. Adzick NS, Harrison MR, Crombleholme TM, Flake AW, Howell LJ. Fetal lung lesions: management and outcome. Am J Obstet Gynecol. 1998;179(4):884–9.
26. Adzick NS. Open fetal surgery for life-threatening fetal anomalies. Semin Fetal Neonatal Med. 2010;15(1):1–8.

27. Derderian SC, Coleman AM, et al. Favorable outcomes in high- risk congenital pulmonary airway malformations treated with multiple courses of maternal betamethasone. J Pediatr Surg. 2015;50(4):515–8.
28. Wilson RD, Baxter JK, Johnson MP, King M, Kasperski S, Crombleholme TM, et al. Thoracoamniotic shunts: fetal treatment of pleural effusions and congenital cystic adenomatoid malformations. Fetal Diagn Ther. 2004;19(5):413–20.
29. Lakhoo K. Management of congenital cystic adenomatoid malformations of the lung. Arch Dis Child Fetal Neonatal Ed. 2009;94(1):F73–6.
30. Wilson RD, Johnson MP, Crombleholme TM, et al. Prenatal diagnosis and outcome of echogenic fetal lung lesions. Fetal Diagn Ther. 2003;18:314–20.
31. Olutoye OO, Gay AN, Andre N, Gay AN, Sheikh F, Akinkuotu AC, et al. In- utero radiofrequency ablation in fetal piglets: lessons learned. J Pediatr Surg. 2016;51(4):554–8.
32. Kumar K, Miron C, Singh SI. Maternal anaesthesia for EXIT procedure: a systematic review of literature. J Anaesthesiol Clin Pharmacol. 2019;35(1):19–24.
33. Van de Velde M, De Buck F. Fetal and maternal analgesia/anesthesia for fetal procedures. Fetal Diagn Ther. 2012;31:201–9.
34. Boris P, Cox PBW, Gogarten W, Strumper D, Marcus MAE. Curr Opin Anaesthesiol. 2004;17:235–40.
35. Hirose S, Farmer DL, Lee H, Nobuhara KK, Harrison MR. The ex utero intrapartum treatment procedure: looking back at the EXIT. J Pediatr Surg. 2003;39:375–80.
36. Rahbar R, Vogel A, Myers LB, Bulich LA, Wilkins-Haug L, Benson CB, et al. Fetal surgery in otolaryngology: a new era in the diagnosis and management of fetal airway obstruction because of advances in prenatal imaging. Arch Otolaryngol Head Neck Surg. 2005;131:393–8.
37. Bouchard S, Johnson MP, Flake AW, Howell LJ, Myers LB, Adzick NS, et al. The EXIT procedure: experience and outcome in 31 cases. J Pediatr Surg. 2002;37:418–26.
38. Bellieni CV, Vannuccini S, Petraglia F. Is fetal analgesia necessary during prenatal surgery? J Matern Fetal Neonatal Med. 2018;31(9):1241–5.
39. Bellieni CV. New insights into fetal pain. Semin Fetal Neonatal Med. 2019;24(4):101001.
40. Anand KJ. Clinical importance of pain and stress in preterm neonates. Biol Neonate. 1998;73(1):1–9.
41. Fisk NM, Gitau R, Teixeira JM, Giannakoulopoulos X, Cameron AD, Glover VA. Effect of direct opioid analgesia on fetal hormonal and Haemodynamic stress response to intrauterine needling. Anaesthesiology. 2001;95:828–35.
42. Handal M, Engeland A, Rønning M, Skurtveit S, Furu K. Use of prescribed opioid analgesics and co- medication with benzodiazepines in women before, during, and after pregnancy: a population based cohort study. Eur J Clin Pharmacol. 2011;67:953–60.
43. Missant C, Van Schoubroeck D, Lewi LE, Marcus MA, Jani JC, Missant C, et al. Remifentanil for fetal immobilisation and maternal sedation during endoscopic treatment of twin-to-twin transfusion syndrome: a preliminary dose-finding study. Acta Anaesthesiol Belg. 2004;55:239–44.
44. Ochsenbein-Kölble N, Krähenmann F, et al. Tocolysis for in utero surgery: atosiban performs distinctly better then magnesium sulphate. Fetal Diagn Ther. 2018;44(1):59–64.

Anesthesia for Uterine Transplant Surgery

29

Michele M. Mele, Kristen K. Burton, Magdy Takla, and Talia K. Ben-Jacob

Key Learning Points

- Uterine transplantation is currently considered an experimental procedure and most appropriately performed inside of IRB approved protocols at academic medical institutions.
- General anesthesia with endotracheal intubation is the standard of care for uterine transplantation.
- A balanced anesthetic approach is utilized to permit extubation in the operating room.
- Dissection and anastomosis involving the large vessels of the pelvis can be associated with significant intraoperative blood loss, therefore, intravenous access, blood availability and autologous cell salvage equipment and personnel should be planned accordingly
- Anesthetic complications have not been reported; recipients of uterus transplantation surgery are at risk for numerous postoperative complications including hemoperitoneum, venous or arterial graft thrombosis and infection resulting in graft necrosis requiring hysterectomy.

Introduction

With the introduction of in vitro fertilization resulting in the first live birth reported by Edwards and Steptoe in 1978, infertility medicine was revolutionized. In the last several decades, this field of medicine has continued to experience tremendous growth with the development of treatments that can remedy most causes of infertility. However, women with absolute uterine factor infertility (AUFI) are one of the few main subgroups of infertility that has remained untreated due to the absence of a functioning uterus. Absolute uterine factor infertility is defined as infertility due to either uterine absence secondary to congenital or surgical causes, or anatomical or functional causes that prevents implantation of an embryo. This untreatable condition affects approximately 1–5% of infertile women of childbearing age [1].

M. M. Mele (✉) · M. Takla
Division of Obstetric Anesthesiology, Department of Anesthesiology, Cooper Medical School of Rowan University, Cooper University Hospital, Camden, NJ, USA
e-mail: Mele-Michele@Cooperhealth.edu; Takla-Magdy@Cooperhealth.edu

K. K. Burton
Anesthesia for Abdominal Organ Transplantation, Department of Anesthesia and Critical Care, Hospital of the University of Pennsylvania, Philadelphia, PA, USA
e-mail: Kristen.burton@pennmedicine.upenn.edu

T. K. Ben-Jacob
Division of Critical Care Medicine, Department of Anesthesiology, Cooper Medical School of Rowan University, Cooper University Hospital, Camden, NJ, USA
e-mail: Ben-Jacob-Talia@Cooperhealth.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_29

Options for women with AUFI to have children have been limited to gestational surrogacy and adoption. However, these routes to motherhood may be unacceptable for some due to religious, financial, ethical or legal concerns. In many countries, surrogacy is not a legal option. Uterine transplantation has been proposed as a solution to AUFI to provide these women with the opportunity to conceive, carry a pregnancy, and give birth to a genetically related child.

Over the last decade, researchers have studied in a stepwise fashion the complex process of uterine transplantation in animals and then in human subjects to optimize the procedure with the aim of clinical implementation. In 2014, the first live birth following uterine transplant was reported in Gothenburg, Sweden [2]. Since then, results of successful uterine transplantation resulting in live births have been published from numerous pioneering centers worldwide including Sweden, the United States, and Brazil [2–4]. At the time of this writing, more than 60 uterine transplantation operations have been performed around the globe, many resulting in live births.

This chapter will outline the unique aspects in the perioperative management of the recipients of uterine transplantation surgery including criteria for selection, preoperative testing related to anesthesia, intraoperative anesthetic management and events and postoperative challenges.

Uterine Transplantation Care Team

Uterine transplantation is currently considered an experimental procedure and is most appropriately performed inside IRB-approved research protocols. Current clinical trials involving uterine transplantation are listed on Clinicaltrials.gov.

Due to the medical and surgical complexity of uterus transplantation as well as the need for long-term maternal, fetal and neonatal follow-up this surgical procedure is mostly conducted at tertiary medical centers. The American Society of Reproductive Medicine (ASRM) recommends teams embarking upon such protocols should be multidisciplinary with the recommended representation as listed in Table 29.1 [1].

Table 29.1 Recommended composition of the uterine transplantation team

Reproductive endocrinologist
Transplant surgeon
Gynecologic surgeon
Maternal-fetal medicine specialist
Anesthesiologist
Infectious disease specialist
Psychiatrist or psychologist
Neonatologist
Pathologist
Radiologist
Bioethicist or professional with bioethics experience
Social worker
Living donor advocate as described by UNOS regulations
Research nurse/coordinator
Transplant medicine specialist

Adapted from ASRM. Uterus transplantation guidance. Fertil Steril 2018, [1]

Recipient Preoperative Patient Selection and Evaluation

As human uterus transplantation is in the beginning stages, the optimal inclusion and exclusion criteria for both donors and recipients are not yet known. For now, these criteria are preliminary. Ideally, development of an international society for uterine transplantation will facilitate collaboration between global teams to allow for official recommendations with regard to inclusion/exclusion criteria as well as create a registry to allow for regulation and safety monitoring. The content of this chapter will focus primarily on the recipient of uterine transplantation.

Potential uterine transplantation recipients undergo extensive testing to ensure medical and psychological appropriateness. Preoperative consultation by the following services: gynecology, transplantation surgery, psychology, maternal fetal medicine, anesthesiology and transplant medicine specialist are also performed. In addition to meeting medical and psychological requirements, the recipient must have evaluated all her other available options for parenthood including adoption, foster parenting and gestational carrier pregnancy before she can be considered for uterus transplantation.

Due to the nature of this type of transplant, all candidates accepted for transplantation are young in age and are usually without chronic medical conditions. The presence of most chronic medical conditions precludes patients from participating in uterine transplantation clinical trials as these medical conditions could increase the surgical risk for the patient and compromise graft success. Patients with a history of hypertension, diabetes, or significant systemic illness, including serious abnormalities of the heart, liver, kidney, hematologic, or central nervous system are usually excluded. Examples of recipient exclusion and inclusion criteria combined from multiple protocols including suggested ASRM criteria for uterine transplantation can be found in Table 29.2.

Table 29.2 Example inclusion and exclusion criteria for recipients of a uterus transplant

Inclusion	Exclusion
• Meets criteria for absolute uterine factor infertility (AUFI) • Reproductive-aged female (18–45 year) with normal ovarian reserve (sufficient number of good prognosis embryos) • Willing and able to undergo criteria of study including psychiatric and social work evaluation • Willing and able to undergo general anesthesia, in vitro fertilization, major gynecologic surgery, pregnancy with potential high risk complications, cesarean delivery and eventual hysterectomy to remove the graft • Willing and able to receive immunosuppressive medications • Willing to receive standard vaccinations • Social support and ability to sign informed consent • Nonsmoker • Approval of multidisciplinary treatment team • Willing and able to follow infection prophylaxis protocols with solid-organ immunosuppression practice, including but not limited to cytomegalovirus and pneumocystis pneumonia prophylaxis	• Age > 45 or poor reproductive status of embryos • History of hypertension, diabetes, or significant systemic illness, including serious abnormalities of the heart, liver, kidney, hematologic, or central nervous system. • Any medical diagnosis placing the subject at high risk of surgical complications based on the transplantation team's review of medical history • Smoker within 3 months of study enrollment • History of malignancy (excluding early-stage cervical cancer or other cancers at low risk for recurrence) • History of HIV or any history of mycobacterium infection (treated or untreated) • Presence of active documented systemic infection or recent systemic infection within the past 3 months • Active chemical and/or alcohol abuse • Anatomical abnormality which would make the pelvic transplantation surgery unlikely to be successful • Body mass index >30 kg/m^2 • Relative or absolute contraindication to immunosuppression • Untreated hepatitis C or active hepatitis B viremia or carrier state

Adapted from ASRM. Uterus transplantation guidance. Fertil Steril 2018, [1]

Uterine Transplant Recipient Selection and Testing

The ideal uterine recipient is a non-smoking, premenopausal patient, BMI 18–30 kg/m^2 with no systemic disease who has absolute uterine factor infertility (AUFI). AUFI refers to fertility that is completely attributable to the uterus. It can be related to congenital absence of the uterus (Mayer-Rokitansky-Küster-Hauser syndrome MRKH), acquired dysfunction of the uterus (e.g. irreversible intrauterine adhesions, radiation damage, inoperable fibromas), or loss of the uterus form malignant or benign pathologies or from postpartum complications. MRKH syndrome (also referred to as Müllerian agenesis) is the congenital absence of a uterus or presence of a rudimentary uterus in combination with absence of the upper third of the vagina. It has an incidence of 1 per 4500–5000 females [5]. Patients with müllerian agenesis usually have normal karyotype, and they can have normal offspring without urogenital malformations when they pursue gestational carrier pregnancy using their own eggs [6–8].

AUFI has emerged as the primary indications for uterine transplantation. Women with uterine factors that contribute to, but do not exclusively cause infertility would not be candidates for uterus transplantation because established medical and surgical infertility treatments exist. Uterus transplantation may be considered for these women when all other therapeutic options have failed.

Recipient Preoperative Testing

There is no standard preoperative workup for uterine transplant candidates and current clinical trials have different testing requirements. However, a thorough preoperative workup for recipients must be performed in order to ensure the patient is an appropriate transplant candidate, without underlying medical conditions and is healthy enough to tolerate general anesthesia with prolonged invasive pelvic surgery. Preoperative testing includes studies to thoroughly evaluate blood chemistry and metabolic function (complete metabolic panel), complete blood count, ABO-RH testing and antibody screen, testing of liver function, coagulation studies, chest x-ray, electrocardiogram and stress electrocardiography.

Preoperative Evaluation of Renal Function

Evaluation of renal function in potential recipients includes a preoperative renal ultrasound. Evaluation of associated congenital anomalies is essential as up to 53% of patients with MRKH syndrome have concomitant congenital malformations especially of the urinary tract [9]. Studies have confirmed the presence of renal abnormalities including unilateral renal agenesis and pelvic kidneys in 27–29% of women with MRKH syndrome [10].

For uterine transplantation candidates, this finding is significant as patients with a single kidney may have a higher risk of having obstetric complications should they become pregnant such as severe preeclampsia [11]. In a Swedish case series, all women who developed preeclampsia had a single kidney, however one woman with a single kidney did not develop preeclampsia in her second pregnancy, which resulted in a live birth [12]. In addition, many of the immunosuppressive medications administered post-transplant are nephrotoxic and can reduce an already limited GFR of a patient with one kidney.

Preoperative Evaluation of Cardiac Function

Evaluation of cardiac function in potential recipients is routinely performed with electrocardiogram and stress echocardiography as MRKH syndrome patients can have cardiac anomalies that are seen with VATER/VACTERL association (vertebral anomalies, anorectal malformation, cardiovascular anomalies, tracheoesophageal fistula, esophageal atresia, renal anomalies, limb defects) [13].

Preoperative Evaluation of Pelvic Anatomy

It is typical that potential recipients are evaluated with MRI (abdominal and pelvic), pelvic magnetic resonance angiogram and trans-vaginal ultrasound. The purpose of these studies is to assess pelvic anatomy, vaginal length and map key aspects of uterine and pelvic vascular anatomy relevant for uterus transplantation.

Vaginal length is important as recipients with congenital absence of the uterus may have a congenitally shortened vagina. Intraoperatively, >7 cm of vaginal cuff is needed to anastomose to the donor uterus [14].

Immunologic and Microbiologic Evaluation

Transplant recipient evaluation also includes testing for infectious diseases that could compromise transplant success. A Pap smear with testing for high-risk human papillomavirus (HPV) is routinely performed. In addition, these patients are tested for relevant viral and bacterial infections including HIV, Hepatitis A, B and C, Cytomegalovirus (CMV) Epstein-Barr virus (EBV) gonorrhea, chlamydia, trichomonas vaginalis and syphilis.

To determine recipient/donor tissue compatibility, genotyping for human leukocyte antigen

(HLA) and screening for HLA and non-HLA antibodies is performed as per the individual institution's transplant protocol.

Psychiatric Evaluation

Psychiatric testing is universally performed to ensure the donor can cope with the mental and emotional stress surrounding the procedure. This evaluation is extensive and includes assessment of cognition, social support, mental illness, substance use, and relationship stress [15, 16]. The organ recipient must have the mental endurance to undergo IVF, multiple surgeries (including the transplant, cesarean delivery if pregnancy is achieved and hysterectomy after child bearing is completed), immunosuppressive treatment, and the challenges of pregnancy, all for a procedure that is not life saving. In addition, the recipient must be prepared for the possibility that the graft could fail or she could have a successful transplant but not achieve a live birth. Despite these challenges, preliminary data suggest that patients and their partners remain psychologically stable throughout the process [15].

Intraoperative Anesthetic Management

Currently, the uterine transplant procedure is still experimental. The following intraoperative anesthetic management is informed by the published successes of global clinical trials [12, 17] and contributing authors' experience.

The operating room is prepared for an open abdominal and vascular general endotracheal anesthetic. Induction of general anesthesia occurs following de-nitrogenation of the lungs with consideration of the use of full stomach precautions, as needed. A balanced anesthetic approach is utilized to permit extubation in the operating room. Included in the regimen is use of a volatile agent or propofol infusion, muscle relaxant, and multimodal analgesia. Patients receive oral acetaminophen preoperatively as well as long-acting opioids and ketorolac intraoperatively. While not routinely placed preoperatively, a low thoracic epidural may be considered in the setting of postoperative pain refractory to intravenous and oral therapy.

In addition to standard American Society of Anesthesiologists (ASA) monitors, a radial arterial line is placed following induction. Intravenous access routinely consists of two large-bore peripheral intravenous catheters (18 gauge or larger). Central venous catheterization in either the subclavian or internal jugular vein is performed in the setting of inadequate peripheral venous access. Femoral access is avoided given the location of the surgery.

In addition to monitoring of anesthesia depth with minimal alveolar concentration, anesthetic depth analysis may be supplemented with monitoring electroencephalographic activity.

The patient is placed in the lithotomy position to facilitate surgical access to the pelvis. The right upper extremity is tucked at the patient's side and the left upper extremity is abducted less than 90° in order to accommodate a Bookwalter retractor. Careful attention is paid to appropriate padding and positioning throughout the procedure given the moderate case duration.

Surgical duration is defined as the period from skin incision to completed skin closure. The surgical duration for the recipients in the Swedish initial trial was 250–365 min with a mean time of 286 min [12]. The U.S. (Dallas) team reported a range of 270–360 min [17] and the ranges were 210–300 and 271–357 min in the Czech [18] and German [19] series, respectively.

Normothermia is maintained using either an under body warming blanket or upper body forced air warming device as well as warmed intravenous fluids. Fluid balance is maintained with a crystalloid solution. Resuscitation is guided by hemodynamic parameters, urine output, and acid-base status.

Infusion of vasoactive medications is additionally utilized as needed to maintain a mean arterial pressure >65 mmHg or within 20% of the patient's preoperative baseline throughout the case, including during creation of the vascular anastomoses.

Given the potential for potassium and acid washout with graft reperfusion, a baseline arterial blood gas is drawn and repeated 20–30 min prior to the reperfusion of the graft (at the start of the iliac

vessel anastomosis). Standard medications for the management of potential hyperkalemia are immediately available, including calcium chloride, insulin, dextrose, and sodium bicarbonate. Significant hemodynamic or acid-base derangements have not been reported with graft reperfusion.

Two to four units of packed red blood cells are cross-matched preoperatively depending on the patient's baseline hemoglobin level and history of prior intraabdominal operations. Intraoperative transfusion of packed red blood cells is considered for Hb < 8 mg/dL. Most uterine transplant trials have reported only modest blood loss with mean estimated blood loss recorded as 367 ± 94 mL (range 300–500). Allogeneic blood transfusion has not been required, though an autologous blood recovery system operated by perfusionists is utilized intraoperatively. The Swedish group has reported transfusing autologous blood to four out of nine study patients with volumes of 200–490 mL [12]. The estimated blood loss for recipients reported by the Dallas series was 300–2000 mL [17], 200–1600 mL for the Swedish series [12] and 400–800 mL in the Indian series [20].

Antibiotic prophylaxis is initiated after uterine cultures are obtained intraoperatively, and include ampicillin-sulbactam and caspofungin. Alternatively, beta lactam allergic patients receive clindamycin and gentamicin.

Methylprednisolone and antithymocyte globulin are administered for immunosuppression induction. An intravenous heparin bolus is given prior to the vascular anastomoses at the discretion of the transplant surgeon.

Postoperative nausea and vomiting (PONV) prophylaxis is standardly achieved with intravenous methylprednisolone and ondansetron; additional anti-emetics including scopolamine or a propofol-based anesthetic are utilized in patients with a significant history of PONV.

Anesthesia-related intra-procedural complications have not occurred to date and are not reported in the literature. Patients are extubated in the operating room and routinely recover postoperatively in the surgical intensive care unit.

Surgical Approach

The majority of uterine transplant grafts have come from living donors. In most published trials, living donor uteri have yielded better results than deceased donor uterus transplantation (20 vs. 2 live births) [21]. The results are superior mainly because living donor uterus transplantation has the advantages of a thorough donor workup and elective timing as compared to deceased donor uterus transplantation [21].

The uterine graft harvesting (from live or deceased donors), and transplantation to recipient surgeries are accomplished synchronously with different surgical teams. As with most transplant surgical procedures, donor and recipient surgeries must be coordinated to avoid long cold ischemic times for the graft and reduce the risk of ischemia-reperfusion injury. The uterus transplantation immediately follows the donor hysterectomy.

The standard surgical approach for recipients is open surgery through a midline infra-umbilical incision regardless of whether the uterus is from a live or deceased donor [17, 22]. In brief, the recipient surgery involves dissection of the vaginal vault to separate it from the rectum posteriorly and bladder anteriorly. The recipient external iliac vessels are dissected free and prepared to allow the arterial and venous anastomosis for the uterine graft [3, 22]. The uterine graft is placed in the pelvis and end-to-side anastomoses are performed between arteries and veins of the uterine graft to the external iliac vessels of the recipient (Fig. 29.1). Naturally, as experience grows, so does the evolution in surgical technique. In recent cases (China, Dallas), surgeons have modified the anastomosis for venous drainage by using utero-ovarian veins instead of uterine veins [17]. Surgeons determine which vascular anastomoses will be more successful based on the patient's anatomy and adjust their technique accordingly. Finally, the vaginal rim of the transplanted uterus is anastomosed to the top of the recipient's vagina and the abdomen is closed.

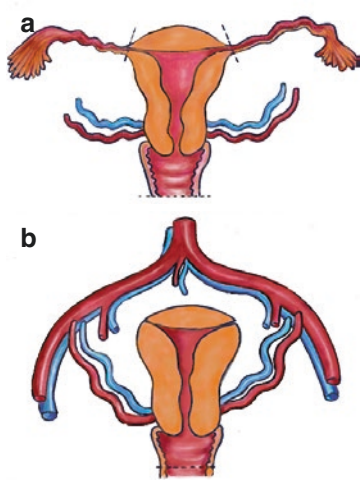


Fig. 29.1 Schematic drawings depicting (**a**) location of surgical transections in donor uterus delineated by dashed lines, (**b**) Donor uterine arteries and veins are anastomosed end to side to recipient external iliac vessels

Complications and Postoperative Course

While complications as a result of the anesthetic have not been reported, recipients of uterus transplantation surgery are at risk for numerous intraoperative and postoperative complications including hemoperitoneum, venous or arterial graft thrombosis and infection resulting in graft necrosis requiring hysterectomy in the immediate postoperative period. The most serious intraoperative complications, in order of descending importance, are lacerations of a vein, artery, ureter, or bladder wall.

Another major intraoperative risk for the uterus recipient is anastomotic leakage. Leakage is typically immediately visible and is repaired at the time of discovery. The routine surgical risks for the recipient are similar to those of the donor and include wound infection and bleeding. A complication that is unique to the graft recipient is the thrombosis of any uterine vessel anastomoses. Some institutions may routinely measure the blood flow with an intraoperative probe during surgery. The graft uterine arteries are monitored with external Doppler measurements using an abdominal probe. If there is concern for vessel thrombosis, the surgeon may repeat the laparotomy to assess the patency of the blood vessels and to clear any thrombosis with possible reconstruction of the graft vessels or anastomosis sites [12].

More common postoperative complications include wound infection, venous thromboembolism, bleeding, vaginal cuff infection or dehiscence, or ureter/bladder injury with fistula formation. In a clinical trial of nine uterus transplantations, one donor was diagnosed with a ureterovaginal fistula on postoperative day (POD) 16, which was treated with a pyelostomy catheter and subsequent ureteral reimplantation on POD 134 [12].

Immunosuppression of the recipient is necessary to minimize graft rejection following uterus transplantation. Levels of immunosuppression are initially high and can be shortly reduced to lower maintenance blood levels after transplantation.

Induction therapy, ie, perioperative prophylactic immunosuppression, is commonly used to prevent acute rejection in the first month after transplantation. The maintenance therapy is normally given as a combination of drugs with different pharmacokinetic mechanisms in order to minimize potential side effects.

Despite immunosuppression recipients are at risk of graft rejection. As uterus transplantation surgery is still in its infancy, the graft failure can be high. In the U.S. series, the first three of the five uterus transplants failed requiring graft hysterectomy on postoperative days 14, 12, and 6 [17]. Graft rejection is discovered by established postoperative protocol of Doppler ultrasound, visual inspection of the cervix and cervical biopsies.

Conclusion

Uterus transplantation is an experimental, complex, multi-step process that involves a uterus donor and uterus recipient. A multidisciplinary uterine transplant team ensures its safety. This chapter shared the current guidelines and protocols for the above mentioned procedure but since human uterus transplantation is in the beginning

stages, protocols for donor/recipient selection, anesthetic and intraoperative management may be revised. Ideally, development of an international society for uterine transplantation will facilitate collaboration between global teams to allow for official recommendations with regard to inclusion/exclusion criteria as well as create a registry to allow for regulation and safety monitoring.

References

1. Practice Committee of the American Society for Reproductive Medicine. American Society for Reproductive Medicine position statement on uterus transplantation: a committee opinion. Fertil Steril. 2018;110(4):605–10.
2. Brännström M, Johannesson L, Bokstrom H, Kvarnström N, Mölne J, Dahm-Kähler P, et al. Livebirth after uterus transplantation. Lancet. 2015;385(9968):607–16.
3. Testa G, McKenna GJ, Gunby RT, et al. First live birth after uterus transplantation in the United States. Am J Transplant. 2018;18(5):1270–4.
4. Ejzenberg D, Andraus W, Baratelli Carelli Mendes LR, et al. Livebirth after uterus transplantation from a deceased donor in a recipient with uterine factor infertility. Lancet. 2019;392(10165):2697–704.
5. Fontana L, Gentilin B, Fedele L, Gervasini C, Miozzo M. Genetics of Mayer-Rokitansky-Kuster-Hauser syndrome. Clin Genet. 2017;91:233–46.
6. Grimbizis GF, Camus M, Tarlatzis BC, Bontis JN, Devroey P. Clinical implications of uterine malformations and hysteroscopic treatment results. Hum Reprod Update. 2001;7(2):161.
7. Folch M, Pigem I, Konje JC. Müllerian agenesis: etiology, diagnosis, and management. Obstet Gynecol Surv. 2000;55(10):644–9.
8. Petrozza JC, Gray MR, Davis AJ, Reindollar RH. Congenital absence of the uterus and vagina is not commonly transmitted as a dominant genetic trait: outcomes of surrogate pregnancies. Fertil Steril. 1997;67(2):387.
9. Oppelt P, Renner SP, Kellermann A, Brucker S, Hauser GA, Ludwig KS, et al. Clinical aspects of Mayer-Rokitansky-Kuester-Hauser syndrome: recommendations for clinical diagnosis and staging. Hum Reprod. 2006;21:792–7.
10. Rall K, Eisenbeis S, Henninger V, Henes M, Wallwiener D, Bonin M, et al. Typical and atypical associated findings in a group of 346 patients with Mayer-Rokitansky-Kuster-Hauser Syndrome. J Pediatr Adolesc Gynecol. 2015;28:362–8.
11. Garg AX, Nevis IF, McArthur E, Sontrop JM, Koval JJ, Lam NN, et al. DONOR Network. Gestation hypertension and preeclampsia in living donors. N Engl J Med. 2015;372(2):124.
12. Brännström M, Johannesson L, Dahm-Kähler P, Enskog A, Mölne J, Kvarnstrom N, et al. First clinical uterus transplantation trial: a six month report. Fertil Steril. 2014;101(5):1228–36.
13. Bjorsum-Meyer T, Herlin M, Qvist N, Petersen M. Vertebral defect, anal atresia, cardiac defect, tracheoesophageal fistula/esophageal atresia, renal defect and limb defect association with Mayer-Rokitansky-Küster-Hauser syndrome in co-occurrence: two case reports and a review of the literature. J Med Case Rep. 2016;10:374.
14. Jones BP, Saso S, Yazbek J, Smith JR. Uterine transplantation: past, present and future. BJOG. 2016;123(9):1434–8.
15. Järvholm S, Johannesson L, Clarke A, Brännström M. Uterus transplantation trial: Psychological evaluation of recipients and partners during the post-transplantation year. Fertil Steril. 2015;104(4):1010–5.
16. Järvholm S, Johannesson L, Brännström M. Psychological aspects in pre-transplantation assessments of patients prior to entering the first uterus transplantation trial. Acta Obstet Gynecol Scand. 2015;94(10):1035–8. 16.
17. Testa G, Koon EC, Johannesson L, McKenna GJ, Anthony T, Klintmalm GB, et al. Living donor uterus transplantation: a single center's observation and lessons learned from early setbacks to technical success. Am J Transplant. 2017;17:2901–10.
18. Chmel R, Navackova M, Janousek L, Matecha J, Pator Z, Maluskova J, et al. Revaluation and lessons learned from the first 9 cases of a Czech uterus transplantation trial: four deceased donor and 5 living donor uterus transplantation. Am J Transplant. 2019;19:855–64.
19. Brucker SY, Brännström M, Taran F-A, Nadalin S, Königsrainer A, Rali K, et al. Selecting living donors for uterus transplantation lessons learned from two transplantations resulting in menstrual functionality and another attempt, aborted after organ retrieval. Arch Gynecol Obstet. 2018;297:675–84.
20. Puntambekar S, Puntambekar M, Telang M, Kulkarni P, Date S, Panse M, et al. Novel anastomotic technique for uterine transplant using utero-ovarian veins for venous drainage and internal iliac arteries for perfusion in two laparoscopically harvested uteri. J Minim Invasive Gynecol. 2019;26:628–35.
21. Tummers P, Göker M, Dahm-Kähler P, et al. Meeting report: first state-of-the-art meeting on uterus transplantation. Transplantation. 2019;103(3):455–8.
22. Ayoubi JM, Carbonnel M, Pirtea P, Kvarnstrom N, Brannstrom M, et al. Laparotomy or minimal invasive surgery in uterus transplantation: a comparison. Fertil Steril. 2019;112:11–8.

30 Anesthesia for Pancreas Transplant

Omar Ben Amer and Jason Kopenitz

Learning Points

- Pancreas alone, or in combination with kidney transplantation, can help patients achieve better glycemic control and curb the systemic effects of long-standing diabetes mellitus.
- Pancreas transplant patients should undergo extensive preoperative cardiac evaluation as coronary artery disease can often go undiagnosed in those with poorly controlled diabetes mellitus.
- Gastroparesis is a common occurrence in patients with diabetes mellitus and should prompt careful evaluation of the aspiration risk following induction of anesthesia. A rapid sequence induction/intubation should be considered in these patients to help minimize risk of aspiration.
- Endocrine drainage of the graft via the portal system is preferable as this method produces less hypoglycemia compared to systemic drainage.
- Close glucose monitoring is essential following graft reperfusion to avoid hyperglycemia-induced islet cell dysfunction

Pancreas transplantation is a treatment modality often utilized in patients with uncontrolled diabetes mellitus and disease burden severe enough to cause metabolic disturbances and frequent hospitalizations. Pancreas transplantation is often performed in combination with renal transplant in patients with co-existing end stage renal disease. As many pancreas transplant candidates have multiple medical co-morbidities, it is essential for the anesthesia provider to conduct a thorough history and physical exam prior to surgery. The determination of functional capacity in each patient is helpful in elucidating their cardiac status and may warrant further investigation through additional testing. The presence of diabetic neuropathy with co-existing gastroparesis should be managed with rapid sequence intubation as the risk of aspiration is significant. Careful intraoperative glucose monitoring is essential in maintaining adequacy of graft function and contributes greatly to successful post-operative outcomes. Pancreas transplant outcomes have steadily improved and are attributable to improved surgical technique and immunosuppressants along with improved anesthetic management.

Introduction

Diabetes mellitus is one of the most common medical problems with widespread implications on the global population. Its physiologic impacts are rooted in major metabolic disturbances that

O. Ben Amer (✉) · J. Kopenitz
Department of Anesthesiology, Thomas Jefferson University Hospital, Philadelphia, PA, USA
e-mail: Omar.ben-amer@jefferson.edu; Jason.kopenitz@jefferson.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_30

span across multiple body systems in the afflicted patient. There currently exist various modalities of therapy that include oral hypoglycemic agents, insulin injections, insulin pumps, islet cell and pancreas transplantation. The nature of diabetes mellitus and its influence on multiple organ systems reinforce the importance of establishing a clear understanding of the pathophysiology for all clinicians, especially the anesthesia provider. The first pancreas transplant was performed on December 17th, 1966 at the University of Minnesota by William Kelly and Richard Lillehei [1]. At present, the majority of these transplants are performed as simultaneous kidney and pancreas transplants from a single deceased donor. Traditionally, pancreas transplantation was reserved for those with type I DM; however, these criteria were recently expanded to include type II DM-affected patients [2]. Listed below are the different classifications of pancreas transplantation along with selection criteria:

1. Pancreas transplant alone: primarily for type I DM with frequent and severe hypoglycemia episodes who may be unaware, have an impaired quality of life and/or poor medication compliance with insulin therapy. These patients tend to have adequate renal function and no uremic symptoms.
2. Simultaneous pancreas-kidney transplant (SPK): organs come from the same deceased donor.
3. Pancreas after kidney: deceased donor pancreas transplant is performed following kidney transplantation from living or deceased donor. Both kidney and pancreas originate from separate donors.
4. Simultaneous deceased donor pancreas and live donor kidney: has the benefit of lower rate of delayed graft function than simultaneous pancreas-kidney transplant and significantly reduced waiting time [3].

As the number of pancreas transplants increase nationally, anesthesia providers will be tasked with managing the co-morbidities of DM with much greater frequency than prior decades. In addition, the expansion of transplantation programs to include some selected type II DM patients, will make the anesthesia providers role more essential to the achievement of successful outcomes. These outcomes include the maintenance of graft survival, hemodynamic and metabolic stability in the peri-operative setting. Due to significant improvements in surgical technique, preoperative screening and postoperative management, there have been significant improvements in graft survival [4].

Pancreas transplantation is an accepted modality of treatment that can lead to better control of blood glucose levels in those patients who have otherwise failed conventional therapy. The decision to proceed to surgery should be weighed against the risk of the surgical procedure and the subsequent use of immunosuppression. The probability of success in pancreatic transplantation is best observed in those patients with end-stage renal disease undergoing simultaneous kidney transplantation or who previously received a renal transplant and are obligated to the use of immunosuppressive treatment [5].

In general, isolated pancreatic transplantation is performed in young patients with type I diabetes who have failed to reach glycemic control, despite strict adherence to optimized medical treatment. In addition, these patients must have preserved kidney function. Simultaneous kidney-pancreas transplantation is more common and limited to diabetic patients who have developed nephropathy and renal insufficiency. The absolute contraindications to pancreas transplant include insufficient cardiovascular reserve, active infection, and malignancy. A diagnosis of HIV can be exclusionary but largely depends on each transplant center's individual policy. The relative contraindications include morbid obesity, significant cardiovascular disease, advanced age, limited life expectancy, or poor psychosocial status [5, 6].

Pre-anesthetic Evaluation

Patients that are under evaluation for pancreas alone or in combination with kidney transplantation are frequently burdened by the systemic effects of diabetes. As such, it is imperative for the anesthesia provider to carefully consider the

impact of diabetes on each organ system in order to construct a safe and effective anesthetic plan. When evaluating the transplant patient, careful attention should be paid to the patient's age and body mass index. In those patients with advanced age, the chronicity and severity of medical comorbidities can make organ transplantation particularly challenging.

Age and Body Mass Index

There exists a reluctance across many transplant centers to accept patients who are more than 50 years old. According to the International Registry of Pancreas Transplant, 2% of pancreas transplants are performed in patients more than 60 years of age [7]. As the data suggests, patients with advanced age can present clear challenges in maintaining hemodynamic and metabolic stability in the perioperative setting. While evidence for the optimal BMI for transplant is lacking, the impact of recipient BMI on morbidity and mortality is clear. Bedat and colleagues demonstrated through analysis of UNOS registry data that patients with overweight (25 kg/m^2 < BMI < 29.9 kg/m^2) and obese (BMI ≥ 30.0 kg/m^2) BMI classifications were associated with moderate increases in early mortality and early pancreas graft loss. In addition, patients classified as obese showed poorer long-term graft survival. The outcomes in patients with a BMI considered underweight (BMI < 18 kg/m^2) were also associated with poorer long-term patient survival [8]. The mechanisms underlying these findings are not completely understood; however, current evidence supports a pre-transplantation BMI of less than 28 kg/m^2 and prevention of post-transplant weight gain as the best ways to improve postoperative glycemic control outcomes [9, 10].

Cardiac Evaluation

To address the importance of medical comorbidities, Pilmore et al. studied all-cause mortality in all patients undergoing renal transplant in Australia and New Zealand between 1980–2007. Cardiovascular events were the most common cause of death at all time points following renal transplantation. Advanced age, prior cardiovascular conditions, and diabetes mellitus were strongly associated with post-transplant cardiovascular events [11]. These observations underscore the importance in conducting a thorough cardiovascular screening assessment for patients set to undergo transplantation.

It is recommended that clinicians utilize the 2014 American College of Cardiology/American Heart association (ACC/AHA) guidelines when assessing cardiac risk factors prior to non-cardiac. As microcirculatory dysfunction may present as cardiovascular disease in the transplant patient, special attention should be paid to the functional status of the recipient and to the presence of nephropathy [5, 7]. The determination of a patient's functional capacity can provide significant insight into their baseline cardiovascular health. A reduced ability to achieve at least four METS is considered a positive prognostication of perioperative or long term cardiac events. Four METS is equivalent to walking up one flight of steps, walking up a hill, or maintaining a pace of 3–4 mph on flat ground. Those patients who are able to complete at least four METS have a more favorable cardiac risk profile. In addition, the following risk factors are predictive of increased likelihood of perioperative cardiac events: history of ischemic cardiac disease, heart failure, cerebrovascular disease, insulin-dependent diabetes mellitus, preoperative serum creatinine >1.5 (NSQIP calculator), increased age or ASA status [12]. It is reasonable to obtain a preoperative resting electrocardiogram in nearly all patients prior to surgery given the universal presence of underlying cardiac risk factors (diabetes, renal dysfunction) in this patient population. The prevalence of significant coronary artery disease in patients with uremic diabetes is estimated to be approximately 40–60% [1, 7]. Silent angina is common in poorly controlled diabetic patients and a high index of suspicion is necessary in order to identify hidden coronary artery disease [6, 13]. The need for additional cardiac testing which can include: echocardiography, exercise or pharmacologic stress testing ± imaging, 24-h ambulatory imaging, and coronary angiography

should be carefully considered in those patients with known cardiac disease or risk factors [11]. These additional tests should be considered along with the need for evaluation by a cardiologist depending on the patient risk profile and functional capacity.

Neurological Evaluation

The neurologic pre-operative evaluation is primarily imaging-based and focused on the vasculature in the head and neck. CT scans or carotid ultrasound can identify evidence of carotid stenosis or presence of plaques. These imaging studies should supplement a pertinent history from the patient with special focus on history of TIA, frequent lightheadedness, or amaurosis fugax. Any positive findings from the history should prompt a bilateral carotid duplex study to quantify the stenosis in the carotid vasculature.

The widespread presence of diabetic neuropathy is an important consideration during the pre-operative evaluation. Diabetic neuropathy can present unintended consequences in the perioperative period – the most severe of which can include sudden cardiac death. Diabetic cardiovascular autonomic neuropathy (DCAN) is a result of prolonged periods of hyperglycemia that can interfere with neuronal signaling and cause permanent damage [14]. Some studies have reported autonomic dysfunction in as many as 90% of potential pancreas transplant recipients [14]. This fact can make the evaluation and treatment of post-operative myocardial infarction a unique challenge as these patients often do not exhibit the classical anginal symptoms given their underlying neuropathy [14]. In patients with autonomic dysfunction, it is important to monitor and correct for intraoperative hypotension to prevent myocardial ischemia/infarction and sudden cardiac death [15]. To ascertain the likelihood of systemic autonomic dysfunction, the anesthesia provider should evaluate for symptoms of orthostatic hypotension, dizziness associated with postural changes and palpitations. A resting electrocardiogram with sinus tachycardia may be indicative of autonomic dysfunction in the right clinical context [15].

Patients with long-standing diabetes mellitus often suffer from gastroparesis as a result of dysfunction of the vagus nerve. A careful history of symptoms of gastroparesis can include history of nausea/vomiting, bloating, or diarrhea. Patients with these symptoms are at increased risk of aspiration on induction of general anesthesia. Treatment with an H_2 blocker or bicitra prior to induction may be prudent to avoid aspiration in this population [15]. It is postulated that chronic hyperglycemia can impair collagen crosslinking via non-enzymatic glycosylation [16]. This can significantly limit the mobility of the cervical spine or temporomandibular joint in patients with long-standing diabetes; thus making laryngoscopy particularly challenging [16]. This was demonstrated by Werner et al. who found that 2% of all patients who underwent renal and/or pancreas transplants between 1985 and 1995 were classified as difficult laryngoscopies [16]. In diabetic patients with particularly stiff tissues and limited range of motion of the cervical spine, it is advisable to consider video laryngoscopy as a useful modality to help manage potentially difficult intubations.

Neurogenic bladder dysfunction is an important consideration especially in those patients who receive a bladder drained pancreas or SPK. In patients with motor or sensory dysfunction, trouble with bladder emptying can result in urine reflux and high postvoid residuals. High post-void residuals can portend poor allograft function and lead to urinary tract infection or graft pancreatitis [5, 17, 18].

Assessment of Peripheral Vascular Disease

The presence of peripheral artery disease should be a featured component of the preoperative evaluation. The anesthesia provider should seek to identify any chronic, non-healing ulcer or gangrenous tissue that might be a source of infection. Many of these infections are often localized to the bilateral lower extremities, and thus it is reasonable to assess the adequacy of the iliac vessels prior to transplantation. This can be accomplished by obtaining a non-contrast CT scan in

order to detect iliac artery calcification and help in operative planning [5, 7].

Assessment of insulin requirements, C-peptide and autoimmunity:

Daily insulin requirements and serum fasting C-peptide levels should be evaluated to categorize DM-type (I or II), as well as to assess the degree of insulin resistance. This evaluation can help identify patients who will benefit most from transplantation. For example, patients with high insulin requirements (>1.0 U/kg/day) and high fasting C-peptide values (>4.0 ng/mL) likely have significant insulin resistance and may not become insulin independent following a pancreas transplant [7, 19]. Transplant candidates must meet the following criteria as set out by The UNOS Pancreas Allocation System to be eligible for transplantation: current insulin use and C-peptide 2 ng/mL or less (presumably T1DM) or insulin use, C-peptide greater than 2 ng/mL, and BMI less than 28–30 kg/m^2 (presumably T2DM) [2, 7, 19, 20].

Assessment of Problematic Hypoglycemia

Many patients with longstanding diabetes have a history of recurrent and severe hypoglycemic episodes. The severity of these episodes is a function of the chronicity of illness. As an example, the release of glucagon and epinephrine in response to hypoglycemia gradually diminishes over the course of illness. These diminished responses result in defective glucose counter regulation, decreased hypoglycemic awareness, glycemic lability and severe hypoglycemic episodes. The consequences of such severe hypoglycemic episodes can increase the urgency for pancreas transplant [7, 17, 19].

Kidney Function

The evaluation of renal function is an essential component of the preoperative assessment and will ultimately guide the appropriate surgical technique. For simultaneous pancreas-kidney transplant candidates, estimated glomerular filtration rate [eGFR] must be ≤20 mL/min or candidates must be dialysis-dependent. For pancreas after kidney (PAK) or pancreas alone (PTA), the adequacy of renal function must be assessed as some patients evaluated for PTA may have marginal kidney function that would make PTA inappropriate. These patients, however, may not have advanced renal dysfunction that would necessitate SPK transplant [2, 20]. In this circumstance, the PTA candidate can undergo a challenge dose tacrolimus therapy to help predict its effect on postoperative native kidney function. If the native kidney function appears insufficient following the tacrolimus therapy, the pancreas transplant should be postponed until there is a further deterioration in the renal function (eGFR ≤ 20 mL/min). At this point, the patient would then be eligible for a SPK transplant [7]. The precise eGFR threshold for eligibility for PTA has not been determined, but many experts recommend PTA candidates have eGFRs of greater than 70–80 mL/min. The presence of macroalbuminuria, but not microalbuminuria, would be exclusionary. The overall goal in this evaluation is to avoid PTA transplant in those patients with poor kidney function secondary to diabetes nephropathy.

Assessment for Retinopathy

Diabetic retinopathy is a common pathology in patients with advanced disease and poor glycemic control. While blindness is not an absolute contraindication for transplantation, the patient should have proper social support to help with travel, immunosuppression medications, and annual eye examinations. This assessment should be carried out pre and post transplantation [7, 19].

Surgical Management

The pancreas transplant consists of heterotopic transplantation with surgical exposure achieved through a laparotomy incision. The location of incision is typically based on surgeon preference. The achievement of good graft function (as in SPK) is reliant on effective perfusion and mini-

mizing the ischemia time of the graft. In the past, the most technically feasible site of exocrine duct drainage and anastomosis was the urinary bladder [5, 21]. However, this technique can lead to significant metabolic abnormalities in the form of chronic metabolic acidosis from loss of bicarbonate rich secretions. As a result of these complications, surgeons will typically perform an enteric exocrine drainage. When bladder drainage is utilized, anatomic limitations can periodically present challenges by reducing the number of available sites for vascular anastomosis. In cases were pancreatic venous drainage occurs in systemic vessels, significant post-operative hypoglycemia can occur due to elevated levels of insulin. Exocrine drainage done through the enteric system promotes pancreatic venous drainage through the portal venous system which often produces systemic insulin levels that closely mirror the nondiabetic population [17].

The close monitoring of blood glucose in the perioperative period is of critical importance as poor glycemic control can impact graft viability. Poor postoperative glycemic control may be an early sign of graft dysfunction, pancreatitis, acute rejection, insufficient graft size, poor perfusion/venous drainage of the graft. These complications should be communicated with the surgeon promptly [22].

Anesthetic Management

Patients undergoing pancreas transplant alone or with renal transplantation are placed under general anesthesia given the long duration of surgery. The induction of general anesthesia is customarily initiated with the administration of an anesthetic agent such as propofol or etomidate. Traditionally, etomidate produces less hypotension on induction and would be an appropriate agent to use in patients with significant history of coronary artery disease [15]. The clinician should be aware of the adrenal suppressing effects of etomidate that arise within the first 24 h following bolus dosing. In addition, it is common practice to co-administer lidocaine and an opioid with hypnotic agents to help blunt the upper airway reflexes and diminish the stimulating nature of intubation. In patients with end stage renal disease or renal dysfunction, cisatracurium may be considered as a reasonable option in order to avoid agents that are renally excreted [5]. In those with preserved renal function, rocuronium may be beneficial on induction and maintenance, especially if reversal agents like sugammadex are available.

As previously discussed, many long-standing diabetics have a co-existing history of gastroparesis which can present increased risk of aspiration in this patient population. Pre-induction treatment with an antacid along with rapid sequence intubation can provide benefit of securing the airway while decreasing the likelihood of aspiration [5]. Succinylcholine may be the preferred agent for RSI even in patients with ESRD. Care should be taken as succinylcholine will produce transient increase in potassium levels that can precipitate fatal cardiac arrythmias. Other agents, such as rocuronium, can be given at RSI doses (1.2 mg/kg) with fast onset but the duration may be significantly prolonged in patients with ESRD or advanced renal dysfunction [5]. Earlier discussion focused on the importance of a thorough airway examination as some diabetics with significant disease burden may have diminished range of motion in the cervical spine. Tracheal intubation with direct laryngoscopy may be difficult in these patients and would likely require more advanced airway methods such as video-laryngoscopy or fiberoptic bronchoscopy.

Maintenance of anesthesia can be achieved by using volatile anesthetic such isoflurane or desflurane with intermittent narcotic boluses for analgesia. Muscle relaxation should be maintained to facilitate surgical exposure with twitch monitoring utilized to assess depth of muscle relaxation. A single twitch on train of four monitoring is recommended to ensure adequate muscle relaxation. While nearly all of the available non-depolarizing muscle relaxant are safe to use, careful consideration should be given to those patients with significant renal disease. In this case, the use of cis-atracurium may be reasonable due to its organ-independent metabolism.

In addition to the standard ASA monitoring, central venous and radial artery catheters should be placed to aid in hemodynamic and intravascular volume monitoring. Also, central venous catheters provide good access for any vasoactive medications that may need to be used during the surgery. In addition, radial artery catheters provide a source for frequent blood sampling. Pulmonary artery catheter placement and a transesophageal echocardiogram are rarely used in pancreas transplantation but may be indicated for patient-specific co-morbidities. Intra-operative blood pressure and heart rate should be maintained within the patient's preoperative baseline readings. It is reasonable to maintain elevated blood pressure values above the patient's baseline readings prior to reperfusion of the new graft. This can help counteract the hypotension and bradycardia that can sometimes occur with graft reperfusion. This can be achieved by the administration of bolus doses of intravenous fluid and vasoactive medication.

Following graft reperfusion, pancreatic beta cells begin secreting insulin in as little as 5 min. Therefore, close monitoring of blood glucose is vital. Blood glucose monitoring should occur every 15 min following graft reperfusion for the first hour followed by every 30 min for the duration of the surgery. The goal of strict glucose control is to prevent hyperglycemia-induced islet cell dysfunction until the metabolic derangements from reperfusion have subsided [22, 23].

Neuromuscular blockade reversal with assessment for extubation is appropriate once surgical skin closure has occurred. It is appropriate to obtain immediate postoperative labs at the conclusion of the surgery in the recovery area which should include an electrolyte panel. In addition, a chest-X-ray should be performed to confirm proper line placement. Postoperative pain management is typically achieved through patient controlled analgesia with either morphine or hydromorphone. In patients with renal failure, the use of hydromorphone is encouraged, as morphine use is associated with accumulation of its principal metabolites: morphine-6-glucuronide and morphine-3-glucuronide. Accumulation of these metabolites can lead to respiratory depression and obtundation (M6G). While the accumulation of morphine-3-glucuronide has a theoretical risk of inducing seizures. An epidural block, while potentially effective, is not usually performed since anticoagulation may be used after the surgery to maintain blood flow through the anastomosis by decreasing the risk of vascular thrombosis [24]. In circumstances of inadequate analgesia, facial plane blocks (transverse abdominis, rectus sheath) can be performed under ultrasound guidance with the added advantage of use in coagulopathic patients. In addition, these blocks can be repeated with exacerbation of pain or the use of indwelling catheters can be utilized to deliver continuous local anesthetics. The use of facial plane blocks has been described for various abdominal surgeries; however, evidence of these blocks specifically in pancreas transplantation is lacking.

Early Complications

Early graft loss is considered an early complication that is most frequently related to graft thrombosis, which complicates 4–8% of pancreas transplants [24]. The causes for graft thrombosis include technical fault, poor graft perfusion, pancreatitis, atherosclerosis and torsion of the vascular pedicle. Graft thrombosis is often suspected with excessive elevation of blood glucose and amylase. The treatment for graft thrombosis is urgent pancreatectomy. Graft pancreatitis is a rare and often difficult complication to diagnose with the added challenge of distinguishing it from acute rejection [5, 24, 25].

Pancreatic Anastomotic Leak

Pancreatic anastomotic leak is a rare but serious complication with it often manifesting clinically as peritonitis which can include fever and leukocytosis. The diagnosis of a pancreatic anastomotic leak is confirmed by computed tomography with oral contrast for enteric drained grafts. Debridement or surgical repair can sometimes serve as adequate treatment for these types of

leaks. If the leak is at the level of duodenal anastomosis, pancreatectomy is often the safest option as the anastomosis is likely contaminated with the pancreatic enzymes and is unlikely to heal [25, 26].

Graft Rejection and Infection

Pancreas transplants are prone to graft rejection with an incidence of 15–21% at 1 year and 27–30% at 5 years [25, 27]. Pancreatic rejection is difficult to diagnose and is often made on the grounds of clinical suspicion. Graft tenderness and fever are two indications that graft rejection may be occurring. In addition, it is useful to utilize serum markers such as glucose, amylase, lipase and C-peptide to further elicit the diagnosis. If a graft rejection is suspected, the patient should undergo a Doppler ultrasound study to rule out vascular thrombosis or other vascular pathologies. The doppler ultrasound can be followed by computed tomography and graft biopsy if the diagnosis is still in question [28]. Pancreas transplant recipients are at risk of posttransplant viral, bacterial and fungal infection given their immunosuppressed state. The clinician should have low suspicion for working up infectious etiologies in the transplant population.

Outcomes

At present, the half-life for SPK pancreatic graft has steadily increased each year [29]. This is likely the result of many factors including: improved surgical techniques, dedication of more specialized anesthesia provider to perform these cases, improvement of immunosuppression protocols, donor and recipient selection, graft surveillance, and greater reliance on graft biopsy [7]. The rates of patient survival are approximately 97% at 1 year and 92% at 3 years after SPK transplantation with similar patient survival rates reported for PAK and PTA recipients. Graft survival rates are variable and depend largely on the type of pancreas transplant performed [30].

Funding and Conflicts of Interest None

References

1. Eller K, Kniepeiss D, Rosenkranz AR. Preoperative risk evaluation: where is the limit for recipients of a pancreatic graft? Curr Opin Organ Transplant. 2013;18(1):97–101. https://doi.org/10.1097/MOT.0b013e32835c9666.
2. Weems P, Cooper M. Pancreas transplantation in type II diabetes mellitus. World J Transplant. 2014;4(4):216–21. https://doi.org/10.5500/wjt.v4.i4.216.
3. Dholakia S, Oskrochi Y, Easton G, Papalois V. Advances in pancreas transplantation. J R Soc Med. 2016;109(4):141–6. https://doi.org/10.1177/0141076816636369.
4. St Michel D, Donnelly T, Jackson T, Taylor B, Barth RN, Bromberg JS, Scalea JR. Assessing pancreas transplant candidate cardiac disease: preoperative protocol development at a rapidly growing transplant program. Method Protoc. 2019;2(4):82. https://doi.org/10.3390/mps2040082.
5. Mittel AM, Wagener G. Anesthesia for kidney and pancreas transplantation. Anesthesiol Clin. 2017;35(3):439–52. https://doi.org/10.1016/j.anclin.2017.04.005.
6. Hariharan S, Pirsch JD, Lu C, Chan L, Pesavento TE, Alexander S, Bumgadner GL, Basadonna G, Hricik DE, Pescovitz M, Rubin N, Stratta R. Pancreas after kidney transplantation. J Am Soc Nephrol. 2002;13:1109–18.
7. Redfield RR, Rickels MR, Naji A, Odorico JS. Pancreas transplantation in the modern era. Gastroenterol Clin N Am. 2016;45(1):145–66. https://doi.org/10.1016/j.gtc.2015.10.008.
8. Bédat B, Niclauss N, Jannot AS, Andres A, Toso C, Morel P, Berney T. Impact of recipient body mass index on short-term and long-term survival of pancreatic grafts. Transplantation. 2015;99(1):94–9. https://doi.org/10.1097/TP.0000000000000226.
9. Young BY, Gill J, Huang E, et al. Living donor kidney versus simultaneous pancreas-kidney transplant in type I diabetics: an analysis of the OPTN/UNOS database. Clin J Am Soc Nephrol. 2009;4(4):845–52. https://doi.org/10.2215/CJN.02250508.
10. Neidlinger N, Singh N, Klein C, Odorico J, Munoz del Rio A, Becker Y, Sollinger H, Pirsch J. Incidence of and risk factors for posttransplant diabetes mellitus after pancreas transplantation. Am J Transplant. 2010;10:398–406. https://doi.org/10.1111/j.1600-6143.2009.02935.x.
11. Pilmore H, Dent H, Chang S, McDonald SP, Chadban SJ. Reduction in cardiovascular death after kidney transplantation. Transplantation. 2010;89(7):851–7.
12. Fleisher LA, Fleischmann KE, Auerbach AD, Barnason SA, Beckman JA, Bozkurt B, et al. 2014

ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;64(22):e77–e137.
13. Knight J, et al. Diabetes management 2: long-term complications due to poor control. Nursing Times [online]. 2017;113(4):45–8.
14. Karayannis G, Giamouzis G, Cokkinos DV, Skoularigis J, Triposkiadis F. Diabetic cardiovascular autonomic neuropathy: clinical implications. Expert Rev Cardiovasc Ther. 2012;10(6):747–65.
15. Beebe D, Cingi E, Harmon JV Jr, Belani K. Anesthetic management of patients undergoing pancreas transplantation. In: Subramaniam K, Sakai T, editors. Anesthesia and perioperative care for organ transplantation. New York, NY: Springer; 2016. p. 309–16.
16. Warner M, Contreras M, Warner M, Schroeder D, Munn S, Maxson P. Diabetes mellitus and difficult laryngoscopy in renal and pancreatic transplant patients. Anesth Analg. 1998;86(3):516–9.
17. Larsen LJ. Pancreas transplantation: indications and consequences. Endocr Rev. 2004;25(6):919–46. https://doi.org/10.1210/er.2002-0036.
18. Halpern H, Miyoshi E, Kataoka LM, Khouri Fo RA, Miranda SB, Marumo CK, et al. Anesthesia for pancreas transplantation alone or simultaneous with kidney. Transplant Proc. 2004;36:3105.
19. Stratta RJ, Farney AC, Orlando G, et al. Pancreas transplantation for type 2 diabetes mellitus: who and why? Curr Transpl Rep. 2015;2:149–58. https://doi.org/10.1007/s40472-015-0055-8.
20. Choudhary P, Rickels MR, Senior PA, et al. Evidence-informed clinical practice recommendations for treatment of type 1 diabetes complicated by problematic hypoglycemia. Diabetes Care. 2015;38(6):1016–29. https://doi.org/10.2337/dc15-0090.
21. Gruessner AC. 2011 update on pancreas transplantation: comprehensive trend analysis of 25,000 cases followed up over the course of twenty-four years at the International Pancreas Transplant Registry (IPTR). Rev Diabet Stud. 2011;8(1):6–16. https://doi.org/10.1900/RDS.2011.8.6.
22. Pichel AC, Macnab WR. Anaesthesia for pancreas transplantation. Cont Educ Anaesth Crit Care Pain. 2005;5(5):149–52. https://doi.org/10.1093/bjaceaccp/mki040.
23. Aniskevich S. Anesthesia for pancreas transplantation. Pancreatic Dis Ther. 2013;3:2. https://doi.org/10.4172/2165-7092.1000122.
24. Farney AC, Rogers J, Stratta RJ. Pancreas graft thrombosis: causes, prevention, diagnosis, and intervention. Curr Opin Organ Transplant. 2012;17(1):87–92. https://doi.org/10.1097/MOT.0b013e32834ee717.
25. Samoylova ML, Borle D, Ravindra KV. Pancreas transplantation: indications, techniques, and outcomes. Surg Clin N Am. 2019;99(1):87–101.
26. Nath DS, Gruessner A, Kandaswamy R, Gruessner RW, Sutherland DE, Humar A. Late anastomotic leaks in pancreas transplant recipients—clinical characteristics and predisposing factors. Clin Transpl. 2005;19:220–4. https://doi.org/10.1111/j.1399-0012.2005.00322.x.
27. Dong M, Parsaik AK, Kremers W, Sun A, Dean P, Prieto M, Cosio FG, Gandhi MJ, Zhang L, Smyrk TC, Stegall MD, Kudva YC. Acute pancreas allograft rejection is associated with increased risk of graft failure in pancreas transplantation. Am J Transplant. 2013;13:1019–25. https://doi.org/10.1111/ajt.12167.
28. Redfield RR, Kaufman DB, Odorico JS. Diagnosis and treatment of pancreas rejection. Curr Transpl Rep. 2015;2:169–75. https://doi.org/10.1007/s40472-015-0061-x.
29. Israni AK, Skeans MA, Gustafson SK, Schnitzler MA, Wainright JL, Carrico RJ, et al. OPTN/SRTR 2012 annual data report: pancreas. Am J Transplant. 2014;14(Suppl 1):45–68.
30. Gruessner RW, Sutherland DE, Gruessner AC. Mortality assessment for pancreas transplants. Am J Transplant. 2004;4(12):2018–26.

31 Anesthetic Management during Surgery for Left Ventricular Aneurysm

William Marion

Learning Points

- Left ventricular aneurysms usually occur as a complication of an acute MI but may also be congenital or the result of other acquired conditions.
- General endotracheal anesthesia with invasive monitoring and transesophageal echocardiography should be employed in all cases
- Rupture of the aneurysm can rapidly lead to catastrophic cardiogenic shock
- Ventricular aneurysms are anatomically different from pseudoaneurysm
- Rapid institution of cardiopulmonary bypass with administration of pressor therapy and massive resuscitation with blood products may become necessary

Introduction

Left ventricular aneurysms (LVA) were first reported in the early 1950s and are defined as thinned areas of the ventricle that contain necrotic or fibrotic tissue but no muscle resulting in an area that bulges paradoxically during systole (dyskinesis). They can be classified as either congenital or acquired with acquired causes being conditions such as MI, myocarditis, hypertrophic cardiomyopathy, sarcoidosis and Chagas Disease. Most commonly, they occur in the anterior wall as a result of an acute infarct that heals without rupture [1]. Although rare, the exact risk of post MI aneurysm is not clear with sources noting a prevalence as low as 0.76% and a wide occurrence range of 3–35% but more recent data have narrowed that range to 8–15% [2, 3].

Some sources may define the aneurysmal section as an area that has "healed" after an MI but this can be misleading. Although the infarct may be resolved and perfusion stabilized, there is still a risk of life-threatening complications. These can include serious arrhythmias, heart failure due to loss of contractile mass, further ischemia, thromboemboli resulting in stroke and rupture of the aneurysmal sack. It is important to note that while an LV aneurysm may rupture, a pseudoaneurysm occurs when the ventricular wall ruptures after an infarction but a tamponade does not occur due to adhesions within the pericardium isolating the ruptured area. Additionally, there is no formation of a thinned and fibrotic wall as the rupture happens acutely during the evolution of the infarction.

Traditionally, LVA were treated with medications such as ACE inhibitors, beta blockers or certain potassium sparing diuretics that antagonize aldosterone receptors. As treatment progressed, PCI was added to that regimen. These

W. Marion (✉)
Division of Cardiothoracic Anesthesia, Department of Anesthesia, Cooper University Healthcare System, Rowan University School of Medicine, Camden, NJ, USA
e-mail: Marion-william@cooperhealth.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_31

modalities were demonstrated to improve survival but patients were still at significant risk for the previously listed complications. However, surgical anterior ventricular restoration (SAVER) with coronary artery bypass grafting (CABG) has demonstrated superior survival, symptom relief and improvement in functional status [4].

Preanesthetic Evaluation

Patients requiring SAVER and CABG may present in varying degrees of distress or may be asymptomatic but it is important to rule out an acute event at the time of presentation. Symptoms may include fatigue, weakness, dyspnea on exertion, orthopnea, dependent edema, ascites and palpitations, all of which, can also occur in the setting of an acute MI. As it takes time for the aneurysmal sack to form, presence of these symptoms may confound the preanesthetic evaluation. In addition to ruling out a new acute event, presence of these symptoms may indicate that a patient is not yet optimized for surgery.

Evaluation of the patient presenting in the preoperative clinic should begin with a thorough history and review of systems followed by a physical exam. The review of systems should focus on the above symptoms to differentiate between noncardiac causes and acute cardiac events. Next, the physical exam should be focused on cardiac and pulmonary symptoms to ensure the patient is in optimal condition but also include important basics such as a detailed airway examination. For example, the presence of JVD or dependent edema may represent inadequate diuresis. Irregular heart tones may indicate poor control of arrhythmias and wheezing may be a sign of inadequate control of asthma or COPD. Patients who are not optimized for cardiac surgery predictably have poorer outcomes and higher rates of complications including cardiac arrest, stroke, renal failure and prolonged intubation.

The next focus should be on pertinent testing. This will again help to rule out acute events and determine optimization. First line testing should include a review of laboratory values to evaluate hemoglobin levels and end organ function. For example, poor blood sugar control as evidenced by high fasting values or an elevated A1C represent a nonoptimized patient who is at risk for poor wound healing and infection while anemia may necessitate early transfusion prior to cardiopulmonary bypass. However, this is not specific to SAVER or CABG but is important prior to anesthetic management of any cardiac procedure.

Testing specifically targeted to the management of patients undergoing the combined SAVER/CABG procedure begins with an electrocardiogram. Patients with LVA may have an ECG that demonstrates precordial ST elevation remote from an AMI, persistent Q waves and T waves with abnormally low amplitude when compared to the QRS complex [5]. This is in contrast to the ECG of an acute MI which may have new ST elevations, acute T waves, an evolving left bundle-branch block or even be completely benign [6]. Next, a recent, post MI echocardiogram is necessary to assess overall structure, ventricular function and left ventricular end diastolic volume which is a primary determinant of a successful SAVER procedure. Additionally, a cardiac catheterization can yield similar information but is necessary to plan the targeted sites of the CABG component. Some institutions may also perform a cardiac MRI to determine the extent of fibrosis, amount of viable tissue and prognosis or CT angiography to confirm the diagnosis [7]. Information from the cardiac MRI, while not necessary, helps the anesthesia provider predict the likelihood of malignant arrythmias requiring defibrillation on induction or prior to the initiation of cardiopulmonary bypass [8].

Anesthetic Management

The anesthetic management of a patient undergoing SAVER/CABG is not unlike the management of patients undergoing other open cardiac procedures requiring bloodless fields. Hemodynamic goals should focus on maintaining a high-normal but not tachycardic heart rate to avoid exacerbating ischemia while decreasing filling time and, in turn, Left Ventricular End Diastolic Pressure.

Additionally, attention should be paid to maintaining a normal blood pressure while avoiding fluid overload. This is because spikes in afterload can lead to rupture of the aneurysmal sack which is generally catastrophic for the patient. Because of this, many centers will opt for placement of an intra-aortic balloon pump both for afterload reduction and to supplement the compromised coronary perfusion.

Monitors and Access

While standard ASA monitors are required, they are not adequate to guide therapy or monitor patient status during the case. Prior to induction, an arterial line should be placed in either the radial, brachial or femoral artery depending on patient anatomy and status. However, it may be safe to wait until after induction if a balloon pump is already in place with an accurate arterial tracing and pressure. Cerebral oximetry is also required to ensure adequate cerebral perfusion during induction, cardiopulmonary bypass and any periods of resuscitation. This is also important as patients with LVA often have vascular anomalies that can lead to embolic stroke.

Next, a central venous catheter is required but may be placed either prior to or after induction depending on center protocols and patient condition. Not only does this allow rapid resuscitation with both fluids and medications if necessary but also provides a conduit through which a pulmonary artery catheter (PAC) can be placed. Although it provides valuable data regarding fluid status, cardiac output and pulmonary artery pressure, the placement of a PAC can be somewhat controversial. This is due to the fact that placement comes with an inherent risk of arrythmia while LVA patients are already at a significantly increased risk of malignant arrythmia and most information can be extrapolated from the data gathered during transesophageal echocardiography (TEE) which carries a much greater safety index. However, a PAC has the advantages of direct measurements and constant monitoring over the intermittent nature of performing TEE. Of course, even with a PAC in place, TEE is still necessary to monitor ventricular function and size as well as ruling out any other structural or functional abnormalities and determining operative success.

Induction

Induction should be tailored to both individual patient needs and the stated hemodynamic goals. Most patients benefit from the anxiolytic and amnestic affect of premedication with midazolam which can help avoid tachycardia and hypertension in the immediate preoperative period. However, this should be avoided in patients at significant risk for cognitive decline, delirium or disinhibition. Additionally, treatment with lidocaine and fentanyl several minutes prior to laryngoscopy can help to mitigate the associated catecholamine release.

Perhaps most important is the choice of the primary sedative based on its hemodynamic profile rather than whether it is hypnotic or dissociative. For instance, although propofol may have favorable effects on afterload in the face of an LVA it may further exacerbate already compromised areas of myocardial perfusion making it less than ideal. Both ketamine and etomidate can provide stable induction without exacerbation of ischemia but etomidate may be more helpful in maintaining heart rate targets. However, the choice is largely based on anesthesia provider preference [9].

As with any open cardiac procedure, muscle relaxant is a necessary component of both induction and maintenance. Patients with GERD, gastroparesis or who don't have the appropriate NPO status should undergo rapid sequence induction with succinylcholine or high-dose rocuronium in the absence of any contraindications. However, this is not inherently necessary for the procedure itself and a slow induction with rocuronium or vecuronium and manual ventilation is appropriate in most situations. It is also important to note that high dose rocuronium should be avoided for induction in patients with nonreassuring airways. For patients with renal failure, cis-atracurium is also appropriate but not always necessary. Once

adequate neuromuscular blockade is achieved, tracheal intubation is performed with an appropriately sized standard endotracheal tube.

Maintenance

Volatile Gasses

Isoflurane has several properties that make it the most common choice of volatile gas for anesthetic maintenance. First, it preserves cardiac output to a greater degree than the other volatile agents as it decreases afterload without significantly blunting baroreceptor reflexes [10]. This decrease in afterload may somewhat reduce the risk of rupture of the aneurysmal sack. While this may raise concerns about coronary steal given the patient's already compromised myocardial perfusion, many studies investigating this have been inconclusive. Additionally, the most recent studies have demonstrated no elevated ischemic risk. Next, it has a high lipid solubility which results in a lower required concentration for the necessary depth of anesthesia [11]. This translates into less of the agent being used over the duration of the procedure. Third, isoflurane reduces CMRO2 further than other agents which may confer some cerebral protection during cardiopulmonary bypass. Fourth, isoflurane undergoes less metabolic degradation than other agents, therefore the potential for generation of toxic metabolites is low enough to be clinically insignificant. Finally, ventricular function is better preserved when compared with other agents.

Sevoflurane is a slightly newer volatile anesthetic which has been gaining popularity in cardiac anesthesia. Like isoflurane, it has cardio-protective effects which may limit damage from new or transient ischemia. It also preserves systolic ventricular function although potentially to a lesser degree. This may be due to it's lower propensity for causing increases in heart rate which maintains a lower myocardial oxygen demand at the expense of maintaining cardiac output. Also, it has a lower lipid solubility which results in a larger volume of the agent being used over the course of the procedure. Given both these similarities and differences, there has been some controversy as to which is the better volatile agent for maintenance. However, Jones et al. have demonstrated both non-inferiority and non-superiority of sevoflurane making the use of either agent somewhat equivocal and up to provider preference [12].

Desflurane, although popular for many procedures, is not appropriate for maintenance of anesthesia during SAVER/CABG for several reasons. First, its very low lipid solubility results in large volumes of the gas being required for maintenance during longer procedures. Next, over these longer time periods, soda lime can become desiccated and its interaction with desflurane results in the production of unacceptable levels of carbon monoxide. Most importantly, rapid increases in concentration result in catecholamine release causing tachycardia and an increased oxygen demand in already compromised myocardium. This occurs without the myocardial protective effects of other volatile agents.

Neuromuscular Blockade

As previously stated, the SAVER procedure and LV aneurysms do not inherently require RSI but comorbidities may make it advisable. Once induction and intubation have been safely achieved, either vecuronium or rocuronium are suitable for maintenance of neuromuscular blockade [9]. In patients with renal failure, cisatracurium may be preferable to either of the previously discussed agents. However, given the duration of the procedure, the availability of train of four monitoring and the additional volume of distribution during cardiopulmonary bypass, both vecuronium and rocuronium can be safely used in renal failure patients.

Regardless of choice of agent, it is important to maintain significant neuromuscular blockade. This can usually be ensured through use of Train of Four twitch monitoring of the adductor pollicis. This is, however, not possible during SAVER/CABG as both arms will be tucked and draped by the surgical team and thus out of view of the anesthesia provider. The next most appropriate target for twitch monitoring is the facial nerve which recovers at a similar but slightly slower rate than the ulnar nerve controlling adductor

pollicis [13]. However, it is important to recognize that diaphragmatic recovery occurs before either facial or ulnar recovery [14].

This is of particular importance as return of spontaneous diaphragmatic function creates difficulty within the surgical field. Depending on the surgical target, this movement may obscure the view of the target site, decrease the available working space or even cause movement of the site itself. Because of this, concerns of limb and body wall movement are secondary as ensuring diaphragmatic blockade ensures blockade of voluntary muscles. Thus, it is ideal to maintain complete neuromuscular blockade with the absence of twitches.

Cardiopulmonary Bypass

Institution of cardiopulmonary bypass is achieved in a fairly standard manner with some subtle variations both in surgical technique and anesthetic management. The most notable surgical difference is the requirement for a bloodless field similar to what is required for valvular surgery. This is achieved through bicaval cannulation with two single-stage cannulas secured and sealed with caval snares. Additionally, a left ventricular vent is often placed to evacuate the air that is entrained due to the ventriculotomy [15]. During placement of this vent, the surgeon will ask the anesthesia provider to ensure proper placement across the mitral valve using TEE. If the vent cannula can't be visualized, color flow doppler may be used. In this mode, the vent can be identified by a discrete linear flow across the valve and parallel to beam direction. Often, once this flow is seen the walls of the cannula can be identified but this is not necessary to ensure proper placement.

When initiating bypass, the perfusionist will perform retrograde autologous priming (RAP) of the pump in order to control the degree of hemodilution that occurs during bypass. This involves allowing the patient's blood to displace the crystalloid solution in the aortic and caval cannulae. This loss of volume can cause significant hypotension if not properly anticipated and supported, usually by the prophylactic administration of an alpha agonist such as phenylephrine prior to the initiation of the RAP. However, this comes with the risk of rupture of the aneurysmal sack with excess afterload. The risk can be somewhat mitigated by decreasing the dose of the alpha agent, setting a lower target systolic pressure or tolerating some degree of hypotension for a short period so that it can treated appropriately rather than prevented. However, if the anesthesia provider chooses to allow the pressure to initially fall the electrocardiogram should be closely monitored to ensue the area around the aneurysm or any areas perfused by the stenosed vessels do become further compromised.

Once the repair is completed, air is evacuated from the left ventricle and the ventricle is filled it is necessary to ensure a successful repair via echocardiography prior to the termination of bypass. This is first accomplished by instructing the perfusionist to allow a moderate amount of LV filling and ejection without terminating bypass and obtaining all views in which the aneurysm was initially visible. Most commonly, this can be achieved through mid esophageal two-chamber and transgastric views as those views can offer the most complete picture of the anterior wall where the majority of LVA occur. In these views, the anesthesia provider inspects the repaired area for apposition of the remaining ventricular epicardium, myocardium and endocardium with gaps in apposition appearing as dark areas [16]. Additionally, any patch tissue should be inspected to ensure good contact with the epicardium. Color flow doppler should also be used to ensure lack of flow through the repair. Finally, if the pericardium is closed, the echocardiographer should pay careful attention to the pericardial space to ensure the absence of an evolving effusion and tamponade [17].

Once bypass has been terminated, hemodynamics and ventricular function need to be adequately supported. However, if the patient had poor ventricular function prior to surgery it is prudent to initiate inotropic therapy prior to the termination of bypass. This can be accomplished with a low dose infusion of epinephrine but excess afterload should be avoided in order to preserve the repair. If hypertension is a concern, milrinone may be the more appropriate choice

and hypotension should be treated with infusions of either norepinephrine or phenylephrine with a target systolic pressure under 120 mmHg.

Intraoperative and Postoperative Complications

The most common complications include rupture of the aneurysmal sack, failure of the repair and new or worsening infarcts. These complications are accompanied by the risk of emergent initiation of bypass, failure to wean from bypass and poor postoperative outcomes. Rupture of the sack is most likely to occur during periods of hypertension seen during induction and laryngoscopy. In contrast, exacerbation of ischemia or infarction are most likely to occur during periods of hypotension. This necessitates tight control of blood pressure during the procedure with a focus on induction and initiation of bypass.

Aneurysmal Rupture

Severe acute increases or lesser sustained increases in afterload represent the greatest risks for rupture. If this occurs prior to median sternotomy the patient is at risk for tamponade resulting in PEA arrest requiring rapid and large volume fluid resuscitation and immediate sternotomy and pericardotomy with rapid cannulation and initiation of bypass if the bleeding cannot be controlled. However, the normal leftward displacement of the heart makes it unlikely but not impossible for sternotomy itself to cause rupture. If rupture occurs after sternotomy and bypass cannot be rapidly initiated, the patient faces the prospect of arrest and intraoperative death secondary to exsanguination. It is also important to note that rapid initiation of bypass also carries serious risks from embolic events or pump failure secondary to thrombosis which may be fatal events.

Repair Failure

Repair failure can occur either during ventricular refilling prior to termination of bypass or during periods of ischemia or hypertension in the early postoperative period. Failures that occur during the filling and weaning period are less likely to result in serious morbidity as full bypass can be reinstituted and the repair can be revised. Additionally, failure that occurs in the postoperative period may evolve slowly with changes in ECG or evidence of tamponade indicating the need for further imaging or investigation and likely reoperation. However, catastrophic failure in that same period carries a significant risk of mortality due to the likelihood of severe tamponade refractory to standard resuscitation measures. If this occurs, it may necessitate reopening of the sternum at the bedside followed by rapid transport to the operating room for revision.

New or Evolving Ischemia

New or worsening ischemia is most likely to result from hypotension intended to preserve the repair or failure of the bypass grafts. Failure of the grafts can be from vasospasm, occlusion or failure of the anastomotic sites but these issues can be seen in any CABG and are not unique to patients undergoing SAVER. This can result in another infarct or further loss of ventricular function up to and including cardiac arrest. Additionally, compromise of the tissue involved in the repair can lead to failure of the repair and the associated complications.

Conclusion

Left ventricular aneurysm is an uncommon but not a rare complication of myocardial infarction. Anesthetic management during repair of the aneurysm is not dissimilar to the management of other open cardiac procedures but with some unique considerations. Safe induction of anesthesia can be achieved in these patients but it is advisable for the anesthesia provider to consider having boluses of medications on hand during this period to avoid dramatic swings in blood pressure. The author would advise having medications such as epinephrine, norepinephrine and nitroglycerine immediately on hand along with the induction medications. Furthermore, stricter than average control of blood pressure is necessary throughout the case and vigilant anesthetic

management contributes to a long term survivability rate of greater than 90% in patients who successfully undergo the SAVER procedure.

References

1. Paraskevaidis S, Stavropoulos G, Vassilikos V, Chatzizisis Y, Polymeropoulos K, Ziakas A, Dakos G, Parcharidis G. Idiopathic left ventricular aneurysm causing ventricular tachycardia with 1:1 ventriculoatrial conduction and intermittent wenckebach block. Open Cardiovasc Med J. 2009;3:105–9.
2. Lee CH, Lee DK, Lim SH, Kim H. Anesthetic management during surgery for left ventricular aneurysm and false aneurysm occurring in stage: a case report. Korean J Anesthesiol. 2016;69(5):518–22.
3. Yonggang S, Teng S, Qian J, Zhao Z, Zhang Q, Yongjian W. Treatment outcomes and therapeutic evaluations of patients with left ventricular aneurysm. J Int Med Res. 2019;47(1):244–51.
4. Restore Group—SAVER update meeting, Toronto 2004.
5. Smith SW. T/QRS ratio best distinguishes ventricular aneurysm from anterior myocardial infarction. Am J Emerg Med. 2005;23(3):279–87.
6. Edhouse J, Brady WJ, Morris F. ABC of clinical electrocardiography: acute myocardial infarction-Part II. BMJ. 2002;324(7343):963–6. Review.
7. https://www.ncbi.nlm.nih.gov/books/NBK555955/.
8. Shanmugam G, Imtiaz A. Surgical ventricular restoration: an operation to reverse remodeling—clinical application (part II). Curr Cardiol Rev. 2009;5(4):350–9.
9. Alwardt CM, Redford D, Larson DF. General anesthesia in cardiac surgery: a review of drugs and practices. J Extracorp Technol. 2005;37(2):227–35.
10. Rivenes SM, Lewin MB, Stayer SA, Bent ST, Schoenig HM, et al. Cardiovascular effects of sevoflurane, isoflurane, halothane, and fentanyl–midazolam in children with congenital heart disease: an echocardiographic study of myocardial contractility and hemodynamics. Anesthesiology. 2001;94:223–9.
11. Dickinson R, Franks NP, Lieb WR. Can the stereoselective effects of the anesthetic isoflurane be accounted for by lipid solubility? Biophys J. 1994;66:2019–23.
12. Jones P, Bainbridge D, Chu M, Fernandes P, Fox S, Iglesias I, Kiaii B, Lavi R, Murkin J. Comparison of isoflurane and sevoflurane in cardiac surgery: a randomized non-inferiority comparative effectiveness trial. Can J Anesth. 2016;63(10):1128–39.
13. Derrington MC, Hindocha N. Comparison of neuromuscular blockade in the diaphragm and the hand. Br J Anesth. 1988;61(3):279–85.
14. Donati F. Neuromuscular monitoring: more than meets the eye. Anesthesiology. 2012;117:934–6.
15. https://www.openanesthesia.org/technical_aspects_of_cardiopulmonary_bypass/.
16. ASE/SCA. ASE/SCA Guidelines for Performing a Comprehensive Intraoperative Multiplane Transesophageal Echocardiography Examination: Recommendations of the American Society of Echocardiography Council for Intraoperative Echocardiography and the Society of Cardiovascular Anesthesiologists Task Force for Certification in Perioperative Transesophageal Echocardiography [Position Paper]. 1999. https://www.asecho.org/wp-content/uploads/2013/05/Performing-a-Comprehensive-Multiplane-TEE-Exam.pdf.
17. Bittar MN, Barnard JB, Khasati N, Richardson S. Should the pericardium be closed in patients undergoing cardiac surgery? Interact Cardiovasc Thorac Surg. 2005;4(2):151–5.

32

Anaesthesia for Catecholamine-Secreting Glomus Jugulare Tumor Resection

Anjan Trikha and Manpreet Kaur

Introduction

Glomus jugulare are benign locally aggressive, extremely vascular tumours originating from the paraganglionic cells of jugular bulb adventitia [1]. They are also called skull base nonchromaffin paragangliomas. These tumours can secrete catecholamines and occasionally serotonin which can mimic pheochromocytoma. Perioperative catecholamine hypersecretion together with unique anatomical position poses a major challenge to the anaesthesiologists when such patients are posted for surgery.

Historical Aspects

Stacy Guild in 1941, reported "flattened, ovoid glomus structures" in temporal bone sections and proposed the name glomus jugularis [2]. In 1953, Rossenwasser proposed that the glomus jugulare tumor proper and the glomus jugulare tympanicus tumor were distinct entities [3]. Alford and Guilford supported this as tympanicum confined to the middle ear and the glomus jugulare relating to the jugular bulb and the skull base [4]. Early reports of surgical management of glomus tumors was by Winship et al. in 1948. Surgical approach is considered challenging due to close proximity to important structures [3, 5, 6]. Hence, feasibility of varied treatment modalities for its management like refinements in the surgical technique (subtotal resection), gamma knife radiosurgery, stereotactic radiosurgery has evolved.

Epidemiology

Head and neck paragangliomas (also called glomus tumors) belong to the pheochromocytoma/paraganglioma (PHEO/PGL) family. Paragangliomas account to 0.5% of all the head and neck tumors [5, 6] and only 1–3% of HNPGL are associated with catecholamines secretion [6]. According to the World Health Organization (WHO) 2004, 2017 classification, term pheochromocytoma is used for intraadrenal paraganglioma [7, 8] while paraganglioma term is used for extradrenal paragangliomas regardless of the secretory status. Based on clinical and biological behaviour, paragangliomas have origin either in parasympathetic system or sympathetic system. Twenty percent of all parasympathetic paraganglia are primarily located in the head and neck region. Nomenclature of HNPGL is based upon anatomical site of origin of the primary tumor like carotid body paraganglioma (commonest), jugulotympanic paraganglioma (middle ear), vagal paraganglioma, and laryngeal paraganglioma. Such tumours are also found in isolated locations

A. Trikha (✉) · M. Kaur
Department of Anaesthesiology, Pain Medicine and Critical Care, All India Institute of Medical Sciences (AIIMS), New Delhi, India

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_32

like the larynx, nasal cavity, nasopharynx, paranasal sinuses, orbit, thyroid gland and along the sympathetic trunk [6, 7]. HNPGL found along the branches of IX or X cranial nerves, in close relation to the temporal bone, primarily in and around the jugular foramen are called glomus jugulare tumors (GJTs) [9, 10]. "Functional paraganglioma"is a tumor that Secretes catecholamines (generally, four- to five-fold higher catecholamines than the upper normal range) and produces clinical symptoms [11]. The combined annual incidence of pheochromocytoma/paraganglioma (PPGL) is 1 in 300,000 [12]. Majority of paragangliomas are diagnosed in the third to fifth decade of life. Hereditary paragangliomas usually develop a decade earlier than the sporadic disease. Further hereditary paragangliomas have equal sexual distribution, but sporadic paragangliomas are more common in women (71% vs. 29%) [13].

Anatomical Aspects

These are the tumors of the neural crest originating at the base of the skull in jugular bulb area. These tumors grow slowly at the rate of about 1 mm/year [14], often are locally infiltrative and rarely metastatic**.** They tend to spread along the path of least resistance i.e.infralabyrinthine and infracochlear cell tracts toward the infratubal part of internal carotid artery, then along the petrous segment and finally to nasopharynx. Medial jugular wall serves as a barrier but once it is breached tumor spreads to involve facial and lower cranial nerves and later intracranially to involve vertebral arteries, the venous sinuses, and the neuraxis (Fig. 32.1). Inferiorly, it spreads to the neck via the carotid foramen and the carotid sheath. As the tumors increase in size, they occlude the venous flow shifting the brains

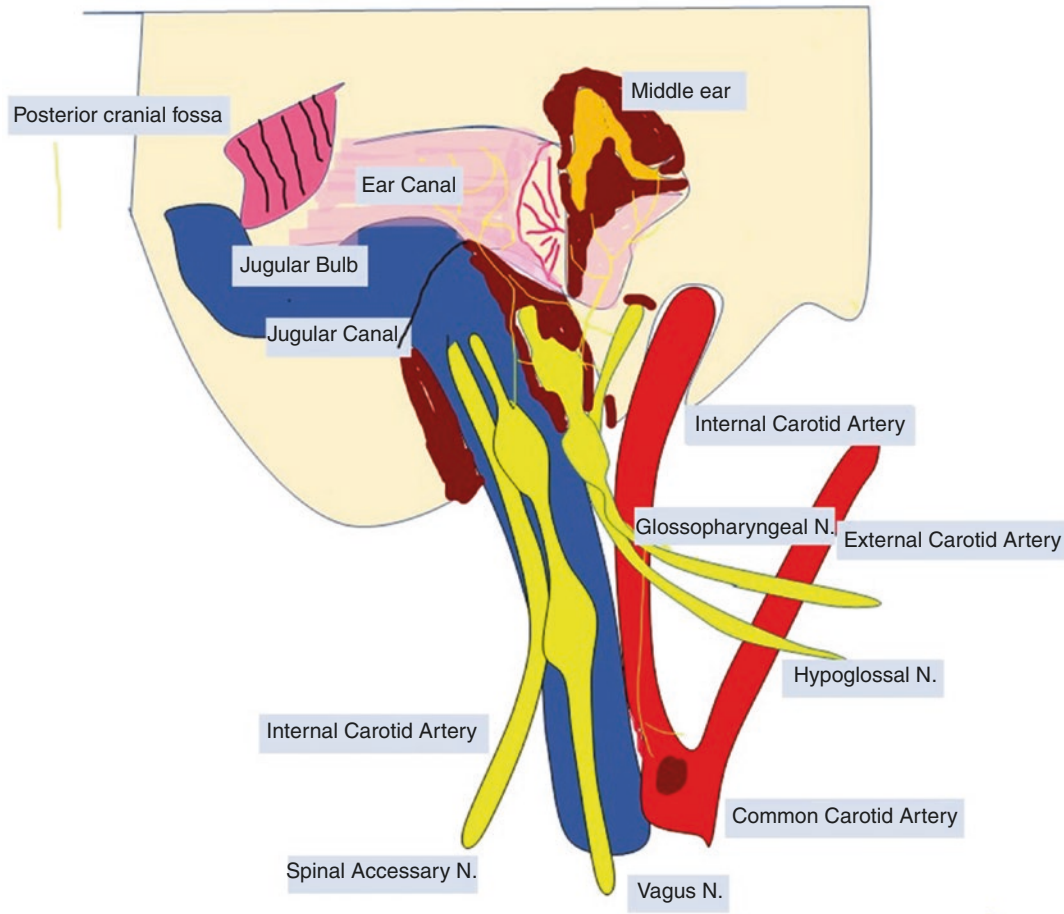


Fig. 32.1 Anatomical correlation of common structures to glomus tumor

venous blood to unaffected sigmoid sinus and jugular bulb. GJTs due to their location at the skull base can spread into the posterior and middle cranial fossae, internal and external auditory canals, middle ear, and inferiorly through the jugular foramen into the neck.

Molecular/Genetic Basis of Glomus Jugulare Tumor

Majority of HNPGL are sporadic and at least 30% of tumors have a familial predisposition [8, 15, 16]. HNPPGL has been linked to multiple susceptibility genes: *NF1*, *RET*, *VHL*, S*DHA*, *SDHB*, *SDHC*, *SDHD*, *SDHAF2* (*SDH5*), and *TMEM127*. Hereditary HNPs are most commonly attributed to *SDHD* gene (>50%), *SDHB* (20–35%) and *SDHC* (15%) mutations while rarely related to mutations of VHL, RET, or NF1 [17, 18]. Patients presenting with symptoms at an earlier age may have the mutation of the succinate dehydrogenase (SDH) enzyme predisposing them for malignant or aggressive behaviour, metastasis, and multicentricity of the tumor [19]. SDHB mutations are associated with multiple tumors of head and neck, a higher percentage of malignant transformation (30%) and <5% risk of concomitant paragangliomas [1, 18]. Patients with the familial occurrence of this tumor necessitate meticulous screening for multifocality, genetic syndromes (multiple endocrine neoplasia types 2A and 2B, von Hippel Lindau (VHL), neurofibromatosis type 1 (NF1), and Carney-Stratakis dyad [20]. Screening protocol for PPGL evaluation for genetic basis has been summarised in Fig. 32.2.

Clinical Presentation

Clinical features vary depending upon the location of the tumor with the mass effect being the commonest presentation. Due to non-specific symptoms, diagnosis is often delayed. Symptoms range from neck swelling, hearing loss, pulsatile tinnitus or cranial nerve failures (IX–XI). Tumors located near the petrous bone, jugular, and tympanic area may present as hearing loss. Initially there is conductive hearing loss due to impairment of ossicle vibration or bone invasion behind the eardrum. Later it is followed by sensorineural hearing loss and/or dizziness which occurs due to inner ear invasion. Occasionally, deficits of other cranial nerves can occur like dysfunctional swallowing and voice huskiness. Since tumor grows slowly, swallowing mechanism and vocal cord function of the opposite side may compensate and mask the disease symptoms. Later, facial nerve invasion can result in facial paralysis and hypoglossal nerve involvement can result in paralysis of half of the tongue. As tumor progresses intracranially, it can cause compression of the brain and/or brainstem [17].

Compared to tumors located in adrenals, abdomen and thorax; HNPGL seldom release catecholamines and are rarely vasoactive. But in 1–3% cases, they secrete catecholamines and patients may present with symptoms of pheochromocytoma such as hypertension, tachycardia, palpitation, headache, and anxiety [22, 23]. Hypertension is the commonest symptom in 90% of catecholamine secreting paragangliomas which might be paroxysmal (lasting minutes or days) or sustained. The classic triad consists of headache, palpitations, and sweating. Patients should be enquired about any episodic symptoms (its frequency, duration), and blood pressure (BP) and heart rate should be checked regularly during these episodes. The commonly advocated "Rule of 10% "for the clinical patterns of pheochromocytoma/paraganglioma, is now out-of-date (10% bilateral/multiple, 10% familial, 10% extra-adrenal, 10% malignant) and is considered not valid.

Rarely, glomus tumors can secrete Serotonin and histamine producing a carcinoid-like syndrome. They may give history of bronchoconstriction, abdominal pain and explosive diarrhea resulting in dehydration and electrolyte abnormalities, violent headaches, cutaneous flushing, and hypertension, hepatomegaly, and hyperglycemia [24, 25].

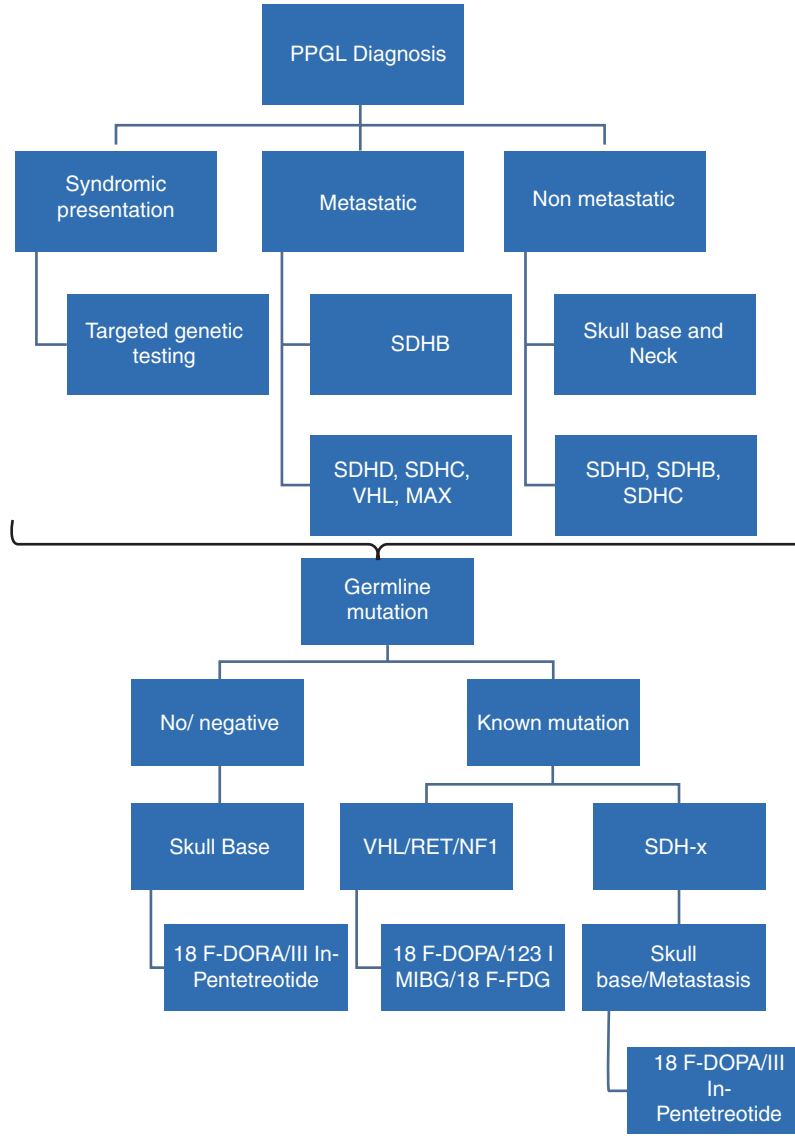


Fig. 32.2 Decision algorithm for proven PPGL for genetic testing and functional imaging. Compiled information from Bholah et al. [21], Taieb et al. [18]

Diagnosis, Staging and Classification

Diagnostic evaluation is aimed to determine the size and extent of the disease (including intracranial extension), detection of any associated lesions, determination of collateral circulation and assessment of major vasculature. Imaging techniques (both anatomical and functional) and angiography aid in determining the above goals. For jugulotympanic paragangliomas staging systems proposed by Fisch and Glasscock/Jackson are currently used which has been summarised in Table 32.1 [8, 26].

Investigation and Imaging

Non secretory HNPGL: Diagnosis is made through Magnetic Resonance Imaging (MRI) with paraganglioma specific functional imaging.

Table 32.1 Classifications of tumor severity and extent for head and neck paragangliomas

Modified Fisch classification for glomus jugulare	
Class C	
C1	Tumors destroying the jugular foramen and bulb with limited involvement of the vertical portion of the carotid canal
C2	Tumors invading the vertical portion of carotid canal (infratubal segment of ICA)
C3	Tumors invading the horizontal petrous segment of carotid canal
C4	Tumors reaching the anterior foramen lacerum and along the internal carotid artery to the cavernous sinus
Class D	
De1	Tumors with upto 2 cm dural displacement
De2	Tumors with more than 2 cm dural displacement
Di1	Tumors with upto 2 cm intradural extension
Di2	Tumors with more than 2 cm intradural extension
Di3	Inoperable intracranial intradural tumors
Class V	
Ve	Tumors engulfing the extradural vertebral artery
Vi	Tumors involving the intradural vertebral artery
Jackson/Glasscock classification	
Type1	Tumor involving the jugular bulb, middle ear, and mastoid process
Type2	ExtenTumor extending under internal auditory canal; may have intracranial extension
Type3	EEE Tumor extending into petrous apex; may have intracranial extension
Type4	Extending beyond petrous apex into clivus or infratemporal fossa; may have intracranial extension

Secretory HNPGL:Secretory nature is confirmed by laboratory workup which includes 24-h urine metanephrines and fractionated catecholamines as well as plasma metanephrines. Diagnosis of HNPGL is made through MRI with paraganglioma specific functional imaging.

Biochemical Analysis/Investigation

Biochemical testing should be done in symptomatic patients, patients with adrenal incidentaloma and in patients with a genetic predisposition for pheochromocytoma/paraganglioma (multiple endocrine neoplasia type 2, Von Hippel-Lindau (VHL) syndrome, neurofibromatosis type 1 (NF 1) and mutations of succinate dehydrogenase (SDH) genes) etc. [27]. Biochemical analysis confirming catecholamine excess is usually done before imaging tests for tumor localizing (Fig. 32.3). Detection of excessive catecholamines or metanephrines (O-methylated catecholamine metabolites) production establishes the secretory nature of tumor. Endocrine Society Clinical Practice Guideline recommend measuring plasma free metanephrines or urinary fractionated metanephrines [28] as these are superior to other tests of catecholamine excess.

Tyrosine through a series of enzymatic reactions is converted to dopamine, which is further converted to norepinephrine and finally to epinephrine. Enzyme Phenylethanolamine-N-methyl-transferase (PNMT), which converts norepinephrine to epinephrine is present only in adrenal medulla, heart, and brain. Hence, Adrenal tumors secrete epinephrine and frequently norepinephrine while extra-adrenal tumors secrete norepinephrine and dopamine. Thus, Pheochromocytomas largely have epinephrine and metanephrine excess while in Paragangliomas norepinephrine and normetanephrine accumulate. Vanillylmandelic acid (VMA) can accumulate in both paragangliomas and pheochromocytomas (Fig. 32.4). Other neurotransmitters like serotonin, vasoactive intestinal peptide, kallikrein, 5-hydroxytryptophan, and neuron specific enolase may also be produced [29].

3-methoxytyramine (a dopamine metabolite): It is a new biochemical marker which is raised in 30% patients of HNPGL.

Tumor Localization/Morphological Imaging

Diagnostic imaging (Table 32.2) is done when patients present with symptomology suggestive of a paraganglioma, or in patients from families with hereditary paragangliomas. These imaging modalities localize the lesion and look for multiplicity. Both Computed tomography scan (CT)

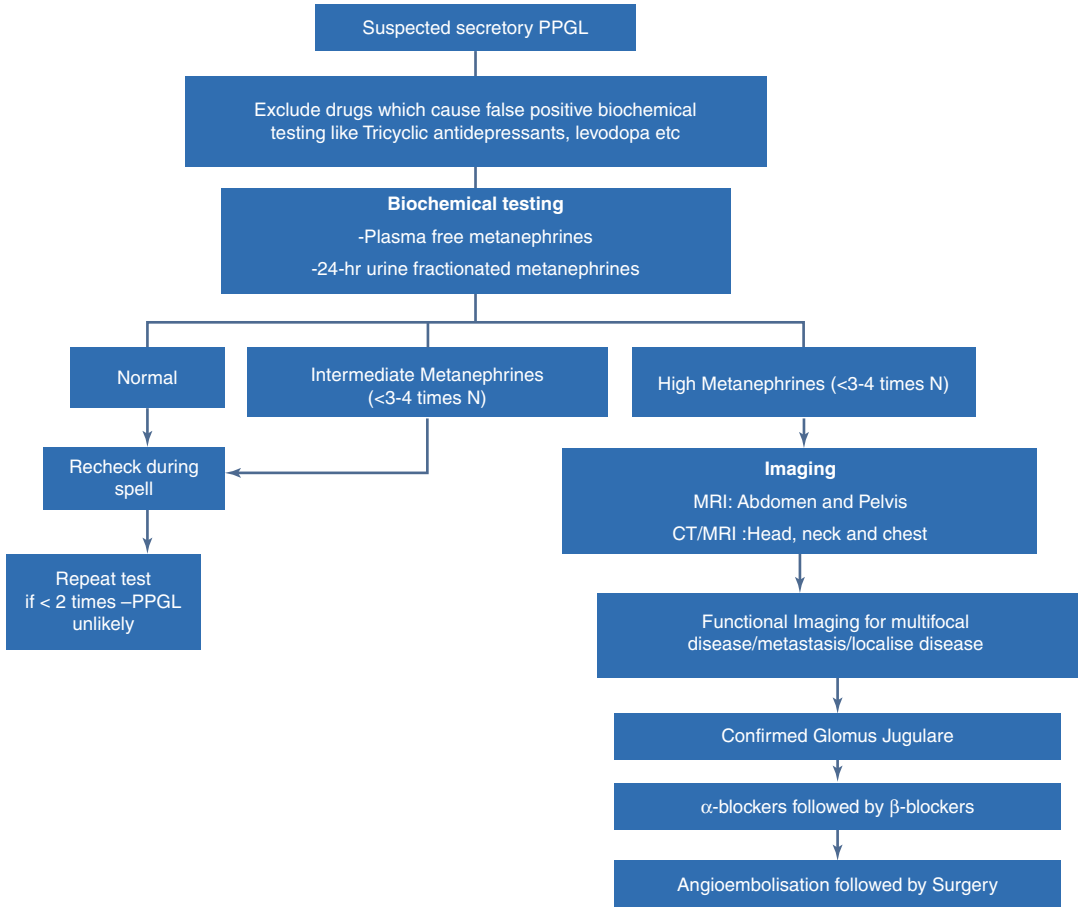


Fig. 32.3 Diagnosis confirmation algorithm for suspected secretory PPGL. Compiled information from Jain et al. [12] and Bholah et al. [21]

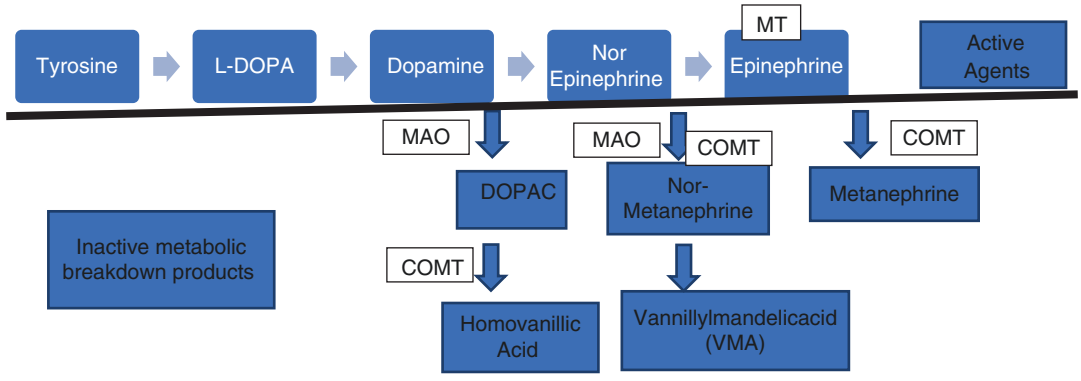


Fig. 32.4 Catecholamine synthesis and metabolism. L- DOPA is 3,4-dihydroxyl-l-phenylalanine, MAO is monoamine oxidase and COMT is Catechol-*O*-methyltransferase. Compiled information from Jain et al. [12], Castrucci et al. [10]

Table 32.2 Comparison of different imaging techniques for head and neck paragangliomas

Imaging technique	Sensitivity (%)	Specificity (%)	Advantages
CT	80–90	90	Accurately delineates temporal bone extension
MRI	80–90	90	No radiation No iodinated media, More accurate than CT for extraadrenal PGL
PET/CT-18F-FDOPA	>90	>95	High tumor/background uptake ratio (TBR) Highly sensitive regardless of genotype Low uptake in normal adrenals
PET/CT-18F-FDG	80	80–90	18F-FDG uptake excellent negative predictive value for SDHx mutations 18F-FDG PET that has become the first-line imaging modality in the follow-up of patients with SDHB-related metastatic tumors Accurately spots concomitant abdominal PGLs which are missed by 18F-FDOPA
PET/CT-68Ga-DOTATATE	>90	90	High TBR

and Magnetic resonance imaging (MRI) have specificities of around 90% [18] for localization of HNPGLs and both are useful for localizing and analyzing glomus tumors for surgical planning. [12].

However, MRI has better sensitivity than CT to locate extra-adrenal tumors and aids in evaluating the spinal canal invasion and major vessels involvement [30]. MRI is recommended in metastatic PPGL, skull base and neck paraganglioma, patients allergic to CT contrast and to limit radiation exposure (Pregnant, children, patients with germline mutations etc.) [28]. T2 weighted MRI images may show flow voids in the tumorgiving "Salt and pepper appearance".MR imaging, and especially 3D Time of Flight (TOF) MRA, is the modality of choice with sensitivities and specificities of 90% and 94% respectively [31]. CT scanning aids when there is bony involvement like the destruction of the temporal bone-like the depiction of expansion and a moth-eaten appearance of the bone of the jugular fossa in jugular paragangliomas [30]. Angiographic embolization is used before surgical resection but can also aid in establishing an unclear diagnosis [32].

Functional Imaging

Functional imaging is indicated for incidental tumors with inconclusive biochemical testing, multicentricity, local extension, and to rule out metastases [12]. Functional imaging can be done with 131-iodine/123-iodine metaiodobenzylguanidine (MIBG) scan/scintigraphy, 18F-DOPA positron emission tomography (PET) (FDOPA), [18F] fluorodeoxyglucose (FDG), [18F] fluorodopamine (FDA), and PET with radiolabeled dodecanetetraacetic acid (DOTA) peptides. The molecular structure of MIBG bear a resemblance to norepinephrine, so is preferentially taken by adrenergic tissues. MIBG scan has a very high specificity for PPGL and especially useful for detection of metastasis. 18F-FDGPET/CT is preferred over 123I-MIBG scintigraphy in subjects with metastatic PPGL [28]. Somatostatin receptor scintigraphy (SRS) may be preferred over MIBG scintigraphy for HNPGL. SRS screening has been used for familial paragangliomas and for detecting recurrence after surgery. F-DOPA has promising role in detecting subcentimeter glomus tumors along with functional study. An approach to functional imaging has been summarised in Fig. 32.2 [33]. Modern PET

modalities use 68Ga-labeled somatostatin analogues (68Ga-DOTA-SSAs) and have excellent results in locating metastatic or extra-adrenal pheochromocytomas [9].

Differential Diagnosis

Tumors which need to be kept in differential diagnosis are Schwannoma, Meningioma, Plasmacytoma, Carcinoma (primary and metastatic), Chondrosarcoma, Tumor extension from nasopharyngeal carcinoma.

Treatment Goals and Options (Non-surgical and Surgical)

Treatment options are determined by tumor location, size, growth rate, neurovascular involvement, malignant potential, and patient factors like age and medical condition [25]. The treatment options include tumor resection, Radiotherapy, stereotactic RT, radiosurgery, and continued observation or conservative management.

Surgery is the preferred option in young patients, catecholamine secretory paraganglioma, and paragangliomas with rapidly progressive neurological deficits [34]. If there is widespread infiltration of lower cranial nerves or the dominant vessels, then a more conservative excision of the lesion is done.

Traditionally, surgical resection with preoperative embolization was the mainstay of treatment targeting complete tumor removal. Surgical resection is challenging because of location near major neurovascular structures and high vascularity. To reduce intraoperative bleeding, digital substruction angiography (DSA) is performed 24–48 h before surgery with agents like polyvinyl alcohol to identify the tumor's vascular pedicle and embolize it. If angioembolization is performed earlier than 24 h, it can result in inflammatory response or revascularization edema [35]. Preoperative selective embolization reduces tumor size, makes it firmer in consistency and decreases blood loss during surgery. Angioembolisation is safe and the effective method but has potential for some neurologic complications because of the overlapping blood supply between these tumors and the CNs [35, 36]. Besides, tumors infiltrate between the CN fascicles and perineurium with reactive fibrosis rendering complete resection challenging without sacrificing these nerves [28]. Hemodynamic variations is common in patients with catecholamine secreting tumor during angioembolization, and even cardiac arrest has been reported [6].

Glomus tumors are relatively radiosensitive, and radiation modalities target arresting the tumorgrowth. Conventional EBRT may adequately prevent reproductive cell growth but does not kill the chief cells immediately, and hence catecholamine levels need to be followed for months. Amongst other radiation modalities, Gamma Knife radiosurgery (GKRS) is gaining popularity in treating lesions with high precision and has the advantage of sparing the nearby critical structures. It is used either as a primary treatment or as a salvage treatment for residual and recurrent tumors. However GKRS is not very suitable for very large tumors as when the target volume of the tumor increases, there is a proportional increase in the radiation dose on the surrounding normal tissues [1]. Even catecholamine-secreting tumors respond to GKRS by reduction in size however there is a latency period for normalization of hormone levels [37]. Patients who are aged and medically unfit with minimum symptoms, a close observation is an option. If they have symptomatology progression then they are subjected to stereotactic radiosurgery [1].

Preoperative Preparation (Pharmacological Preparation, Cardiovascular Evaluation, Angioembolisation)

GJT which are secretory pose a formidable anaesthetic challenge.Early multidisciplinary involvement of endocrinology, anesthesiology, and surgery speciality is a must for the successful management of secretory paragangliomas. Most paragangliomas and large pheochromocytomas

need an open resection [28, 38] but for small, non-invasive paragangliomas in surgically favourable locations laparoscopic resection can be performed [28]. Patients are at increased risk for hypertensive crisis during its surgical resection due to catecholamine surge and hypotension after its successful removal due to withdrawal of the catecholamines. These hemodynamic variations become lessened if patients are adequately prepared preoperatively [39]. There are subset of patients who might have normal BP recordings usually due to low circulatory levels of catecholamines [27]. Even these patients have comparable instability intraoperatively if not properly prepared for surgery [40]. The preoperative goals include evaluation of cardiovascular sequel due to high circulating catecholamines, optimising cardiac dysfunction and achieving adequate BP control to prevent intraoperative hemodynamic instability. Endocrine Society Clinical Practice (ESCP) Guidelines and Roizen's criteria guide in the management of Pheochromocytoma and secretory paraganglioma [28, 41].

Another subset of tumors which are Serotonin and histamine secreting, may mimic carcinoid like syndrome during surgical manipulation causing profound hypotension and even shock. Severe bronchoconstriction produced by histamine and bradykinin is refractory to conventional therapy such as corticosteroids but responds to inhaled β-agonists (best), inhaled anticholinergics (ipratropium bromide).

Cardiac Evaluation

There is a wide myriad of Cardiovascular Disorders Associated With PPGL which include Hypertension (Sustained/Paroxysmal/Hypertensive emergency), orthostatic hypotension, arrhythmias (Sinus tachycardia/Atrial arrhythmias/Supraventricular tachycardia/Torsade's de pointes/Atrioventricular reentrant tachycardia/Asystole), cardiomyopathy (Hypertrophic/Dilated/Peripartum/Takotsubo), myocardial ischemia, and even aortic dissection [42]. These diverse manifestations are due to excessively circulating catecholamines which stimulate adrenergic receptors in cardiovascular system and are responsible for significant morbidity and mortality. Symptoms associated with catecholamine excess can be controlled with pharmacological blockade with drugs like α-blockers and β- blockers. Cardiac function, structure and conduction abnormalities improve after pharmacological intervention [40]. For the evaluation of functional capabilities of cardiovascular system detailed history, physical examination and laboratory testing should include complete blood count, metabolic panel, electrocardiogram (ECG) and echocardiogram (ECHO).

Antihypertensives

Due to the low incidence of PPGL, there are no prospective randomised control trials comparing efficacy of different antihypertensive regimens and the evidence of its utility has been derived from retrospective analysis [28]. Management of secretory glomus jugulare tumor is done on lines similar to secretory pheochromocytoma. Administration of antihypertensive therapy is recommended even in normotensive patients [28] with secretory tumours. There are no prospective RCTs for determination of optimal blood pressure but based upon retrospective studies it is reasonable to target blood pressure of less than 130/80 mmHg and heart rate of 60–70 bpm while seated and greater than 90 mmHg systolic while standing seems reasonable and heart rate of 70–80 bpm while standing [28]. Endocrine Society Clinical Practice Guidelines recommend alfa blockers as the first line of antihypertensive regimen in all hormonally functional PPGL for the prevention of perioperative complications [28]. On the basis of retrospective studies, targeting a Blood pressure <130/80 mmHg in sitting position and systolic >90 mmHg systolic in standing position and heart rate of 60–70 bpm seated and 70–80 bpm while standing is advised which can be modified based upon patients age and comorbidities [39, 43]. Medical treatment for 7–14 days is recommended for the optimization of blood pressure and heart rate. Pharmacological

Table 32.3 Preoperative pharmacological hypertensive control

Drug therapy	Dosage	Specific concern
Alpha blocker		Administered 10–14 days prior to surgery
Phenoxybenzamine	10 mg BD to intravenous infusion of 0.5 mg/kg/day for 5 h/day for 3 days	Irreversible long acting Alpha blocker (pharmacological half-life of 24 h). It has significant adverse effect profile (reflex tachycardia, postural hypotension, sedation) by α-2 blockade. It causes significant hypotension after PPGL removal due to long duration of action
Prazosin	0.05–0.1 mg/kg/day/8 h Max. 0.5 mg/kg/day (20 mg/day)	Selective short acting α-1 blocker
Doxazosin	2 mg QID	Selective long acting α-1 blocker. (Half-life: 16–30 h)
Beta blocker		Started only after Alpha blocker
	Usually stared for persistent tachycardia	
Propranolol	20 mg TDS	Non-selective β1 and β2 blocker. Asthma can flare up
Atenolol	25 mg QID	Adverse effects are: Dizziness Fatigue
Calcium channel blocker		Used as an adjuvant
Amlodipine	5 mg QD	Adverse effects include Headache, Oedema, Palpitations
Other		
Alpha-methyl-para-tyrosine	20 mg/kg/day/6 h Maximum: 250 mg TDS	Used with α-blocker. Adverse effects include extra-pyramidal symptoms, depression, galactorrhoea, and sedation on prolonged use. Its use is limited to management of large tumors and prior to the radiofrequency ablation of metastatic disease

agents used for optimal hemodynamic management has been summarised in Table 32.3.

Non-Selective α-blockers: (Phenoxybenzamine) It is a non-selective long acting α-blocking agent with irreversible action at the receptor. It is administered at a starting dose of 10 mg twice a day for 1–2 weeks. However, in case of time limitation, it is administered as intravenous infusion of 0.5 mg/kg/day for 5 h/day for 3 days. Due to its significant adverse effect profile (reflex tachycardia, orthostatic hypotension, nasal congestion, excessive somnolence and peripheral edema) patients can become non-compliant. Preoperative and intraoperative hemodynamics are better controlled with phenoxybenzamine but it carries a risk of postoperative hypotension after tumor removal.

Selective α-1 blockers: Selective α_1-blockers like prazosin, doxazosin and terazosin cause lesser side effects, and hence are preferred in many centres. Amongst them, Doxazocin is administered once daily due to longer duration of action while prazosin and terazosin have shorter half-lives and hence are administered more frequently. All α-1 blockers cause adverse effects like postural hypotension, syncope and nasal stuffiness and hence should be carefully titrated.

Table 32.4 Roizens criteria for diagnosing adequacy of alfa blockade

	Roizen's criteria
1	I. BP <160/80 mm/Hg
2	II. Orthostatic hypotension not less than 80/60 mm/Hg
3	III. No more than 1 VPC in 5 min
4	IV. No new ST-Tchanges on the ECG over the last week

Adequacy of blockade is assessed by Roizen's criteria [41] which is summarised in Table 32.4:

β-adrenergic blockers: β- blockers are only started after establishing adequate α-adrenergic blockade and never before α-blockers due to possibility of hypertensive crisis occurring due to unopposed stimulation of α-adrenergic receptors. Utility of β- blockers is to control tachycardia or any tachyarrhythmias. Both selective and non-selective β- blockers can be used. Cardio selective agents like atenolol, metoprolol and esmolol are preferred as they cause lesser side effects. However, agents with both α- and β- blocking properties like Labetalol with more potent β-

action compared to α- action (5:1) should not be used as initial therapy due to the risk of hypertensive crisis [28].

Calcium channel blockers: These agents cause smooth muscle relaxation in peripheral vessels and coronary arteries. These are used as add-on drugs for controlling BP and monotherapy with calcium channel blockers is usually not recommended unless they have mild preoperative hypertension or severe orthostatic hypotension with α-adrenergic receptor blockers or in normotensive patients with paroxysmal hypertension [28].

α Methyl-para-tyrosine: It is a catecholamine synthesis inhibitor (tyrosine hydroxylase) and can be used along with α-adrenergic receptor blockers immediately before surgery to further optimise blood pressure control and volume depletion [44, 45]. But due to its adverse effect profile (extra-pyramidal side effects, depression, galactorrhoea, and sedation), it is used only in the management of large tumors and before radiofrequency ablation of the metastatic disease [46].

Preparation in Serotonin secreting glomus tumors: Patients suspected of Serotonin and histamine secretion based upon history are evaluated fordehydrationand electrolyte abnormalities and corrected for them. Somatostatin analogue, Octreotide which inhibits the release of serotonin is administered in the perioperative period (100 μg subcutaneously, BD/TDS) starting 2 weeks before surgery in symptomatic patients.

Other measures: Due to excessive catecholamines, vasoconstriction results in relatively reduced circulating plasma volume. High-sodium diet and fluid intake is recommended for reversal of catecholamine induced blood volume contraction which in turn would prevent severe hypotension after tumor removal. In histamine and bradykinin secreting tumors there is possibility of bronchospasm, tachycardia and hypotension. BP, heart rate, and blood glucose levels should be monitored beginning from preoperative period to postoperatively and drug therapy should be regulated accordingly [28]. Compared to pheochromocytomas, volume loading after GJT excision should be carefully performed as it can result in intracranial pressure elevation.

Angioembolisation

For reduction of blood loss in these highly vascular tumors, digital subtraction angiography (DSA) is performed 24–48 h prior to surgery. Angioembolization reduces tumor size, makes it firmer in consistency and decreases blood loss during surgery but it has potential for some neurologic sequel due to overlapping blood supply of these tumors and the CNs [35, 36].

Anaesthetic Management (Premedication, Preparation of OR, Induction, Maintenance, Analgesia)

Catecholamine secreting glomus jugulare tumor is a rare entity. But when secretory, they may secrete a wide variety of neuropeptide hormones, including adrenocorticotropic hormone, serotonin, catecholamine, and dopamine. However, if secretory nature goes unrecognised, serious complications of an intra- or perioperative hypertension crisis can occur. Anaesthetic management of these GJT is like management of a secretory PPGL with a few additional concerns.

Additional Considerations in Glomus Jugulare tumor Compared to PPGL

Measures to control intracranial pressure in cases with intracranial extension (involvement of posterior cranial fossa, lower cranial nerves, internal carotid artery) are needed. There is risk of air embolism which can occur during ligation of the internal jugular vein and sigmoid sinus. Management of these highly vascularised tumours may be challenging. CN monitoring might be needed in case of intracerebral extent.

Premedication

Anxiolytic like oral benzodiazepine and H2 blockers are administered preoperatively. Long acting α-blockers like Phenoxybenzamine and Doxazocin are stopped 12–24 h preoperatively

while short acting α 1-blockers like prazosin are continued on the morning of surgery. Risk of gastroparesis is increased in patients with large glomus tumors due to compression of the lower cranial nerves predisposing them to airway compression by obstruction or aspiration.

Preparation of OR: Preparation of antihypertensive agents like sodium nitroprusside (SNP) 0.01%, nitro glycerine (NTG) 0.1%, esmolol and norepinephrine and vasoactive drugs (magnesium sulphate, labetalol, diltiazem, lidocaine 2%, Dexmedetomidine) should be done prior to induction. These infusions should be kept attached to the central line according to the choice of the agent intended to be used. Due to the anticipated blood loss; large bore Intravenous canulae, hot line and rapid infusers should be kept ready.

Monitoring: Besides standard ASA monitors (SpO_2, 5-lead ECG, NIBP, temperature), invasive arterial line for beat to beat analysis of hemodynamic variations and central venous access for infusing vasoactive agents is recommended. Invasive BP monitoring is started before induction of anaesthesia under local anesthetic infiltration for real time monitoring of hemodynamic fluctuations. Before placement of central venous line, assessment for tumor involvement of internal jugular vein (IJV) and superior vena cava should be done. If IJV but not the superior vena cava has been invaded by the tumor, consider inserting central line in the contralateral basilic, external or internal jugular vein. Urine output monitoring is routinely done during surgeries for excision of PPGL to monitor perfusion in view of anticipated excessive blood loss. Monitoring for venous air embolism can be achieved with frequent ABG, $ETCO_2$, N_2 and precordial doppler. Additional monitors like Cerebral Oximetry provide information along with NIBP and mean arterial pressure about accurate estimation of cerebral desaturation. Cerebral perfusion monitoring becomes clinically relevant if the carotid artery is to be occluded intraoperatively. For assessment of Cerebral Perfusion monitors which can be used are EEG, somatosensory evoked responses, arterial stump pressure assessments and transcranial Doppler measurement of middle cerebral artery flow velocities [47]. Cranial nerves like facial nerve may need to be monitored intraoperatively and in that case total intravenous anaesthesia needs to be administered to the patients.

Induction

Large bore intra venous access (14G/16G) should be ensured before induction for all such patients. Intravenous induction agents are considered safe except ketamine due to its sympathetic stimulation and catecholamine release. Dexmedetomidine and remifentanil also have been used success/fully [48] in pheochromocytomas and can be used in PPGL.

Total intravenous anaesthesia administered using propofol target-controlled infusion has been recognized technique for maintaining surgical anaesthesia. Its utility in head and neck surgeries might provide additional benefit especially in the setting of neurophysiological monitoring for cranial nerve preservation [49]. TIVA provides stable physiological and anaesthetic milieu to facilitate interpretation of signal changes and aid in surgical guidance.

Drugs which cause sympathetic stimulation (ketamine, ephedrine, and meperidine) or elicit histamine release (morphine) or trigger hypertension (droperidol) must be avoided. Hence, opioids and neuromuscular blocking agents which do not release histamine should be used.

Amongst neuromuscular blocking agents vecuronium, rocuronium, and cisatracurium are widely used during anaesthetic management due to absence of any autonomic effects and absence of histamine release. Succinyl choline must be avoided as the fasciculations may induce release of catecholamines from the tumor. Pancuronium is avoided due to its vagolytic effect which may result in tachycardia and an intense hypertensive response.

Magnesium use is gaining popularity during surgical removal of pheochromocytoma in view of its antiarrhythmic properties, calcium-blocking properties, inhibits catecholamine release, and acts as vasodilator. It is administered in a dose of

40–60 mg/kg over 10 min [12]. Additionally, it has neuroprotective effect by action as *N*-methyl-D-aspartate antagonist and has favourable effect on intracranial surgery [6].

Maintenance: Inhalational volatile anesthetics in moderate dose can be used safely. However, halothane due to its arrhythmogenicity and desflurane due to its sympathetic stimulation is not recommended for use in the surgery for excision of secretory PPG. Intense vigilance and preparedness for assessing blood loss, hypertension, hypotension, bradycardia venous air embolism and tumor parts embolization is necessary. In case there is intracranial extension of the tumor, measures are taken to reduce intracranial pressures which include appropriate positioning to optimize venous return from brain, moderatehyperventilation ($PaCO_2$ 25–30 mmHg), administration of mannitol and assessment for CSF drainage by inserting lumbar subarachnoid catheter if needed.

Analgesia: Preoperative analgesia can be provided with any of the commonly used opioids-fentanyl, hydromorphone, remifentanil, and sufentanil. Opioids like Morphine, Alfentanyl,Pethidine which causes histamine release should not be used.

Measures to reduce intraoperative blood loss: Since GJT are large, highly vascular tumors located near sinuses, there is a potential risk of massive blood loss during their surgical removal. Major sources of bleeding are the sigmoid sinus, the inferior petrosal sinus, and the tumor itself. Preoperative angioembolization of the feeder vessel is done 24–48 h before surgery and is a reasonable option to reduce it. Simple measures like elevation of the surgical site reduces arterial pressure and reduces venous congestion thereby facilitating venous drainage away from the wound. Other methods used by surgeons are external carotid and jugular vein ligation. Controlled hypotension/hypotensive anaesthesia may aid in decreasing intraoperative blood loss thereby providing clear surgical field. Various agents employed to achieve controlled hypotension include magnesium sulphate, sodium nitroprusside, nicardipine, nitroglycerine, esmolol, α_2-agonists, labetalol and high-dose potent inhalational anaesthetics [50]. These agents have their individual side effects which include vasodilation, tachyphylaxis, cyanide toxicity with nitroprusside and long postanaesthetic recovery period with high dose inhalational agents etc. Another simple measure to reduce blood loss is to avoid hypothermia as low temperatures adversely affect platelet function [50].

Fluid Management: Hypotension can occur due to residual effect of long acting preoperative antihypertensives like phenoxybenzamine, inadequate intravascular volume in a patient with prolonged peripheral vasoconstriction or due to hypovolemia resultant of excessive blood loss. It usually occurs after the removal of paraganglioma and it is managed by administering fluids and vasopressors. In case of persistent hypovolemia, vasopressors have reduced effect and are likely to be ineffective without fluid resuscitation. All pressor agents norepinephrine, phenylephrine, vasopressin, and dopamine have been successfully used during surgical removal of paragangliomas. In case there is catecholamine induced cardiomyopathy, fluids should be used judiciously due to the risk of volume overload.

Intraoperative Hypertensive Crisis

Different medications with a quick onset of action have been used for perioperative control of high blood pressure and have been summarised in Table 32.5. Hypertensive response is expected during preoxygenation while application of tight-fitting mask, laryngoscopy and during tumour manipulation. Suggested risk factors for developing hypertensive crisis during surgery are – a large tumour, preoperative high levels of NE, sub optimal preoperative preparation of patient and presence of significant postural hypotension after α- blockade. Nearly all available antihypertensive agents have been used intraoperatively for control of blood pressure surges – depend on personal preferences and institutional practices. If Norepinephrine crisis occurs, it is.characterised by profound hypertension and bradycardia. For its management, ensure adequate depth of anaesthesia and adequate neuromuscular blockade and

Table 32.5 Intraoperative pharmacological management of hypertension

Drug	Mechanism of action	Dosage	Specific concern
Sodium Nitroprusside (SNP)	Vasodilator	Prepared as 0.01%	Protect it from light. Caution about cyanide toxicity
Nitro-glycerine	Venodilator	Prepared as 0.1%	It can cause reflex tachycardia
Esmolol	Selective β 1 antagonist	Prepared as 1 mg/mL 500–600 μg/kg IV	Can be used to treat intraoperative tachyarrhythmias
Labetalol	Combined α and β blocker (1:7)	5–15 mg boluses	Can be used to treat intraoperative tachyarrhythmias
Magnesium sulphate	↓ Catecholamine release from adrenal medulla and sympathetic nerve endings – Blocks catecholamine receptors – Vasodilation	40–60 mg/kg intravenously followed by a continuous infusion of 1–2 gm/h	Be cautious in patients with renal dysfunction, elevated creatinine levels, urine output <30 mL/h
Dexmedetomidine	– Central α 2 agonist – ↓ Availability of norepinephrine at the axon terminals of sympathetic postganglionic neurons via α_2-adrenoceptor activation	0.5–1 μg/kg followed by 0.2–0.7 μg/kg/h	Additional sedative and analgesic effects

still if blood pressure remains high, control of BP is done using agents like Sodium nitroprusside, Nitro-glycerine, Diltiazem, Labetalol, Second-generation calcium channel antagonists, especially dihydro-pyridines (nicardipine), Lidocaine and Magnesium sulphate [51].

Intraoperative carcinoid-like syndrome: GJTs may release 5-Hydroxytryptamine (serotonin), kallikrein, and 5-hydroxytryptophan, a precursor of serotonin and histamine. Serotonin appears to be the primary marker associated with the syndrome. Patient may present with episodic facial flushing, hypotension, tachycardia, diarrhea, bronchoconstriction, venous telangiectasia, dyspnea etc. Intraoperative tumor manipulation can result in histamine and bradykinin release causing bronchospasm, decreased lung compliance, profound hypotension, and even shock. Severe hypertension can occur as 5-Hydroxytryptamine may increase vascular response to catecholamines by inhibiting the Norepinephrine uptake. The 5HT2 antagonist ketanserin may offer benefit in both provoked and spontaneous attacks of flushing, diarrhoea due to carcinoid syndrome [52]. Management should focus upon either blocking the chemical modulators release or blocking their actions. Somatostatin analogue, octreotide 100 μg intravenously administered at induction can inhibit serotonin release [53] and can be continued postoperatively for 72 h.

Extubation: Extubation after surgical excision can be carried out in the operation theatre itself, however prior to extubation evaluate for airway swelling and neck hematoma, brain stem injury in intracranial extension and any sequel of pulmonary embolism. During surgical resection of glomus jugulare lower CN may get damaged, hence extubation should be performed after careful assessment [47, 54]. These patients may need care in critical care unit and postoperative ventilation especially when they have intraoperative crisis, hemodynamic instability, hypothermia and major blood loss.

Postoperative Management

Potential complications expected in the postoperative period are hypotension, hypertension and hypoglycaemia. ESCP guidelines recommend that blood pressure, heart rate and plasma glu-

cose levels should be monitored for 24–48 h after surgery [28]. Postoperative hypotension is multifactorial and is likely to be due to one or all of the following: residual effect of long acting α- blockers like phenoxybenzamine, persistent effect of antihypertensive agents given during surgical removal persistent circulating catecholamine with downregulated adrenergic receptors after tumor removal [12]. Hypotension is managed by administering fluids and vasopressors. Persistence of hypertension in a few patients may indicate persistent residual mass, possibility of other tumors at various other sites secreting catecholamines or volume overload. Postoperative hypoglycaemia is due to rebound hyperinsulinemia after catecholamine withdrawal and increased peripheral glucose uptake. Thus, these patients should be closely monitored for glycaemic control for the first 48 h according to endocrine society practice guidelines [28, 55].

Follow up Examination: ESCP guidelineslong-term follow-up of postsurgical PPGL [56]. The recommendation is to assay plasma or urinary meta nephrines within 2–6 weeks after surgery to confirm adequate resection and then annually to screen for local or metastatic recurrences or new tumours. The follow-up (biochemical testing and imaging) should be done for at least 10 years in all the operated PPGL. The High-risk patients (young patients,genetic disease, a large PPGL) should be offered a lifelong annual follow-up [28, 56].

Conclusion

Early multidisciplinary involvement of endocrinology, anaesthesiology, and endocrine surgeon for catecholamine secreting tumors is desirable for successful perioperative management. The same preoperative pharmacological stabilization is done in patients with secretory glomus jugulare tumor as in pheochromocytoma. Optimal preoperative preparation/stabilisation, and intensive perioperative monitoring can result in successful management of GJT.

References

1. Jayashankar N, Sankhla S. Current perspectives in the management of glomus jugulare tumors. Neurol India. 2015;63(1):83–90.
2. Guild ST. A hitherto unrecognized structure, the glomus jugularis, in man. Anat Rec. 1967;79(Suppl 2):28.
3. Rosenwasser H. Carotid body tumor of the middle ear and mastoid. Arch Otolaryngol. 1945;41(1):64–7.
4. A Comprehensive Study of Tumors of the Glomus Jugulare—PubMed [Internet]. https://pubmed.ncbi.nlm.nih.gov/13860392/?from_term=Alford+B%2C+Guilford+F.+A+comprehensive+study+of+tumors+of+the+glomus+jugulare.+Laryngoscope++1962%3B+72%3A+765-787. Accessed 30 March 2020.
5. Winship T, Klopp CT, Jenkins WH. Giomus-jugularis tumors. Cancer. 1948;1(3):441–8.
6. Teranishi Y, Kohno M, Sora S, Sato H, Haruyama N. Perioperative management of catecholamine-secreting glomus jugulare tumors. J Neurol Surg Rep. 2014;75(1):e170–4.
7. Pathology and Genetics of Tumours of Endocrine Organs. Third edition—WHO—OMS—[Internet]. https://apps.who.int/bookorders/anglais/detart1.jsp?codlan=1&codcol=70&codcch=8. Accessed 6 March 2020.
8. Lam AK-Y. Update on adrenal tumours in 2017 World Health Organization (WHO) of endocrine tumours. Endocr Pathol. 2017;28(3):213–27.
9. Tokgöz SA, Saylam G, Bayır Ö, Keseroğlu K, Toptaş G, Çadallı Tatar E, et al. Glomus tumors of the head and neck: thirteen years' institutional experience and management. Acta Otolaryngol (Stockh). 2019;139(10):930–3.
10. Castrucci WA, Chiang VLS, Hulinsky I, Knisely JPS. Biochemical and clinical responses after treatment of a catecholamine-secreting glomus jugulare tumor with gamma knife radiosurgery. Head Neck. 2010;32(12):1720–7.
11. Batsakis J. Tumors of the head and neck: clinical and pathological considerations. 2nd ed. Baltimore: Williams & Wilkins; 1979.
12. Jain A, Baracco R, Kapur G. Pheochromocytoma and paraganglioma-an update on diagnosis, evaluation, and management. Pediatr Nephrol Berl Ger. 2020;35(4):581–94.
13. Boedeker CC, Neumann HPH, Maier W, Bausch B, Schipper J, Ridder GJ. Malignant head and neck paragangliomas in SDHB mutation carriers. Otolaryngol Head Neck Surg. 2007;137(1):126–9.
14. Jansen JC, van den Berg R, Kuiper A, van der Mey AG, Zwinderman AH, Cornelisse CJ. Estimation of growth rate in patients with head and neck paragangliomas influences the treatment proposal. Cancer. 2000;88(12):2811–6.
15. Bayley J-P, van Minderhout I, Weiss MM, Jansen JC, Oomen PHN, Menko FH, et al. Mutation analysis of

SDHB and SDHC: novel germline mutations in sporadic head and neck paraganglioma and familial paraganglioma and/or pheochromocytoma. BMC Med Genet. 2006;7:1.
16. van der Mey AG, Maaswinkel-Mooy PD, Cornelisse CJ, Schmidt PH, van de Kamp JJ. Genomic imprinting in hereditary glomus tumours: evidence for new genetic theory. Lancet Lond Engl. 1989;2(8675):1291–4.
17. Offergeld C, Brase C, Yaremchuk S, Mader I, Rischke HC, Gläsker S, et al. Head and neck paragangliomas: clinical and molecular genetic classification. Clinics. 2012;67(Suppl 1):19–28.
18. Taïeb D, Kaliski A, Boedeker CC, Martucci V, Fojo T, Adler JR, et al. Current approaches and recent developments in the management of head and neck paragangliomas. Endocr Rev. 2014;35(5):795–819.
19. Heth J. The basic science of glomus jugulare tumors. Neurosurg Focus. 2004;17(2):E2.
20. Medline ® Abstract for Reference 20 of "Paragangliomas: Epidemiology, clinical presentation, diagnosis, and histology"—UpToDate [Internet]. https://www.uptodate.com/contents/paragangliomas-epidemiology-clinical-presentation-diagnosis-and-histology/abstract/20. Accessed 9 Mar 2020.
21. Bholah R, Bunchman TE. Review of pediatric pheochromocytoma and paraganglioma. Front Pediatr. 2017;5:155.
22. Ganz JC, Abdelkarim K. Glomus jugulare tumours: certain clinical and radiological aspects observed following Gamma Knife radiosurgery. Acta Neurochir. 2009;151(5):423–6.
23. Gandía-González ML, Kusak ME, Moreno NM, Sárraga JG, Rey G, Álvarez RM. Jugulotympanic paragangliomas treated with Gamma Knife radiosurgery: a single-center review of 58 cases. J Neurosurg. 2014;121(5):1158–65.
24. Farrior JB, Hyams VJ, Benke RH, Farrior JB. Carcinoid apudoma arising in a glomus jugulare tumor: review of endocrine activity in glomus jugulare tumors. Laryngoscope. 1980;90(1):110–9.
25. Jager RM, Polk HC. Carcinoid apudomas. Curr Probl Cancer. 1977;1(11):1–53.
26. Fisch U, Mattox D. Microsurgery of the skull base. Stuttgart, New York: Thieme; 1988. 149 p.
27. Zelinka T, Eisenhofer G, Pacak K. Pheochromocytoma as a catecholamine producing tumor: implications for clinical practice. Stress Amst Neth. 2007;10(2):195–203.
28. Lenders JWM, Duh Q-Y, Eisenhofer G, Gimenez-Roqueplo A-P, Grebe SKG, Murad MH, et al. Pheochromocytoma and paraganglioma: an endocrine society clinical practice guideline. J Clin Endocrinol Metab. 2014;99(6):1915–42.
29. McCaffrey TV, Myssiorek D, Marrinan M. Head and neck paragangliomas: physiology and biochemistry. Otolaryngol Clin N Am. 2001;34(5):837–44.
30. Ilias I, Pacak K. Current approaches and recommended algorithm for the diagnostic localization of pheochromocytoma. J Clin Endocrinol Metab. 2004;89(2):479–91.
31. van den Berg R, Schepers A, de Bruïne FT, Liauw L, Mertens BJA, van der Mey AGL, et al. The value of MR angiography techniques in the detection of head and neck paragangliomas. Eur J Radiol. 2004;52(3):240–5.
32. van den Berg R. Imaging and management of head and neck paragangliomas. Eur Radiol. 2005;15(7):1310–8.
33. Hoegerle S, Ghanem N, Altehoefer C, Schipper J, Brink I, Moser E, et al. 18F-DOPA positron emission tomography for the detection of glomus tumours. Eur J Nucl Med Mol Imaging. 2003;30(5):689–94.
34. Lieberson RE, Adler JR, Soltys SG, Choi C, Gibbs IC, Chang SD. Stereotactic radiosurgery as the primary treatment for new and recurrent paragangliomas: is open surgical resection still the treatment of choice? World Neurosurg. 2012;77(5–6):745–61.
35. Karaman E, Isildak H, Yilmaz M, Edizer DT, Ibrahimov M, Cansiz H, et al. Management of paragangliomas in otolaryngology practice: review of a 7-year experience. J Craniofac Surg. 2009;20(4):1294–7.
36. Gaynor BG, Elhammady MS, Jethanamest D, Angeli SI, Aziz-Sultan MA. Incidence of cranial nerve palsy after preoperative embolization of glomus jugulare tumors using Onyx. J Neurosurg. 2014;120(2):377–81.
37. Gartrell BC, Hansen MR, Gantz BJ, Gluth MB, Mowry SE, Aagaard-Kienitz BL, et al. Facial and lower cranial neuropathies after preoperative embolization of jugular foramen lesions with ethylene vinyl alcohol. Otol Neurotol. 2012;33(7):1270–5.
38. Shen J, Yu R. Perioperative management of pheochromocytoma: the heart of the issue. Minerva Endocrinol. 2013;38(1):77–93.
39. Pacak K. Preoperative management of the pheochromocytoma patient. J Clin Endocrinol Metab. 2007;92(11):4069–79.
40. Naranjo J, Dodd S, Martin YN. Perioperative management of pheochromocytoma. J Cardiothorac Vasc Anesth. 2017;31(4):1427–39.
41. Roizen MF, Hunt TK, Beaupre PN, Kremer P, Firmin R, Chang CN, et al. The effect of alpha-adrenergic blockade on cardiac performance and tissue oxygen delivery during excision of pheochromocytoma. Surgery. 1983;94(6):941–5.
42. Gu YW, Poste J, Kunal M, Schwarcz M, Weiss I. Cardiovascular manifestations of pheochromocytoma. Cardiol Rev. 2017;25(5):215–22.
43. Melmed S, Polonsky KS, Reed Larsen P, Kronenberg HM. Williams textbook of endocrinology. 12th ed. Philadelphia, PA: Elsevier; 2011.
44. Naruse M, Satoh F, Tanabe A, Okamoto T, Ichihara A, Tsuiki M, et al. Efficacy and safety of metyrosine in pheochromocytoma/paraganglioma: a multi-center trial in Japan. Endocr J. 2018;65(3):359–71.
45. Wachtel H, Kennedy EH, Zaheer S, Bartlett EK, Fishbein L, Roses RE, et al. Preoperative metyrosine

improves cardiovascular outcomes for patients undergoing surgery for pheochromocytoma and paraganglioma. Ann Surg Oncol. 2015;22(Suppl 3):S646–54.
46. Tsirlin A, Oo Y, Sharma R, Kansara A, Gliwa A, Banerji MA. Pheochromocytoma: a review. Maturitas. 2014;77(3):229–38.
47. Jensen NF. Glomus tumors of the head and neck: anesthetic considerations. Anesth Analg. 1994;78(1):112–9.
48. Erdoğan MA, Uçar M, Özkan AS, Özgül Ü, Durmuş M. Perioperative management of severe hypertension during laparoscopic surgery for pheochromocytoma. Turk J Anaesthesiol Reanim. 2016;44(1):47–9.
49. Castillo-Monzón CG, Marroquín-Valz HA, Fernández-Villacañas-Marín M, Moreno-Cascales M, García-Rojo B, Candia-Arana CA. Comparison of the macintosh and airtraq laryngoscopes in morbidly obese patients: a randomized and prospective study. J Clin Anesth. 2017;36:136–41.
50. Rabinowitz MR, Cognetti DM, Nyquist GG. Blood-sparing techniques in head and neck surgery. Otolaryngol Clin N Am. 2016;49(3):549–62.
51. Lentschener C, Gaujoux S, Tesniere A, Dousset B. Point of controversy: perioperative care of patients undergoing pheochromocytoma removal-time for a reappraisal? Eur J Endocrinol. 2011;165(3):365–73.
52. Robertson JI. Carcinoid syndrome and serotonin: therapeutic effects of ketanserin. Cardiovasc Drugs Ther. 1990;4(Suppl 1):53–8.
53. Roy RC, Carter RF, Wright PD. Somatostatin, anaesthesia, and the carcinoid syndrome. Perioperative administration of a somatostatin analogue to suppress carcinoid tumour activity. Anaesthesia. 1987;42(6):627–32.
54. Motegi H, Terasaka S, Yamaguchi S, Kobayashi H, Asaoka K, Iwasaki Y. A case of catecholamine-secreting glomus jugulare tumor: treatment strategy and perioperative management. No Shinkei Geka. 2008;36(11):1029–34.
55. Hack HA. The perioperative management of children with phaeochromocytoma. Pediatr Anesth. 2000;10(5):463–76.
56. Plouin PF, Amar L, Dekkers OM, Fassnacht M, Gimenez-Roqueplo AP, Lenders JWM, et al. European society of endocrinology clinical practice guideline for long-term follow-up of patients operated on for a phaeochromocytoma or a paraganglioma. Eur J Endocrinol. 2016;174(5):G1–10.

Anesthesia for the EXIT Procedure

33

Anna Gitterman, Matthew Reschke, and David J. Berman

Introduction

The Ex *Utero* Intrapartum Treatment procedure is a rarely-performed but transformative surgery performed at the time of cesarean delivery. Usually used as a method of controlling difficult airways in neonates, the EXIT procedure is gaining increasing popularity for a wide variety of indications. As the accuracy and precision of prenatal diagnosis continues to improve, the frequency of EXIT procedures is expected to increase.

Initially described in 1989 [1], the EXIT procedure typically consists of an open uterine incision, delivery of the fetal head and upper chest, and management of the fetal airway while maintaining uteroplacental perfusion for fetal oxygenation. This is followed by fetal delivery, with the potential for immediate definitive management versus direct NICU admission. As the fetus remains on placental support until complete delivery, the EXIT procedure allows the neonatal team precious time to manage an airway that would otherwise pose difficulty, allowing protection from hypoxic-ischemic encephalopathy during complicated airway management.

Key to the EXIT procedure are maternal hemodynamic management, maintenance of uterine relaxation, and preparedness for the rare but catastrophic potential for major hemorrhage. Additionally, the need for fetal anesthesia during these procedures often necessitates creative maternal anesthetic approaches: contrary to a traditional cesarean delivery, during the EXIT procedure fetal sedation and immobility are desired and sometimes essential.

Indications

Fetuses with neck masses and potential airway management challenges form the majority of EXIT procedure candidates. Significant compressive tumors or intrinsic airway stenosis are typical candidates for the procedure, where traditional vaginal or cesarean delivery would present a significant challenge in maintaining neonatal oxygen delivery during airway management attempts.

Since the development of the procedure, it has been used for a variety of other pathologies presenting challenges in neonatal management. These include conjoint twin separation [2], EXIT-to-ECMO procedure for cannulation of fetuses with otherwise lethal cardiac anomalies or cases of impossible airway management [3, 4],

A. Gitterman · M. Reschke · D. J. Berman (✉)
Department of Anesthesiology and Critical Care Medicine, Johns Hopkins Hospital, Baltimore, MD, USA
e-mail: agitter1@jhmi.edu; mreschk1@jhmi.edu; DaveBerman@jhmi.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_33

congenital high airway obstruction syndrome (CHAOS) [5], and removal of temporary clips applied to allow for lung development in severe congenital diaphragmatic hernia [6]. While thought of as a short-term method for oxygenation during airway management, the EXIT procedure has been successfully used to maintain fetal perfusion for greater than 1 h while surgical resection and airway management were ongoing [7]. Given the variety of fetal conditions which could benefit from repair on placental bypass, the indications for an EXIT procedure will likely continue to expand over time.

Perioperative Planning

Fetal Prenatal Assessment

Prenatal assessment first begins with accurate prenatal diagnosis to facilitate multidisciplinary discussions, determine candidacy for an EXIT procedure, and subsequently begin operative planning. A detailed anatomical screen is performed as part of routine prenatal care between 18–20 weeks of gestation. As ultrasound technology allows for a very detailed assessment of fetal anatomy, abnormalities are often identified early allowing for referral to a fetal therapy center. Early identification allows time for additional prenatal testing and serial scans as indicated. Ultrasound also can identify placental pathology such as placenta previa or placenta accreta spectrum disorders which may impact surgical planning.

While prenatal testing is underway, a multidisciplinary team can begin to assemble. It is paramount that these discussions include the parents so they have an in-depth understanding of the procedure along with the associated risks/benefits and knowledge of alternative options. The multidisciplinary team can be tailored based upon the specific fetal pathology but will likely include members from maternal fetal medicine, obstetrics, pediatric surgery, pediatric otolaryngology, neonatal intensive care, pediatric cardiothoracic surgery, obstetric anesthesiology, pediatric anesthesiology, radiology, social work, and operating room support staff including nursing and scrub technologists [8].

A thorough understanding of the fetal pathophysiology is critical for success. Fetal prenatal testing considered may include fetal echocardiography, genetic testing, and anatomic modeling [9]. Fetal echocardiography should be strongly considered to assess for heart failure which may limit the ability of the fetus to tolerate the EXIT procedure. The team must also monitor for the development of fetal hydrops from cardiac failure, lymphatic abnormalities, or venous obstructions that would likely expedite timing of delivery [9].

Polyhydramnios is often identified in patients considered for EXIT procedures given the compression and/or obstruction of the esophagus and trachea by large neck or mediastinal masses. A thorough history of amnioreductions and any resulting complications such as preterm contractions requiring tocolytic therapy can help guide management. This may not only impact the timing of delivery but can impact anesthetic management.

Timing of an EXIT procedure must be decided in conjunction with the multidisciplinary team. Ideal timing of delivery takes into consideration complications of prematurity, maternal and fetal well being, and performance of the procedure before the onset of labor.

Procedural Steps

Prior to the procedure, the entire team must be ready and have the appropriate equipment available. Ideally, the team should be aware of all the members and their associated roles. There should be a detailed plan in terms of potential airway management strategies with clear communication to change techniques if one is not successful. Plans for managing acute complications such as maternal hemorrhage or premature placental separation should be in place.

Perioperative ultrasound evaluation is utilized to identify the location of the placenta and fetal position as well as to estimate fetal weight to calculate intraoperative medication dosages [10].

Skin and Uterine Incisions

The location and extent of skin and uterine incisions depend on the location of the placenta as well as the extent of fetal exposure needed for the procedure. While skin incisions are almost always transverse, midline vertical incisions have been performed depending on the indication for the procedure. For instance, in the case of fetuses with large neck masses, larger exposure may be necessary. Additionally, as the placenta will be used for fetal oxygenation and perfusion for a period of time after uterine incision, careful mapping out of placental edges is often undertaken by the surgical team to avoid disrupting the placental interface with the myometrium. If possible, the incision is made in the less-muscular lower uterine segment to reduce bleeding [9]. Hysterotomy is often made with a single use surgical stapling instrument or vascular clamps to minimize intraoperative bleeding [8].

Amniotic fluid serves as a barrier against uterine contraction and placental separation: when uterine entry is made, amniotic fluid will be lost and this can potentially lead to uterine contraction, placental separation, umbilical cord vessel compression or spasm, and heat loss. For this reason, warmed isotonic crystalloid is often infused via intravenous tubing directly into the uterine cavity to maintain adequate amniotic fluid volume. Tocolysis is also required as surgical stimulation can incite uterine contractions which in and of themselves can compromise fetal blood supply. Contractions can also precipitate premature separation of the placenta, further damaging fetal blood flow and inciting maternal hemorrhage [11].

Fetal Monitoring/Delivery

Following hysterotomy and delivery of the fetal head and torso, it is now possible to monitor fetal hemodynamics and administer medications to the fetus via IV or IM routes as needed. Fetal monitoring can be relatively simple involving a pulse oximeter or more involved with a scrubbed sterile cardiologist providing continuous echocardiography monitoring with information about heart rate, contractility, preload, and any wall motion abnormalities [10]. The chosen technique should be based upon the fetal pathology and information necessary to perform appropriate interventions.

Considerations for fetal medications/equipment to be immediately available:

- Pulse oximeter for fetal use
- Neonatal ambu bag for resuscitation or other oxygen supply
- End tidal CO_2 indicator
- Pediatric intravenous catheters
- Tourniquet (can use penrose drain)
- Resuscitation meds:
  - Epinephrine IV/ET 0.1 mg/mL—dosing 0.1–0.3 mL/kg
  - 1 mL syringe of atropine 0.01–0.03 mg/kg
  - Fentanyl, non depolarizing muscle relaxant
  - 10 mL NS syringes
  - Packed red blood cells for fetus
- Airway equipment with various ETT sizes, stylets, options for DL, VL, rigid bronchoscope or fiberoptic intubation, LMA size 1 if term baby
- Suction equipment
- Temperature probe
- Chemical mattress for warming and neonatal warmer
- Hat and blankets
- Supplies to place an umbilical vein line

Once the airway has been established or appropriate intervention complete, the umbilical cord is clamped and the remainder of the fetus is delivered and handed off to the appropriate neonatal team for resuscitation and possible interventions.

Uterine Tone Augmentation

Once the umbilical cord is clamped, return of maternal uterine tone is desired to reduce hemorrhage following delivery of the placenta. High dose inhalational volatile anesthetics are discon-

tinued in favor of intravenous anesthetics which do not affect uterine tone. Any uterine relaxants such as nitroglycerin are also stopped. Uterotonic medications are then administered in stepwise fashion until adequate uterine tone is achieved.

Manual uterine massage and closure of the hysterotomy are performed to improve tone and reduce bleeding. Ongoing hemorrhage despite maximal medical therapy must prompt consideration for surgical management including uterine artery embolization and/or hysterectomy.

Extubation/Emergence

Following hemostasis and achievement of adequate uterine tone, the remainder of the incision is closed. Considerations for extubation, in the case of general anesthesia, are similar to any anesthetic case. If the patient is hemodynamically stable without ongoing blood loss and demonstrates appropriate oxygenation and ventilation on minimal ventilation settings, extubation can be considered. The anesthetic agents are weaned as the procedure concludes and the mother should show signs that she is able to protect her airway such as the ability to follow commands prior to extubation. If any of these criteria are not met, mechanical ventilation should be continued with transfer to an intensive care unit for ongoing care until extubation is deemed safe.

Anesthetic Management Considerations

Main anesthetic concerns:

- Adequate uterine relaxation—often requiring 2 MAC (minimum alveolar concentration) of volatile anesthetic in addition to nitroglycerin [8]
- Critically important to maintain maternal hemodynamics; uterine vasculature is maximally dilated and the absence of autoregulation makes maintenance of mean arterial blood pressure paramount for fetal wellbeing
- Direct fetal anesthesia may be required, either given via direct intrasmuscular injection or via umbilical cord injection [8]

Maternal Perioperative Assessment

Maternal preoperative assessment requires a profound knowledge of maternal physiology and associated changes during pregnancy. Routine preoperative assessment documenting any pre existing comorbidities and anesthetic history should be thorough and detailed. Any personal or family history of malignant hyperthermia or difficult airway should be elicited. Pertinent to the choice of uterotonic agents is any history of hypertension, hypertensive disorders of pregnancy or reactive airway disease. Basic laboratory studies including complete blood counts should be obtained to evaluate platelet count prior to consideration of neuraxial anesthesia. A type and screen should be collected and communication with the institutional blood bank should take place to make sure blood is available the day of the procedure. In assessing the airway of a pregnant patient, it is important to remember that hormonal changes lead to vascular enlargement and often edema, which predisposes women to mucosal bleeding which can complicate airway management [8]. Some institutions, including our own, will have separate units of maternal and fetal blood in the operating room routinely during an EXIT procedure.

Personnel Available

Two separate anesthesiology teams are frequently present: one team provides maternal anesthesia, whereas the other provides monitoring and vascular access for the fetus on placental bypass. While institution-to-institution practices differ, at our institution the obstetric anesthesiology team

provides care to the mother whereas the pediatric anesthesiology team manages fetal concerns.

Key Decision: Neuraxial vs. General

While EXIT procedures are occasionally performed under neuraxial anesthesia, the majority of these procedures are performed under general anesthesia. This serves multiple purposes, namely to relax the uterus during the period of placental bypass as well as to provide some measure of anesthetic for the fetus. The choice between neuraxial and general anesthesia is a key decision and will affect all subsequent aspects of management. Primary considerations include the patient's medical history, airway exam noting any history or concern for a difficult airway, contraindications to neuraxial placement, and patient preference.

With neuraxial anesthesia, careful patient selection is required as the mother will be awake and conversant. Supplemental pharmacologic agents will be required to produce uterine relaxation necessary for surgical operating conditions. However, operations performed under neuraxial anesthesia have been shown to have less blood loss and less need for transfusion [12]. Additionally, the duration of placental bypass should be taken into consideration: if the duration of placental bypass is expected to be significant, neuraxial anesthesia is likely not the optimal choice.

After thorough explanation of the associated risks and benefits, patient preference must be considered. Given uncertainty surrounding ability to manage the fetal airway or other interventions that may be required, an awake patient must be prepared for the emotional strain this may cause.

Positioning and Monitoring

Once the mother is brought into the operating room, she will be laid supine with left uterine displacement to avoid aorto-caval compression and maintain maternal preload and cardiac output. Sequential compression devices should be placed on the bilateral lower extremities to reduce risk of venous stasis. Given potential for hemorrhage following placental separation with profound uterine relaxation, large bore peripheral IV access should be assured. Central access can also be considered for volume and/or circulatropic medication administration as indicated. Arterial access for precise blood pressure management is also recommended given the reliance of the fetus on maternal hemodynamics. Both high dose volatile anesthetic administration and possibly nitroglycerin, can have profound influences on mean arterial pressure. Additionally, given the risk of life threatening hemorrhage, arterial access is beneficial for frequent lab monitoring of acid/base status, hemoglobin measurements, and to precisely measure and treat any coagulopathy.

Induction/Intubation

Intubation is typically performed in a rapid-sequence fashion to minimize the risk of pulmonary aspiration. Aspiration prophylaxis with a non-particulate antacid such as sodium citrate can be considered prior to induction. While there are a variety of agents used for this purpose, our traditional approach in healthy mothers is to induce with propofol and high-dose rocuronium. Airway management is provider-specific, but judicious providers will often use video laryngoscopy to increase first-attempt success.

Unlike during a standard cesarean section, the goal of an EXIT procedure is to provide maximum uterine relaxation and adequate anesthesia to both the mother and the fetus. Although it is prudent to minimize the duration of the operation as feasible, there is no urgency in delivery following induction of anesthesia. This places an EXIT procedure in contrast to a normal cesarean delivery, where the aim is often for surgical incision immediately following intubation.

Uterine Relaxation Techniques/ Tocolysis

Multiple techniques have been successfully described to provide adequate maternal uterine relaxation and tocolysis to facilitate partial delivery for the EXIT procedure. Duration of placental bypass under general anesthesia described has ranged from 3–93 min [12].

Volatile anesthetics cause a dose-dependent reduction in uterine tone. The benefits of the halogenated vapors are multifold: they provide surgical anesthesia to the mother, have tocolytic effects, and supply intraoperative anesthesia for the fetus. Drawbacks to high dose volatile administration do exist and must be recognized and appropriately managed including maternal vasodilation and cardiac depression which can result in hypotension, placental hypoperfusion, and fetal cardiovascular depression [11]. In vitro studies have suggested that the tocolytic effects of sevoflurane and desflurane are greater than that of isoflurane [13]. Sevoflurane or desflurane over isoflurane use may also be advantageous in that recovery of uterine tone following discontinuation will be faster given the lower blood gas solubility.

There is some evidence to suggest that reducing the fetal exposure time to high dose volatile anesthetic may be advantageous. A retrospective review by Boat et al. analyzed records of 36 mothers and fetuses who underwent an EXIT procedure, half received high dose desflurane for maintenance anesthesia, and half had supplemental intravenous anesthesia (SIVA) with propofol and remifentanil with desflurane added for uterine relaxation at an appropriate interval after induction just prior to hysterotomy [11]. A significant increase in moderate-severe left ventricular systolic dysfunction was noted in the high dose desflurane group when compared with the SIVA group. The authors also noted a significant reduction in percentage of fetuses that required resuscitative interventions (fluid bolus, epinephrine or atropine) in the SIVA group (61% compared with 22%). This data suggests that limiting the time of exposure to high dose inhalational agents may be beneficial but further studies are required.

Intravenous pharmacologic agents to induce uterine relaxation are required in the case of neuraxial anesthesia and may be required as adjuncts if sufficient relaxation is not achieved with high dose volatile anesthesia alone. Nitroglycerin is often used for this purpose. Dosing strategies commonly use a loading dose of 25–100 μg followed by an infusion at 1–20 μg/kg/min [12]. Placental transfer of nitroglycerin has not been shown to have any significant fetal hemodynamic effects. Advantages of nitroglycerin include quick onset and offset in addition to ease of titration [14]. It must be recognized that nitroglycerin can cause headache in the awake parturient and can cause methemoglobinemia with prolonged high dose infusions [10].

Other medications commonly used in obstetric patients for tocolysis include magnesium and terbutaline. Magnesium is a calcium antagonist and acts to relax smooth muscle. Magnesium is often used in preterm labor for fetal neuroprotection [15]. Prior to induction of anesthesia it is important to be aware that magnesium can increase sensitivity to depolarizing and non depolarizing neuromuscular medications [10]. Terbutaline, a **β**2 agonist, is also a smooth muscle relaxant acting through the adenylyl cyclase pathway [15]. Neither magnesium nor terbutaline are easily titratable or reversible and thus are not optimal choices for uterine relaxation in EXIT patients.

Administration of high dose volatile anesthesia with adjunctive uterine relaxants can have profound impact on maternal blood pressure [16]. Often vasopressor infusions such as phenylephrine or norepinephrine are required to maintain uteroplacental perfusion. Although not commonly employed at our institution, dopamine and angiotensin II infusions have also been used to maintain adequate mean arterial pressures [12].

Fetal Anesthetics

The choice of anesthetic agents for maternal anesthesia directly influences fetal anesthesia. As previously discussed, the inhaled volatile anesthetics readily cross the placenta and provide fetal anesthesia. Similarly, remifentanil, an ultrashort acting opioid medication undergoes extensive placental transfer as evidenced by a UV: MA of 0.88. Infusion doses at 0.1–0.15 μg/kg/min have been used safely in mothers with mild sedation with no adverse respiratory outcomes. Furthermore, remifentanil redistributes and is metabolized by nonspecific blood and tissue esterases in the fetus with low umbilical artery:umbilical vein ratio 0.29 limiting adverse fetal events [12, 17]. Remifentanil can be used to supplement neuraxial anesthesia or general anesthesia as it will provide fetal analgesia and fetal immobility [17].

A second pediatric anesthesiology team is present to provide care specifically for the fetus perioperatively. This anesthesia provider will also be in charge of providing anesthesia to the fetus should procedures be required after delivery. Following delivery of the fetal head and torso, intravenous access can be obtained and medications administered directly to the fetus via IV or IM injections. Commonly used medications include opioids such as fentanyl for analgesia and neuromuscular blocking drugs to facilitate operating conditions. Emergency drugs such as atropine and epinephrine should also be readily available.

A technique used in fetoscopic surgery can also be employed for administration of medication directly to the fetus prior to hysterotomy. Ultrasound is used to guide instruments into the uterus where medications are injected intramuscularly or into the umbilical cord.

Reversal of Uterine Relaxation

Following delivery of the fetus, establishment of uterine tone is desired to prevent hemorrhage. High dose inhalational agents and any uterotonins are discontinued and uterotonics administered. Oxytocin is most often the first line uterotonic. This synthetic version of the posterior pituitary hormone binds to receptors in the myometrium. Receptor binding stimulates increased sodium permeability and incites uterine smooth muscle contraction. If adequate uterine contraction has not been achieved after administration of oxytocin, additional uterotonics are warranted and selected based on maternal comorbidities. Second line agents include methylergonovine and carboprost. Methylergonovine is an ergot alkaloid that causes tetanic contractions. Its use can precipitate severe hypertension and should be used cautiously in parturients with pre-existing hypertension or preeclampsia. Carboprost (Hemabate) is an prostaglandin $F_2\alpha$ analog that increases calcium concentrations augmenting uterine contractions [18].

Postoperative Pain Management

At many institutions, epidural catheters are placed preoperatively for perioperative and postoperative use. Typically, the epidural catheter is bolused with lidocaine, bupivacaine and/or fentanyl prior to emergence in order to ensure adequate maternal analgesia. Some advocate for a single injection of spinal morphine prior to the procedure rather than leaving an epidural catheter in place due to lower perceived risk and ability to ambulate postoperatively. This is typically added to a multimodal regimen including scheduled acetaminophen, non-steroidal anti-inflammatory medications, and breakthrough systemic opiate therapy as necessary. Even for procedures performed under general anesthesia, consideration should be made for a single-shot spinal injection of morphine.

An emerging area of clinical practice is the non-neuraxial anesthetic approach for post-EXIT analgesia. At our institution, in the event of maternal contraindication to neuraxial anesthesia, we offer quadratus lumborum (QL) or transversus abdominal plane (TAP) blocks for post-cesarean analgesia as part of a multimodal pain pathway [19, 20]. Some groups have begun offering erector spinae plane (ESP) blocks for

post-cesarean analgesia, though experience in the EXIT procedure is limited [20, 21].

The Society for Obstetric Anesthesia and Perinatology recently released their consensus statement on Enhanced Recovery after Cesarean consensus statement, detailing optimal post-cesarean analgesia [22]. From a postoperative standpoint, an EXIT procedure recovery is similar to a standard cesarean delivery.

Outcomes

Maternal risks to the EXIT procedure include hemorrhage, wound infections, and future risk of uterine dehiscence/rupture. Hemorrhage is of particular concern given the significant uterine relaxation required for the procedure. Estimated blood loss with the EXIT procedure is reported to be approximately 1ooo mL [9, 12], with 23% of mothers requiring transfusion [23]. When compared with matched controls who underwent cesarean delivery, a retrospective review reported a significantly higher estimated blood loss in EXIT patients (1104 mL vs. 883 mL) [24].

A recent metaanalysis assembled 224 patients (214 managed with general anesthesia, 10 using regional anesthesia) [12]. The analysis reported only eight postpartum hemorrhages (blood loss > 2000 mL) in the general anesthesia group, five of whom required transfusion. No maternal deaths were reported in either group. Fetal mortality rate was 10.31% (23/223). Causes of fetal mortality included failure to oxygenate and intubate, parental refusal of tracheostomy, hemorrhage, pulmonary hypoplasia and cardiac failure in the neonatal intensive care unit.

Wound complications have been reported to be higher in EXIT patients compared with cesarean delivery patients (15% vs. 2%) [24]. It is important to note that the EXIT patients in this cohort had undergone previous open or laparoscopic fetal surgery an average of 24–29 days prior to an EXIT procedure. Previous uterine instrumentation may have placed them at a higher risk of infection. A more recent study showed wound complications in only 8% of EXIT patients [23]. The rate of surgical site infections following cesarean sections worldwide is reported at 3–15% [25]. Surgery duration over 1 h has also been identified as a risk factor for the development of SSI [25].

In a review of maternal morbidity and reproductive outcomes following fetal surgery including EXIT procedures and mid-gestation open maternal fetal surgery based on survey response, 100% of women who attempted future pregnancies following EXIT procedures were successful, with 8% complicated by uterine dehiscence [23]. 17% of EXIT patients even had a successful trial of labor after cesarean delivery. An interval at least 2 years is recommended following EXIT procedure prior to subsequent pregnancy [23].

Fetal outcomes reported are also largely favorable. A recent literature review examined 24 reports of 28 prenatally diagnosed cases of upper airway obstruction management by EXIT with tracheostomy [26]. The survival rate for infants with complete laryngeal atresia is reported as 94%, which is higher than the 50% reported for those infants with tracheal atresia.

Ethical Issues

Despite the fact that there are two patients in the operating room, the mother must be the first priority of the team. No intervention can be performed that places undue risk upon the mother. As indications for the EXIT procedure expand, it will be critical to continue to analyze and evaluate maternal and fetal outcomes.

Parents must have a full understanding of the fetal pathology and any other complex comorbidities that exist for the neonate that would be life-limiting. Involvement of neonatology and social work during the planning period must take place to guide parents in understanding the implications of caring for a child with complex medical conditions. Finally, questions still surround the effect of inhalational anesthetic agents on the fetus early in life. This is an area of ongoing research [10].

Conclusions

The EXIT procedure is a remarkable intervention that allows for the management of the fetal airway while maintaining uteroplacental perfusion and fetal oxygenation. This technique allows survival for previous lethal fetal conditions while avoiding ischemic injury to the fetus. Key to the procedure is an integrated multidisciplinary team who work together with constant communication. The EXIT procedure has been performed safely and successfully under both general and neuraxial anesthesia.

Individual patient factors and considerations will help guide an individualized anesthetic plan. Other vital components of anesthetic management include maintaining adequate uterine relaxation, sustaining placental perfusion, determining if additional fetal analgesia/anesthesia is required, and monitoring for complications such as post partum hemorrhage.

Thankfully, maternal complications following EXIT procedures seem to be similar to a traditional cesarean delivery. While ongoing research is required to continue to evaluate and refine the EXIT procedure, it remains a safe clinical technique when correctly indicated.

Funding Disclosures and Conflicts of Interest None to disclose as related to this project.

References

1. Norris MC, Joseph J, Leighton BL. Anesthesia for perinatal surgery. Am J Perinatol. 1989;6:39–40.
2. Marwan A, Crombleholme TM. The EXIT procedure: principles, pitfalls, and progress. Semin Pediatr Surg. 2006;15:107–15.
3. Michel TC, Rosenberg AL, Polley LS. EXIT to ECMO. Anesthesiology. 2002;97:267–8.
4. Matte GS, Connor KR, Toutenel NA, Gottlieb D, Fynn-Thompson F. A modified EXIT-to-ECMO with optional reservoir circuit for use during an EXIT procedure requiring thoracic surgery. J Extra Corpor Technol. 2016;48:35–8.
5. Bouchard S, Johnson MP, Flake AW, Howell LJ, Myers LB, Adzick NS, Crombleholme TM. The EXIT procedure: experience and outcome in 31 cases. J Pediatr Surg. 2002;37:418–26.
6. Harrison MR, Adzick NS, Flake AW, et al. Correction of congenital diaphragmatic hernia in utero VIII: Response of the hypoplastic lung to tracheal occlusion. J Pediatr Surg. 1996;31:1339–48.
7. Rahbar R, Vogel A, Myers LB, et al. Fetal surgery in otolaryngology: a new era in the diagnosis and management of fetal airway obstruction because of advances in prenatal imaging. Arch Otolaryngol Head Neck Surg. 2005;131:393–8.
8. Kuczkowski KM. Advances in obstetric anesthesia: anesthesia for fetal intrapartum operations on placental support. J Anesth. 2007;21:243–51.
9. Bence CM, Wagner AJ. Ex utero intrapartum treatment (EXIT) procedures. Semin Pediatr Surg. 2019;28:150820.
10. Garcia PJ, Olutoye OO, Ivey RT, Olutoye OA. Case scenario: anesthesia for maternal-fetal surgery: the ex utero intrapartum therapy (EXIT) procedure. Anesthesiology. 2011;114:1446–52.
11. Boat A, Mahmoud M, Michelfelder EC, Lin E, Ngamprasertwong P, Schnell B, Kurth CD, Crombleholme TM, Sadhasivam S. Supplementing desflurane with intravenous anesthesia reduces fetal cardiac dysfunction during open fetal surgery. Paediatr Anaesth. 2010;20:748–56.
12. Kumar K, Miron C, Singh SI. Maternal anesthesia for EXIT procedure: a systematic review of literature. J Anaesthesiol Clin Pharmacol. 2019;35:19–24.
13. Yoo KY, Lee JC, Yoon MH, Shin M-H, Kim SJ, Kim YH, Song TB, Lee J. The effects of volatile anesthetics on spontaneous contractility of isolated human pregnant uterine muscle: a comparison among sevoflurane, desflurane, isoflurane, and halothane. Anesth Analg. 2006;103:443–7, table of contents.
14. Benonis JG, Habib AS. Ex utero intrapartum treatment procedure in a patient with arthrogryposis multiplex congenita, using continuous spinal anesthesia and intravenous nitroglycerin for uterine relaxation. Int J Obstet Anesth. 2008;17:53–6.
15. Arrowsmith S, Kendrick A, Wray S. Drugs acting on the pregnant uterus. Obstet Gynaecol Reprod Med. 2010;20:241–7.
16. Oliveira E, Pereira P, Retroz C, Mártires E. Anesthesia for EXIT procedure (ex utero intrapartum treatment) in congenital cervical malformation—a challenge to the anesthesia provider. Braz J Anesthesiol. 2015;65:529–33.
17. Fink RJ, Allen TK, Habib AS. Remifentanil for fetal immobilization and analgesia during the ex utero intrapartum treatment procedure under combined spinal-epidural anaesthesia. Br J Anaesth. 2011;106:851–5.
18. Vallera C, Choi LO, Cha CM, Hong RW. Uterotonic medications: oxytocin, methylergonovine, carboprost, misoprostol. Anesthesiol Clin. 2017;35:207–19.
19. Gupta A, Sondekoppam R, Kalagara H. Quadratus lumborum block: a technical review. Curr Anesthesiol Rep. 2019;9:257–62.

20. Kelly S, Kelly S, Malhotra R. Ultrasound-guided transversus abdominis plane blocks for analgesia post cesarean section. Compar Effective Res. 2011;1:35–8.
21. Rincón C, Moreno DA, Moore A. Erector spinae plane block for post-cesarean delivery analgesia. Int J Obstet Anesth. 2020;41:120–2.
22. Bollag L, Tiouririne M, Lim G, Carvalho B, Zakowski M, Bhambhani M, Hunt E, Landau R, Habib A. Enhanced recovery after cesarean (ERAC)—beyond the pain scores. Int J Obstet Anesth. 2020;43:36–8.
23. Zamora IJ, Ethun CG, Evans LM, Olutoye OO, Ivey RT, Haeri S, Belfort MA, Lee TC, Cass DL. Maternal morbidity and reproductive outcomes related to fetal surgery. J Pediatr Surg. 2013;48:951–5.
24. Noah MMS, Norton ME, Sandberg P, Esakoff T, Farrell J, Albanese CT. Short-term maternal outcomes that are associated with the EXIT procedure, as compared with cesarean delivery. Am J Obstet Gynecol. 2002;186:773–7.
25. Zuarez-Easton S, Zafran N, Garmi G, Salim R. Postcesarean wound infection: prevalence, impact, prevention, and management challenges. Int J Women's Health. 2017;9:81–8.
26. Kumar M, Gupta A, Kumar V, Handa A, Balliyan M, Meena J, Roychoudhary S. Management of CHAOS by intact cord resuscitation: case report and literature review. J Matern Fetal Neonatal Med. 2019;32:4181–7.

34 Anesthesia for Placenta Accreta Spectrum (PAS) Disorders

Swarup Sri Varaday and Andrew Pauszek

Learning Points

- Placenta accreta spectrum is becoming increasingly more common and carries a significant morbidity and mortality. The risk is higher in patients with placenta previa and prior cesarean section.
- It is important for the obstetricians to know the risk factors and have a low threshold for antenatal ultrasound and other imaging studies that can help guide the diagnosis.
- It is strongly emphasized on early anesthesia consultation and multidisciplinary approach to preparation for delivery and postpartum care.
- Cesarean hysterectomy is associated with massive bleeding and should be performed by the most experienced surgeons and anesthesiologists.
- General anesthesia for cesarean hysterectomy is preferred over neuraxial anesthesia because of increase risk of massive bleeding and hemodynamic stability.

Introduction

The placenta accreta spectrum (PAS) refers to a group of disorders in which placental tissue abnormally adheres to or invades through the uterine myometrium. It may be further subclassified into three pathologies depending on the degree of placental translocation across the decidua basalis layer of endometrium—placenta accreta vera, placenta increta, and placenta percreta(Fig. 34.1). Placenta accreta vera involves attachment of the placental villi through the endometrium to the outer myometrium. Placenta increta reflects deeper invasion into the myometrium. Finally, placenta percreta indicates extension through the myometrium and uterine serosa with possible invasion into surrounding pelvic structures.

First described in the international literature in 1937 at the Boston Lying-In Hospital by obstetrician Frederick C. Irving and pathologist Arthur T. Hertig, PAS disorders have long caused challenges for the obstetrician and anesthesiologist. In their original case series of 18 patients with placenta accreta, Irving and Hertig observed major hemorrhage after attempts were made to remove the placenta. In 14 of the cases, emergency or secondary hysterectomy was required to control the bleeding [1].

Indeed, to this day, PAS disorders are a significant cause of maternal morbidity and mortality as a result of peripartum hemorrhage. The average

S. S. Varaday (✉) · A. Pauszek
Washington University School of Medicine,
Saint Louis, MO, USA
e-mail: Varadays@wustl.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_34

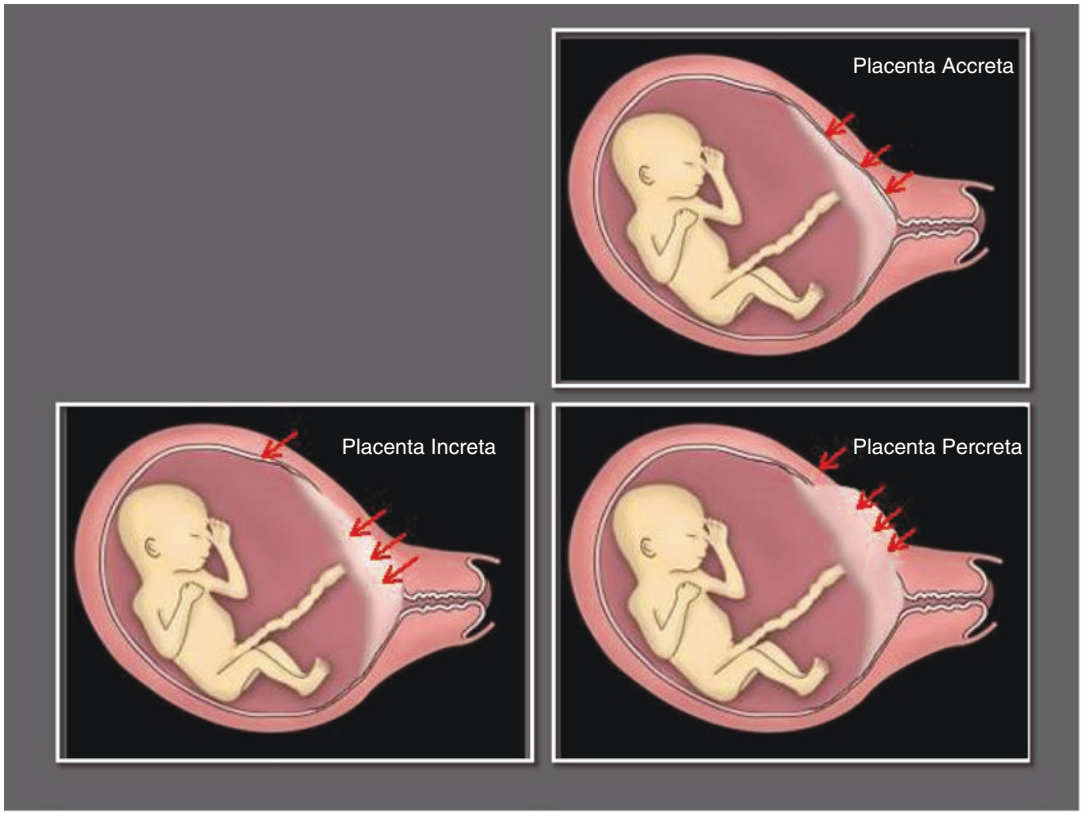


Fig. 34.1 Placenta accreta syndrome. Courtesy: www.obimages.net

blood loss at delivery has been reported to range from 3000 to 5000 mL [2]. Blood loss is often even more significant in cases of increta or percreta with greater extension of placental tissue. Subsequent disseminated intravascular coagulation (DIC), multiorgan failure, thromboembolism, and even death may ensue as a result of hemorrhage [3]. Parturients with PAS disorders frequently require blood products and ICU admission. Additional surgery is often necessary to control bleeding. In fact, PAS disorders are the most common indication for a peripartum hysterectomy. Surgical intervention itself is associated with incidental cystotomy, ureteral injury, vesicovaginal fistula, and need for reoperation [4].

PAS disorders are estimated to occur in 1 per 333–533 deliveries [5]. Interestingly, the incidence has increased over the past 50 years from 1 in 4000 deliveries in the 1970s, to 1 in 2500 deliveries in the 1980s, and, most recently, to the current rate [6, 7]. This increase has mirrored the increasing rate of caesarian delivery. For example, in the United States, the caesarian section rate jumped from 12.5% in 1982 to 23.5% in 2002 [8]. As any anomaly or injury to the uterine wall (even iatrogenic) can lead to PAS disorders, it is very likely that the increased incidence of PAS disorders is at least partially a consequence of the increased caesarian rate.

Fittingly, the recent increase in PAS disorders has spawned a considerable amount of research on the optimal diagnosis and treatment strategies, both from an obstetric and anesthetic perspective. While multidisciplinary care at centers of excellence (CoE) has been shown to reduce maternal morbidity, there is still much debate on the best way to care for patients with PAS disorders [9]. The purpose of this chapter is to review the most up-to-date literature and guidelines pertaining to the peripartum anesthetic management of this disease.

Pre-anesthesia Evaluation of PAS Disorder

Risk Factors and Pathophysiology

Although PAS disorders are most often diagnosed before delivery in the developed world, peripartum hemorrhage still contributes to 150,000 maternal deaths around the world each year [10]. Despite advances in available diagnostic techniques, the anesthesiologist should be keenly aware of the risk factors for the disorder and have a detailed plan for potential massive hemorrhage when one or several of these factors are present. The single strongest risk factor is the presence of placenta previa, which is is found in approximately half of all cases [11]. Coupled with a history of prior caesarian section (Fig. 34.2), the risk for PAS disorder has been estimated at 11% for a history of 1 previous caesarian section, 40% for 2 prior, 61% for 3, and 67% for 4 or more [12].

Because the proposed pathophysiology of PAS disorders centers on the abnormal decidualization of the endometrial epithelium and, thus, abnormal trophoblast invasion, any structural abnormality of or local injury to the uterine endometrium may lead to the disorder. In this regard, the following conditions have all been implicated (Fig. 34.3), bicornate uterus and submucosal fibroids, as well as histories of prior D + C, hysteroscopic surgery, pelvic radiation, and anterior myomectomy. Finally, other risk factors include advanced maternal age (age > 36 years), multiparity, prior history of PAS disorder, use of assisted reproduction techniques (ART), hypertensive disorders, and tobacco use [13].

Diagnosis

PAS disorders are often first diagnosed on second trimester ultrasound. An early diagnosis is key to facilitating adequate peripartum counseling and planning. Ultrasound modalities, including greyscale, color, and 3D power Doppler, have been shown to have a high degree of sensitivity and specificity in several studies. A systematic review and meta-analysis in 2013 yielded a sensitivity of 90.7% along with a specificity of 96.94% [14]. Likewise, another systematic review in 2017 showed a sensitivity of 90.9% [15]. Ultrasound findings (Fig. 34.4) suggesting a PAS disorder include the presence of large or irregular placental lacunae, a loss of hypoechoic retroplacental zone (representing abnormal extension of chorionic villi), and patterns of hypervascularization within the placenta [16]. Despite their merits, ultrasound techniques can only identify abnormal placentation. They cannot be used to discern the degree of invasion and cannot distinguish between accreta and percreta.

On the other hand, MRI does provide the increased spatial resolution to determine the degree of invasion in increta or percreta. It shows similar sensitivity and specificity when compared to ultrasound and may be utilized when adequate ultrasound views are difficult to obtain. A 2014 systematic review and meta-analysis found a sen-

Fig. 34.2 Increased risk of placenta accrete with prior cesarean section

History of Prior C-Section	Risk of Placenta Accreta
1 Prior C-Section	11%
2 Prior C-sections	40%
3 Prior C-sections	61%
4 or more C-sections	67%

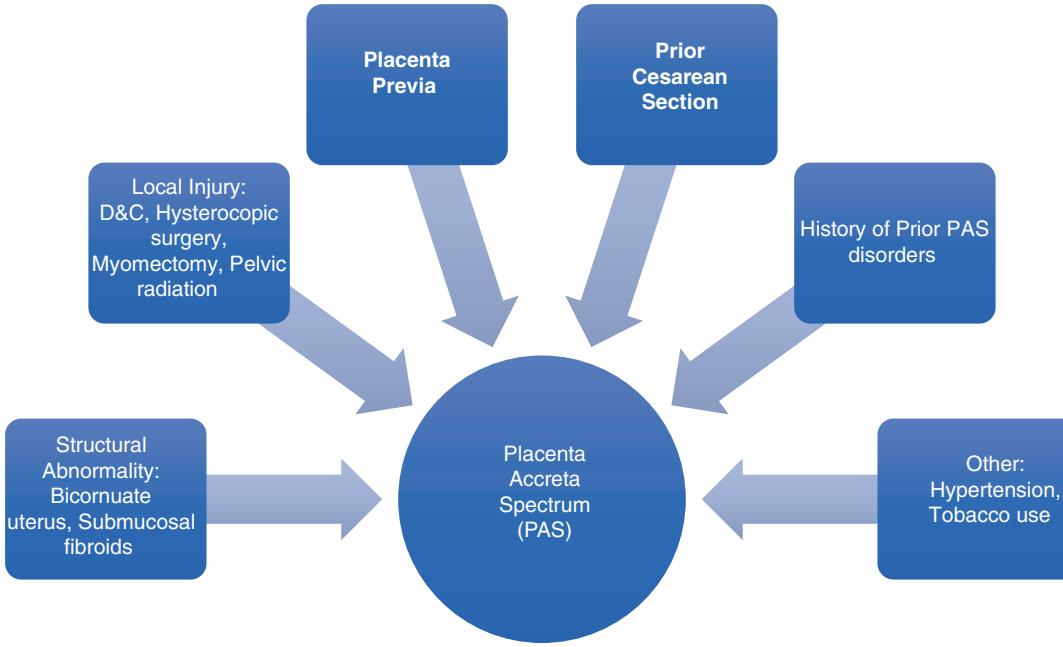


Fig. 34.3 Factors causing placenta accreta spectrum

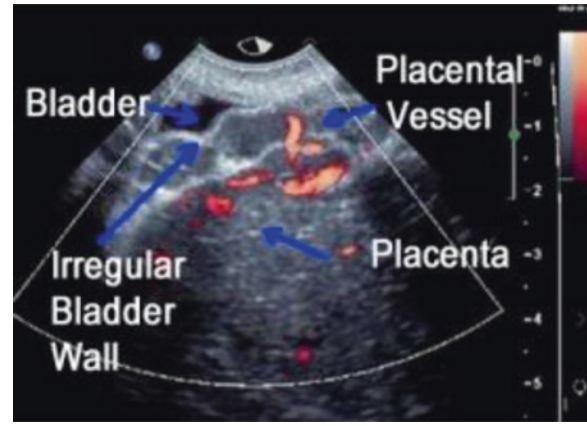


Fig. 34.4 U/S Doppler showing placental invasion of bladder wall. Courtesy: www.obimages.net

sitivity of 94.4% and specificity of 84% in a pooled set of 18 studies [17]. However, as it is often not available in resource poor environments and ultrasound is comparable in efficacy, MRI should not be considered an essential tool for screening purposes.

Overall, the modalities available today for the diagnosis of PAS disorders suggest high reliability. However, many of the studies focus on data collected by experts at centers specializing in prenatal diagnosis, not by nonexpert operators during routine midtrimester ultrasounds. This may overestimate the diagnostic utility of these tools. Screening for PAS disorders is not routinely taught in ultrasound training, and there is no universally defined set of diagnostic criteria for either modality. In fact, there is evidence from population studies that 50–66% of cases of PAS disorder are not diagnosed before delivery [16]. Thus, when reviewing a parturient's diagnostics

to develop an anesthetic plan for delivery, the anesthesiologist should consider the context of the studies and be prepared for all possible scenarios.

Obstetric Management

When PAS disorders are diagnosed prenatally, the usual management strategy is planned caesarian hysterectomy. Scheduled deliveries that are nonemergent have been associated with lower maternal morbidity. However, there is no consensus on what the optimal gestational age is to pursue a planned delivery. Case series from different centers show planned deliveries ranging from 34 to 38 weeks gestation [18, 19]. Since a considerable number of cases of PAS disorder are accompanied by placenta previa, most centers opt for late preterm (34–35 weeks) or early term (37 weeks), as further postponement of delivery may pose an increased risk for prepartum hemorrhage or emergent surgery. These considerations are always weighed on a case-by-case basis against the potential neonatal issues associated with a nonterm delivery.

While caesarian hysterectomy and avoidance of purposeful placental removal may reduce blood loss during delivery, performance of the hysterectomy itself often still leads to significant blood loss. The hysterotomy alone in cases of PAS disorder may cause 500–800 mL of blood loss [19]. Additionally, many cases of PAS disorder are also accompanied by bladder adherence to the lower uterine segment and neovascularization of several pertinent surgical planes [20]. These issues have prompted obstetricians to begin to employ new surgical approaches such as the use of linear cutters for the hysterotomy and vessel sealing systems for mobilization of the bladder with some possible benefit [20]. In addition to seeing a rise in the use of novel surgical techniques from their obstetric colleagues, anesthesiologists are increasingly finding themselves working alongside interventional radiologists in the care of patients with PAS disorder.

Both the use of balloon occlusion catheters and bilateral uterine artery embolization have been proposed as adjunctive treatments to decrease blood loss and maternal morbidity. Balloon occlusion catheters are devices typically inserted into the bilateral internal iliac or uterine arteries by an interventional radiologist, which can then be inflated during a caesarian hysterectomy. Several studies have posited their efficacy. For example, in a 2012 retrospective study of 117 patients with PAS disorders, those who received uterine artery balloons (UABs) preoperatively had a lower mean estimated blood loss (EBL) intraoperatively as well as less need for massive transfusion (>6 units of packed red blood cells.) [21] However, it is not clear that there is equal benefit to this in all forms of PAS disorders. A 2014 prospective study of 23 patients found that the use of internal iliac balloon catheters decreased the mean EBL and number of blood products transfused only in the subset of patients with placenta percreta and not in the accreta or increta groups [22].

Indeed, beyond the question of which subset of patients may benefit from balloon occlusion, questions also remain as to when to inflate the balloons. Data in some studies actually show increased bleeding with balloon inflation. There is a possibility that routine inflation without the presence of massive hemorrhage can paradoxically lead to increased bleeding due to the recruitment of collateral circulation in the pelvis. Thus, at the present time, there is no definitive role that balloon occlusion catheters play for patients with PAS disorder.

The other major adjunctive tool being used in the care of PAS disorder is uterine artery embolization (UAE.) Relying on the same mechanistic reasoning as balloon occlusion, UAE has been studied in patients with PAS disorder both as a way to decrease blood loss with caesarian hysterectomy and also as a means to achieve uterine preservation. In a systematic review of 177 cases of PAS disorder, ~90% of the patients were able to make it through delivery without immediate hysterectomy. Further, a secondary hysterectomy was needed in only 11.3% of cases [23]. Still, this study and most others do not clearly define the indications for hysterectomy or document the degree of placental invasion. This may account

for the finding that, overall, the use of UAE in uterine preservation strategies is still associated with notable maternal morbidity, including sepsis and uterine necrosis [24].

Conversely, when UAE is used prophylactically during a caesarian hysterectomy, there is some evidence of efficacy. UAE following the caesarian delivery but prior to hysterectomy may contribute to decreased blood loss and accelerate placental tissue absorption [25]. In a 2018 retrospective review of 31 patients, UAE was found to be safe and effective in decreasing EBL and transfusion requirements in a subgroup of patients with placenta increta [26]. Another promising application of UAE during caesarian hysterectomy is its use in hybrid operating rooms also capable of radiologic interventions. A case series from 2019 at a university hospital in Japan describes such a method in the successful management of three patients with placenta percreta [27]. Of note, a specific benefit of this approach to the anesthesiologist may be minimizing the transport time of unstable parturients.

Finally, the obstetric team may opt for expectant management, which is also known as leaving the placenta *in situ*. The reasoning behind this approach is that, while attempting to remove placental tissue during delivery is a well-established potential cause of massive hemorrhage, caesarian hysterectomy also comes with a high rate of maternal morbidity as well as mortality (~7% in placenta percreta) [25]. Leaving the placenta behind after delivery avoids both issues and relies on the progressive necrosis, involution, and detachment of tissue. This technique may be employed in scenarios when the parturient desires future fertility and can also maintain close follow up after delivery.

Anesthesia Management

Choice of Anesthesia: Neuraxial Versus General

Deciding on the best approach to the anesthetic management of PAS disorder can often be difficult. Nevertheless, the anesthesia plan should consider the usual maternal and fetal factors pertinent to care during a caesarian section but should also take into account the type of PAS pathology present and the availability of facility resources and personnel.

In the absence of major contraindications, neuraxial anesthesia is the standard of care for routine caesarian deliveries due to the ability to avoid parturient airway manipulation and the adverse effects of general anesthetics on the fetus. With PAS disorders, the expectation of significant blood loss has traditionally led to the routine use of general anesthesia [28]. Possible benefits of general anesthesia include the improved ease of performing large volume resuscitation without concerns for sympathectomy and the avoidance of a neuraxial catheter in the setting of potential coagulopathy.

However, with improved diagnostics and use of elective delivery, PAS disorders are increasingly being managed under neuraxial anesthesia as well. Neuraxial anesthesia provides an overall reliable anesthesia, a means to address postoperative analgesia via long-acting neuraxial opioids, and an opportunity for early maternal-newborn bonding after delivery. A relatively large retrospective cohort study (n = 129) looking over an 18-year period showed that in those cases requiring caesarian hysterectomy, 75% were successfully managed with neuraxial anesthesia alone [29]. The independent predictors for the need to convert to general anesthesia were longer surgical duration and history of >3 prior caesarian deliveries [29]. Indeed, practical demands such as the waning of a spinal anesthetic over a longer surgery may warrant conversion, and this can often be accomplished in a safe manner. Still, as noted in this study, where 60% of the conversion patients ended up having pathologic diagnoses of placenta percreta (versus 16% in the neuraxial only group), it is prudent to consider general anesthesia from the beginning of the case if placenta percreta is documented or if several risk factors for it are present. This is because conversion to general anesthesia does come with the risk of having to secure a potentially difficult airway in a dynamic setting and the challenge of safely inducing general anesthesia in the face of

an already present neuraxial sympathectomy. In another retrospective study from 2017, the authors found similar data trends of conversion. They recommend the use of general anesthesia in cases of placenta percreta and spinal anesthesia in all others [30].

The choice of general versus neuraxial anesthesia may also come down to the resources available in a facility and the personnel involved. For example, centers in low-income countries in which higher rates of blood loss are often seen and where potentially helpful therapies such balloon occlusion catheters or UAE are not available, general anesthesia may be preferred [31]. On the other side of the spectrum, there is evidence that care of PAS disorder patients with a multidisciplinary team (MDT) of experienced providers (namely, those specializing in complex pelvic surgery) can positively affect outcomes such as transfusion requirements, the need for reoperation, and early morbidity [32]. In such environments, the risk to benefit ratio may favor the use of neuraxial anesthesia first.

Additionally, the choice may be influenced by institutional culture and the individual anesthesiologist's comfort with converting from one technique to the other. In a 2017 retrospective review (n = 43) from a tertiary care center, the authors describe the successful use of combined spinal epidural (CSE) with planned conversion to general anesthesia during caesarian hysterectomy in 70% of the cohort [33]. Such an approach encompasses the strengths of neuraxial anesthesia while proactively having general anesthesia in place prior the portion of the case that can be fraught with instability. It may or may not be feasible at other centers due to provider comfort and care team buy-in. No matter what the anesthesia plan is, it is paramount to involve the patient and her family in the preoperative discussion and tactfully counsel that a postoperative ICU stay is always within the realm of immediate possibility.

Preprocedural Considerations

As part of the process of formulating the anesthetic plan, it is important to perform a full history and physical exam with attention paid to both the obstetric and anesthetic histories. Specifically, the anesthesiologist should identify any risk factors for peripartum hemorrhage and comorbidities (cardiovascular, pulmonary, or renal) predisposing to end-organ damage in the setting of potential hemodynamic instability [34]. In addition, a detailed airway exam and assessment of the patient's back is key to adequate preparation. Indicated laboratory studies to obtain include a complete blood count (CBC), basic metabolic panel (BMP), type and screen (T&S), and coagulation tests (PT/INR, aPTT, and fibrinogen level). In cases of elective management, preoperative communication among all services (obstetrics, anesthesia, radiology, blood bank, etc.) planning to take part in care may streamline events the day of surgery. Administration of appropriate aspiration prophylaxis and confirmation of blood product availability may then follow prior to transport to the operating room.

Induction of Anesthesia

Before the delivery of either general or neuraxial anesthesia, application of standard ASA monitors is required. In cases of general anesthesia, a BIS monitor can help guide the delivery of an appropriate depth of anesthesia. Access with at least two large bore peripheral IVs is also crucial to facilitate rapid resuscitation with both fluid and blood products. In cases where IV access is difficult or contraindicated, central venous access with a large bore central line or introducer sheath is warranted. However, routine central venous access may not be typical. Invasive blood pressure monitoring via an arterial line is often employed to closely observe hemodynamics and sample serial blood gases to guide resuscitation. With regards to the choice of induction agent for general anesthesia, propofol, etomidate, or ketamine may be used, depending on the hemodynamic state of the mother. Standard local anesthetics and opioids such as lidocaine, bupivacaine, fentanyl, and morphine may be utilized for neuraxial anesthesia.

Maintenance of Anesthesia

Typical regimens for the maintenance phase of a general anesthetic for a caesarian hysterectomy include halogenated inhalational agents prior to fetal delivery. After delivery, due to concerns for uterine atony, nitrous oxide with or without intravenous opioids is then added, and the inhalational agent concentration is reduced or eliminated altogether.

Given the potential for rapid hemodynamic shifts in the setting of PAS disorders, it may be prudent to use rapidly titratable inhalational agents such as sevoflurane or consider the use of adjunctive agents such as remifentanil. As an ultra-short acting opioid with a low context sensitive half time, remifentanil may be an option to supplement anesthesia and analgesia during a long procedure. Further, due to rapid fetal metabolism, there is evidence that it does not negatively affect neonatal Apgar scores or the need for respiratory intervention at birth [35]. Dexmedetomidine has been studied for use in standard caesarian deliveries and can potentially add to an anesthetic regimen without negative neonatal outcomes [36]. However, due to its hemodynamic effects of attenuating sympathetic outflow, it should be avoided as a first line agent in the anesthetic care of PAS disorders. In all cases, vasoactive agents including phenylephrine, ephedrine, and epinephrine should be readily available.

When neuraxial anesthesia is employed, the anesthesiologist should carefully weigh the pros and cons of a spinal technique versus a catheter-based technique such as an epidural or CSE. While a spinal may afford the fastest onset, having a neuraxial catheter to supplement the anesthetic already in place may be key with longer operating times. With the advent of MDTs and CoEs, even as outcomes have improved, surgical interventions may take more time. In a 2017 retrospective study, the use of a multidisciplinary management strategy resulted in average operating times of 260 min (versus 181 min in the non-MDT group) [37].

Blood Product Management

One of the most central concerns for the anesthesiologist in the intraoperative care of PAS disorder is blood product management. Indeed, while it is universally known that PAS disorders often lead to massive obstetrical hemorrhage, the data on average EBL totals and transfusion requirements ranges significantly. Reported average blood loss in caesarian hysterectomies for PAS disorder was 6655 mL (±3798 mL) in one retrospective review [38]. In another, the range was 590–10,500 mL [39]. Traditionally, case series have reported transfusion requirements of 4–6 units of packed red blood cells [40]. However, different providers and institutions have different criteria for transfusion. Postoperative transfusion rates have sometimes been included in totals as well, thus altering the results and making comparison difficult.

Further, there is not a definitive body of evidence to predict which patients will bleed the most. A 2011 retrospective review (n = 77) sought to answer this question and identify risk factors for blood loss >5000 mL and need for transfusion of >10 units of packed red blood cells. None of the typical risk factors, including number of previous caesarian deliveries or degree of known placental invasion, were associated [41]. On the other hand, it has been suggested that patients with placenta percreta may suffer increased blood loss secondary to sources of extrauterine blood supply [40]. The only factor that has backing from data is the timing of intervention, as emergency surgery has been associated with higher blood loss versus elective surgery (e.g., a mean of 2526 mL versus 1319 mL in one study) [42].

In any case involving a PAS disorder, at least 2–4 units of packed red blood cells should be in the operating room prior to incision [43]. Use of a massive transfusion protocol may also be warranted in order to maintain an adequate supply of blood products and to avoid specific factor deficiencies leading to coagulopathy. Although there have been no controlled studies on the optimum ratio of blood product administration in obstetric

hemorrhage [44], a ratio of 1:1:1 of packed red blood cells, plasma, and platelets has been used successfully in other surgical fields and may be applied in the care of PAS disorder. Cryoprecipitate should be available as a therapy for DIC that may sometimes accompany massive obstetric hemorrhage. Finally, the anesthesiologist should warm intravenous fluids and blood products before delivery to the patient, maintain normothermia, and appropriately treat hypocalcemia during large volume resuscitation.

Blood Conservation Strategies

The role of blood conservation strategies has also been explored in the care of PAS disorder. Two major interventions are the use of anti-fibrinolytics such tranexamic acid (TXA) and the implementation of cell salvage. Although there is no data on the use of anti-fibrinolytics in the management of PAS disorders to date, there is evidence to support their use in other scenarios of postpartum hemorrhage. The 2017 WOMAN trial, a large, placebo-controlled trial, showed that compared to placebo, TXA significantly reduced maternal mortality secondary to bleeding after delivery [45]. During caesarian delivery, the use of TXA may also decrease overall blood loss and transfusion requirements without increased risk of thromboembolism [46]. Therefore, administration of TXA before or during caesarean hysterectomy for PAS disorders is reasonable and possibly effective. The other option to decrease transfusion requirements is autologous cell salvage. Such techniques may be warranted as an adjunct or replacement for transfusion in cases of rare blood type or in patients who are Jehovah's witnesses.

Postoperative Considerations

It is well known that surgery for PAS disorder management often results in the need for postoperative monitoring and treatment in an ICU setting. Specifically, evidence shows that ~9–40% of patients fall into this category [47–49]. It is therefore important to plan and arrange for a potential ICU stay before surgery to easily transfer care postoperatively.

Conclusions

Placental accreta spectrum (PAS) disorders pose difficult challenges to anesthesia providers today. Preoperative considerations include obtaining a detailed understanding of the parturient medical history, diagnostics, and laboratory data. Intraoperative care, often in the form of a caesarian hysterectomy, should prioritize not only the presence of adequate blood products but also the means to prevent and assist in abating obstetric hemorrhage. Often, this is accomplished via the availability of specialized personnel (multidisciplinary teams) and tools (interventional radiology techniques). Postoperatively, the anesthesiologist should be prepared to transfer care to an ICU setting.

In the last 83 years since PAS disorders were first described by Irving and Hertig, countless new diagnostic and treatment modalities have been developed. All may play a role in the care for this pathology. However, the best way to deliver effective anesthetic care is likely determined on a case-by-case basis and should consider both facility resources and personnel available.

References

1. Irving FC, Hertig AT. A study of placenta accreta. Surg Gynecol Obstet. 1937;38(6):1088–200.
2. Pinto PV, Machado AP, Montenegro N. Risk of hemorrhage in abnormally invasive placenta according to its management. J Matern Fetal Neonatal Med. 2016;30(18):2139–45.
3. Silver RM. Abnormal placentation: placenta previa, vasa previa, and placenta accreta. Obstet Gynecol. 2015;126(3):654–68.
4. Silver RM, Branch DW. Placenta accreta spectrum. N Engl J Med. 2018;378(16):1529–36.

5. Bailit JL, et al. Morbidly adherent placenta treatments and outcomes. Obstet Gynecol. 2015;125(3):683–9.
6. Read JA, Cotton DB, Miller FC. Placenta accreta: changing clinical aspects and outcome. Obstet Gynecol. 1980;56(1):31–4.
7. Miller DA, Chollet JA, Goodwin TM. Clinical risk factors for placenta previa-placenta accreta. Am J Obstet Gynecol. 1997;177(1):210–4.
8. Jauniaux E, Chantraine F, Silver RM, Langhoff-Roos J. FIGO consensus guidelines on placenta accreta spectrum disorders: epidemiology. Int J Gynaecol Obstet. 2018;140(3):265–73.
9. Allen L, Jauniaux E, Hobson S, Papillon-Smith J, Belfort MA. FIGO consensus guidelines on placenta accreta spectrum disorders: nonconservative surgical management. Int J Gynaecol Obstet. 2018;140(3):281–90.
10. Devine PC. Obstetric hemorrhage. Semin Perinatol. 2009;33(2):76–81.
11. Thurn L, et al. Abnormally invasive placenta-prevalence, risk factors and antenatal suspicion: results from a large population-based pregnancy cohort study in the Nordic countries. BJOG. 2016;123(8):1348–55.
12. Silver RM, et al. Maternal morbidity associated with multiple repeat cesarean deliveries. Obstet Gynecol. 2006;107(6):1226–32.
13. Papanikolaou IG, et al. Abnormal placentation: Current evidence and review of the literature. Eur J Obstet Gynecol Reprod Biol. 2018;228:98–105.
14. D'Antonio F, Iacovella C, Bhide A. Prenatal identification of invasive placentation using ultrasound: systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2013;42(5):509–17.
15. Jauniaux E, Bhide A. Prenatal ultrasound diagnosis and outcome of placenta previa accreta after cesarean delivery: a systematic review and meta-analysis. Am J Obstet Gynecol. 2017;217(1):27–36.
16. Jauniaux E, et al. FIGO consensus guidelines on placenta accreta spectrum disorders: Prenatal diagnosis and screening. Int J Gynaecol Obstet. 2018;140(3):274–80.
17. D'Antonio F, et al. Prenatal identification of invasive placentation using magnetic resonance imaging: systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2014;44(1):8–16.
18. Camuzcuoglu A, et al. Surgical management of 58 patients with placenta praevia percreta. Wien Klin Wochenschr. 2016;128(9-10):360–6.
19. Grace Tan SE, et al. Surgical management of placenta accreta: a 10-year experience. Acta Obstet Gynecol Scand. 2013;92(4):445–50.
20. Belfort MA, Shamshiraz AA, Fox K. Minimizing blood loss at cesarean-hysterectomy for placenta previa percreta. Am J Obstet Gynecol. 2017;216(1):78.e1–2.
21. Turan OM, Shannon A, Asoglu MR, Goetzinger KR. A novel approach to reduce blood loss in patients with placenta accreta spectrum disorder. J Matern Fetal Neonatal Med. 2019;27:1–10.
22. Ballas J, et al. Preoperative intravascular balloon catheters and surgical outcomes in pregnancies complicated by placenta accreta: a management paradox. Am J Obstet Gynecol. 2012;207(3):216.e1–5.
23. Cali G, et al. Prophylactic use of intravascular balloon catheters in women with placenta accreta, increta and percreta. Eur J Obstet Gynecol Reprod Biol. 2014;179:36–41.
24. Mei J, et al. Systematic review of uterus-preserving treatment modalities for abnormally invasive placenta. J Obstet Gynaecol. 2015;35(8):777–82.
25. Sentilhes L, et al. Maternal outcome after conservative treatment of placenta accreta. Obstet Gynecol. 2010;115(3):526–34.
26. Sentilhes L, Kayem G, Chandraharan E, Palacios-Jaraquemada J, Jauniaux E. FIGO consensus guidelines on placenta accreta spectrum disorders: Conservative management. Int J Gynaecol Obstet. 2018;140(3):291–8.
27. Wang M, et al. Uterine artery embolization following cesarean delivery but prior to hysterectomy in the management of patients with invasive placenta. J Vasc Interv Radiol. 2019;30(5):687–91.
28. Yamada T, et al. Cesarean hysterectomy in a hybrid operating room for placenta percreta: a report of three cases. JA Clin Rep. 2019;5(1):9.
29. Ioscovich A, et al. Israeli survey of anesthesia practice related to placenta previa and accreta. Acta Anaesthesiol Scand. 2016;60(4):457–64.
30. Markley JC, Farber MK, Perlman NC, Carusi DA. Neuraxial anesthesia during cesarean delivery for placenta previa with suspected morbidly adherent placenta: a retrospective analysis. Anesth Analg. 2018;127(4):930–8.
31. Wang Y, Zeng H, Guo XY, Rong XY. Anesthetic choice for patients undergoing cesarean section complicated with placenta implantation. Beijing Da Xue Xue Bao. 2017;49(2):322–5.
32. Muñoz LA, Mendoza GJ, Gomez M, Reyes LE, Arevalo JJ. Anesthetic management of placenta accreta in a low-resource setting: a case series. Int J Obstet Anesth. 2015;24(4):329–34.
33. Eller AG, et al. Maternal morbidity in cases of placenta accreta managed by a multidisciplinary care team compared with standard obstetric care. Obstet Gynecol. 2011;117(2 Pt 1):331–7.
34. Riveros-Perez E, Wood C. Retrospective analysis of obstetric and anesthetic management of patients with placenta accreta spectrum disorders. Int J Gynaecol Obstet. 2018;140(3):370–4.
35. Warrick CM, Rollins MD. Peripartum anesthesia considerations for placenta accreta. Clin Obstet Gynecol. 2018;61(4):808–27.
36. Shaylor R, et al. Pre-delivery remifentanil infusion for placenta accreta cesarean delivery under general anesthesia: an observational study. J Matern Fetal Neonatal Med. 2016;29(17):2793–7.
37. El-Tahan MR, Mowafi HA, Al Sheikh IH, Khidr AM, Al-Juhaiman RA. Efficacy of dexmedetomi-

dine in suppressing cardiovascular and hormonal responses to general anaesthesia for caesarean delivery: a dose-response study. Int J Obstet Anesth. 2012;21(3):222–9.
38. Smulian JC, et al. Invasive placental disease: the impact of a multi-disciplinary team approach to management. J Matern Fetal Neonatal Med. 2017;30(12):1423–7.
39. Takahashi H, et al. Factors contributing to massive blood loss on peripartum hysterectomy for abnormally invasive placenta: who bleeds more? Obstet Gynecol Int. 2016;2016:5349063.
40. Kato R, et al. Anesthetic management for cases of placenta accreta presented for cesarean section: a 7-year single-center experience. Masui. 2008;57(11):1421–6.
41. Reitman E, Devine PC, Laifer-Narin SL, Flood P. Case scenario: perioperative management of a multigravida at 34-week gestation diagnosed with abnormal placentation. Anesthesiology. 2011;115(4):852–7.
42. Wright JD, et al. Predictors of massive blood loss in women with placenta accreta. Am J Obstet Gynecol. 2011;205(1):38.e1–6.
43. Zelop CM, Harlow BL, Frigoletto FD Jr, Safon LE, Saltzman DH. Emergency peripartum hysterectomy. Am J Obstet Gynecol. 1993;168(5):1443–8.
44. Kuczkowski KM. A review of current anesthetic concerns and concepts for cesarean hysterectomy. Curr Opin Obstet Gynecol. 2011;23(6):401–7.
45. American College of Obstetricians and Gynecologists; Society for Maternal-Fetal Medicine. Obstetric care consensus no. 7: placenta accreta spectrum. Obstet Gynecol. 2018;132(6):e259–75.
46. WOMAN Trial Collaborators. Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with postpartum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial. Lancet. 2017;389(10084):2105–16.
47. Simonazzi G, et al. Tranexamic acid for preventing postpartum blood loss after cesarean delivery: a systematic review and meta-analysis of randomized controlled trials. Acta Obstet Gynecol Scand. 2016;95(1):28–37.
48. Mitric C, Desilets J, Balayla J, Ziegler C. Surgical management of the placenta accreta spectrum: an institutional experience. J Obstet Gynaecol Can. 2019;41(11):1551–7.
49. Esakoff TF, et al. Diagnosis and morbidity of placenta accreta. Ultrasound Obstet Gynecol. 2011;37(3):324–7.

Anesthesia for Parturient with Peripartum Cardiomyopathy

35

Christopher Hoffman

Learning Points

- Peripartum cardiomyopathy is a heart failure diagnosis of exclusion that occurs in the late stage pregnancy and postpartum period.
- Optimizing therapies range from mild measures to reduce fluid retention and reduce afterload to aggressive interventions including ventricular assist devices and cardiac transplantation.
- Anesthetic care may warrant invasive monitoring and early analgesic interventions to mitigate cardiac compromise.
- Prognosis is poor when cardiac function does not return. Prognosis may be good if function returns but recurrence and longterm functional decline has been documented and warrants continuing surveillance.

Introduction

Peripartum cardiomyopathy (PC) is defined as a form of heart failure that develops during the final month of pregnancy through 6 months postpartum. As its mechanism is unknown, it is a diagnosis of exclusion in parturients with no other clear etiology. It is a rare condition that can become dire. Its diagnosis is limited by a narrow window of opportunity to investigate. When PC is suspected, multi-disciplinary management in a high-risk perinatal center is crucial to curtail lethality. Return to baseline function is not guaranteed, and long-term sequelae may present both in future pregnancies and in nongravid life.

Pathophysiology

It has been shown that transient left ventricular (LV) remodeling and hypertrophy can develop in pregnancy, leading to reversible decrease in left ventricular systolic function. However, there is no data supporting the hypothesis that these changes exaggerate to the extent of clinically devastating decline in function [1, 2]. Thus, a general consensus is that the mechanism is not strictly the exacerbation of an underlying subclinical cardiomyopathy. While it has not been observed to be ubiquitous, myocarditis confirmed via endomyocardial biopsy has been found in many patients with PC. One study found positive biopsies in 76% of PC patients [3]. The fetal-maternal immune interaction may increase susceptibility to viral infected mediated myocarditis. While the myocarditis wasn't universally present, resolution of the inflammatory process via immunosuppressive therapy was successful in improving function. Other immune mediated responses are postulated, including reported chi-

C. Hoffman (✉)
Department of Anesthesiology, Thomas Jefferson University Hospital, Sidney Kimmel Medical College, Philadelphia, PA, USA
e-mail: Christopher.Hoffman2@jefferson.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_35

meric progenitor cells in the fetus moving into maternal circulation. If the immunogenicity of the new cell line does not trigger a response in maternal circulation, foreign cells may persist [4]. Progenitor cell lines have been detected in maternal blood decades postpartum [5]. If foreign cell lines are transmitted and stored in cardiac tissue, an inflammatory response could lead to myocytotoxicity. This causality is supported by higher titers of autoantibodies against cardiac tissue proteins in PC patients [6]. Other postulated mechanisms include abnormally increased proinflammatory cytokines (e.g. tumor necrosis factor α and interleukin 1) and decreased hormone and trace minerals (e.g. relaxin and selenium, respectively) operating in tandem to promote a proinflammatory and autoantigen process in cardiac tissue that induces cardiac injury [7–9].

Epidemiology and Risk Factors

PC incidence estimates may be limited by lack of diagnostic services, misdiagnosed or undiagnosed milder form of disease, lack of access to care, regionality, and risk factor prevalence, among other variables. Epidemiologic reports vary considerably. PC incidence in the United States varies by report from 2.5 to 10.3 per 10,000 live births [10, 11]. Incidence varied by ethnicity within the United States, with PC occurring the greatest in African-Americans, which was 2.9-fold higher compared with whites and seven-fold that of Hispanics [12]. Incidence is as high as 10 per 10,000 live births in South Africa and 33 per 10,000 live births in Haiti [13, 14]. Mortality rates follow similar trends, with reported mortality rates occurring in 3.3% of PC cases in the U.S. compared to 15.3% in Haiti [14, 15].

Incidence and morbidity trends are not favorable. An 8-year investigation of trends in the United States shows that PC incidence is on the rise and major adverse event occurrence (in-hospital mortality, cardiac arrest, heart transplant, mechanical circulatory support, acute pulmonary edema, thromboembolism, implantable cardioverter defibrillator/permanent pacemaker implantation, and cardiogenic shock) have either persisted or increased over that period [11]. Investigated cardiac morbidity in this population emphasizes long-term impairment. A 4 year follow up of diagnosed PC patients showed their initial mean ejection fraction (EF) was 20%. Upon follow up, 62% of patients improved, 25% were unchanged, and 4% declined. 10% eventually required transplant. Among those who recovered, 75% eventually had an EF >45% [15].

Risk factors for PC are reproduced in multiple studies, but no strict recommendations exist regarding potential screening in higher risk populations. Women with PC are more likely to be advanced maternal age, multiparous, non-Hispanic African American or Filipino women. Multifetal pregnancy, preeclampsia, and gestational hypertension are also associated [16]. Given the nature of these associated conditions, it also subsequently correlates that women with PC are more likely to develop anemia, gestational diabetes mellitus, HELLP syndrome (i.e. hemolysis, elevated liver enzymes, low platelets), and cesarean delivery [12]. Risk factors for lack of recovery postpartum include a LV end-diastolic dimension >5.6 cm, the presence of LV thrombus, and African American ethnicity. Recovery of LV function was not predictable by the initial EF [15].

Evaluation and Assessment

Diagnostic Criteria

Diagnosing peripartum cardiomyopathy on clinical evaluation alone is challenging because many symptoms of normal pregnancy during the last month (i.e., dyspnea, fatigue, lower extremity edema) can overlap with heart failure-related symptomatology. Milder PC may go unrecognized in the absence of echocardiographic screening.

The National Heart, Lung and Blood Institute and the Office of Rare Diseases of the National Institutes of Health established a set of four criteria to establish a PC diagnosis:

- Development of heart failure in the last month of pregnancy or within 5 months postpartum.
- Absence of identifiable cause of heart failure.

- Absence of recognizable heart disease before the last month of pregnancy.
- Left ventricular systolic dysfunction demonstrated by left ventricle ejection fraction of less than 45%, fractional shortening of less than 30%, or both, with or without a left ventricle end-diastolic dimension less than 2.7 cm/m^2 of body surface area [17].

Clinical Evaluation

Notable evidence of heart failure exacerbation or decompensation is typically required in order to raise suspicion beyond typical signs of late stage pregnancy. This includes chest pain, jugular venous distension, pulmonary exacerbation (orthopnea, pleural effusion), worsening murmurs (P2 accentuation, S3 and S4 heart sounds, valvular regurgitation), and hepatomegaly. The timing of these more severe features may prove crucial to increasing suspicion. An unremarkable prenatal history and otherwise asymptomatic early pregnancy is commonly seen. 60–70% of PC patients develop symptoms in the postpartum period [18, 19]. Chest radiography will likely exhibit cardiomegaly, pleural effusion, pulmonary venous congestion, or basilar infiltrate. Electrocardiography commonly exhibits ST-T wave changes, left ventricular hypertrophy, and prolonged PR and QRS intervals [20]. When heart failure has been confirmed, PC still remains a diagnosis of exclusion. Laboratory studies, ECG, and echocardiography should be utilized to evaluate for idiopathic cardiomyopathy, congenital heart disease, ischemic heart disease, valvulopathy/rheumatic disease, arrhythmia, coronary disease, and toxicity-related failure.

Further testing has been reported with varying results. Cardiac magnetic resonance imaging may be able to evaluate ventricular function via T2 ratio, late gadolinium enhancement, and early gadolinium enhancement ratio to gauge severity of myocarditis and myocardial hyperemia, capillary leakage, fibrosis, and necrosis [21]. Endomyocardial biopsy has been investigated but its use is limited by the degree of its invasiveness and the potential for sampling error. Inflammatory infiltrates can be mild or focal in nature or be primarily positioned on myocardium inaccessible by biopsy needle, contributing to false-negative results. Other diagnostic criteria may provide an accurate enough picture to warrant proceeding with PC therapy without requiring endomyocardial biopsy [22].

Management

Clinical Interventions

PC treatment is similar to heart failure from other etiologies, with some restrictions if symptoms require intervention during the antepartum period. Therapy selection is based on severity of pathophysiology, but general goals are to reduce afterload and preload, increase contractility, and mitigate fluid retention. Mild symptoms should be treated with a combination of salt and water restriction and modest exercise. Prior recommendations included bed rest; however, PC is associated with an increased thromboembolic risk [23, 24]. Modest exercise can reduce this risk as well as mobilize free fluid and improve vascular tone. If exercise is not plausible then prophylactic anticoagulation may be warranted. Low-molecular-weight heparins are optimal, as warfarin is teratogenic and unfractionated heparin has a decreased bioavailability in pregnancy [25].

In scenarios where moderate symptoms present or mild symptoms persist despite more benign interventions, diuretics can be employed to prevent retention, reduce preload, and decrease pulmonary congestion. Persistent signs of congestive heart failure at this point would require vasodilators. Angiotensin converting enzyme (ACE) inhibitors and receptor blockers improve cardiac function and prevent cardiac remodeling and are considered first line therapy in the setting of heart failure. However, they are indicated only in the postpartum setting due to teratogenicity and neonatal renal failure [26]. Hydralazine is typically first line therapy in this scenario prior to delivery, and is an agent already commonly used in the obstetric population to control hemodynamics in the setting of pregnancy induced hypertension or

preeclampsia [27]. Calcium channel blockers are safe in pregnancy, but many have negative inotropic properties. Amlodipine has minimal negative inotropic effect, observable in vitro but not reliably in vivo, and has been shown to improve survival [28]. Longterm utilization of beta-adrenergic antagonists is associated with low fetal birth weight. The drug class is effective in decreasing heart rate, improving diastolic function, and mitigating arrythmias. Labetalol and carvedilol have been shown to be particularly effective in improving mortality due to additional afterload reduction via alpha-1 adrenergic blockade [29]. Minimizing antepartum dosing and maximizing its utilization in the postpartum PC period is widely accepted.

Patients in severe failure may require aggressive support in an intensive care setting to implement intravenous inotropes, supplemental oxygen, invasive monitoring, and controlled ventilation. Inotropic agents may be included at this stage to improve contractility. Digoxin is utilized in this setting not only for its efficacy in cardiomyopathy but also for its safety profile in pregnancy and puerperium both to mother and fetus [30]. While digoxin is considered first line therapy, other inotropic agents including dobutamine, dopamine, and milrinone have also been utilized. Intravascular vasodilators such as nitroglycerin and nitroprusside may be administered concomitantly to reduce afterload. Nitroprusside is less desirable in the antepartum setting due to the potential accumulation of thicyanate and cyanide [26]. Effective and appropriate titration of these agents may require invasive monitoring including arterial, central venous, and Swan-Ganz catheterization. Each can be of value in the critically ill, though their placement has its own risk benefit ratio.

Impending cardiovascular collapse failing medical management may warrant the placement of intra-aortic balloon pumps, ventricular assist devices or extracorporeal membrane oxygenators. These devices can be used as a bridge to recovery or to cardiac transplantation. 10% of patients eventually require transplantation. Follow-up reports show that PC patients receiving transplantation demonstrate similar survival and complication rates, laboratory values, and hemodynamic status as any other indications for cardiac transplant. Most of those using bridging methods to clinical recovery and not transplantation observe functional status return within 1 year post-delivery [31, 32] Given the inflammatory pathophysiology present in PC, limited studies have attempted to deploy immunosuppressive and immunomodulating therapies. Prior investigations yield varying results. Reductions in inflammatory markers (e.g. tumor necrosis factor alpha) have been shown to improve outcomes. Utilizing suppressive drugs in specific patients with proven lymphocytic myocarditis has also shown some benefit. Investigations have been limited but these modalities may play a future role in treating PC when improvement is not seen in more benign interventions [33, 34].

Anesthesia Considerations

A multidisciplinary team is required to assess disease severity and progression if discovered prior to delivery. Medical management and the anticipated mode of delivery may vary on an individualized basis and may change over time if physiology and symptomatology improves or worsens. Concerns surround the ability to compensate for fluid shifts, sympathomimetic activity, and Valsalva maneuvers present during vaginal delivery. Suspected intolerance to these changes warrants surgical delivery. Preventing fluid overload and sympathomimetic activity are crucial goals in this period and thus continuous invasive hemodynamic monitoring may be warranted in any scenario. Case reporting documents PC patients delivering under both strategies [35]. Regardless of mode of delivery, adequate analgesia is necessary to mitigate pain and associated with increased cardiac output and afterload. Unless cardiomyopathy or other comorbidities are cause for contraindication (e.g. anticoagulation), neuraxial anesthesia is the superior modality of labor or surgical analgesia. Avoidance of neuraxial may lead to other regional or systemic analgesic strategies for labor and general anesthesia for cesarean section.

Prognosis

Recovery from PC has been typically defined as normalization of ventricular size and function within 6 months postpartum. About 30–50% of PC patients achieve this criterion. However, among those who do not experience full recovery, there is a 5-year mortality rate of 85%. Patients who survive in this observed period also have insidious decline in function (e.g. lower ejection fraction, larger ventricular cavity size) [24, 36, 37]. Recommendations regarding future pregnancy is complicated by reported PC recurrence. It is generally recommended that those who do not return to baseline function avoid future pregnancy, given the aforementioned incidence of cardiovascular collapse. While sample sizes are limited, some data suggests that at least 25% of "recovered" PC patients develop the same symptomatology in a subsequent pregnancy [16, 36]. While heart rate, blood pressure, ventricular dimension, and ventricular function return to baseline in this group, data supports that contractile reserve (assessed via dobutamine challenge) does not [37]. Thus evidence suggests that despite return of baseline function, cardiac pathophysiology may be irreversible.

Conclusions

Peripartum cardiomyopathy is a rare disease with significant peripartum and postpartum morbidity and mortality. The diagnosis requires a high index of suspicion, as it shares clinical presentation with other conditions and includes symptoms commonly seen in pregnancy. Research regarding its pathophysiology is multifactorial and at times still theoretical. Aggressive medical management and surveillance is crucial to optimizing outcomes when dysfunction is moderate to severe. Treatment may warrant end-of-line critical interventions including ventricular assist devices, extracorporeal membrane oxygenators, and cardiac transplantation. Return to functional baseline takes extensive time and is often not achieved. Prognosis may be favorable but recurrence in subsequent pregnancies and longterm cardiac function are not well defined. Gaps in knowledge persist largely due to the variability in incidence, presentation, and recovery. Future laboratory and clinical research is warranted to clarify and educate.

Funding and Conflicts of Interest None

References

1. Geva T, Mauer MB, Striker L, Kirshon B, Pivarnik JM. Effects of physiologic load of pregnancy on left ventricular contractility and remodeling. Am Heart J. 1997;133:53–9.
2. Mone SM, Sanders SP, Colan SD. Control mechanisms for physiological hypertrophy of pregnancy. Circulation. 1996;94:667–72.
3. Midei MG, DeMent SH, Feldman AM, Hutchins GM, Baughman KL. Peripartum myocarditis and cardiomyopathy. Circulation. 1990;81:922–8.
4. Nelson JL. Pregnancy, persistent microchimerism and autoimmune disease. J Am Med Wom Assoc. 1998;53:31–2.
5. Bianchi BW, DeMaria MA, Sylvester S, Weil GJ. Male fetal progenitor cells persist in maternal blood for as long as 27 years post partum. Proc Natl Acad Sci U S A. 1996;93:705–8.
6. Ansari AA, Neckelmann N, Wang YC, Gravanis MB, Sell KW, Herskowitz A. Immunologic dialogue between cardiac myocytes, endothelial cells, and mononuclear cells. Clin Immunol Immunopathol. 1993;68:208–14.
7. Mann DL. Stress activated cytokines and the heart. Cytokine Growth Factor Rev. 1996;7:341–54.
8. Kothari SS. Aetiopathogenesis of peripartum cardiomyopathy: prolactin-selenium interaction? Int J Cardiol. 1977;60:111–4.
9. Ansari AA, Fett JD, Carraway RE, Mayne AE, Onlamoon N, Sundstrom JB. Autoimmune mechanisms as the basis for human peripartum cardiomyopathy. Clin Rev Allergy Immunol. 2002;23(3):301–24.
10. Brar SS, Khan SS, Sandhu GK, Jorgensen MB, Parikh N, Hsu JW, et al. Incidence, mortality, and racial differences in peripartum cardiomyopathy. Am J Cardiol. 2007;100:302–4.
11. Kolte D, Khera S, Aronow WS, Palaniswamy C, Mujib M, Ahn C, Jain D, Gass A, Ahmed A, Panza JA, Fonarow GC. Temporal trends in incidence and outcomes of peripartum cardiomyopathy in the United States: a nationwide population-based study. Am Heart J. 2014;3(3):e001056.
12. Gunderson EP, Croen LA, Chiang V, Yoshida CK, Walkton D, Go AS. Epidemiology of peripartum cardiomyopathy: incidence, predictors, and outcomes. Obstet Gynecol. 2011;118(3):583–91.

13. Desai D, Moodley J, Naidoo D. Peripartum cardiomyopathy: experiences at King Edward VIII Hospital, Durban, South Africa and a review of the literature. Trop Dr. 1995;25:118–23.
14. Fett JD, Christie LG, Carraway RD, Murphy JG. Five-year prospective study of the incidence and prognosis of peripartum cardiomyopathy at a single institution. Mayo Clin Proc. 2005;80(12):1602–6.
15. Amos AM, Jaber WA, Russell SD. Improved outcomes in peripartum cardiomyopathy with contemporary. Am Heart J. 2006;152:509–13.
16. Demakis JG, Rahimtoola SH, Sutton GC, et al. Natural course of peripartum cardiomyopathy. Circulation. 1971;44:1053–61.
17. Pearson GD, Veille JC, Rahimtoola S, Hsia J, Oakley CM, Hosenpud JD, Ansari A, Baughman KL. Peripartum cardiomyopathy national heart, lung, and blood institute and office of rare diseases (national institutes of health) workshop recommendations and review. JAMA. 2000;283(9):1183–8.
18. Mishra TK, Swain S, Routray SN. Peripartum cardiomyopathy. Int J Gynaecol Obstet. 2006;95:104–9.
19. Duran N, Gunes H, Duran I, Biteker M, Ozkan M. Predictors of prognosis in patients with peripartum cardiomyopathy. Int J Gynaecol Obstet. 2008;101:137–40.
20. Brown CS, Bertolet BD. Peripartum cardiomyopathy: a comprehensive review. Am J Obstet Gynecol. 1998;178:409–14.
21. Renz DM, Röttgen R, Habedank D, Wagner M, Böttcher J, Pfeil A, et al. New insights into peripartum cardiomyopathy using cardiac magnetic resonance imaging. Fortschr Röntgenstr. 2011;183(9):834–41.
22. Hauck AJ, Kearney DL, Edwards WD. Evaluation of postmortem endomyocardial biopsy specimens from 38 patients with lymphocytic myocarditis: implications for role of sampling error. Mayo Clin Proc. 1989;64(10):1235–45.
23. Jha P, Jha S, Millane TA. Peripartum cardiomyopathy complicated by pulmonary embolism and pulmonary hypertension. Eur J Obstet Gynecol Reprod Biol. 2005;123:121–3.
24. Murali S, Baldisseri MR. Peripartum cardiomyopathy. Crit Care Med. 2005;33:S340–6.
25. Bennani SL, Loubaris M, Lahlou I, Haddour N, Badidi M, Bouhouch R, et al. Postpartum cardiomyopathy revealed by acute lower limb ischemia. Ann Cardiol Angeiol (Paris). 2003;52:382–5.
26. Abboud J, Murad Y, Chen-Scarabelli C, Saravolatz L, Scarabelli TM. Peripartum cardiomyopathy: a comprehensive review. Int J Cardiol. 2007;118:295–303.
27. Cohn JN, Johnson G, Ziesche S, Cobb F, Francis G, Tristani F, et al. A comparison of enalapril with hydralazine-isosorbide dinitrate in the treatment of chronic congestive heart failure. N Engl J Med. 1991;325:303–10.
28. Packer M, O'Connor CM, Ghali JK, et al. for the PRAISE Study Group. Effect of amlodipine on morbidity and mortality in severe chronic heart failure. N Engl J Med. 1996;335:1107–14.
29. Packer M, Bristow MR, Cohn JN, et al. The effect of carvedilol on morbidity and mortality in patients with chronic heart failure. N Engl J Med. 1996;334:1349–55.
30. Rathore SS, Curtis JP, Wang Y, Birstow MR, Krumholz HM. Association of serum digoxin concentration and outcomes in patients with heart failure. JAMA. 2003;289:871–88.
31. Gevaert S, Van Belleghem Y, Bouchez S, Herck I, De Somer F, De Block Y, et al. Acute and critically ill peripartum cardiomyopathy and 'bridge to' therapeutic options: a single center experience with intra-aortic balloon pump, extra corporeal membrane oxygenation and continuous-flow left ventricular assist devices. Crit Care. 2011;15:R93.
32. Keogh A, Macdonald P, Spratt P, Marshman D, Larbalestier R, Kaan A. Outcome in peripartum cardiomyopathy after heart transplantation. J Heart Lung Transplant. 1994;13:202–7.
33. liwa K, Skudicky D, Candy G, Bergemann A, Hopley M, Sareli P. The addition of pentoxifylline to conventional therapy improves outcome in patients with peripartum cardiomyopathy. Eur J Heart Fail. 2002;4(3):305–9.
34. Bültmann BD, Klingel K, Näbauer M, Wallwiener D, Kandolf R. High prevalence of viral genomes and inflammation in peripartum cardiomyopathy. Am J Obstet Gynecol. 2005;193(2):363–5.
35. Ramachandran R, Rewari V. Trikha. Anaesthetic management of patients with peripartum cardiomyopathy. J Obstet Anaesth Crit Care. 2011;1(1):5–12.
36. Sutton MS, Cole P, Plappert M, Saltzman D, Goldhaber S. Effects of subsequent pregnancy on left ventricular function in peripartum cardiomyopathy. Am Heart J. 1991;121:1776–8.
37. Lampert MB, Weiner L, Hibbard J, Korcarz C, Lindheimer M, Lang RM. Contractile reserve in patients with peripartum cardiomyopathy and recovered left ventricular function. Am J Obstet Gynecol. 1997;176(1):189–95.

Anesthesia for Intrapartum Fetal Surgery

36

Matthew Reschke, Anna Gabrielian, and David J. Berman

Learning Points

- Fetal surgery intrapartum is a growing field with many new procedures being developed that can improve neonatal outcomes
- These are procedures that should only be performed at experienced institutions with the appropriate multidisciplinary teams in place
- It is important to understand the physiologic changes in pregnancy as some of these procedures are performed later in gestation
- There are risks to both the mother and fetus, and it is important to appreciate and understand how to optimize both
- Some procedures can be performed minimally invasively and only require some local anesthesia, others require general anesthesia with complex management plans

Introduction

History and Development

Observation of the fetus and its physiology was recorded in medical text as early as the 1500s—by Andreas Vesalius in his *De Humani Corporis Fabrica.* Practical experimentation on mammalian fetuses lagged behind, with the first studies performed in the 1800s on guinea pigs. The twentieth century unfolded with the discovery that a viable pregnancy could be delivered after in utero manipulation of the fetus and, by the 1960s and 1970s, multiple animal models were used to simulate various congenital abnormalities found in human fetuses [1].

The first successful human fetal surgery was performed on Mother's Day in 1981 to relieve hydronephrosis from obstruction via vesicostomy [2]. Since that time fetal surgery has been a rapidly evolving field with more physicians being trained in it. New procedures are being researched and trialled and the outcomes for many of them are quite promising. These are complicated procedures that require a multidisciplinary approach and therefore should only be performed at experienced centers that have an appropriate structure in place and the resources should complications ensue.

These are altruistic procedures as the parturient herself does not gain any benefit from them directly—so it is paramount to minimize the risks to the mother, all while optimizing fetal outcomes.

M. Reschke (✉) · A. Gabrielian · D. J. Berman
Department of Anesthesiology and Critical Care Medicine, The Johns Hopkins Hospital, Baltimore, MD, USA
e-mail: mreschk1@jhmi.edu; agabrie9@jhmi.edu; DaveBerman@jhmi.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_36

Types of Surgery

Intrapartum fetal surgery is a developing field that includes a wide array of procedures. Fetal surgeries can be performed in a minimally invasive manner either via needle or fetoscope. These include procedures such as serial amniocentesis, septostomy, or laser therapy for *twin-twin transfusion syndrome (TTTS); radiofrequency ablation or bipolar coagulation for twin reversed arterial perfusion (TRAP);* fetal blood transfusion; release of *amniotic bands*, fetoscopic endotracheal occlusion (FETO), and balloon valvuloplasty to name a few. More complex procedures that require open abdominal incisions are myelomeningocele (MMC) repairs, Ex-Utero Intrapartum Treatment (EXIT) procedures, and Sacrococcygeal Teratoma Resections. The anesthetic management of these cases depends on the complexity of the condition and the approach of the surgery. Minimally invasive procedures can typically be performed with local anesthesia with or without sedation. In certain instances neuraxial anesthesia may be preferable. Open surgery requires a more complex general anesthetic that will be discussed in depth later.

Minimally Invasive Procedures

Twin-Twin Transfusion Syndrome (TTTS)

TTTS is a condition in monochorionic gestations where an arteriovenous vascular anomaly exists that leads to uneven distribution of volume between the fetuses. Twin Anemia Polycythemia Syndrome is a variation of this process where the result is anemia in one and polycythemia in the other. The incidence of TTTS is estimated to be present in 9–15% of diamniotic pregnancies and 6% for monoamniotic [3]. Surgical management of these patients can be by Fetoscopic Laser Ablation of Anastomotic Vessels, Amnioreduction, or Selective Twin Reduction. A small incision to allow for trocar insertion is required to gain access for the procedures.

Twin Reversed Arterial Perfusion (TRAP)

In monochorionic gestations where one fetus is acardiac, the other fetus is the "pump twin" and its cardiac system performs the work of supplying blood to both fetuses. This puts the "pump twin" at risk for cardiac failure. Fetal intervention can be performed to selectively reduce the acardiac twin—which is often not fully formed and may be missing body parts—via radiofrequency ablation or fetoscopic cord coagulation.

Fetal Blood Sampling (FBS)

FBS involves inserting a 20–22 g spinal needle and obtaining blood from the umbilical cord or intrahepatic vein (rarely intracardiac). It is performed to evaluate and treat severe fetal anemia. Diagnostic testing can typically be performed with local anesthesia—however for longer, therapeutic procedures sedation may be added, or some institutions may choose to perform neuraxial anesthesia due to concerns of conversion to cesarean delivery.

Amniotic Band Sequence (ABS)

ABS refers to a class of anomalies where amniotic strands may constrict the fetus's extremities. Fetoscopic laser or scissors can be used to lyse the bands to relieve the constriction and allow for more normal development.

Fetoscopic Endotracheal Occlusion (FETO)

Patients who are diagnosed intrapartum with fetal congenital diaphragmatic hernias may be candidates for intervention. FETO is the percutaneous endoscopic insertion of a balloon into the fetus' trachea. This minimizes compression of the lung tissues and allows more lung growth [4].

This is a newer procedure with only a select few institutions performing it currently.

Congenital Pulmonary Airway Malformation (CPAM)

These rare tumors may be treated by fetal intervention in severe cases by drainage or placement of thoracoamniotic shunts. These are typically performed under neuraxial with or without sedation. Open fetal surgery can also be performed in the worst of cases with lobectomy.

Fetal Hydronephrosis

Fetal hydronephrosis most commonly caused by either obstruction or posterior urethral valves can lead to renal disease and poor lung development. Placement of a vesicoamniotic shunt can help in decompression and allow for greater lung development.

Invasive Procedures

Myelomeningocele (MMC)

MMCs are the most common form of spina bifida: these are congenital defects that result in the extrusion of the meninges and spinal cord into a sac filled with cerebrospinal fluid. Fetal surgery can be performed to improve quality of life for the patient and parents and for improved motor function and development compared to postnatal repair [5]. Early postnatal surgical repair still results in irreversible damage which, depending on defect size, includes paralysis and bowel and bladder dysfunction. The current hypothesis regarding the severity of the damage entails a two-hit injury: the first part is the failure of the neural tube to close, the second part is the exposure of the neural elements to the intrauterine environment. Given this theory it becomes clear that early closure of the defect would minimize the secondary damage incurred. The MOMS trial was an NIH sponsored multicenter trial investigating early closure at 26 weeks gestational age and post-natal repair: the benefits of intrauterine repair were so apparent that the trial had to be stopped early, with 183 of the planned 200 patients recruited. Early repair was associated with decreased risk of death or shunt placement as well as improvement in mental development and motor function [6].

Ex-Utero Intrapartum Treatment (EXIT)

EXIT procedures are used to secure the fetal airway or allow it to be placed on ECMO prior to separation from maternal placental support. The specifics of this procedure are discussed elsewhere. Briefly, the fetus is partially delivered via c-section while remaining connected to the maternal circulation via the placenta. Its airway and circulation are stabilized through extraneous intervention—intubation, ECMO—and only then is the placental connection severed. Such procedures are performed when the fetus has a known congenital malformation which would not be compatible with life upon delivery.

Sacrococcygeal Teratoma (SCT)

SCTs are arteriovenous malformations that can lead to high output cardiac failure for the fetus. In certain cases they can be partially resected in utero in order to allow further development of the fetus with definitive treatment postnatally. Alternatively these fetuses can be delivered via EXIT procedures and subsequently managed.

Anesthesia Concerns

Physiologic Changes in Pregnancy

The state of pregnancy causes notable derangements in normal physiologic parameters, and all organ systems of the parturient are affected to

varying degrees. This is discussed in greater detail in earlier chapters. It is crucial for successful surgical and anesthetic intervention that the practitioner be very familiar with the physiologic changes brought about by pregnancy.

A high degree of vigilance is warranted from patient intake to post-operative care. For example, hematocrit and creatinine levels that are "normal" in a non-pregnant state may signify dehydration in the parturient. A dilutional anemia occurs in pregnancy that results in a 15% decreased hematocrit due to increases in plasma volume, and creatinine levels fall due to an increase in GFR. The ability to identify and appreciate the subtle changes is tantamount in providing appropriate care to both patients—mother and fetus.

Another physiologic parameter that should be observed closely in the parturient is blood pressure. In the non-pregnant patient previously undiagnosed hypertension warrants a workup but is generally not considered urgent: in the parturient, however, unexplained elevations in blood pressure could herald the onset of the hypertensive disorders of pregnancy. These could potentially have more substantial effects for mother and fetus if not treated appropriately. Thus, a sudden elevation in blood pressure in the setting of prior normotension should prompt a thorough workup and careful monitoring for progression at all points of the pregnancy process.

The knowledge of maternal physiology will also guide the choice of anesthetic management for the mother during surgery on the fetus. Increased oxygen consumption and a decreased functional residual capacity lead to rapid desaturation and hypoxia. Cephalad displacement of the stomach by the uterus and decreased lower esophageal sphincter tone lead to a higher risk of aspiration. These all preclude general anesthesia from being the first choice of anesthetic, with preference given to neuraxial anesthesia. When general anesthesia is unavoidable or chosen for other factors, aggressive antiemetic management is important and the airway should be secured expertly following rapid sequence induction. Appropriate preoxygenation is even more crucial in the pregnant patient. Airway changes along with an increased incidence of difficult tracheal intubation are more common in parturients so it is important to understand the risks of endotracheal intubation and to prepare accordingly—such as readying smaller endotracheal tubes and rapidly converting to video laryngoscopy if direct laryngoscopy is inadequate.

Conversely, it is important to gauge the appropriateness of neuraxial anesthetics in the setting of bleeding disorders of pregnancy. These range from the benign thrombocytopenia of pregnancy, to Von Willebrand disease, to iatrogenically administered anticoagulants, to HELLP syndrome—amongst many others. The appropriate practitioner of anesthesia for fetal surgery will be familiar with the diagnosis, pathophysiology, and treatment of all these [7].

Fetal Hemodynamics

It is important to understand fetal hemodynamics, particularly when discussing open procedures where the fetus is exposed. Hypothermia in the fetus is a serious risk and is associated with poor outcomes. Due to a lack of ability to shiver, an immature skin barrier leading to increased evaporative losses, and immature thermogenesis the fetus is susceptible to significant temperature shifts. The hypovolemia and hypoperfusion that can follow leads to hypoxia. As a result, the surgeons try to expose as little of the surgical field through the hysterotomy and warmed fluids replace the lost amniotic fluid which is imperative to the wellbeing of the fetus. Large volumes of amniotic fluid are oftentimes replaced during these procedures so rapid infusion devices must be utilized and connected to the sterile operative field [8].

Another concept that is frequently discussed is the role of fetal pain. In the third trimester neurologic pathways responsible for noxious stimuli are still developing. However, physiologic responses are observed and measurable increases in stress hormones such as cortisol and B-endorphin are seen. The long term neurodevelopmental and behavioral responses to pain have not been studied, but the general consensus is that

the fetus in the third trimester warrants anesthesia and analgesia during surgery. This can be administered indirectly via the mother—by way of the placenta—or directly via intramuscular or umbilical vein injection [9].

Moreover, the fetus exists in exquisite balance with the mother and it is essential to recognize how interventions administered to the mother will affect the fetus. This ranges from basic physiology, such as when the mother becomes hypotensive, placental perfusion will decrease and negative effects can be detected in the fetus, to more complex pharmacologic principles. Neuraxial anesthesia does not significantly decrease uterine blood flow, barring significant decreases in blood pressure. Intravenous anesthetics tend to preserve uterine blood flow and placental perfusion. The volatile anesthetics may cause a decrease in placental perfusion: although the uterus vasodilates to preserve placental perfusion initially, eventually this is not enough to compensate for the decrease in blood pressure. Recent studies suggest that both phenylephrine and ephedrine are effective for hemodynamic support under these circumstances [10].

In general, placental transfer of medications is facilitated by small size (<500 Da), uncharged state, low protein binding, and lipophilicity. Caveats to the above are that ionic forms, when they do cross the placenta, may preferentially be sequestered in the fetus since it tends to have a lower pH than the mother; medications with high protein binding still have a fraction that is nonbound, and this can cross the placenta; excessive lipophilicity can paradoxically cause placental accumulation so less medication than anticipated will reach the fetus [11].

In terms of anesthetic management and placental drug transfer, both volatile and intravenous anesthetics readily cross the placenta. Local anesthetics and opiates cross the placenta to varying degrees and may be affected by the ion trapping described above, with preferential fetal accumulation. Paralytic agents do not cross the placenta, although repeated doses of succinylcholine may have fetal effects. When reversing neuromuscular blockade for the mother it is important to remember that, while neostigmine crosses the placenta, glycopyrrolate does not due to its larger size. To avoid fetal bradycardia it is thus preferable to pair neostigmine with placenta-crossing atropine during reversal.

Determining what agents are able to reach the fetus is only part of the complex picture of fetal pharmacokinetics. Few studies exist to elucidate this area, and fetal pharmacokinetics are often extrapolated from neonate studies. Key points are that the fetal organ systems are not fully developed, with earlier gestational age corresponding to lesser functionality: this results in greater fetal drug levels than may otherwise be anticipated.

Anesthesia Management

The anesthetic management of these cases is complex and multidisciplinary. It requires the coordination between anesthesia, obstetrics/MFM/fetal surgery, neonatology, ultrasonography and the surgical services. An ideal anesthetic balances the needs of the mother, fetus and optimization or surgical conditions. The mother is not without risk as some of the procedures require major surgical intervention with all the inherent risks associated. The risks to the fetus include placental abruption, membrane separation, PPROM, preterm labor, and uterine rupture [12].

The extent of anesthetic involvement depends on the complexity of the procedure. For most ultrasound guided and minimally invasive fetoscopic procedures local anesthesia is often sufficient. It can be supplemented with maternal sedation. Occasionally neuraxial may be preferred by the surgeons. This also allows for the ability to convert to an emergent cesarean delivery in case of fetal intolerance. Otherwise, the anesthesiology team should be prepared to rapidly convert to general anesthesia in case of emergency.

Open Abdominal Procedures

Open abdominal surgery require more complicated management. These procedures are performed under general anesthesia. Appropriate

intravenous access is required (typically two large bore peripheral IVs) along with an arterial line to closely monitor vitals due to the expected usage of vasodilators and vasopressors. An epidural can be placed preoperatively to facilitate postoperative pain control which is important to minimize uterine irritation. A difficult airway is to be appreciated in the parturient population and therefore indirect laryngoscopy can be used first line to secure the airway in a rapid sequence. Many institutions choose to bridge anesthesia with TIVA (propofol and remifentanil) during the planning and preparation phase until incision is made to minimize uterine relaxation during laparotomy. Tocolysis is maintained throughout the procedure with preoperative indomethacin and a magnesium infusion (typically 4–6 g bolus given over 30 min after incision to be followed by an infusion at 2–4 g/h) which is continued postoperatively and managed by the fetal team. It is important to be careful with titration of nondepolarizing muscular blockers as their duration of action is prolonged by the high doses of magnesium and high levels of inhaled anesthetics so close monitoring of relaxation is important.

Upon skin incision the anesthetic is converted from intravenous to volatile with high doses of gas to provide hypnosis and uterine relaxation. Prior to uterine incision, the nitroglycerin infusion is started for further relaxation. There is variation between protocols and physician preference relating to the ratio of gas and nitroglycerin. Some prefer using higher MAC of volatiles with a continuous nitroglycerin rate while others prefer to titrate higher doses of nitroglycerin. Phenylephrine or low dose norepinephrine will almost certainly be required with the combination of these vasodilators to ensure maintenance of baseline blood pressure to optimize uteroplacental perfusion. Upon exposure of the fetus, the surgeons will administer an intramuscular medication cocktail that contains a long acting paralytic, fentanyl, and atropine. Weight based doses of medication based on the most recent estimated fetal weight should either be prepared by the pharmacy or drawn up by the team prior to the procedure. The fetal team will frequently monitor the status of the fetal heart rate via ultrasonography and intervene as required. Fetal temperature optimization is imperative during procedures with open hysterotomies and exposure. The operating room is warmed as it would for other neonatal cases and the lost amniotic fluid is aggressively replaced by rapid transfusers of warmed crystalloid. It is typical for large volumes to be required, sometimes up to 20 L.

Once the fetal procedure is completed the hysterotomy is carefully closed in multiple layers. The nitroglycerin is titrated down or turned off once the uterus is internalized and closure is begun. Consider weaning your inhaled anesthetic early or converting to TIVA knowing that the patient may have ample deposits. Wait to administer reversal until after postoperative doptones are performed. The epidural can be run throughout the procedure or can be activated and bolused prior to extubation.

Several other considerations are worth mentioning that are unique to these procedures. It is important to be conservative with fluid management, and typical goals are less than 2 L of fluid total, as postoperative pulmonary edema is one of the more common sources of maternal morbidity. The volume of the infusions alone are substantial throughout the case so vasopressors are preferred to additional fluid boluses for hypotension. The team should be prepared to deliver and resuscitate the fetus in case of emergency so the appropriate equipment and personnel must be available. Aliquots of fetal blood should be immediately available that are O-negative, CMV-negative, irradiated, leukocyte depleted, and have been crossmatched with maternal blood. These patients must subsequently be delivered by cesarean section at 37 weeks, if possible.

Conclusion

This is a promising field with constantly developing procedures that can improve neonatal morbidity and mortality. These should only be performed at the appropriate centers because of the complexity and required support. The scope of anesthesia management for these procedures varies from institution to institution but certain procedures can be performed minimally invasively with little sedation and at other times may

require a much more extensive plan. An appreciation for the nuisances of the pregnant mother and fetus in utero are required to safely deliver an anesthestic that also optimizes surgical conditions.

Funding Disclosures and Conflicts of Interest None to disclose as related to this project.

References

1. Jancelewicz T, Harrison MR. A history of fetal surgery. Clin Perinatol. 2009;36:227–36.
2. Harrison MR, Golbus MS, Filly RA, Callen PW, Katz M, de Lorimier AA, Rosen M, Jonsen AR. Fetal surgery for congenital hydronephrosis. N Engl J Med. 1982;306:591–3.
3. Baxi LV, Walsh CA. Monoamniotic twins in contemporary practice: a single-center study of perinatal outcomes. J Matern Fetal Neonatal Med. 2010;23:506–10.
4. Baschat AA, Rosner M, Millard SE, et al. Single-Center Outcome of Fetoscopic Tracheal Balloon Occlusion for Severe Congenital Diaphragmatic Hernia. Obstet Gynecol. 2020;135:511–21.
5. Houtrow AJ, Thom EA, Fletcher JM, et al. Prenatal repair of myelomeningocele and school-age functional outcomes. Pediatrics. 2020;145(2):e20191544. https://doi.org/10.1542/peds.2019-1544.
6. Adzick NS, Scott Adzick N, Thom EA, et al. A randomized trial of prenatal versus postnatal repair of myelomeningocele. N Engl J Med. 2011;364:993–1004.
7. Chestnut DH, Wong CA, Tsen LC, Ngan Kee WD, Beilin Y, Mhyre J. Chestnut's obstetric anesthesia: principles and practice e-book. Amsterdam: Elsevier Health Sciences; 2014.
8. De Buck F, Deprest J, Van de Velde M. Anesthesia for fetal surgery. Curr Opin Anaesthesiol. 2008;21:293–7.
9. Lin EE, Tran KM. Anesthesia for fetal surgery. Semin Pediatr Surg. 2013;22:50–5.
10. Singh PM, Singh NP, Reschke M, Ngan Kee WD, Palanisamy A, Monks DT. Vasopressor drugs for the prevention and treatment of hypotension during neuraxial anaesthesia for Caesarean delivery: a Bayesian network meta-analysis of fetal and maternal outcomes. Br J Anaesth. 2020;124:e95–e107.
11. Griffiths SK, Campbell JP. Placental structure, function and drug transfer. Continuing education in anaesthesia. Crit Care Pain. 2015;15:84–9.
12. Kabagambe SK, Jensen GW, Chen YJ, Vanover MA, Farmer DL. Fetal surgery for myelomeningocele: a systematic review and meta-analysis of outcomes in fetoscopic versus open repair. Fetal Diagn Ther. 2018;43:161–74.

37 Anesthesia for Deep Brain Stimulation

Muthuraj Kanakaraj

Introduction

Deep Brain Stimulation (DBS) is a functional stereotactic neurosurgical treatment used effectively in movement disorders such as Parkinson's disease (PD), Essential Tremor and Dystonia refractory to medical management. It's application is also increasingly explored in the treatment of psychiatric disorders like Obsessive Compulsive Disorder and Major Depression. This technique has been increasingly used over the last two decades and has proven to improve the quality of life of the patients especially with PD [1].

It is a minimally invasive procedure which includes the placement of electrodes into the deep structures of the brain and connecting them to a pulse generator implanted in the chest wall through subcutaneously tunneled leads. In most institutions it is performed in two stages where the placement of electrodes is achieved with the patient being awake under Magnetic Resonance Imaging (MRI) guidance unless contraindicated and the pulse generator implantation under general anesthesia [2].

The role of the anesthesiologist is vital in facilitating the accurate placement of the electrodes in the deep brain structures as well as keeping the patient comfortable. The anesthesiologist is faced with challenges in providing anesthesia in a remote location (MRI suite), optimal surgical conditions, ensuring a patent airway, maintenance of stable cardiopulmonary status, monitoring of neurology/cognition, awareness to the pharmacokinetics in patients with PD, drug interactions with the procedure and prompt management of perioperative complications.

History

In 1987, Benabid et al. laid the foundation for the modern era of DBS by successfully demonstrating reduction of tremor in a PD patient through stimulation of the Ventral intermediate (Vim) nucleus of the thalamus [3]. The introduction of Albin-Delong model of basal ganglia function in 1989–1990, based on the hypothesis that there are isolated circuits within the basal ganglia-thalamocortical network each with a distinct function of its own provided the scientific basis for the DBS [4, 5]. In 1998, Limousin et al. demonstrated that bilateral subthalamic nucleus (STN) DBS was not only safe and effective in advanced PD but also reduced the dose of dopamine replacement therapy [6]. In 2000, Coubes

M. Kanakaraj (✉)
Department of Anesthesiology, Washington University in Saint Louis, St Louis, MO, USA
e-mail: muthuraj.kanakaraj@wustl.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_37

et al. demonstrated DBS of Globus Palladium pars interna (GPi) for the treatment of dystonia.

The Federal Drug Administration (FDA) approval encouraged the expansion of the practice of DBS in many centers.

1997: Thalamic DBS for Essential Tremor and PD-related tremor.

2003: STN DBS and GPi DBS for PD.

A humanitarian device exemption for STN DBS and GPi DBS for primary generalized and segmental dystonia was granted in 2003 and for Obsessive Compulsive Disorder in 2004.

Advantages of DBS Over Invasive Neuro-Ablative Procedures

Invasive procedures like thalamotomy, pallidotomy and cingulotomy were performed before the invention of DBS in which the outcomes were irreversible including permanent side effects. In DBS, the outcomes are not only reversible, but the stimulation can also be applied bilaterally and titrated according to the desired effects. It is also proven to be safe and effective in the long term, thereby providing a better quality of life.

Device

The DBS has got four components:

1. The multi-contact intracranial quadripolar DBS electrodes, which are inserted into the deep brain either unilaterally or bilaterally as indicated.
2. A plastic ring and cap seated onto a burr hole to fix the electrodes to the skull.
3. A single or dual channel internal pulse generator (IPG)
4. A subcutaneously tunneled extension cable to connect the DBS electrode and the IPG.

Indications and the targets [7]

Parkinson's disease	Subthalamic nucleus(STN); Globus pallidus interna(GPi)
Essential tremor	Ventral intermediate thalamus(Vim)
Dystonia	Globus pallidus interna(GPi)
Obsessive Compulsive Disease	Anterior limb of internal capsule(AIC)
Epilepsy	Anterior nucleus of thalamus
Chronic pain	Ventrocaudal thalamus; Periventricular gray
Major depression	Subcallosal cingulate gyrus; Nucleus Accumbens; AIC
Tourette syndrome	Centromedian-parafascicular nucleus of thalamus; Nucleus Acumbens; GPi

Contraindications

- Dementia
- Patients who are unable to follow instructions
- Patients with unsuccessful test stimulation
- Patients with increased bleeding risk as in coagulopathy and uncontrolled hypertension

Surgical procedure with anesthetic implications.

Deep brain stimulation placement is achieved in two stages.

Stage 1: Insertion of the electrodes close to the target nuclei in the brain.

1. Generally done under MAC with local anesthesia or conscious sedation as it requires patient co-operation and vigilant monitoring by the anesthesiologist.
2. Done under MRI guidance unless there is a contraindication to MRI. All the safety precautions for MRI should be strictly followed.
3. The first step is the placement of a rigid stereotactic head frame to the patient's skull under local anesthesia or scalp block. When this head frame is fixed to the operating table, it restricts the access to the airway (Fig. 37.1). So, if a GA

Fig. 37.1 Awake patient with the head in a rigid stereotactic frame fixed to the operating table

is planned, the patient should be intubated before the head frame is placed. Further, it poses a challenge for emergency intubation. The anesthesiologist should have a plan to deal with that situation. There are reports from some centers that STN-DBS can be placed without the need for the rigid stereotactic head frame, but GPi and Vim DBS still need the stereotactic head frames.

4. The second step is the visualization of the target nuclei under MRI and establishment of references to external coordinates for accurate insertion of the electrodes. If MRI is contraindicated, the patient is taken to CT scan to get the images and further establish the coordinates.
5. Next, the patient is positioned either supine or in a semi-sitting position with the rigid head frame fixed to the operative bed and a burr hole is created in the cranium for the insertion of the electrode. The patient is at risk for the development of venous air embolism with the creation of a burr hole.
6. Then the electrode is placed 10–15 mm above the target site. The surgeon does this in coordination with a neurophysiologist who uses a method called microelectrode recording (MER). The electrode is advanced 0.5–1 mm along the path towards the target. This facilitates the accurate placement of the electrode. It is important that the anesthesiologist uses the appropriate sedation, if needed, that will not interfere with the MER.
7. With the patient awake, stage 1 is completed by observing the clinical improvement and side effects by macrostimulation of the target nuclei through the inserted electrode.

Stage 2: Implantation of the internal pulse generator and connecting the electrodes with it through subcutaneously tunneled leads. This is done under general anesthesia with endotracheal intubation because the subcutaneous tunneling is done on the side of the neck which restricts the airway access and also can be very stimulating.

Depending on the institution, both the stages can be done on the same day or the second stage is done in about 3 days to 2-weeks after the first stage. Initially, the electrodes can cause edema around the implanted site (microlesion effect), which can result in an improvement of the symptoms. This in turn can interfere with the response to the actual stimulation of the target sites. So the microlesion effect can impair the functioning of DBS by 1–2 weeks.

Anesthetic Implications in Microelectrode Recording (MER)

MER is done in coordination with a neurologist or neurophysiologist to improve the accuracy in the placement of the electrode [8]. Specific brain structures can be identified by their unique patterns of spontaneous neuronal firing. These patterns of neuronal firing are simultaneously recorded as the microelectrode is advanced along the path towards the target nuclei. The neuronal discharges are viewed on an oscilloscope and listened through an audio monitor as they are best appreciated as sound waves [9]. As the microelectrode is advanced, the neurophysiologists make a scaled drawing of the

cells encountered at each depth. This information is superimposed on the brain atlas to assist in determining the electrode's exact location.

Sedatives which act by enhancing the GABAergic neurons can theoretically interfere with the neuronal firing rate, MER and the accurate placement of the electrodes. The GPi neurons have a higher GABA input than the STN neurons. Further, the neuronal firing rates in GPi, was significantly decreased in patients with PD than in dystonia. Compared with local anesthesia, the neuronal activity is decreased with long pauses from GPi under general anesthesia with Propofol, in patients with dystonia [10]. In practice, successful MERs have been obtained from STN nuclei irrespective of the choice of anesthetic technique with Propofol and dexmedetomidine. The varied MER response from GPi may be due to its GABAergic input. But it doesn't affect its ability to facilitate the accuracy in the placement of the electrode.

Anesthetic Implication in Macrostimulation Testing

This is the final step in stage 1 of DBS implantation. The patient needs to be awake and be able to cooperate to determine the expected treatment response and any adverse effects.

If the electrodes are misplaced, dysarthria, dyskinesia, paresthesia, eye movements, muscle cramps and cerebellar signs can be observed. If conscious sedation is used, it should be discontinued well in advance to minimize its effects. General anesthesia can suppress tremors and rigidity and impair the success of macrostimulation testing [11]. Flash visual evoked potentials for GPi DBS, high intensity stimulation for internal capsule and MRI confirmation of the implanted electrode are used in patients who need general anesthesia for stage 1 of the procedure [12, 13].

Anesthetic Implications in Specific Disorders [14, 15]

Parkinson Disease

1. Upper airway dysfunction may cause aspiration pneumonia and laryngospasm.
2. Restrictive lung disease can impair oxygenation.
3. Hypovolemia, orthostatic hypotension and autonomic dysfunction can cause hemodynamic instability.
4. Patients may have dysphagia resulting in poor nutrition status.
5. Patients can have depression and dementia which could impair their ability to cooperate.
6. Drug interactions between anti-Parkinson and anesthetic drugs.
7. The "off drug state" can worsen the symptoms intra and postoperatively.

Dystonia

1. Laryngeal dystonia can cause laryngospasm
2. Hypovolemia can cause hemodynamic instability
3. Spasmodic dysphonia can interfere with communication.
4. Poor nutrition.

Essential Tremors

- Betablocker therapy can cause cardiac arrhythmias.

Epilepsy

1. Developmental delay can be detrimental in obtaining a consent.
2. Seizures.
3. Drug interactions between anti-epileptics and anesthetic drugs.

Preoperative Evaluation

A comprehensive evaluation should be made with a multidisciplinary involvement and patient selection is made on an individual basis taking into account the risk of the procedure against the benefit in improvement in the quality of life after the procedure. The multidisciplinary team includes the neurologist, neurosurgeon, neurophysiologist, neuropsychologist, psychiatrist and anesthesiologist.

Patient selection is based on the following factors [16, 17]:

1. Diagnosis and indication for the procedure based on the disease severity.

In PD, dopamine sensitive symptoms respond well to DBS. Further PD patients with moderate to severe motor fluctuations, levodopa induced dyskinesia, refractory tremor and intolerance to medications benefit with DBS.

2. Cognitive function.

   Patient's cooperation is vital during stage 1 of the procedure. Further pre-existing dementia may worsen after surgery. A Mini Mental State Exam (MMSE) score of <24 or a Mattis Dementia Rating Scale (MDRS) total score of <120 are indicators of poor response to surgery.

3. Psychiatric status.

   Patients with claustrophobia and extreme anxiety may not tolerate the procedure being awake.

4. Patient's motivation and realistic expectations from the procedure.

Preanesthetic Assessment Specific to DBS

(a) MRI: Patients are checked for the presence of any ferromagnetic devices such as pacemaker, internal cardioverter-defibrillator (ICD), aneurysm clips or cochlear implants.

(b) Position: Patients with musculoskeletal problems and severe dystonia can pose a challenge in positioning especially during stage 1 of the procedure.

(c) Airway: In addition to routine airway assessment and the risk for aspiration, a plan for urgent intubation when the patient's head is fixed to the operating table with the head frame should be evaluated.

(d) Obstructive Sleep Apnea: Patients can develop upper airway obstruction during conscious sedation. A plan for nasopharyngeal airway should be discussed with the patient.

(e) Psychiatric evaluation: As discussed earlier, patient's fitness to tolerate the procedure by being awake should be assessed.

(f) Chronic pain: Clear instructions should be given to continue the patient's regular pain medicines.

(g) Psychological preparation: A detailed verbal and written instructions should be given to the patient and the family on the realistic expectations during as well as after the procedure. Their questions and concerns should be addressed in a reassuring way. A good psychological preparation can alleviate anxiety to a great extent.

(h) Pharmacology:

Drug off state: The neurosurgeons expect the patients to be off their regular medicines for PD, essential tremor and dystonia to enable intraoperative MER, neuronal mapping and clinical testing. Patients with severe symptoms may have worsening of their symptoms in this state. A detailed discussion should be made with the neurosurgeon to assess if the patient could have a reduced dose of their regular medications.

Anti-platelets/Anti-coagulants: After discussing with the primary care providers or the cardiologists, these drugs should be stopped well in advance and any need for a bridging therapy should be discussed with the cardiologists and the neurosurgeons.

Anti-hypertensives: Uncontrolled hypertension can lead to intracerebral hemorrhage especially in stage 1. Optimal blood pressure control should be a priority and there is evidence that continuation of ACE inhibitors and ATR blockers can reduce the need for intraoperative blood pressure control therapy.

Premedication: Benzodiazepines and GABA agonists can interfere with patient cooperation, tremor interpretation and MER. So they are better avoided.

Intraoperative Management

Monitoring

ASA basic standards of monitoring are to be attached to the patient. It is important to deliver oxygen through face masks or nasal prongs with outlets for $ETCO_2$ monitoring during MAC or con-

scious sedation. Invasive blood pressure monitoring is indicated in patients with poor cardiac reserve and uncontrolled movement disorders or dystonia.

Position

As the patient have to be awake for a long time during stage 1 of the procedure, appropriate positioning will contribute to patient comfort. With the head in a rigid frame attached to the operating table, flexion at the lower cervical spine and extension at the atlanto-occipital joint will enable a patent airway and ensure the anesthesiologist to access the airway in an emergency. The legs should be flexed and supported under the knees to maintain stability in a semi-sitting position.

Airway

Patients with their head turned 180° away from the anesthesiologist and fixed in a rigid head frame, limits the anesthesiologist's ability to immediately secure it. During conscious sedation, patients at risk of developing upper airway obstruction may need a nasopharyngeal airway. In patients with severe OSA, the continuous positive airway pressure (CPAP) face mask should be fitted to the patient before the head frame is fixed and the CPAP machine should be readily available. If general anesthesia is planned for stage 1, airway should be secured with an endotracheal tube or laryngeal mask airway (LMA) before the head is fixed to the rigid stereotactic frame. Intubation may be extremely difficult if attempted with the head fixed to the frame especially in an emergency. Video laryngoscopy or Optical laryngoscopy can be useful. Fiberoptic endotracheal intubation may not be quick enough to secure the airway. The risk of regurgitation and aspiration has to be considered when using an LMA.

Blood Pressure Control

As discussed earlier, uncontrolled hypertension may cause intracranial hemorrhage. The risk is higher in an awake and anxious patient. Invasive BP monitoring is useful if there is an increased risk for uncontrolled hypertension. Intravenous anti-hypertensives such as nicardipine, esmolol, hydralazine, labetalol and nitroglycerine are used. A systolic BP of <140 mmHg or a 20% increase of the patient's normal BP is acceptable.

Fluid Management

Since no major blood loss or fluid shifts are expected in this procedure, fluids should be administered cautiously to avoid both hypovolemia and hypervolemia. Hypervolemia can cause bladder distension and patient discomfort. Patients can be advised to void before surgery. In an awake patient, urinary catheter will be very uncomfortable. Patients can be advised to void before surgery to prevent the discomfort from bladder distension.

Communication and Reassurance

This is a very crucial part of the procedure, especially for the anesthesiologist. During MAC as well as conscious sedation, regular communication and reassurance helps in alleviating the anxiety of the patient, macrostimulation testing, early recognition of airway or neurological compromise and prompt response to deal with any emergency. Covering the face with a clear drape can help in a more efficient face to face communication with the patient.

Monitored Anesthesia Care (MAC)

MAC with local anesthesia is considered to provide patient comfort as well as facilitate accurate placement of the electrode without any interference on MER and macrostimulation. Most neurosurgeons prefer this unless the patient cannot tolerate the procedure under MAC. Either subcutaneous infiltration of local anesthesia or a scalp block can be established

[18]. If the patient feels any discomfort during establishment of LA, small doses of dexmedetomidine can be administered. Although there is no evidence of difference between LA infiltration and scalp block in the accurate placement of the electrode, it has been observed that with scalp block, the hemodynamics are better with less requirement of anti-hypertensives [19]. If the procedure is prolonged, it is important to supplement further local anesthetics to maintain patient comfort. Bupivacaine, ropivacaine and lignocaine with or without epinephrine are the local anesthetics commonly used. The anesthesiologist should check the dose of the local anesthetics used and be vigilant for Local Anesthetic Systemic Toxicity (LAST) presentations such as seizures, respiratory and cardiovascular arrest.

Conscious Sedation

Patients may require some comfort during the attachment of the head frame under local anesthesia as well as during closure of the scalp wounds. Since the subcortical brain areas are extremely sensitive to GABA receptor mediated medicines, sedatives can abolish tremor, MER and interfere with the accurate placement of the electrode. It is imperative to use only a short acting sedation that should be stopped well before the neurophysiological testing [20].

Benzodiazepines should not be used in conscious sedation for DBS.

Propofol is commonly used because it is short acting and has got a predictable emergence [21]. The infusion rate should be titrated to the individual patient needs. Titrating the infusion rate according to Bispectral Index (BIS) in DBS, has not shown any difference in the amount of drug consumption, arousal and hemodynamic instability. One should be aware that the pharmacokinetics in PD patients is different from the pharmacokinetic model used to develop target controlled infusion for propofol [22]. It is not known to interfere with MER, but can cause dyskinesia and abolish the tremor.

Dexmedetomidine is an α-2 adrenoceptor agonist acting on local coeruleus (LC) through non-GABA mediated mechanism. LC modulates arousal, sleep and anxiety. So, dexmedetomidine through its action on LC, provides adequate anxiolysis, analgesia and patients can be easily arousable for verbal stimuli. It does not affect respiration. It maintains stable hemodynamics and reduces the need for any anti-hypertensive treatment intraoperatively. Further it does not ameliorate the PD signs. Overall it satisfies the requirements for an ideal sedative for Functional awake neurosurgery [23]. BIS can be used to titrate the infusion for STN-DBS insertion [24]. A BIS >80 is equivalent to MER from subthalamic nucleus in an awake state. However BIS <80 results in suppression of MER as in deep sedation.

General Anesthesia

General anesthesia is used in patients with psychiatric disorders, exacerbation of symptoms on "off drug state" and anxiety with uncontrolled hypertension. Although dexmedetomidine sedation can be used in pediatric patients for awake craniotomy, general anesthesia is better tolerated in children. Although some studies show that the electrode placement under GA may be less accurate, the evidence is not clear on the difference in outcome in patients having the procedure under GA or MAC. The accuracy of the placement of electrodes can be improved by flash visual evoked potentials, high intensity stimulation and confirmation by MRI as discussed earlier.

Postoperative Management

Patients should be recovered in a Post Anesthesia Care Unit as in any other surgery.

With the patients in an "off drug state", for a long time, it is vital that the anti-PD medications are restarted as soon as possible.

Complications

The incidence of intraoperative complications is about 16% that requires a high index of clinical suspicion and immediate response to avoid any serious catastrophe [25].

Respiratory

Acute airway obstruction can occur due to over sedation, seizures or intracranial hemorrhage. The anesthesiologist should have an advanced plan to secure the airway as discussed earlier.

Restrictive lung disease as in PD can result in hypoxemia.

Cardiovascular

Uncontrolled hypertension can be due to poor preoperative optimization of blood pressure, an awake, anxious and agitated patient. It can even result in intracranial hemorrhage (ICH). The blood pressure must be controlled before the insertion of electrode to prevent ICH.

Orthostatic hypotension occurs as a result of the effect of anti-PD medications, hypovolemia and autonomic dysfunction.

Venous air embolism is less common but a serious complication. Burr hole in a supine or semi-sitting patient with hypovolemia is a risk factor. Sudden vigorous coughing is the most common initial symptom followed with tachypnea, hypoxemia, chest discomfort, tachycardia and hypotension. Anesthesiologist should have a high index of clinical suspicion due to limitations in the usage of precordial doppler and $ETCO_2$ monitoring. Prompt communication with the surgeon should be followed with the standard management of a venous air embolism.

Neurological

Seizures can be focal or generalized tonic-clonic. They are usually self-limiting or respond to boluses of Propofol or midazolam.

Altered neurological status can be due to fatigue from being awake for a long time, uncomfortable position, drug withdrawal, seizures and intracranial hemorrhage.

Intracranial hemorrhage is due to uncontrolled hypertension as discussed earlier.

Akinetic crisis occurs in severe PD in which the patient is awake and alert but unable to communicate.

Tension pneumocephalus has been reported as well.

Paresthesia, involuntary movements, cognitive dysfunction and movement changes can occur due to inaccurate placement of the electrodes.

Long Term Complications

Long term complications can be hardware related with infection, migration or misplacement of the electrode, lead fracture, skin erosion and sudden DBS failure.

Parkinsonian crisis can be due to DBS failure with reduced dopamine replacement therapy.

Anesthesia for DBS Battery Replacement

The battery life of the internal pulse generator is usually 2–5 years. Conscious sedation supplemented with opioids or general anesthesia with LMA or endotracheal intubation is provided depending on the patient's airway and other comorbidities. Once on the DBS, the patients are neurostimulator dependent. So, to prevent any Parkinsonian crisis, the anti-PD medications should be continued in the perioperative period and the DBS should be activated immediately after the battery replacement.

Anesthesia for Patients with Pre-existing DBS

It may be not uncommon to have a patient with a DBS for an elective or an emergency surgery.

A thorough history and review of medical records is crucial to identify the presence of a DBS.

A DBS has got almost similar implications as a pacemaker or an ICD.

A discussion with the corresponding neurologist or neurophysiologist has to be made on whether to turn off and reprogram the DBS during and after the surgery. Also it is vital to ensure that the patient is on treatment for the relevant disorder during the perioperative period to avoid any crisis.

Electrocautery: Intraoperative electrocautery can cause thermal damage to the neural tissue around the electrodes [26]. It is recommended to either turn off the DBS during the procedure or use a bipolar diathermy. If a monopolar diathermy is strongly indicated, the grounding pad should be placed as far as possible from the internal pulse generator and the lowest possible energy is used in short irregular pulses. Shortwave diathermy should not be used in a patient with DBS because it induces radiofrequency current and heating of the electrode resulting in devastating neural injury.

External and Internal Cardiac Defibrillators: The paddles must be placed perpendicular and as far as possible to the pulse generators in the event of a defibrillation. The DBS should be checked after a defibrillation.

Electrocardiogram can be interfered with artifacts by a functioning DBS.

Electroconvulsive therapy [27], radiofrequency neuroablation and peripheral nerve stimulation are all safe when the DBS is turned off.

MRI has the potential to increase the temperature of the DBS electrodes and cause brain damage. The Medtronic DBS has been certified as MRI conditional by its manufacturer.

Summary

DBS insertion is a complex procedure with a number of critical steps in which the neurosurgeon, neurophysiologist and the anesthesiologist should work in a very close coordination.

The anesthesiologist faces a number of challenges throughout the procedure. So a comprehensive preoperative assessment, preparing the patient in a reassuring manner with realistic expectations, optimizing the existing comorbidities and a clear plan for the various challenges that may arise throughout the procedure is essential for a successful outcome. Appropriate airway assessment and management plan in an emergency is a key aspect of the care. MAC with local anesthetics or conscious sedation with dexmedetomidine can facilitate the accurate placement of the electrode. A high index of clinical suspicion and monitoring is vital in the prompt recognition and management of the complications.

References

1. Kocabicak E, Temel Y, Höllig A, Falkenburger B, Tan SKH. Current perspectives on deep brain stimulation for severe neurological and psychiatric disorders. Neuropsychiatr Dis Treat. 2015;11:1051.
2. Miocinovic S, Somayajula S, Chitnis S, Vitek JL. History, applications, and mechanisms of deep brain stimulation. JAMA Neurol. 2013;70(2):163–71.
3. Benabid AL, Pollak P, Louveau A, Henry S, de Rougemont J. Combined (thala-motomy and stimulation) stereotactic surgery of the VIM thalamic nucleus for bilateral Parkinson's disease. Appl Neurophysiol. 1987;50(1–6):344–6.
4. Albin RL, Young AB, Penney JB. The functional anatomy of basal ganglia disorders. Trends Neurosci. 1989;12(10):366–75.
5. DeLong MR. Primate models of movement disorders of basal ganglia origin. Trends Neurosci. 1990;13(7):281–5.
6. Limousin P, Krack P, Pollak P, et al. Electrical stimulation of the subthalamic nucleus in advanced Parkinson's disease. N Engl J Med. 1998;339(16):1105–11.
7. Suchorska B, Ruge MI. Deep brain stimulation: current applications and future prospects. Discov Med. 2015;20(112):403.

8. Venkatraghavan L, Luciano M, Manninen P. Review article: anesthetic management of patients undergoing deep brain stimulator insertion. Anesth Analg. 2010;110:1138–45.
9. Ruskin DN, Bergstrom DA, Kaneoke Y, Patel BN, Twery MJ, Walters JR. Multisecond oscillations in firing rate in the basal ganglia: robust modulation by dopamine receptor activation and anesthesia. J Neurophysiol. 1999;81:2046–55.
10. Hutchison WD, Lang AE, Dostrovsky JO, Lozano AM. Pallidal neuronal activity: implications for models of dystonia. Ann Neurol. 2003;53:480–8.
11. Anderson BJ, Marks PV, Futter ME. Propofol-contrasting effects in movement disorders. Br J Neurosurg. 1994;8:387–8.
12. Lozano AM, Kumar R, Gross RE, Giladi N, Hutchison WD, Dostrovsky JO, Lang AE. Globus pallidus internus pallidotomy for generalized dystonia. Mov Disord. 1997;12:865–70.
13. Krause M, Fogel W, Kloss M, Rasche D, Volkmann J, Tronnier V. Pallidal stimulation for dystonia. Neurosurgery. 2004;55:1361–8.
14. Nicholson G, Pereira AC, Hall GM. Parkinson's disease and anesthesia. Br J Anaesth. 2002;89:904–16.
15. Frost EA, Osborn I. Deep brain stimulation—surgery for movement disorders and Parkinson's disease. Int Anesthesiol Clin. 2009;47:57–68.
16. Rodriguez RL, Fernandez HH, Haq I, Okun MS. Pearls in patient selection for deep brain stimulation. Neurologist. 2007;13:253–60.
17. Poon CC, Irwin MG. Anaesthesia for deep brain stimulation and in patients with implanted neurostimulator devices. Br J Anaesth. 2009;103(2):152–65.
18. Watson R, Leslie K. Nerve blocks versus subcutaneous infiltration for stereotactic frame placement. Anesth Analg. 2001;92:424.
19. Krauss P, Marahori NA, Oertel MF, Barth F, Stieglitz LH. Better hemodynamics and less antihypertensive medication: comparison of scalp block and local infiltration anesthesia for skull-pin placement in awake deep brain stimulation surgery. World Neurosurg. 2018;120:e991.
20. Martinez-Simon A, Alegre M, Honorato-Cia C, Nuñez-Cordoba JM, Cacho-Asenjo E, Trocóniz IF, et al. Effect of dexmedetomidine and propofol on basal ganglia activity in parkinson disease: a controlled clinical trial. Anesthesiology. 2017;126(6):1033.
21. Kim W, Song IH, Lim YH, Kim MR, Kim YE, Hwang JH, et al. Influence of propofol and fentanyl on deep brain stimulation of the subthalamic nucleus. J Korean Med Sci. 2014;29(9):1278.
22. Fábregas N, Rapado J, Gambús PL, Valero R, Carrero E, Salvador L, et al. Modeling of the sedative and airway obstruction effects of propofol in patients with Parkinson disease undergoing stereotactic surgery. Anesthesiology. 2002;97(6):1378–86.
23. Rozet I. Anesthesia for functional neurosurgery: the role of dexmedetomidine. Curr Opin Anaesthesiol. 2008;21(5):537–43.
24. Elias WJ, Durieux ME, Huss D, Frysinger RC. Dexmedetomidine and arousal effect of subthalamic neurons. Mov Disord. 2008;23:1317–20.
25. Venkatraghavan L, Manninen P, Mak P, Lukitto K, Hodaie M, Lozano A. Anesthesia for functional neurosurgery review of complications. J Neurosurg Anesthesiol. 2006;18:64–7.
26. Martinelli PT, Schulze KE, Nelson BR. Mohs. Micrographic surgery in a patient with a deep brain stimulator: a review of the literature on implantable electrical devices. Dermatol Surg. 2004;30(7):1021–30.
27. Bailine S, Kremen N, Kohen I, Linder H, Schwartz GJ, Mogilner AY, et al. Bitemporal electroconvulsive therapy for depression in a Parkinson disease patient with a deep-brain stimulator. J ECT. 2008;24(2):171.

38

Anesthesia for Hyperthermic Intraperitoneal Chemotherapy (HIPEC)

Eilish M. Galvin, Emma C. Boer, and Sanne H. Hidding

Learning Points

- Cytoreductive surgery (CRS) with HIPEC (hyperthermic intraperitoneal chemotherapy) uses extensive surgical resection and locally infused heated chemotherapeutic agents as a treatment for peritoneal malignancy.
- Significant pathophysiological changes can be expected during CRS and HIPEC; including blood loss, coagulation disorders and/or cardiopulmonary compromise.
- CRS-HIPEC is a complex procedure with various challenges, therefore standardized protocols and dedicated teams are preferable.

Introduction

CRS-HIPEC surgery is complex and perioperative management depends on many factors; including patient's preoperative health status, disease load, surgical factors, intraoperative events, in addition to the type of chemotherapeutic drug(s) used for HIPEC. HIPEC is a highly concentrated, heated chemotherapy treatment that is delivered directly into the abdominal cavity after cytoreductive surgery (CRS).

CRS with HIPEC (hyperthermic intraperitoneal chemotherapy) is a procedure with various challenges for both anaesthesiologist and surgeon. Traditionally, primary peritoneal malignancy and peritoneal metastasis from gastrointestinal and gynaecological malignant neoplasms have a poor prognosis [1]. Since the start of CRS-HIPEC surgery the outcome of these patients has improved [2]. In mesothelioma and appendix peritoneal metastasis, CRS-HIPEC has significantly improved 5-year survival from less than 10% to 50% to 90%, and is now considered the standard of care for these tumor types. For colorectal peritoneal metastases median survival ranges from 22 to 47 months, with 5-year survival increasing from 27% to 54% with CRS-HIPEC. For ovarian cancer CRS-HIPEC surgery shows a median survival of 73 months with an overall survival benefit of 11 months [3].

The importance of anesthesia management is often underestimated. A good clinical pathway is key to success, focused on patient selection, nutrition, renal protection, pain management, prevention and early detection of complications [4, 5].

Surgical Procedure

CRS-HIPEC surgery is difficult and associated with a high morbidity and mortality rate [6]. Patient selection, standardisation of surgical

E. M. Galvin (✉) · E. C. Boer
S. H. Hidding
Department of Anesthesiology Erasmus Medical Centre, University of Rotterdam the Netherlands, Rotterdam, The Netherlands
e-mail: e.galvin@erasmusmc.nl; e.c.boer@erasmusmc.nl; s.hidding@erasmusmc.nl

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_38

technique and degree of surgical experience are important contributors in reducing morbidity and mortality rates.

Patient Selection

In patient selection for HIPEC-procedure many factors play a crucial role, such as the tumor entity (with no extra-abdominal metastases), limited tumor extent and good general status with a Karnofsky index of ≥80 (normal activity with effort; some signs or symptoms of disease) Fig. 38.1 [7]. The peritoneal Carcinomatosis Index (PCI) is used to make a quantitative assessment of the extent of disease within the peritoneal cavity Fig. 38.2 [8]. Some centers have exclusion criteria for HIPEC (i.e. advanced age, ASA IV, significant cardiac or pulmonary comorbidity, renal failure). It is important that each case should be assessed individually and discussed in a multidisciplinary team in case of frailty.

The CRS-HIPEC procedure is distinguished in two stages.

Able to carry on normal activity and to work; no special care needed.	100	Normal no complaints; no evidence of disease.
	90	Able to carry on normal activity; minor signs or symptoms of disease.
	80	Normal activity with effort; some signs or symptoms of disease.
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed.	70	Cares for self; unable to carry on normal activity or to do active work.
	60	Requires occasional assistance, but is able to care for most of his personel needs.
	50	Requires considerable assistance and frequent medical care.
Unable to care for self; requires equivalent of instituitional or hospital care; disease may be progressing rapidly.	40	Disable; requires special care and assistance.
	30	Severely disabled; hospital admission is indicated although death not imminent,
	20	Very sick; hospital admission necessary; active supportive treatment necessary.
	10	Moribund; fatal processe progressing rapidly.
	0	Dead

Fig. 38.1 Karnofsky performance status scale definitions rating (%) criteria

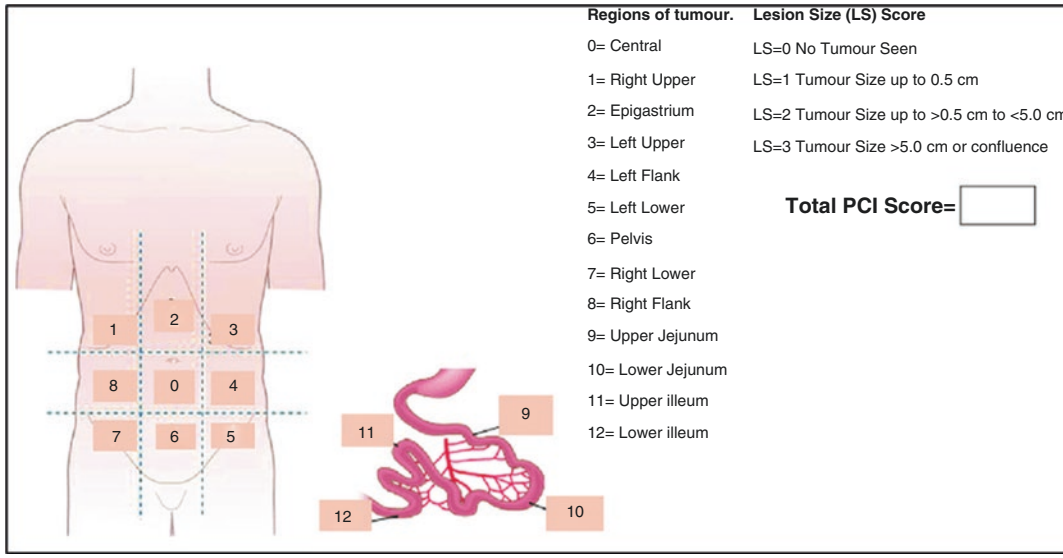


Fig. 38.2 Sugarbaker's peritoneal carcinomatosis index scoring

First Stage: Cytoreduction Surgery (CRS)

The first stage, cytoreduction, consists of macroscopic removal of tumor tissue including affected organs and peritoneum. The "Completeness of Cytoreduction (CC) score" is an important prognostic indicator on basis of the visible tumor left after cytoreduction. (CC-0 no visible tumor; CC-1 persisting tumor nodule <2.5 mm; CC-2 tumor nodule between 2.5 mm-2.5 cm and CC-3 tumor nodule >2.5 cm) [9]. Patients with intraoperative scores of CC-0 or CC-1 are ideal candidates for HIPEC after cytoreduction [10].

Second Stage: Hyperthermic Intraperitoneal Chemotherapy (HIPEC)

The cytoreduction is followed by intraperitoneal hyperthermic chemotherapy (HIPEC) which is the second stage of the procedure. The choice of the intraperitoneal chemotherapy used depends on the entity of the tumor. The target is to maximize exposure of the involved tissue to high concentrations of chemotherapeutic drugs (20–100 times greater than plasma level) while minimizing exposure of the non-affected tissue. The application of hyperthermia causes direct cytotoxic effects through inhibition of DNA repair mechanisms, denaturing of proteins and activation of heat shock proteins and as well as causing an immune mediated attack on tumor cells [9]. Most common chemotherapeutic agents used during this procedure are cisplatin, Oxyplatin, Doxurubicin, Mitomycin C and Irinotecan.

The HIPEC procedure can be performed with an open or closed technique. The open technique (Fig. 38.3), otherwise known as "Coliseum technique", allows direct access to the abdominal cavity during administration of chemotherapeutic drugs and allows for manipulation of fluid and bowel for optimal distribution of drugs within the abdomen. The challenge is to achieve and maintain the so called, hyperthermic state due to the heat dissipation by the exposed abdomen. The infusate is warmed to a temperature of 43–45 °C to ensure that the temperature of the intraperitoneal fluid is maintained at 41–43 °C (Fig. 38.4).

As an alternative a peritoneal cavity expander (PCE) can be used. This involves a modified open technique consisting of an acrylic cylinder with in-flow and out-flow tubes that are secured over

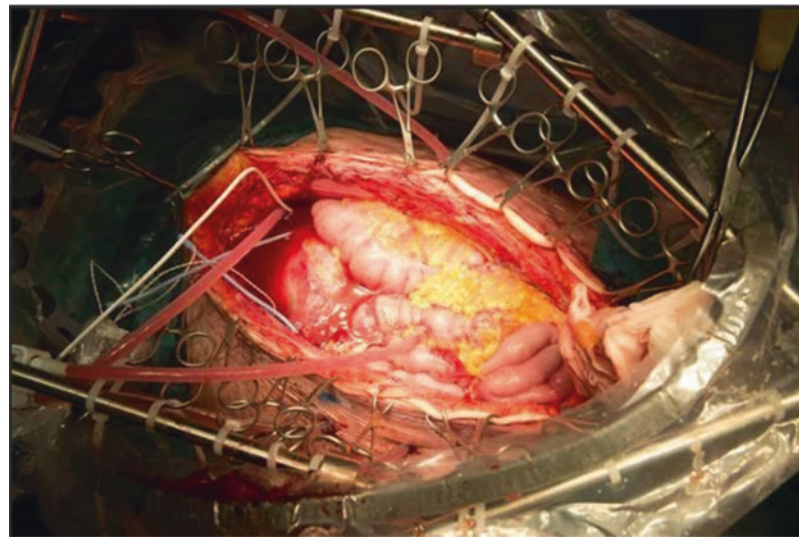


Fig. 38.3 Laparotomy and inserted cannulas for HIPEC procedure

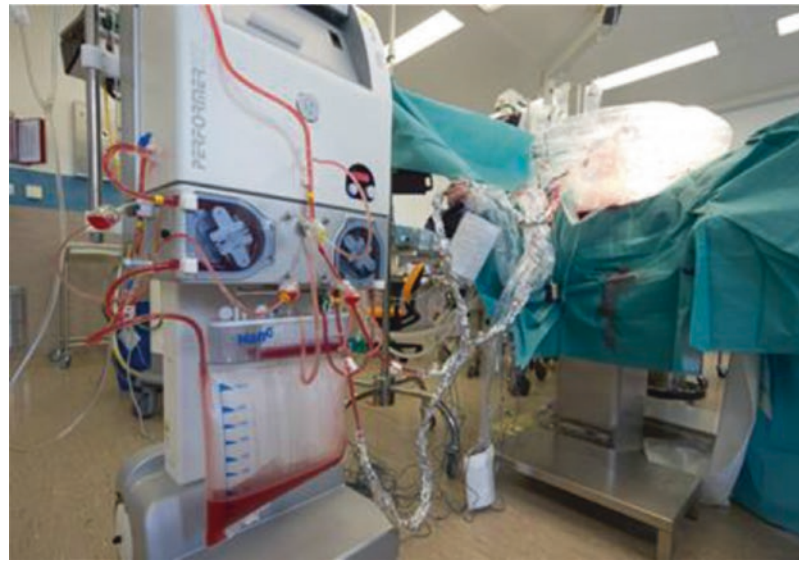


Fig. 38.4 Perfusor pump setup

the wound. The small bowel floats freely and is manually manipulated in the PCE filled with heated perfusate [10].

In the closed technique the temperature probes and catheters are placed after cytoreductive surgery and the abdominal wall is sutured prior to infusion of chemotherapy. During infusion intra-abdominal pressure rises which improves deeper tissue penetration by the chemotherapeutic drug. The closed abdomen keeps heat loss to minimum and ensures that hyperthermia is easy to achieve and maintain. The other important advantage of the closed technique is that there is minimal exposure of the operating theatre personnel to aerosolized chemotherapy. However, the disadvantage of closed technique is that it may lead to uneven distribution of the hyperthermic chemotherapy, as the drug may pool and accumulate in dependent parts of the abdomen potentially causing postoperative ileus, bowel perforation, and fistula [10].

Anesthesia Management

Preoperative Evaluation

In general, preoperative anesthesiological risk stratification does not differ from other large surgical interventions. Risk stratification is based on the recommendation of the European Society of Anaesthesiology (ESA)/American Heart Association (AHA) from 2014. The fitness for surgery should be assessed and particular attention should be paid to the presence of pre-existing cardiac disease which may also be due to the toxic side effects of previous chemotherapy [7]. Additionally, large fluid shifts may occur during the cytoreductive phase, due to extreme surface exposure following peritonectomy, ascitic drainage or significant blood loss during the procedure. Patients often have pre-existing ascites and pleural effusion prior to surgery causing basal atelectasis and predisposing these patients to increased risk of postoperative respiratory complications. Furthermore, increased intra-abdominal pressure during surgery and enlargement of pleural effusion due to possible leakage of chemotherapy solution into the pleural space can cause a further reduction in respiratory capacity. In addition to, a detailed medical history on pulmonary function, pulmonary function tests or cardiopulmonary exercise testing may be indicated to objectively measure pulmonary function [10]. In our hospital, we consider a preoperative FEV1 $\geq$ 1 L as favourable.

Preoperative malnutrition is prevalent in 30–67% of the patients undergoing CRS-HIPEC [11]. Poor nutritional status and preoperative hypoalbuminemia is used as an independent predictor of major postoperative complications and of prognostic relevance [1, 7]. The presence of large amounts of ascitic fluid can lead to further protein losses during the procedure; hence, preoperative optimization of nutritional status is essential.

Haematopoiesis is often impaired in patients with disseminated malignant disease [1]. Preoperative anemia should be identified and corrected for iron deficiency or other underlying disorder before surgery [7].

Perioperative Management

The CRS-HIPEC procedure requires general anesthesia with endotracheal intubation. Rapid sequence induction should be considered in the presence of abdominal distention related to ascites fluid collection predisposing patients to relatively rapid oxygen desaturation as well as aspiration. Careful pre induction oxygenation and preventative measures against aspiration are essential.

A lung protective ventilation regime (tidal volumes of 6–8 mL/kg is recommended, especially in the case of pre-existing impaired lung function. Further cranial movement of the diaphragm occurs during the perfusion phase, which results in increased airway pressures and a simultaneously reduction in functional residual capacity (FRC). During hyperthermia in the HIPEC phase, increased oxygen consumption is to be expected due to the hypermetabolic state which requires an increase in minute volume. Normalization of ventilation and oxygenation occurs within 30 min after the end of the hyperthermic perfusion [7]. Both inhalational anesthesia and total intravenous anesthesia are suitable and no clear advantage of either technique has been reported in the literature. To reduce the chance of spill or splash incidents during the HIPEC-phase, continuous monitoring of muscle relaxation is indicated.

Monitoring

Pulse oximetry (SpO_2), non-invasive blood pressure, electrocardiography (ECG), capnometry and core temperature monitoring are regarded as standard monitors. The placement of an arterial line is strongly recommended to monitor beat to beat blood pressure and to facilitate (arterial) blood samples which are regularly required during this procedure for assessment of ventilation, volume status, haemoglobin, electrolytes, albumin and coagulation. At least one large bore peripheral intravenous line is recommended for rapid fluid resuscitation or administration of blood products if necessary. Invasive functional

hemodynamic monitoring such as cardiac output measurements, may be considered useful in high risk patients [10]. The choice of placing a central venous line should be individualized, however, it is useful for intraoperative volume management, administration of vasopressors and for postoperative parenteral nutrition and is placed regularly at our institution. Central venous pressure (CVP) can be used as an additional parameter to achieve adequate fluid status, however, it is not always a reliable indicator of preload, especially in the presence of increased abdominal pressure during HIPEC. Due to both the duration of the procedure and the changing volume status, a urinary catheter is placed for hourly urine output measurement [7].

Temperature Regulation

Temperature regulation can be quite challenging during the CRS-HIPEC procedure. During the first phase of surgery, the debulking phase, patients may become hypothermic as a result of extensive surgical resection, volume loss and duration of surgery. Hypothermia must be prevented as coagulation, metabolic homeostasis, anti-inflammatory cascade and neurological status are all dependent on thermal homeostasis [7]. Administration of warm fluids, convective warming systems (forced warm air blankets) or increased operating room temperature should be considered.

In contrast, during the actual HIPEC stage, patients develop an increased body temperature secondary to the hyperthermic intraperitoneal solution. Body temperature rises up to as high as 40.5 °C (mean 37.7) and leads to peripheral vasodilation [7]. There follows a hypermetabolic phase with increased oxygen demand and a hyperdynamic circulation. The aim in this phase is to restore normothermia with cold intravenous infusions or ice packs. If the temperature remains ≥39 °C, the perfusionist can reduce the temperature of the instilled fluid solution [10]. Temperature can be measured transoesophageal, vesical or intra-abdominal. Temperature probes are also placed at the entrance and outlet cannulas of the perfusion system (Fig. 38.5).

Fluids

A significant challenge during CRS-HIPEC is optimizing organ perfusion through adequate fluid therapy. Inadequate fluid resuscitation may lead to hypovolemia which results in impaired perfusion of major organs and increased postoperative morbidity [12]. Patients lose significantly more fluid with CRS-HIPEC in comparison with other abdominal surgery; volume loss averages 10–12 mL/kg/h in comparison to 6–8 mL/kg in

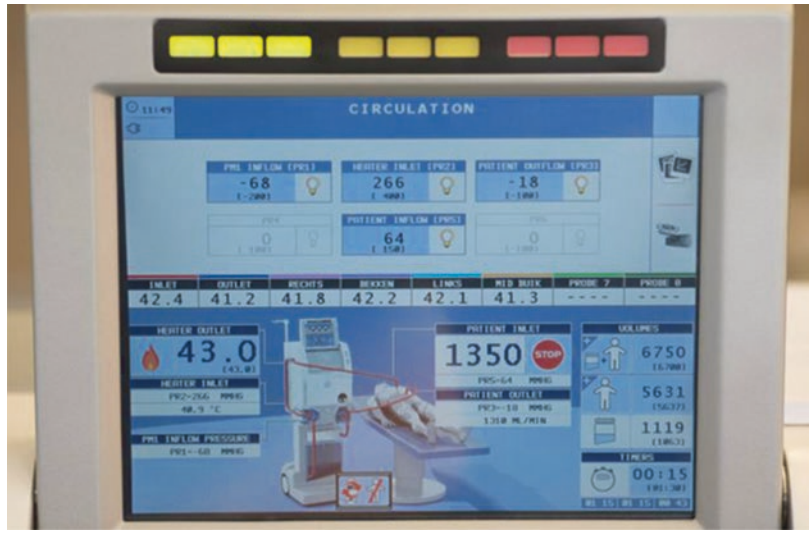


Fig. 38.5 Detail of perfusor system, with temperature and volume indications

other major abdominal surgery. Blood loss during the resection stage can also be extensive. Transfusion of blood products is necessary in about 50% of all patients perioperatively [7].

The removal of the peritoneum and the following HIPEC procedure causes loss of protein-containing exudate into the abdominal space due to extended capillary leak. Loss of blood, plasma, proteins and coagulation factors lead to considerable quantitative and qualitative fluid loss. However, the heated hyperthermia phase leads to vasodilatation and hyperdynamic circulation with tachycardia and increased cardiac output. Changes in abdominal pressure during the HIPEC phase by infusion of fluids into the abdominal cavity also affect cardiac output due to a reduction in the venous return by compression of the inferior vena cava [7, 13].

To ensure adequate regional and systemic perfusion adequate fluid resuscitation is essential. The choice of fluid in terms of crystalloids or colloids is still under debate [10]. Whether a liberal or restrictive substitution regime influences the outcome of these patients is still unknown and requires further evaluation [7]. Liberal volume replacement is associated with development of oedema, cardiopulmonary impairment and abdominal complications such as anastomotic leakage. However, restrictive use of fluids is also associated with increased morbidity and mortality. A partially restrictive and goal directed fluid therapy seems to offer advantages. Based on experience, several authors recommend a continuous administration (about 1–2 mL/kg/h) of (balanced) crystalloids. Further fluid substitution can be done with bolus administration of crystalloids, colloids or blood products. Transfusion of Fresh Frozen Plasma (FFP) is recommended in order to maintain sufficient oncotic pressure and in the event of significant blood loss. Albumin can be used in the case of a profound decrease in serum albumin levels. In addition to volume substitution, catecholamine therapy is usually required to maintain adequate perfusion pressure during this procedure.

The changes in hemodynamics, hyperthermia and the additional use of cytotoxic chemotherapy increases the risk of renal injury. Estimating the absolute lack of intravascular volume and renal function during individual procedures remains difficult. A target urinary output of 0.5 mL/kg/h during cytoreduction, 1–2mk/kg/h during HIPEC phase and 1–2 mL/kg post-HIPEC are recommended [10]. Routine use of furosemide to improve urinary output (and thereby prevent AKI (Acute Renal Failure) is not recommended by the recent KDIGO-ICU guidelines [14]. The retrospective study bij Schmidt et al. showed unaltered perioperative creatinine levels in patients with CRS-HIPEC by maintaining normovolemia [15]. The early use of vasopressors to avoid hypervolemia and goal directed fluid therapy appears to be beneficial in reducing perioperative morbidity [16].

Blood Loss and Coagulation

Various factors are held responsible for the occurrence of coagulation disorders during CRS and HIPEC. Preexisting coagulation disorders often exist due to factors such as malnutrition, hypoalbuminemia or ascites. Such patients also show an increased bleeding tendency due to coagulation disturbances; an increased INR (international ratio), a fall in AT III and fibrinogen values, as well as prolonged aPTT (activated partial thromboplastin time) have been reported. Other issues contributing to impaired coagulation include; volume shifts, protein loss, extreme variations in temperature, intraoperative blood loss and dilution caused by volume substitution [7, 10, 15]. Point of care measurements such as thromboelastography (TEG) or rotational thromboelastography (ROTEM) are useful in detecting a specific cause of coagulopathy. Coagulation abnormalities generally stabilize within 24–48 h following surgery and recover within the first five postoperative days [7].

Electrolyte Disturbances

Chemotherapy agents may lead to disturbances in electrolyte balance, such as hypomagnesaemia, hyperglycemia, and abnormalities in cal-

cium and potassium levels. The chemotherapeutics are dissolved in various solutions (such as glucose 5% or Ringer's solution) and absorb rapidly over the large wound area, leading to a risk of hyponatremia and hyperglycemia. A lactate increase of up to four times the initial value is usually observed and is attributed to volume losses, increased temperature and hypermetabolism [7]. Electrolyte levels must be monitored by frequent blood sampling and supplemented as necessary [10].

Pain Management

Good analgesia management is key to postoperative recovery in these patients who have a large laparotomy incision and tumour resection. Preoperatively, many of these patients are already using opioids to manage pain caused by tumor masses, therefore an adequate prolonged multimodal pain plan is essential. Adequate pain management can play an important role in early extubation, mobilisation and reducing postoperative pulmonary complications [7]. Many centers highly recommend providing thoracic epidural anesthesia for the CRS-HIPEC procedure. However, epidural analgesia may lead to an increased risk of hemodynamic disturbance and the presence of coagulation abnormalities during placement or removal of the catheter must be considered [10]. Other analgesic options worth considering are single or continuous paravertebral or subcostal transversus abdominis plane blockade. Paravertebral blocks provide excellent intraoperative anaesthesia and postoperative analgesia. There have not been any reports of systemic toxicity despite the large doses of local anaesthetic required in paravertebral blocks, and the incidence of pneumothorax and hypotension is low [12]. One of the main disadvantages of opioid-based analgesia is respiratory depression, which is clearly of significance in this group of patients who may already have compromised pulmonary function. Inadequate analgesia due to its ceiling analgesic effect is also a disadvantage. In our center, a thoracic epidural is given to patients undergoing CRS-HIPEC surgery. In presence of a contra-indication to epidural analgesia, good postoperative pain management is achieved by continuous intravenous esketamine and PCA (patient controlled analgesia) containing opioids.

Safety Precautions with the use of Chemotherapeutic Agents

Every chemotherapeutic drug administered in HIPEC has its own specific side effects in addition to common adverse effects, such as allergic reactions, nausea and vomiting. The most common end organ toxicity is nephrotoxicity [9, 10]. Cisplatin is known to have a direct cardiotoxic effect on myocardial cells leading to prolongation of the QT-interval and selective renal magnesium wasting. Intraperitoneal administration of chemotherapy is designed to achieve high intraperitoneal concentrations and low systemic toxicity. Depending on the agent used, a certain amount still will get into the systemic circulation. Its bioavailability is short lived due to first-pass effect in the liver or renal excretion [17]. However, a case of arrhythmia has been described due to intraperitoneal use of cisplatin [18].

Safety precautions should also be taken for the staff involved in HIPEC surgery. At high temperatures, aerosols and vapours are produced from chemotherapy drugs [10]. Handling of intraoperative intraperitoneal chemotherapy has been demonstrated to be safe for patients and staff by ambient air and biological monitoring, provided that standard protective equipment is used [9]. A protocol of how to handle the administration of chemotherapeutic agents during surgery should be locally available (Table 38.1). In our hospital, high risk groups like pregnant women, breastfeeding mothers and those who are planning pregnancy are advised not to take part in the HIPEC team. Chemotherapeutics are also excreted by the patient through urine and sweat. Therefore, using gloves whilst having contact with the patient and regularly changing gloves is recommended. There should be a proper disposal system for chemotherapy drugs and the tubing of the HIPEC equipment [10]. Even after surgery,

Table 38.1 Example of safety procedures using Chemotherapeutics

Operating room
• Warning sign on operating theatre door "chemotherapeutics used"
• Disposables (i.e. sterile dressings, tubes, cannulas, gauzes and surgical clothing) are collected in biohazard bin
• Thorough cleaning of OR after procedure
Staff
• If pregnant, lactating or planning pregnancy advised not to take part in HIPEC-team
• During HIPEC-phase, only necessary staff is near the patient
• Protective clothing during HIPEC-phase
Surgery
• Surgical face mask (IIR)
• Splash goggles
• Water resistant gown
• Latex-free, preferably elbow-length, "indicator" gloves[a]
• Disposable shoe protection is advised
Anaesthesia
• Surgical face mask (IIR)
• Splash goggles
• Disposable surgery gown
• Non-sterile gloves
• Disposable shoe protection is advised
Spill
• If available, use the chemotherapy spill kit[b]
• In case of chemotherapeutic spill on the skin, the area should be washed with soap and water

[a]Tested on the penetration of mitomycin- or other relevant chemotherapeutic drug

[b]Usually containing a chemotherapy resistant gown, absorber pads

all materials in direct contact with the patient and all excreta should be treated as contaminated.

Postoperative Care

In anticipation of direct postoperative instability and complications, patients are usually transferred to ICU or similar monitored high care unit after surgery. The average duration of ICU admission is 1–2 days [7]. Vasopressor support for blood pressure is generally required in the immediate post-operative days. Close monitoring and management of fluid balance, coagulation profile and electrolytes is essential. Postoperative fluid loss during the first 72 h after surgery can be considerable, up to 4 L, mostly via abdominal drains [19]. However, urine, nasogastric and drain fluid loss must also be carefully measured.

Patients are at risk of developing thrombosis and thromboprophylaxis is needed. Heparin or low molecular weight heparin (LMWH) should be started once the risk of bleeding has stabilised. In addition mechanical devices like intermittent pneumatic compression or compression stockings can be applied. Like all patients undergoing (upper) abdominal surgery, CRS-HIPEC patients are prone to postoperative respiratory complications. This risk is increased due to ascites, pleural effusion and atelectasis. Some patients require postoperative ventilation due to hemodynamic instability, diaphragmatic injury or other comorbidities preventing safe extubation [10]. If possible, an early extubation is favourable and attention should be given to early mobilisation to prevent pulmonary complications. Routine implementation of thoracic epidural analgesia can also play an important role in preventing pulmonary complications.

One must be aware of Infectious complications that can occur due to immunosuppression caused by chemotherapy and antibiotic therapy should be considered [10]. Early starting of enteral feeding is safe and beneficial in these patients. If enteral nutrition is not possible due to postoperative ileus or other intra-abdominal complications, early supplementary parenteral nutrition should be considered, since this patient population is already malnourished or at risk for malnutrition. About 40% of patients develop at least one postoperative in hospital complication with a low incidence of need for organ support and other significant critical care interventions [9].

A temporary increase in serum creatinine is common in this patient group however the incidence of acute kidney injury (AKI) and permanent renal dysfunction is low. Septic shock and multisystem organ failure is the leading cause of mortality in patients undergoing CRS-HIPEC. This is likely attributable to the extensive nature of the procedure, immunosuppression due to previous chemotherapy, peritoneal inflamma-

tion and the inflammatory response. Other major surgical complications include anastomotic leaks, intra-abdominal abscesses, intestinal perforation/peritonitis, fistulas and prolonged ileus [9].

Conclusions

The anesthesia provider has a crucial role during HIPEC and cytoreductive procedure. Unique aspects of HIPEC surgery are hemodynamic fluctuations, hypothermia and induced hyperthermia and the potential for chemotherapeutic drug induced nephrotoxicity. Anesthesia providers need to manage intravenous fluid therapy, electrolyte balance and blood transfusion to maintain optimal end-organ perfusion and prevent renal injury. Hemodynamic stability, adequate pain relief and early extubation are important targets. A team approach in this type of surgery is key to improving patient outcomes.

Key Points

- **Preoperative**
  - Routine blood investigations and 12-lead electrocardiogram, additional pulmonary function tests if indicated
  - If possible, nutritional status, cardiac, pulmonary and kidney function should be optimized
- **Perioperative**
  - Endotracheal intubation, higher PEEP levels may be required
  - Standard monitoring required (ECG, SpO_2, capnography), arterial line and central venous line, urine catheter strongly recommended.
  - Be aware of major fluid shifts, goal directed therapy might be beneficial, substitution of coagulation factors if necessary
  - Electrolyte disturbances may occur
  - Temperature management: aim normothermia in hypermetabolic and hyperdynamic state
  - Be aware of safety precautions using chemotherapy
- **Postoperative**
  - Prolonged postoperative hemodynamic monitoring is advised
  - Adequate multimodal/epidural pain management is key to early mobilisation and preventing complications

Funding and Conflicts of Interest None

References

1. Solanki SL, Mukherjee S, Agarwal V, Thota RS, Balakrishnan K, Bhatia Shah S, et al. Society of onco-anaesthesia and perioperative care consensus guidelines for perioperative management of patients for cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC). Indian J Anaesth. 2019;63(12):972–87.
2. Sugarbaker PH. Surgical management of peritoneal carcinosis: diagnosis, prevention and treatment. Langenbecks Arch Chir. 1988;373:189–96.
3. Foster JM, Sleightholm R, Patel A, Shostorm V, Hall B, Neilsen B, et al. Morbidity and mortality rates following cytoreductive surgery combined with hyperthermic intraperitoneal chemotherapy compared with other high-risk surgical oncology procedures. JAMA Network Open [Internet]. 2019;2(1):e186847.
4. Fichmann D, Roth L, Raptis DA, Kadji ME, Gertsch P, Vonlanthen R, et al. Standard operating procedures for anesthesia management in cytoreductive surgery and hyperthermic intraperitoneal chemotherapy improve patient outcomes: a patient cohort analysis. Ann Surg Oncol. 2019;26:3652–62.
5. Passot G, Vaudoyer D, Villeneuve L, Wallet F, Beaujard AC, Boschetti G, et al. A perioperative clinical pathway can dramatically reduce failure-to-rescue rates after cytoreductive surgery for peritoneal carcinomatosis: a retrospective study of 666 consecutive cytoreductions. Ann Surg. 2017;265(4):806–13.
6. Newton AD, Barlett EK, Karakousis GC. Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy: a review of factors contributing to morbidity and mortality. J Gastrointest Oncol. 2016;7(1):99–111.
7. Raspe C, Piso P, Wiesenack C, Bucher M. Anesthetic management in patients undergoing hyperthermic chemotherapy. Curr Opin Anaesthesiol. 2012;25(3):348–55.
8. Coccolini F, Catena F, Glehen O, Yonemura Y, Sugarbaker PH, Piso P, et al. Complete versus incomplete cytoreduction in peritoneal carcinosis from gastric cancer, with consideration to PCI cut-off. Systematic review and meta-analysis. Eur J Surg Oncol. 2015;41(7):911–9.

9. Raspé C, Flöther L, Schneider R, Bucher M, Piso P. Best practice for perioperative management of patients with cytoreductive surgery and HIPEC. Eur J Surg Oncol. 2017;43(6):1013–27.
10. Gutpa N, Kumar V, Garg R, Jee Barthi S, Mishra S, Bhatnagar S. Anesthetic implications in hyperthermic intraperitoneal chemotherapy. J Anaesthesiol Clin Pharmacol. 2019;35(1):3–11.
11. Reece L, Dragicevich H, Lewis C, Rothwell C, Fisher OM, Carey S, et al. Preoperative nutrition status and postoperative outcomes in patients undergoing cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. Ann Surg Oncol. 2019;26(8):2622–30.
12. Thong SY, Chia CS, Ng O, Tan G, Ong ET, Soo KC, et al. A review of 111 anaesthetic patients undergoing cytoreductive surgery and hyperthermic intraperitoneal chemotherapy. Singap Med J. 2017;5(8):488–96.
13. Raue W, Tsilimparis N, Bloch A, Menenakos C, Hartmann J. Volume therapy and cardiocircular function during hyperthermic intraperitoneal chemotherapy. Eur Surg Res. 2009;43(4):365–7.
14. Kellum JA, Lameire N. Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1). Crit Care. 2013;17:204.
15. Schmidt C, Creutzenberg M, Piso P, Hobbhan J, Bucher M. Perioperative anesthetic management of cytoreductive surgery with hyperthermic intraperitoneal chemotherapy. Anesthesia. 2008;63(4):389–95.
16. Eng OS, Dumitra S, O'Leary M, Raoof M, Wakabayashi M, Dellinger TH, et al. Association of fluid administration with morbidity in cytoreductive surgery with hyperthermic intraperitoneal chemotherapy. JAMA Surg. 2017;152(12):1156–60.
17. Thix CA, Königsrainer I, Kind R, Wied P, Schroeder TH. Ventricular tachycardia during hyperthermic intraperitoneal chemotherapy. Anaesthesia. 2009;64(10):1134–6.
18. Goodman MD, McPartland S, Detelich D, Wasif SM. Chemotherapy for intraperitoneal use: a review of hyperthermic intraperitoneal chemotherapy and early post-operative intraperitoneal chemotherapy. J Gastrointest Oncol. 2016;7(1):45–57.
19. Cooksley TJ, Haji-Michael P. Post-operative critical care management of patients undergoing cytoreductive surgery and heated intraperitoneal chemotherapy (HIPEC). World J Surg Oncol. 2011;9:169.

39 Anesthetic Management of Tracheal/Airway Stents

Narinder P. Singh, Jeetinder K. Makkar, Anudeep Jaffra, and Inderpaul Singh Sehgal

Learning Points

- Airway stents are the endobronchial prosthetic devices that maintain the patency of the compromised airways, primarily for malignant conditions but can be used for benign conditions as well.
- Placement of stent poses a great challenge both for the pulmonologist and the anesthesia provider owing to shared, severely stenotic airway segments.
- A thorough understanding of the airway anatomy, level and size of obstruction and meticulous planning is required for stent placement.
- Airway management depends on the location of lesion and type of stent. Placement of stent generally requires general anesthesia with muscle relaxant.

Introduction

Tracheobronchial stenosis caused by benign and malignant pathologies is an important clinical problem. Surgical resection and reconstruction is considered the standard of care for definitive management. Endoscopic management plays an important role in non-surgical patients or those coming for palliation and includes forceps debulking, brachytherapy, cryotherapy, argon plasma coagulation, and tracheobronchial stents [1–3]. Recent technological advances have seen an increase in the popularity of tracheobronchial stents because these effectively manage both extraluminal and intraluminal lesions and rapidly alleviate acute distress due to airway obstruction [4].

An airway stent is an endobronchial prosthesis that provides support and framework to the airway in order to maintain its patency and improve ventilation [5]. Airway stents are most commonly placed in the trachea, main stem bronchi, or the intermediate bronchus.

Indications of Airway Stenting

Indications for stent placement can be broadly classified as obstructive and defect in the airway wall (Table 39.1). The obstruction in the airways can further be classified as endoluminal (lesion causing obstruction from with-in), extraluminal

N. P. Singh
Department of Anaesthesia, MMIMSR, MM (DU), Mullana-Ambala, India

J. K. Makkar (✉) · A. Jaffra
Department of Anaesthesia and Critical Care, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India

I. S. Sehgal
Department of Pulmonary Medicine, Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh, India

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_39

Table 39.1 Indications for tracheobronchial stent placement

Malignant disease	Benign disease
• Malignant airway obstruction from extrinsic compression	• Tracheal stenosis- post intubation, tracheostomy
• Endobronchial tumor with residual obstruction	• Post-transplant airway stenosis
• Loss of cartilage support from tumor destruction	• Complex benign stricture >4 cm
• Malignant tracheoesophageal fistula	• Benign tracheoesophageal fistula
	• Tracheobronchomalacia: therapeutic trial before tracheoplasty
	• Inflammatory lesion like Wegener's granulomatosis, sarcoidosis, radiation, relapsing polychondritis, amyloidosis,
	• Vascular compression like aortic aneurysm
	• Post infection (tuberculosis)

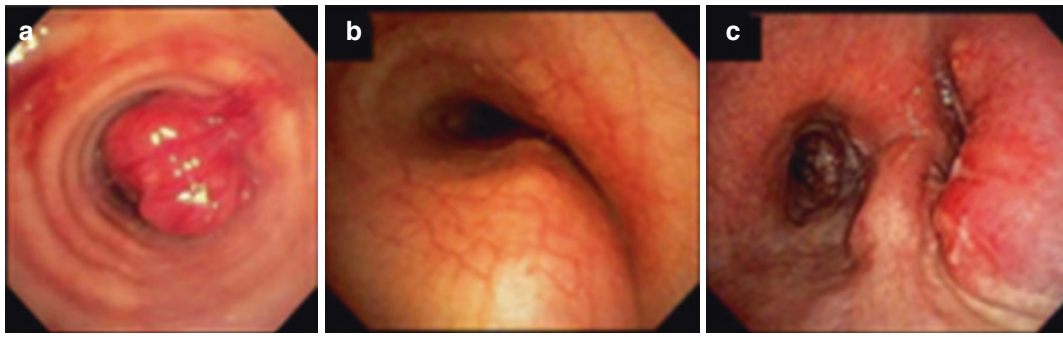


Fig. 39.1 Endoscopic view during flexible bronchoscopy demonstrating endobronchial obstruction (**a**), extrinsic compression (**b**), and a mixed obstruction (**c**)

(lesion compressing the airways extrinsically), or mixed (having both intrinsic and extrinsic component) (Fig. 39.1). Endobronchial obstruction can be due to either benign causes or due to malignant aetiology. The endobronchial obstruction can also be due to defect in the airway cartilage that causes dynamic airway collapse and thus central airway obstruction. Extrinsic obstruction is generally due to malignant causes like esophageal cancer, thyroid cancer, and other head and neck tumors that are adjacent to the airway and produce obstructive symptoms.

Defect in the airway wall can be classified as tracheoesophageal fistula, bronchoesophageal fistula, or tracheobronchial mediastinal fistula (Fig. 39.2). Fistula can be due to benign (post-surgical, traumatic, caustic injury, and others) or malignant aetiologies.

Bronchial anastomotic strictures occur in over 1.6–32% of recipients after lung transplant [6, 7]. Dilatation of stricture and laser debridement is

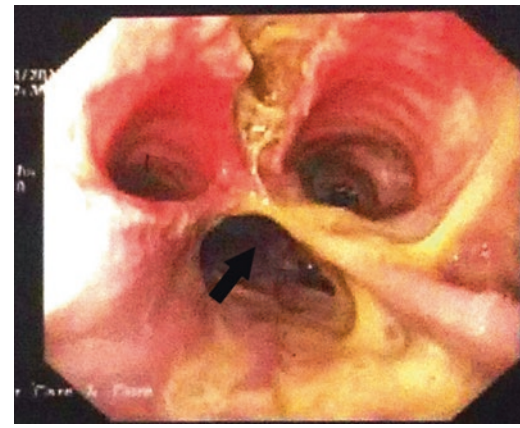


Fig. 39.2 Endoscopic view during flexible bronchoscopy demonstrating a tracheoesophageal fistula (arrow). There is also loss of integrity at the anterior wall of the carina. The tracheoesophageal fistula in this case was secondary to road traffic accident and is best suited for surgical repair. However, a silicone stent may be considered as a bridge before definitive surgery for stabilization. The index case had features of sepsis that required systemic antibiotics and stabilization before surgery

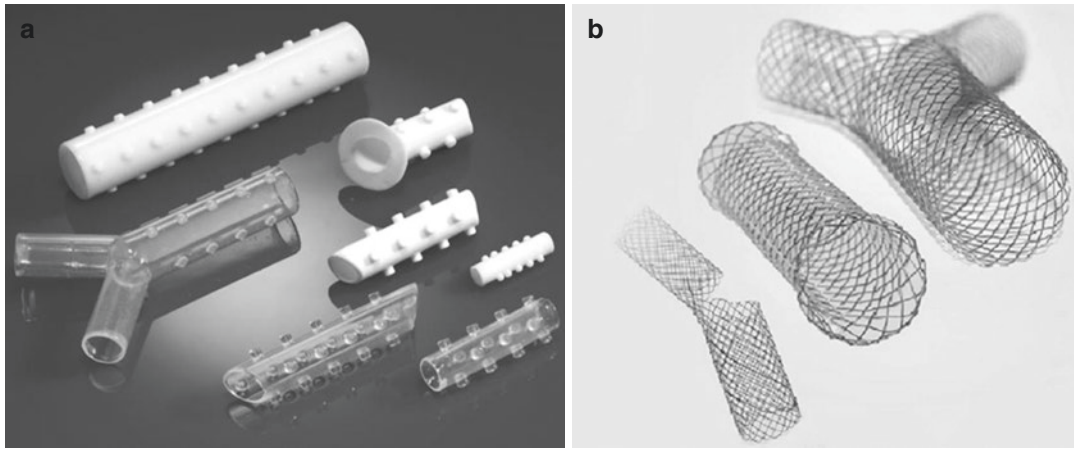


Fig. 39.3 Photograph demonstrating straight and Y-shaped silicone stents (**a**), and uncovered metallic stents (**b**)

the preferred initial management strategies while airway stents accords rapid relief of dyspnea and are mostly safe [8].

Stenosis secondary to prolonged intubation or tracheostomy burns of airway, tracheomalacia and inflammatory diseases (Wegener's granulomatosis, sarcoidosis, radiation, relapsing polychondritis, amyloidosis, tuberculosis) are the nonmalignant indications for stenting.

Types of Stents

The optimum choice for airway stent depends on the anatomy of the lesion and airway as well as experience of the bronchoscopist. These can be broadly classified as metallic or silicon stents (Fig. 39.3). The metallic stents are either bare stents or may be covered by silicone material (covered metallic stents) [9]. The stents can be straight (tracheal or bronchial stents) or Y-stents. The advantages and disadvantages of the stents are enumerated in Table 39.2.

Table 39.2 Advantages and disadvantages of airway stents

Type of stent	Advantages	Disadvantages
Silicone stents	• Can be placed for prolonged duration of >6 months • Customizable • Can be retrieved • Lesser granulation tissue formation • Lesser mucous impaction • Lesser chances for tumor ingrowth • Can be used both for benign or malignant etiologies	• Costlier • Stent displacement • Require rigid bronchoscopy and general anesthesia for placement
Metallic stents	• Lesser chances of displacement • Relatively cheaper • Can be placed using flexible bronchoscopy under moderate sedation and local anaesthesia	• Can only be placed for malignant etiologies where life expectancy is less than 3–6 months • Higher risk of tumor ingrowth, mucous impaction and granulation tissue formation • Cannot be retrieved • Cannot be customized

Treatment Planning and Selection of a Patient

The initial step in the management of a patient presenting with central airway obstruction (CAO) is to determine the extent of the disease and the assessment of severity [10]. There are several scoring systems that have been proposed to access the extent of CAO. These include the Myer-Cotton, McCaffrey, Nouraei, Freitag and others. Briefly, these score study the extent of

obstruction (% of airway lumen compromised), type of structural abnormality (intraluminal, extrinsic, or mixed), location of disease (upper trachea, middle trachea, or lower trachea with or without carinal involvement), and the extent of physical limitation (dyspnoea) [11–14].

To correctly characterize the extent and type of disease, the initial step is imaging (type and extent of disease) followed by either flexible bronchoscopy or virtual bronchoscopy to gauge the extent of disease and to plan the procedure and deciding the type and the size of the stent required (Fig. 39.4). Generally, for lesions involving the lower one-third of trachea, carina, or main stem bronchi a Y-shaped stent is preferred and for the lesions involving the upper two-third of trachea, a straight stent is usually chosen. The size of the stent is selected so that a 5 mm margin on either side of the lesion is covered with the stent.

Preprocedural assessment: Pre procedural assessment should be individualized to avoid intra operative complications.

History: Duration of dyspnea and speed of onset indicates the duration, extent and severity of disease. Generally, patients do not get symptomatic until the extent of airway involvement is >50% of the lumen and patients become symptomatic at rest when the tracheal diameter reduces to less than 8 mm [15]. History of decrease in respiratory distress associated with any specific posture would enable the anesthesia provider to induce anesthesia in that posture.

Physical examination: Breathing pattern should be observed at rest and on mild exertion. Presence of stridor is an indicator of potentially narrowed upper airway. The respiratory phase-specific noises (or stridor) on auscultation is usually helpful in localizing the stenotic site. Inspiratory stridor is associated with extrathoracic obstruction (more than 50% reduction in diameter at the glottis or periglottis) while expiratory or biphasic stridor is associated with intrathoracic obstruction (pathology well below the vocal cords). Patients with stridor can develop acute airway obstruction at the time of induction of general anesthesia due to collapse, secretions, or minor airway swelling. This can make airway management difficult or even impossible.

A qualitative sense of the degree of dynamic respiratory function can be obtained by performing "birthday candle" test. In this, airflow obstruction in setting of high positive intratho-

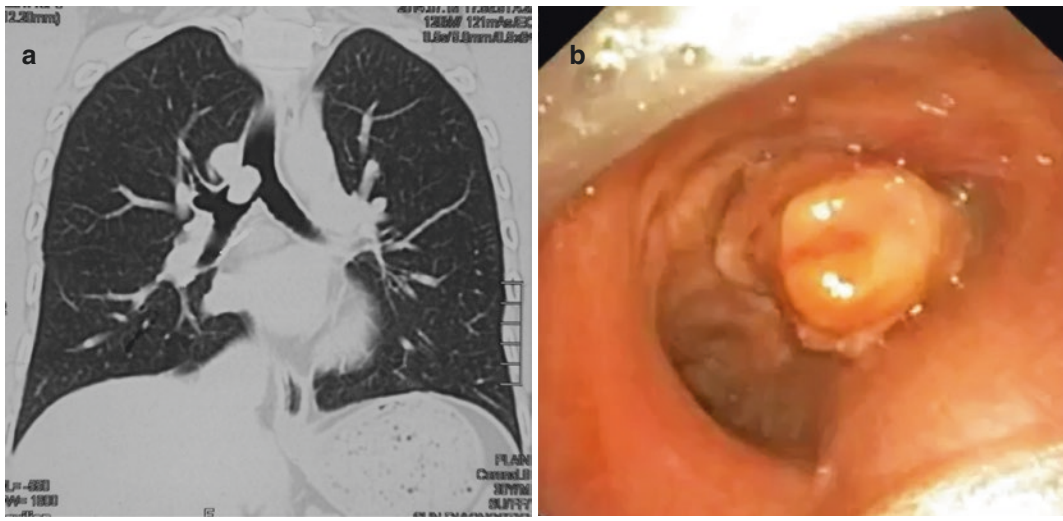


Fig. 39.4 Computed tomography of the thorax demonstrating an endobronchial growth arising from the right upper lobe bronchus occluding 70–80% of the right main bronchus (**a**); endoscopic view during rigid bronchoscopy of the same patient confirming the presence of an endobronchial growth completely occluding the right main bronchus. The tumor was removed by mechanical coring

racic pressure generated during forced exhalation can be gauged by asking the patient to blow forcibly on hand of physician.

Imaging studies: Various imaging modalities like conventional radiography, chest computed tomography and chest magnetic resonance imaging can accurately establish the location, size and spread of the tumor mass and the extent of the airway obstruction [16]. This information helps in determining the endotracheal tube (ETT) size, safe depth for its placement, and, for proximal lesions, whether an ETT is possible or not. Progression of airway disease can occur very quickly and therefore, it is desirable to have a recent scan to understand the current state of airway invasion.

Flow-volume loops: These might help in identifying inspiratory and expiratory inconsistency or etiology (fixed or dynamic obstruction) of tracheal stenosis. Variable obstructions are effected by respiratory phases whereas fixed obstructions are not. A variable extra thoracic and intrathoracic obstruction produced flattening of both the limbs (inspiratory as well as expiratory) of flow volume loop. Airway stenting is performed for lesions that are below the cords. Hence, such lesions act as variable intrathoracic blockade and hinder the expiratory flow. Whereas inspiratory flow is not compromised as the airway expands on inspiration [15].

Preoperative team planning: Preoperative communication with the bronchoscopy team and joint planning are necessary to avoid or immediately manage loss of airway patency or inability to ventilate and oxygenate the patient during induction or emergence from general anesthesia. Thus, briefing in the pre procedure period should provide team members information about procedural plan, need for modification, anesthetic technique for airway management, back up plans and strategies to manage a situation when there is loss of airway leading to cannot intubate and cannot ventilate scenario.

An antisialogouge, glycopyrrolate 0.004 mg/kg given intramuscularly 30–60 min prior to induction of anesthesia, counteracts the vagolytic action of bronchoscope placement, reduces the secretions and prevent the thickening of secretions during airway manipulation. Steroids reduces mucosal edema resulting due to airway manipulation. Airway reactivity can be reduced by nebulizing the awake patient with 4% lidocaine.

Anesthesia Management

The anesthetic challenges for insertion of tracheobronchial stents include- a shared airway, patients with multiple co morbidities, advanced malignancy of thorax in some patients and possibility of failure of stent placement. It also demands maintaining airway patency, adequate oxygenation and ventilation. A technique which caters to maintenance of adequate anesthetic depth, working across a stenotic segment, suppression of stress response during bronchoscope insertion and provision of a still and dry field is the ideal one, however difficult to attain. The stenosis involving the middle and lower trachea are more troublesome and challenging as options of emergency airway management like transtracheal ventilation, tracheostomy and a surgical airway access cannot be obtained. During the procedure, complete airway obstruction can be precipitated by coughing or airway instrumentation. The anesthesia provider and the bronchoscopist must realize that the airway is tenuous and a fit of coughing or irritation because of airway instrumentation or instillation of local anesthetic can cause complete airway obstruction during the procedure and can be fatal.

Anesthetic plan depends upon the condition of the patient, location, severity and nature of the lesion, type of stent and it's deployment technique. Placement, of an airway stent can be performed with sedation after topicalization of airway. However, procedure is sufficiently stimulating and warrants general anesthesia in majority of the patients. One of the following techniques can be used for providing anesthesia in these patients [17–19].

1. Anesthesia with rigid bronchoscope
2. Anesthesia with supraglottic airway devices (SGA)

3. Anesthesia with endotracheal tube (ETT)
4. Inhalational anesthesia with spontaneous ventilation

ASA standards for basic anesthetic monitoring should be followed - electrocardiogram, end tidal carbon dioxide monitoring, pulse oximetry and non-invasive blood pressure. Invasive monitoring is indicated for severely compromised patients.

Induction of anesthesia: Induction technique for general anesthesia is based on surgical needs and potential for compromised ventilation. Critical decisions include timing of endotracheal intubation (awake or asleep), selection of an intravenous or inhalation induction technique, whether to use a neuromuscular blocking agent, and timing for initiation of positive pressure ventilation [20]. These decisions are based on the knowledge gleaned during the preoperative assessment and consultation with the bronchoscopist.

While the aforementioned factors help gauge the risk, maintenance of airway patency at the time of induction is usually not smooth and backup plans and equipment must be kept ready. Briefly, flexible bronchoscopy is performed to assess the airway before stent placement, whenever feasible to ascertain the airway anatomy, site of obstruction and/or tracheoesophageal fistula and its severity. Maneuvering the bronchoscope across the area of obstruction allows the estimation of the lumen size in comparison to the outer diameter of the bronchoscope being used. After establishing that the stenosis can be cleared with the bronchoscope or tube, one can proceed with the induction of anesthesia. It is worthwhile to mention that transition from spontaneous ventilation to positive pressure ventilation can lead to critical airway obstruction from previous partial stenosis. Hence, preoxygenation/denitrogenation has vital role and will take considerably longer than usual.

Induction of anesthesia should be done either using sleeping doses of propofol (1–2 mg/kg) or incremental doses of inhalational anesthetic "sevoflurane" which ensures intact spontaneous ventilation especially in cases with more than 50% airway stenosis or distal airway obstruction,. In case, the airway narrowing is not significant, shorter acting muscle relaxants (succinylcholine) provide a motionless field for airway manipulation and stent placement. The stress response to bronchoscope insertion can be blunted with the use of short acting opioids like fentanyl boluses or remifentanil infusion.

Maintenance of anesthesia: Total intravenous anesthesia (TIVA*)* is the preferable anesthesia maintenance technique. Major advantage includes ability to administer anesthetic agents independent of ventilation, without waste of anesthetic agents or operating room pollution. TIVA using Propofol infusion along with remifentanil infusion is the technique of choice. Dexmedetomidine has come up as a promising agent secondary to its anxiolytic, sedative and analgesic properties.

Maintenance of airway: Securing the airway with a device makes procedure easier and faster as bronchoscopist can introduce the bronchoscope through the adapter with port attached to LMA or ETT and there is no need to navigate the bronchoscope through the mouth and vocal cords each time. LMA is preferred for shorter duration procedures where anticipated ventilator pressures are low and when stent has to be placed in glottis [21]. Tracheal intubation should be employed when higher peak pressures are anticipated and in patients with high risk of aspiration.

Ventilation strategies: One of the following methods can be used:

- Topical anesthesia or nerve block+ Spontaneous ventilation with inhalational anesthetic
- Apneic oxygenation with or without oxygen insufflation
- Intermittent positive pressure ventilation (IPPV) through the side port of rigid bronchoscope
- Jet ventilation along with total intravenous anesthesia

Placement of the Stent

Once the appropriately sized stent has been selected the placement of the airway stents is done either during the flexible bronchoscopy or the rigid bronchoscopy. Flexible bronchoscopy can only be used to place the metallic stents and requires fluoroscopic guidance whereas silicone stents can only be placed during rigid bronchoscopy. At author's center, all airway stents are placed during rigid bronchoscopy (Fig. 39.5) as it provide a better airway control and management. The size of the stent is decided on the basis of the airway measurements performed on CT thorax and flexible bronchoscopy. The silicone stent is first folded in a stent folding assembly (Tonn tracheobronchial stent applicator, Novatech, France). The stent folding assembly (with the stent in situ) is then placed over the introducer tube and the stent is loaded in the introducer tube by pushing the loading rod. The stent is placed using the "pull technique" wherein the distal end of the rigid bronchoscope is positioned just distal to the site of obstruction (for a straight stent) and in the left main bronchus (for the Y-stent). The introducer tube with the stent-in-situ is introduced into the rigid barrel and with the help of a pusher rod, the stent is then pushed gently along with simultaneous retraction of the rigid bronchoscope barrel, until the entire stent is deployed. After deploying the stent, the introducer tube is removed and the proper placement of the stent is confirmed using flexible bronchoscopy. If required, the stent is gently manipulated with a rigid forceps and pulled until the stent is properly positioned. A controlled radial expansion (CRE™, Boston Scientific) balloon is inflated within the collapsed stent, to open the stent, if needed. It is important to realize that the placement of the stent is a blind procedure and a short period of apnea is unavoidable during the stent deployment and positioning. The placement of the metallic stent is almost similar to the silicone stent except that the metallic stents come preloaded in introducer sheath [22, 23].

Fig. 39.5 Photograph demonstrating barrels of a rigid bronchoscope of different sizes. The proximal end of the rigid bronchoscope has a port for ventilation, jet ventilation, attaching a light source, and a working channel through which the instrumentation is done

Intraprocedural Complications [24–29]*:*

- Partial or complete airway obstruction can occur due to bleeding, tissue dislodgement, secretions, breakage or malposition of the stent and can lead to progressive hypoxemia and hypercarbia with subsequent cardiovascular collapse.
- Negative pressure pulmonary edema although rare can develop due to coughing or forced inhalation in spontaneously ventilated patients across the obstructed airway.
- Tracheobronchial wall perforation
- Surgical emphysema
- Tension pneumothorax
- Pneumoperitoneum

Emergence and Extubation

This is more challenging than the induction of anesthesia as placing a stent does not immediately lead to reversal of respiratory symptoms. There could be precipitation of airway obstruction leading to hypoxemia and reintubation after extubation of trachea. Airway should be extubated once patient is fully awake, responding and is not in respiratory distress. Coughing after emergence can be a persistent problem because of foreign body placed in the airway and this can be blunted by small doses of short acting opioids.

Post Procedure Care

There is limited data on post procedural management for airway stents; each institution has individualized policies which are followed. Immediate post procedure recommendations are round the clock nebulization with saline to prevent thickening of secretions along with a cover of steroids and antibiotic prophylaxis for duration of 3–4 days, along with adequate hydration of the patient. A post procedure chest roentgenogram is obtained which could be followed by a flexible bronchoscopy after a period of 2–3 weeks if there is no symptomatic improvement in patient's obstructive features.

Post Procedural Complications [24–29]

Immediate Complications

1. Migration—resulting in mild to total airway obstruction
2. Retention of secretions
3. Obstruction of bronchial orifices
4. Cough
5. Infection

Long Term Complications

1. Sputum retention
2. Granulation tissue at proximal or distal end of stent
3. Halitosis
4. Metal fatigue
5. Respiratory infections

Patients with Stents for Other Surgeries

Patients with stents in situ may present for some other surgery. A thorough assessment should be done regarding type of stent, size of stent and the exact site of stent. As placement of endotracheal tube can lead to stent displacement and migration and can also lead to airway obstruction due to stent dislodgement or formation of extra luminal tract. Hence, a direct communication with the bronchoscopist who placed the stent should be done. Laryngeal mask airway can be safely used; however, ETT should be guided by flexible bronchoscopes that the distal end of ETT is placed above the stent or within the lumen of the stent [30].

Funding and Conflicts of Interest None

References

1. Witt C, Ortner M, Ewert R, Schmidt B, Steiniger L, Baumann G, et al. Multiple fistulas and tracheobronchial stenoses require extensive stenting of the central airways and esophagus in squamous-cell carcinoma. Endoscopy. 1996;28(4):381–5.
2. Witt C, Dinges S, Schmidt B, Ewert R, Budach V, Baumann G. Temporary tracheobronchial stenting in malignant stenoses. Eur J Cancer. 1997;33(2):204–8.
3. Marquette CH, Mensier E, Copin MC, Desmidt A, Freitag L, Witt C, et al. Experimental models of tracheobronchial stenoses: a useful tool for evaluating airway stents. Ann Thorac Surg. 1995;60(3):651–6.
4. Shin JH. Interventional management of tracheobronchial strictures. World J Radiol. 2010;2(8):323–8.
5. Ernst A, Silvestri GA, Johnstone D, American College of Chest Physicians. Interventional pulmonary procedures: Guidelines from the American College of Chest Physicians. Chest. 2003;123(5):1693–717.
6. Garfein ES, McGregor CC, Galantowicz ME, Schulman LL. Deleterious effects of telescoped bronchial anastomosis in single and bilateral lung transplantation. Ann Transplant. 2000;5(1):5–11.
7. Herrera JM, McNeil KD, Higgins RS, Coulden RA, Flower CD, Nashef SA, et al. Airway complications after lung transplantation: treatment and long-term outcomes. Ann Thorac Surg. 2001;71(3):989–93.
8. Sonnett JR, Keenan RJ, Ferson PF, Griffith BP, Landreneau RJ. Endobronchial management of benign, malignant and lung transplantation airway stenoses. Ann Thorac Surg. 1995;59(60):1417–22.
9. Dumon JF. A dedicated tracheobronchial stent. Chest. 1990;97(2):328–32.
10. Conacher ID. Anaesthesia and tracheobronchial stenting for central airway obstruction in adults. Br J Anaesth. 2003;90(3):367–74.
11. Myer CM, O'connor DM, Cotton RT. Proposed grading system for subglottic stenosis based on endotracheal tube sizes. Ann Otol Rhinol Laryngol. 1994;103(4 Pt 1):319–23.
12. Mc Caffrey TV. Classification of laryngotracheal stenosis. Laryngoscope. 1992;102(12 Pt 1):1335–40.
13. Freitag L, Ernst A, Unger M, Kovitz K, Marquette CH. A proposed classification system of central airway stenosis. Eur Respir J. 2007;30(1):7–12.

14. Nouraei SAR, McPartlin DW, Nouraei SM, Patel A, Ferguson C, Howard DJ, et al. Objective sizing of upper airway stenosis: a quantitative endoscopic approach. Laryngoscope. 2006;116(1):12–7.
15. Brodsky JB. Bronchoscopic procedures for central airway obstruction. J Cardiothorac Vasc Anesth. 2003;17(5):638–46.
16. Weber AL. Radiologic evaluation of the trachea. Chest Surg Clin North Am. 1996;6(4):637–73.
17. Paes ML, Conacher ID, Snellgrove TR. A ventilator for carbon dioxide laser bronchoscopy. Br J Anaesth. 1986;58(6):663–9.
18. Teh J, Platt H. Inhalational induction with sevoflurane in central airway obstruction. Anaesth Intensive Care. 1998;26(6):458–9.
19. Watters MP, McKenzie JM. Inhalational induction with sevoflurane in an adult with severe complex central airways obstruction. Anaesth Intensive Care. 1997;25(6):704–6.
20. Conacher ID, Paes ML, McMahon CC. Anesthetic management of laser surgery for central airway obstruction. J Cardiothorac Vasc Anesth. 1998;12(2):1–5.
21. Tanigawa N, Sawada S, Okuda Y, Sougawa M, Komemushi A, Kojima M, et al. Expandable metallic stent placement in upper tracheal stenosis: Value of laryngeal masks. AJR Am J Roentgenol. 2001;177(6):1423–6.
22. Saad CP, Murthy S, Krizmanich G, Mehta AC. Self-expandable metallic airway stents and flexible bronchoscopy: Long-term outcomes analysis. Chest. 2003;124(5):1993–9.
23. Schmidt B, Olze H, Borges AC, John M, Liebers U, Kaschke O, et al. Endotracheal balloon dilatation and stent implantation in benign stenoses. Ann Thorac Surg. 2001;71(5):1630–4.
24. Ernst A, Feller-Kopman D, Becker HD, et al. Central airway obstruction. Am J Respir Crit Care Med. 2004;169(12):1278–97.
25. Thornton RH, Gordon RL, Kerlan RK, LaBerge JM, Wilson MW, Wolanske KA, et al. Outcomes of tracheobronchial stent placement for benign disease. Radiology. 2006;240(1):273–82.
26. Gaissert HA, Grillo HC, Wright CD, Donahue DM, Wain JC, Mathisen DJ. Complication of benign tracheobronchial strictures by self-expanding metal stents. J Thorac Cardiovasc Surg. 2003;126(3):744–7.
27. Bolliger CT, Mathur PN, Beamis JF, et al. ERS/ATS statement on interventional pulmonology. European Respiratory Society/American Thoracic Society. Eur Respir J. 2002;19(2):356–73.
28. Noppen M, Pierard D, Meysman M, Claes I, Vincken W. Bacterial colonization of central airways after stenting. Am J Respir Crit Care Med. 1999;160(2):672–7.
29. Chen W, Ruan Y. Late complications of nickel-titanium alloy stent in tracheal stenosis. Laryngoscope. 2012;122(4):817–20.
30. Davis N, Madden BP, Sheth A, Crerar-Gilbert AJ. Airway management of patients with tracheobronchial stents. Br J Anaesth. 2006;96(1):132–5.

40 Anesthetic Management of Minimally Invasive Pulmonary Thrombo-embolectomy

Anand Lakshminarasimhachar

Learning Points

- Patients having percutaneous thromboembolectomy for massive or sub-massive acute pulmonary embolism (PE) are very high-risk patients with severe cardiorespiratory compromise.
- Acute right heart dysfunction is a significant complication following acute pulmonary embolism and accurate preprocedural assessment and planning for perioperative management of right heart failure is the key to successful outcomes in these patients.
- A multidisciplinary approach involving the PERT (Pulmonary Embolism Response Team) including the Emergency Physician, Cardiac Surgeon, Vascular Surgeon, Interventional Radiologist, Anesthesia provider, and Critical care physician is very essential for managing these challenging patients.
- The patients are at high risk for a cardiorespiratory collapse in the perioperative period and may need mechanical circulatory support with ECMO (Extra Corporeal Membrane Oxygenation)
- A cardiac anesthetist should also be considered for critically ill patients with multiple comorbidities.
- The procedure is usually done in either a hybrid operating room or in an interventional radiology suite and anesthetizing these high-risk cases in these locations will be a challenge for the anesthesia provider.
- Assessment of the heart function with a TTE (Transthoracic Echocardiography) preoperatively and cardiovascular management of the patient intraoperatively with a TEE (Transesophageal Echocardiography) is very crucial for appropriately managing inotropes, vasopressors and pulmonary vasodilators in these unstable patients.

Introduction

Pulmonary thromboembolism is the third leading cause of cardiovascular mortality after myocardial infarction and stroke in the United States [1]. Unlike the acute management of Myocardial infarction and stroke, the management of acute PE (Table 40.1) remains poorly standardized. In the last 5 years, there has been a lot of interest and research focused on novel technologies like percutaneous catheter-based techniques aimed at reducing morbidity and mortality from this disease([3] PE response teams (PERTs) are being established around the world to provide rapid, individualized, and expert-based care for patients with acute PE [4].

A. Lakshminarasimhachar (✉)
Washington University School of Medicine, Saint Louis, MO, USA
e-mail: lakshmia@wustl.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_40

Table 40.1 Comparison of key features of treatment modalities in acute PE [2] is shown in the table below

Treatment	Major benefits	Major drawbacks
Systemic anticoagulation	Inexpensive, ease	Time to effect Treatment failure Limited data on novel oral anticoagulants in intermediate-risk PE
Systemic thrombolysis	Rapid initiation of reperfusion without specialized equipment	Major bleeds including intracranial bleed
Catheter directed fibrinolysis	Hybrid mechanical and pharmacological approach	Special expertise needed Lack of randomized data
Ultrasound-assisted catheter-directed thrombolysis	Lower dose of thrombolytics required	Special expertise needed
Percutaneous thrombectomy	En bloc removal of thrombi	Special expertise needed Large bore access May not reach distal thrombi
Surgical pulmonary thrombo-embolectomy	Comprehensive proximal thrombectomy	Sternotomy Specialized surgical expertise needed
Vena-caval filters	Aim to prevent further thrombus migration, avoid anticoagulation	Multiple late mechanical complications because of failure to monitor and to retrieve the filter

Table 40.2 Comparison of available endovascular devices for pulmonary embolism [2]

Device	Mechanism
AngioVac	Veno-venous bypass Funnel-shaped inflow tip to engage thrombi
Flowtriever	Nitinol discs engage and mechanically retrieve clot with simultaneous aspiration
Angiojet	Rheolytic thrombectomy with option of thrombolytic vs. saline spray
Indigo system	Mechanical clot engagement with mechanized aspiration
Unifuse	CDF, catheter-directed fibrinolysis
EkoSonic	USAT Ultrasound-Assisted Catheter-Directed Thrombolysis
Cragg-McNamara	CDF, catheter-directed fibrinolysis

Percutaneous Catheter-based techniques (Table 40.2) can be rapidly instituted in most tertiary care centers that are equipped with Hybrid operating rooms and interventional radiology suites. These less invasive percutaneous procedures are better tolerated in tenuous patients whose comorbidities frequently preclude consideration of surgical embolectomy. The advantage of these techniques is that thrombolytics can be directly infused into the pulmonary circulation at doses that are a fraction of those used for systemic thrombolysis thus avoiding the complications of giving a higher dose systemically. Technical advances in endovascular devices now allow for combining mechanical thrombus disruption and aspiration with pharmacological thrombolysis. This is called pharmaco-mechanical therapy [5]. Pharmacological therapy allows a rapid reduction in RV afterload in patients with hemodynamic instability, whereas mechanical therapy reduces thrombus burden via longer, catheter-directed infusion of a low-dose thrombolytic. Even partial mechanical removal and fragmentation of thrombus (Fig. 40.1), however, can be sufficient to restore RV function (Fig. 40.2) and reverse circulatory collapse. There is a growing interest in clinical applications and large-scale investigations of these pharmaco-mechanical therapies in patients with massive PE and selected patients with sub-massive PE.

Patients with massive or sub-massive PE presenting for pulmonary thrombo-embolectomy are very high-risk patients and have a higher rate of morbidity and mortality. Providing anesthesia

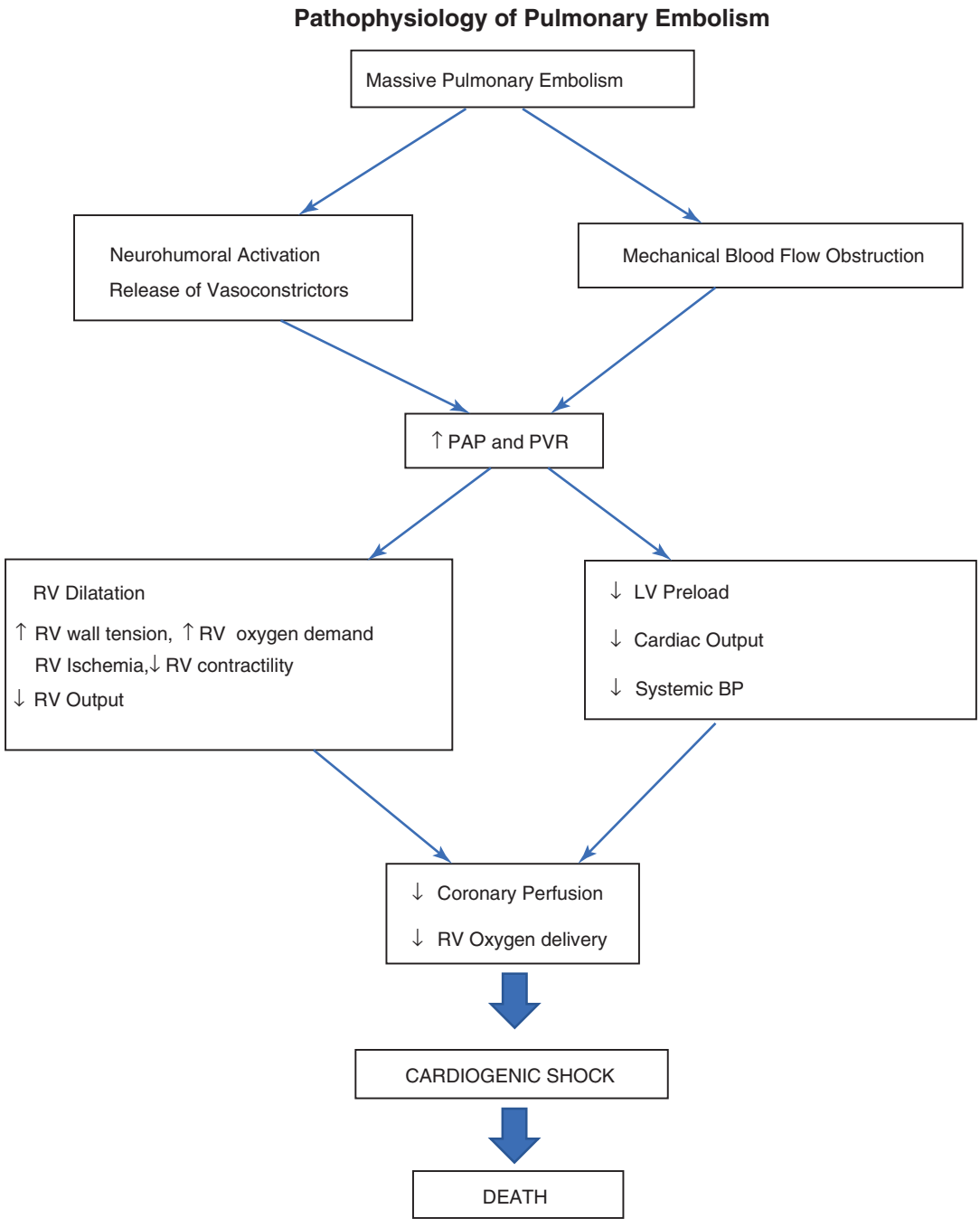


Fig. 40.1 Key factors contributing to hemodynamic collapse and death in acute pulmonary embolism. *RV* right ventricle, *LV* left ventricle, *BP* blood pressure, *PAP* pulmonary artery pressure, *PVR* pulmonary vascular resistance

to these patients having these high-risk procedures could be very challenging. These patients can have a variety of cardio-respiratory issues and they need a well-coordinated, multidisciplinary approach for successful management. They must be done in high volume centers with adequate expertise in managing these kinds of patients.

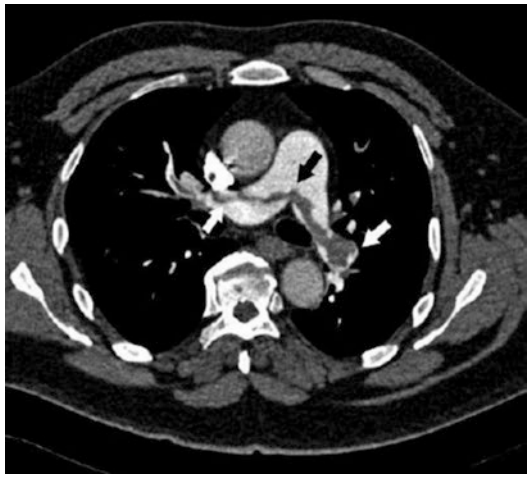


Fig. 40.2 Chest CT angiogram showing a saddle thrombus with filling defects. Arrow showing a saddle thrombus extending into the right and left PA

Table 40.3 Definition of acute hemodynamic Instability following acute PE

1. Cardiac arrest	Need for cardiopulmonary resuscitation
2. Obstructive shock	Systolic BP <90 mmHg or vasopressors required to achieve a BP ⩾90 mmHg despite adequate filling status and End-organ hypoperfusion (altered mental status; cold, clammy skin; oliguria/anuria; increased serum lactate)
3. Persistent hypotension	Systolic BP <90 mmHg or systolic BP drop ⩾40 mmHg, lasting longer than 15 min and not caused by new-onset arrhythmia, hypovolemia, or sepsis

Adapted from the ESC Guidelines [13]

Anesthetic Management

Epidemiology

In epidemiological studies, annual incidence rates for PE range from 39 to 115 per 100,000 population; for DVT (Deep Vein Thrombosis), incidence rates range from 53 to 162 per 100,000 population. Longitudinal studies have revealed a rising tendency in annual PE incidence rates over time [6].

Predisposing Factors

Major trauma, surgery, lower-limb fractures, joint replacements, and spinal cord injury are strong provoking factors for VTE (Venous Thrombo-Embolism). Cancer is a well-recognized predisposing factor for VTE. Estrogen-containing oral contraceptive agents are associated with an elevated VTE risk, and contraceptive use is the most frequent VTE risk factor in women of reproductive age. Infection is a common trigger for VTE. Blood transfusion and erythropoiesis-stimulating agents are also associated with an increased risk of VTE [7]. VTE may be viewed as part of the cardiovascular disease continuum, and common risk factors such as cigarette smoking, obesity, hypercholesterolemia, hypertension, and diabetes mellitus are shared with arterial disease, notably atherosclerosis. Other risk factors include patients with risk of HIT (Heparin Induced Thrombocytopenia), patients who are pregnant, patients with antiphospholipid syndrome, and inherited thrombophilia.

Clinical Manifestation

The clinical signs and symptoms of acute PE are non-specific. In most cases, PE is suspected in a patient with dyspnea, chest pain, pre-syncope or syncope, or hemoptysis [8]. Hemodynamic instability (Table 40.3) is a rare but important form of clinical presentation, as it indicates central or extensive PE with severely reduced hemodynamic reserve. Syncope may occur and is associated with a higher prevalence of hemodynamic instability and RV dysfunction [9]. Conversely, and according to the results of a recent study, acute PE may be a frequent finding in patients presenting with syncope (17%), even in the presence of an alternative explanation [10]. In some cases, PE may be asymptomatic or discovered incidentally during diagnostic workup for another disease. Dyspnea may be severe in central PE but in small peripheral PE, it is often mild and may be transient. In patients with pre-existing heart

Fig. 40.3 Flow triever embolectomy device

Transthoracic Echocardiography Findings in Pulmonary Embolism

1. Parasternal long axis view - Enlarged right ventricle
2. Parasternal short axis view - Flattened interventricular septum
3. Apical Four chamber view –
   Dilated RV with basal RV/LV ratio >1.0 and McConells' sign (Akinesia of the mid free wall of the RV with normal motion of the apex)
   Right heart mobile thrombus detected in the right heart cavities
   Decreased tricuspid annular plane excursion (TAPSE) measured with M-mode (<16 mm)
   Decreased peak systolic (s') velocity of the tricuspid annulus (<9.5 cm/s)
4. Subcostal view - Distended inferior vena cava with diminished inspiratory collapsibility
5. RV inflow outflow view - 60/60 sign : Coexistence of acceleration time of pulmonary ejection < 60 ms and mid-systolic notch with mildly elevated (<60 mmHg) peak systolic gradient at the tricuspid valve

failure or pulmonary disease, worsening dyspnea may be the only symptom indicative of PE. Chest pain is a frequent symptom of PE and is usually caused by pleural irritation due to distal emboli causing pulmonary infarction [11]. In central PE, chest pain may have a typical angina character, possibly reflecting RV ischemia, and requiring differential diagnosis from an acute coronary syndrome or aortic dissection.

A clue to the presence of massive/sub-massive PE is tachycardia with or without hypotension (heart rate/systolic blood pressure > 1.0). Blood gas analysis shows hypoxemia with hypocapnia. A sensitive sign for massive/sub-massive PE is increased right ventricular load. Acute PE is a life-threatening complication for hospitalized patients, a multidisciplinary approach is important to save critically ill patients. Treatment to stabilize respiratory and hemodynamic status should be carried out simultaneously [12].

Flowtriever Device (Fig. 40.3)

Acute PE interferes with both pulmonary blood flow and gas exchange. There is a sudden increase in afterload to the right ventricular (RV) which may lead to RV failure that is the primary cause of death in severe PE. Pulmonary artery pressure (PAP) increases if >30–50% of the total cross-sectional area of the pulmonary arterial bed is occluded by thromboembolism [14]. PE-induced vasoconstriction, mediated by the release of thromboxane A2 and serotonin, contributes to the initial increase in pulmonary vascular resistance (PVR) after PE (Fig. 40.4). Anatomical obstruction and hypoxic vasoconstriction in the affected lung area lead to an increase in PVR and a proportional decrease in arterial compliance [15]. The abrupt increase in PVR results in RV dilation (Fig. 40.5), which alters the contractile properties of the RV myocardium via the Frank-Starling mechanism. There is an increase in wall tension and myocyte stretch as the RV pressure and volume increase (Fig. 40.5). The contraction time of the RV is prolonged, while neurohumoral activation leads to inotropic and chronotropic stimulation. Together with systemic vasoconstriction, these compensatory mechanisms increase PAP, improving flow through the obstructed pulmonary vascular bed and thus temporarily stabilizing systemic blood pressure (BP). The thin-walled RV is unable to generate a mean PAP > 40 mmHg as is not preconditioned and cannot adapt acutely. Prolongation of RV contraction time into the early diastole of the left ventricle (LV) leads to leftward bowing of the interventricular septum. The desynchronization of the ventricles may be exacerbated by the development of the right bundle branch block. As a result, LV filling is impeded in early diastole, and this may lead to a reduction in the cardiac output (CO) and contribute to systemic hypotension and hemodynamic instability [16].

Fig. 40.4 Risk Assessment in PE

LOW RISK	No imaging evidence of RVS Normal Cardiac biomarkers PE may be asymptomatic, incidental
INTERMEDIATE - LOW RISK	Normotensive, with either 1. Imaging evidence of RVS, or 2. Elevated cardiac biomarkers
INTERMEDIATE - HIGH RISK	Normotensive, with both 1. Imaging evidence of RVS, and 2. Elevated cardiac biomarkers Hypotension Acute Respiratory Failure Ventricular Tachyarrhythmias
HIGH RISK	Cardiac arrest Cardiogenic shock Paradoxical bradycardia Vasopressor requirement

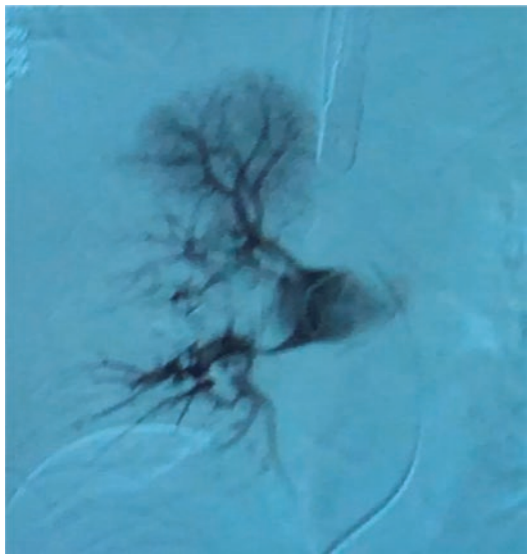


Fig. 40.5 Intra procedure angiogram showing decreased perfusion of the right lung

Diagnostic Studies

1. **D-Dimers**: D-dimer levels are elevated in plasma in the presence of acute thrombosis because of the simultaneous activation of coagulation and fibrinolysis. The negative predictive value of D-dimer testing is high, and a normal D-dimer level renders acute PE or DVT unlikely. On the other hand, the positive predictive value of elevated D-dimer levels is low and D-dimer testing is not useful for confirmation of PE [17].
2. **CT Pulmonary Angiography** (CTPA): Multidetector CTPA is the method of choice for imaging the pulmonary vasculature in patients with suspected PE (Fig. 40.6). It allows adequate visualization of the pulmonary arteries down to the subsegmental level

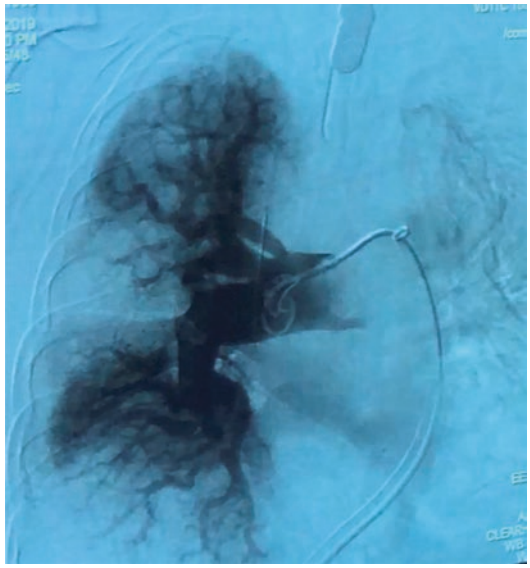


Fig. 40.6 Significantly improved blood flow to the right lung after the embolectomy

[18]. The Prospective Investigation On Pulmonary Embolism Diagnosis (PIOPED) II study observed a sensitivity of 83% and a specificity of 96% for CTPA in PE diagnosis [19].

3. **Enhanced chest computed tomography** (CT) using multi-detector CT is a useful tool for detecting pulmonary emboli in the pulmonary arteries with high specificity and sensitivity [20]. It is also useful to exclude cardiovascular emergencies such as acute aortic dissection or ruptured thoracic aortic Aneurysm.
4. **Lung V/Q Scintigraphy**: The planar ventilation/perfusion [V/Q (lung scintigraphy)] scan is an established diagnostic test for suspected PE. Perfusion scans are combined with ventilation studies, for which multiple tracers such as xenon-133 gas, krypton-81 gas, technetium-99m-labeled aerosols, or technetium-99m-labeled carbon microparticles can be used. The purpose of the ventilation scan is to increase specificity: in acute PE, ventilation is expected to be normal in hypo-perfused segments thus increasing the V/Q mismatch [21].

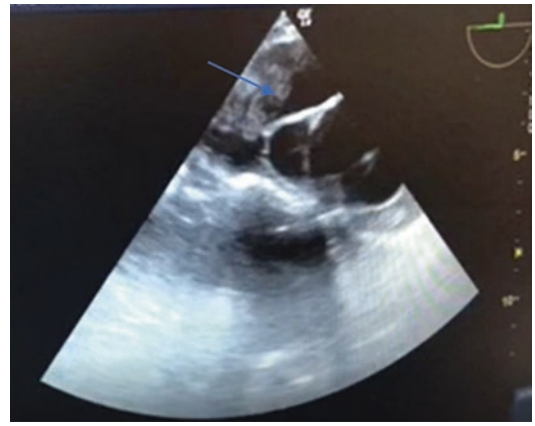


Fig. 40.7 Thrombus in the right PA

5. **Compression Ultrasonography:** Ultrasonography is also useful to detect proximal deep vein thrombosis in the femoral vein.
6. **Echocardiography:** An echocardiogram is a useful tool to detect right ventricular load, floating right ventricular thrombi, and a straddling embolus on the patent foramen ovale [22]. McConnell's sign is a distinct echocardiographic feature of acute massive pulmonary embolism. It is defined as a regional pattern of right ventricular dysfunction with akinesia of the mid free wall and hypercontractility of the apical wall. The advantage of echography is its portability whereas the advantage of CT is that it provides a precise three-dimensional understanding of how the pulmonary emboli occupy the pulmonary arteries (Fig. 40.7).
7. **EKG**: May show ST-segment abnormalities, T-wave inversion, right axis deviation, RBBB, S1Q3T3 pattern
8. **Chest X-Ray**: Maybe non-specific but excludes diseases that may mimic PE like pneumothorax
9. **Laboratory Testing**: CBC, BMP, EKG, NT-BNP, Troponin (Elevation is associated with RV dysfunction and with adverse short-term outcomes) [23]
10. **Blood Gas**: Arterial PH, PaO_2, Serum Lactate

Risk Assessment

The risk stratification of patients with PE is shown in the diagram below. Patients with PE are risk-stratified based on hemodynamic consequences and indices, including biomarkers and imaging evidence of RVS (Fig. 40.8).

Key Anesthetic Management Considerations

Pre-op Assessment

Patients with a sub-massive and massive PE coming in for percutaneous thrombectomy are usually very sick patients with cardiovascular compromise and severe RV strain. Hence it is important to obtain an anesthesia consultation for the procedure and explain the risks and benefits of the anesthesia technique (Sedation vs. General Anesthesia). The possibility of perioperative complications and expected course should be explained to the patient and their family. A thorough preoperative evaluation is very essential for the optimal management of these patients. The patients may be in the ICU or a step-down unit and hence it is necessary to clinically evaluate these patients and check the labs, imaging, echo, assess access for intravenous lines and monitoring lines. It is also very important to discuss with the team taking care of the patient and also the team operating on the patient to have a good understanding of the planned procedure and steps to take in case of any perioperative complications. It is always advisable to have the ECMO(Extra Corporeal Membrane Oxygenation) team on stand-by in case of cardiorespiratory collapse.

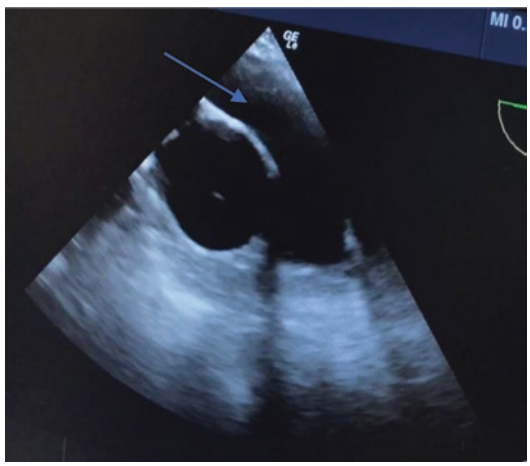


Fig. 40.8 Right PA cleared of the thrombus

MAC (Monitored Anesthesia Care): It may be very challenging to provide MAC for these patients as any degree of hypoxia or hypercarbia is very poorly tolerated by these patients. There may be a subset of patients (Low risk and Intermediate, low, and high risk) who may have a significant PE and maybe hemodynamically and neurologically stable. If the patient is not needing high amounts of oxygen to maintain adequate oxygen saturation and able to lie flat on the procedure table for the duration of the procedure, it may be possible to consider MAC anesthesia. Caution should be exercised in minimizing the sedation and a plan to convert to general anesthesia in case of decompensation should be in place. Patients with respiratory issues may not be good candidates for a MAC. General anesthesia though challenging could be a safer option in these circumstances. In a case series of 46 patients having percutaneous thrombo-embolectomy published by Wible et al. about 75% of the patients had their procedure successfully under MAC [24].

Patients may be on ECMO for Cardiopulmonary support. In such cases, a cardiac anesthetist should be available for managing these critically ill patients with multiple comorbidities. It may be prudent to have a Cardiac Anesthetist on standby in patients with severe hemodynamic instability and also for intra-op TEE monitoring, The procedure is done in an interventional suite which may be remote from the operating rooms, hence it is essential to have a discussion with the cardiac surgical team and have a plan in place in case the patient needs to go to the operating room for any emergencies. The average blood loss for the procedure is about 300–500 mL and the average procedural time is 90–150 min [24].

Preprocedural ultrasound of the common femoral or internal jugular vein should be done to

confirm patency. Pre-operative TTE may be needed to quickly assess the RV function and size, LV function, any clot in transit, IVC diameter and variation with respiration, pericardial effusion, and (tricuspid regurgitation)TR. This will help in selecting the appropriate medications for the induction and maintenance of anesthesia.

Physical Examination: Heart Rate, Elevated Jugular Venous Pulse, Oxygen Saturation, Respiratory Rate, Hypotension (sustained hypotension or need for vasopressors and inotropes indicates severe PE), CNS-Cognitive Impairment.

Intra-op Management

Set-up: Prepare for GA (even if you do a MAC on certain patients), TEE/TTE, Fluids, Pumps, Vasopressor, Inotrope infusion, Pulmonary vasodilators (Inhaled Nitric oxide, Epoprostenol).

Some of the patients may already be on ECMO when coming in for the procedure. Consider TIVA along with inhaled anesthetics and BIS (Bispectral Index) monitoring in case the patient is on ECMO.

Monitoring

- Standard ASA Monitors
- Arterial Line: Preferably pre-induction even if the patient is stable
- Central Venous Monitoring: Preferable for infusion of Vasopressors and Inotropes as needed. It can be placed post-induction or can be slaved from the interventionalist's central venous access
- TEE if the patient has a GA or TTE if the patient has a MAC
- ACT monitoring for the administration and management of heparin
- Point of care Blood Gas

Induction

Patients undergoing PTE are highly vulnerable to right heart failure and cardiac arrest. Invasive arterial blood pressure monitoring is instituted before the induction of anesthesia. It should be noted that sedatives and induction drugs used for intubation and positive pressure ventilation may decrease preload, increase PVR, worsen RV function, and cause hypotension [25]. Preoperatively, severe TR, dilated RV with depressed function, flattened septum with D shaped ventricle may all be impending signs of cardiovascular collapse during induction and in such instances, the institution of inotropic support with either Dobutamine or Epinephrine may be considered before induction. In the case of preoperative hemodynamic instability, it may be necessary to start an infusion of vasopressors in the form of norepinephrine or vasopressin as giving a general anesthetic with an intravenous agent and the IPPV will invariably decrease the blood pressure. Repeated small boluses of a vasoconstrictor may be needed to maintain the BP during induction and maintain the RV perfusion. Bradycardia is avoided to maintain an adequate right ventricular output. It is important to avoid and correct factors increasing PVR like hypoxia, hypercarbia, acidosis, and high airway pressures [26].

A cardio stable induction technique with Etomidate or Ketamine may be necessary in most cases. Propofol must be used very judiciously as these patients may be susceptible to profound hypotension. A rapid sequence induction with either succinylcholine or Rocuronium will mitigate the need to give positive pressure ventilation in these patients and avoid a further decrease in preload which may be detrimental. It is important to rule out any difficult intubation and any evidence of hyperkalemia before doing an RSI.

Intravascular Access

It is advisable to have at least two working intravenous lines for access during induction, one for vasopressors and inotropes, and the other for pushing the induction medications. It is preferable to have at least one 16G IV in case there is a need for fluid and blood resuscitation in the event of bleeding, even if the case is done under

MAC. A central venous line should be placed in consultation with the operating team as they might have to access specific vessels. A double lumen or a triple lumen CVC would be optimal access for infusion of inotropes and vasopressors. It may be necessary to access the central access placed by the interventionalist in case the patient is unstable and there is no time to place the central line.

Intra-op Hemodynamic Goals

Preload: Hypovolemia can aggravate the hypotension caused by pulmonary thromboembolism. Maintain adequate preload and be aware of the decrease in preload with positive pressure ventilation.

Contractility: Depending on the RV and LV function it may be necessary to use inotropes. In cases with PTE depending on the size of the thrombus the RV function could be significantly affected. Dobutamine is sometimes used to increase myocardial contractility in patients with circulatory shock from PE. However, it also results in systemic vasodilation which worsens hypotension, particularly at low doses. To mitigate this effect, it may be necessary to add norepinephrine to dobutamine; as the dose of dobutamine is increased, the effects of dobutamine-induced myocardial contractility exceed those of vasodilation, potentially allowing norepinephrine to be weaned off. Other alternatives include dopamine and epinephrine, but tachycardia, which can exacerbate hypotension, can occur with these agents. Milrinone can cause a significant drop in SVR and hence may not be the appropriate choice for an inotrope [27].

Afterload: These patients will have an increased pulmonary afterload which may be detrimental to the patient. As they are hemodynamically unstable and drop in systemic vascular resistance could be disastrous. Intravenous vasopressors are administered when adequate perfusion is not restored with intravenous fluids. The optimal vasopressor for patients with shock due to acute PE is unknown, but norepinephrine is generally preferred. Norepinephrine is the most frequently utilized agent in this population because it is effective and less likely to cause tachycardia [28].

In patients with pulmonary hypertension or right ventricular dysfunction, vasopressin is preferred to other vasoconstrictors since it can selectively support systemic vascular tone without increasing pulmonary vascular resistance and right ventricular afterload. Vasopressin provides a dual benefit to the failing right ventricle. Initially, the increased systemic vascular tone increases coronary perfusion pressure to increase myocardial oxygen delivery [29]. Also, the increased oxygen supply due to increased coronary perfusion pressure is not at the cost of increasing right ventricular afterload. Consequently, in combination with an inhaled selective pulmonary vasodilator, vasopressin advances the perioperative management of clinically significant pulmonary hypertension and right ventricular dysfunction. This dual drug strategy can be considered a ‘pharmacologic balloon pump’ for the failing right ventricle.

Pulmonary Vasodilators

Inhaled Nitric Oxide

Inhaled nitric oxide (iNO) has been proposed as a potential therapeutic agent in cases of acute PE with associated increased pulmonary vascular resistance. Inhaled NO (iNO) has been reported to improve oxygenation and hemodynamics in conjunction with either chemical and/or mechanical thrombolysis in massive PE. iNO has multiple effects that suggest a potential therapeutic role in the treatment of acute PE [30]. Also, in both human and animal studies, NO has been shown to inhibit platelet adhesion and aggregation, prolong bleeding times, and reduce fibrinogen binding; these factors may prevent additional clot formation in acute PE. It has not been shown to have any mortality benefit.

Epoprostenol

Aerosolized epoprostenol has been shown in case reports to be transiently beneficial for acute pulmonary hypertension in patients with acute PE following systemic thrombolysis. Aerosolized flolan can improve right ventricular function through targeted vasodilation in the pulmonary vasculature and alveolar gas exchange due to increased surface area. In patients with excessive clot burden, there is always a theoretical risk of worsening V/Q mismatch by dilating a pulmonary capillary bed with proximal emboli. Proper patient selection and the exact timing of therapy is not very clear [31].

Heart rate: It is important to avoid tachycardia to facilitate adequate ventricular filling in these patients. Some inotropes like dobutamine and epinephrine can cause tachycardia and the practitioner should be mindful of this. Bradycardia from poor RV perfusion can be deleterious.

Rhythm: Patients with significant embolism and RV failure and hypotension and hypoxemia can have life-threatening arrhythmias. This may be precipitated by acid-base and electrolyte imbalances. Hence it is very essential to maintain adequate RV and LV perfusion and correct any acid-base and electrolyte abnormalities to prevent malignant arrhythmias and maintain sinus rhythm.

Surgical Procedure

The percutaneous access for the procedure is usually through the femoral vessels in the groin. The internal jugular vein can be used for additional access in certain situations. The embolectomy catheters are introduced through a sheath placed in the femoral vein. Angiograms are performed before (Fig. 40.9) and after the procedure (Fig. 40.10) to access the improvement in lung perfusion after the thromboembolectomy.

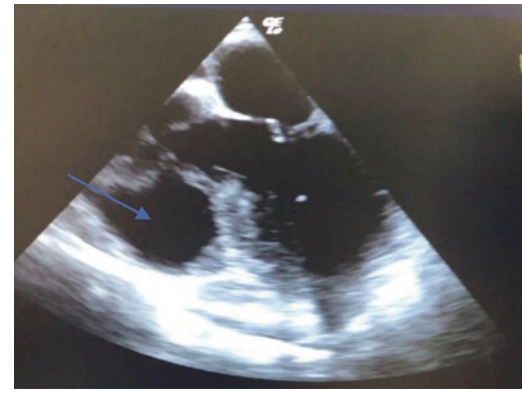


Fig. 40.9 RV dilatation from increased afterload from PE

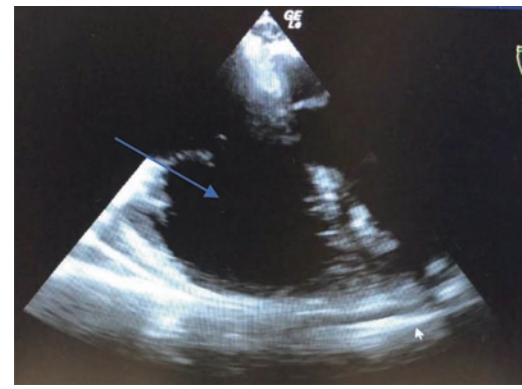


Fig. 40.10 Decreased RV size after embolectomy

Maintenance of Anesthesia

Anesthesia can be maintained with a general anesthetic with Air, Oxygen, and an inhaled anesthetic agent.

Intra-Procedure TEE Can be used to Assess

1. Severity of TR
2. RV Size and Function: TAPSE, RV FAC, RV EF, RVSP, PASP, Pulse doppler velocity at annulus – Fig. 40.5 shows the RV dilatation from increased afterload and Fig. 40.2 shows

the decreased size of RV after the thrombus was removed.
3. LV and the Septum
4. Dilated IVC
5. Assessment of PA: Main PA and the Branches. Figure 40.11 shows the thrombus in the main PA and Fig. 40.12 shows the right PA cleared of the thrombus.
   - TAPSE Tricuspid annular plane systolic excursion (Normal 15–22 mm).
   - RV FAC fractional area change (Normal 35% or higher).
   - RVEF RV Ejection Fraction (Normal >45%).
   - RVSP RV Systolic Pressure.
   - PASP PA Systolic Pressure (Normal 18–25 mmHg).

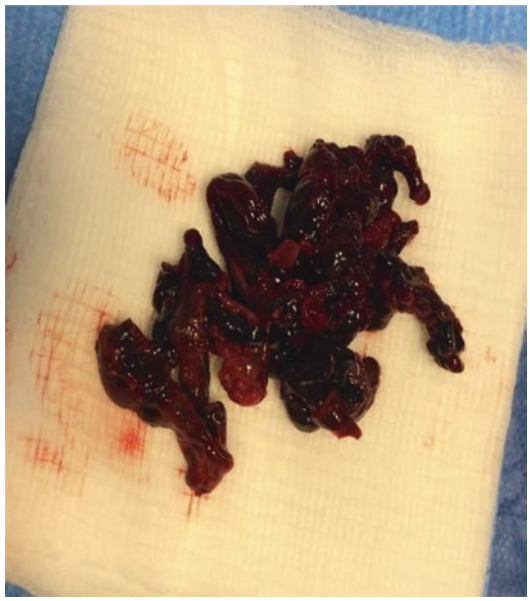


Fig. 40.11 Thrombus from the right PA

Other Intraoperative Considerations

Before traversing the right heart en-route to catheterizing the main PA, the presence of left bundle branch block should be excluded. For patients with a left bundle branch block, transvenous pacing should be available before the procedure, as manipulation of wires and catheters in the right heart may cause the right bundle branch block and consequently complete heart block. A variety of transvenous pacing options are now available and can be provided by cardiology [32].

The patient may have a vena-caval filter. So, access to the PA through the femoral vein may require the removal of the filter. The filter may have to be retrieved through access from the Internal jugular vein. However, after removal, the IJV may be used for central venous access.

ECMO back up may be needed if the patient decompensates during the procedure. So, if this is suspected it may be prudent to cannulate the femoral vein and artery with catheters which may be used to place the ECMO cannulas if needed. Hence it is wise to have the ECMO team on standby during the percutaneous procedure.

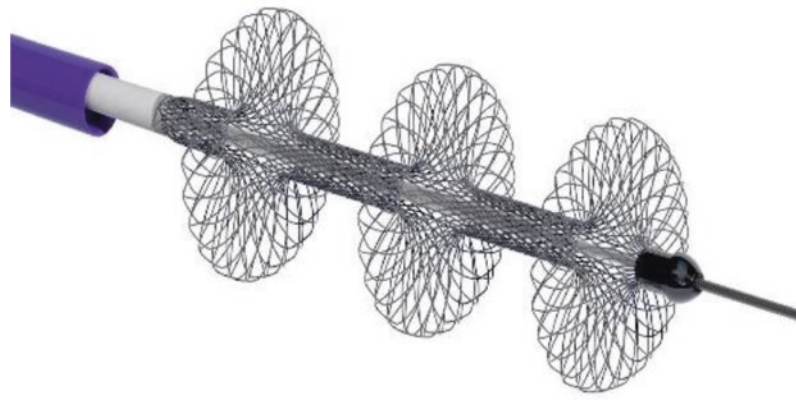


Fig. 40.12 FlowTriever Embolectomy Device

ECMO

In patients with high-risk PE and cardiogenic shock, cardiac arrest, or impending hemodynamic collapse, further mechanical support should be considered. Veno-arterial extracorporeal membrane oxygenation (VA ECMO) is effective when used in combination with any of the above treatments with good survival rates and low complication risks [33]. VA ECMO provides complete hemodynamic support with up to 5–6 L of output in conjunction with an oxygenator, which provides oxygenation and ventilation support. Importantly, as it bypasses the pulmonary circulation, it reduces the RV pre-load and reduces RV distention while having no effect on the pulmonary artery pressure.

Respiratory Support—Patients with massive and sub-massive pulmonary thromboembolism can have significant problems with oxygenation and hemodynamic stability. Importantly, patients with coexistent right ventricle failure are prone to hypotension following intubation and positive pressure ventilation. In these cases, it may be prudent to avoid high plateau pressures to prevent the decrease in pre-load and avoid significant hypotension. These patients will have a very high V/Q mismatch from the massively decreased lung perfusion. So, they might need a higher amount of oxygen to maintain adequate oxygen saturation. If the patient has severe hemodynamic compromise to the point that it is impossible to maintain oxygenation, then consideration should be given to VA ECMO for hemodynamic support and oxygenation.

Periprocedural Complications

Many complications of PE interventions are intrinsic to the pulmonary anatomy and are independent of the type of device used. The thin-walled PA branches are prone to perforation, prompting many clinicians to recommend limiting interventions to the main PA and the larger segmental branches of the lower lobes. Perforation can result in pericardial tamponade or life-threatening hemoptysis. Concomitant use of even low doses of thrombolytic agents carries the risk of bleeding complications, but cumulative experience suggests that major procedural complications, including bleeding, can be as low as 2.4%. Catheter fragmentation techniques have been reported to cause paradoxical elevation of pulmonary arterial pressures and worsening hemodynamic status, likely via embolization of proximal thrombus into the distal branches [34].

Post-op Considerations

Extubation can be considered depending on the preoperative stability of the patient and the intraoperative course. If the patient is hemodynamically stable with a minimal amount of vasopressors and inotropes, is not needing any pulmonary vasodilator for right heart support, has minimal oxygen requirements, the metabolic status is normal on the blood gas and the TEE shows reasonable right and left heart function it may be possible to go ahead with a trial of extubation. If any of these above criteria are not met it may be prudent to keep the patient intubated and ventilated on the ICU till the patient is stabilized.

Successful PTE results in an immediate decrease in right ventricular afterload. Cardiac output is generally dependent on the optimization of right ventricular function. Maintaining appropriate right ventricular preload, sinus rhythm, and heart rate are important to achieve optimization of right ventricular function. Pericardial effusion and tamponade are possible complications following this procedure and it should be ruled out by the TEE at the end of the procedure. Most patients experience some degree of reperfusion injury ranging in severity from mild to life-threatening. Onset is typically within 24–72 h of the procedure, though reperfusion injury can occur immediately after the thrombo-embolectomy. Mild reperfusion injury typically results in pulmonary edema and postoperative hypoxemia for which supportive care typically allows resolution while severe reperfusion injury presents as profound alveolar hemorrhage with

persistently increased pulmonary artery pressure [35]. The use of inhaled nitric oxide to improve oxygenation and gas exchange has been described, but subsequent clinical trials have not demonstrated significant benefit [36]. Besides, long-term use of nitric oxide may lead to rebound pulmonary hypertension. Inhaled and intravenous prostacyclin analogs have been reported in case series as a successful, short-term treatment option, but the evidence is limited, and long-term efficacy has not been demonstrated [37]. Extracorporeal membrane oxygenation may be used for hemodynamic or respiratory support in severe cases. Current management strategies include diuretic administration, avoidance of inotropes and vasodilators, and lung-protective ventilatory strategies including the early use of positive end-expiratory pressure. Pulmonary arterial steal occurs as blood flow from previously perfused alveoli is shunted to the newly perfused areas of the lung. Severe hypoxemia develops when these lung segments are not yet contributing to oxygenation [38]. This phenomenon decreases over time, suggesting that remodeling of the pulmonary vasculature occurs leading to improved ventilation-perfusion matching.

Conclusions

Minimally invasive Percutaneous Pulmonary Thrombo-embolectomy is a very high-risk procedure that is done in remote anesthesia locations and involves a multidisciplinary team approach involving Interventional radiologists, ED physicians, Intensivists, Cardiologist, Cardiac surgeons, and the Anesthesia provider. A thorough pre-procedural exam with a review of the CT angiogram and echocardiogram, careful monitoring and management of hemodynamics, and a judicious anesthetic technique is very crucial for the successful management of these patients. It may be prudent to have the involvement of a cardiac anesthesia provider for such complex patients as their expertise in TEE/TTE, management of inotropes, vasopressors, pulmonary vasodilators, and ECMO may be very useful in taking care of these very complicated patients.

References

1. Venous Thromboembolism in Adult Hospitalizations—United States, 2007–2009 [Internet]. https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6122a1.htm. Accessed 23 Jun 2020.
2. Dudzinski DM, Jay G, Kenneth R. Interventional treatment of pulmonary embolism. Circ Cardiovasc Interv. 2017;10(2):e004345.
3. Barnes GD, Kabrhel C, Courtney DM, Naydenov S, Wood T, Rosovsky R, et al. Diversity in the pulmonary embolism response team model: an organizational survey of the national PERT consortium members. Chest. 2016;150(6):1414–7.
4. Tu T, Toma C, Tapson VF, Adams C, Jaber WA, Silver M, et al. A prospective, single-arm, multicenter trial of catheter-directed mechanical thrombectomy for intermediate-risk acute pulmonary embolism. JACC Cardiovasc Interv. 2019;12(9):859–69.
5. Piotr S. Catheter-assisted pulmonary embolectomy. Circulation. 2012;126(15):1917–22.
6. Wendelboe AM, Raskob GE. Global burden of thrombosis. Circ Res. 2016;118(9):1340–7.
7. Anderson Frederick A, Spencer Frederick A. Risk factors for venous thromboembolism. Circulation. 2003;107(23_suppl_1):I–9.
8. Miniati M, Prediletto R, Formichi B, Marini C, Di Ricco G, Tonelli L, et al. Accuracy of clinical assessment in the diagnosis of pulmonary embolism. Am J Respir Crit Care Med. 1999;159(3):864–71.
9. Wells PS, Ginsberg JS, Anderson DR, Kearon C, Gent M, Turpie AG, et al. Use of a clinical model for safe management of patients with suspected pulmonary embolism. Ann Intern Med. 1998;129(12):997–1005.
10. Barco S, Ende-Verhaar YM, Becattini C, Jimenez D, Lankeit M, Huisman MV, et al. Differential impact of syncope on the prognosis of patients with acute pulmonary embolism: a systematic review and meta-analysis. Eur Heart J. 2018;39(47):4186–95.
11. Prevalence of Pulmonary Embolism among Patients Hospitalized for Syncope | NEJM [Internet]. https://www.nejm.org/doi/full/10.1056/NEJMoa1602172. Accessed 23 Jun 2020.
12. Konstantinides SV, Torbicki A, Agnelli G, Danchin N, Fitzmaurice D, Galiè N, et al. 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. Eur Heart J. 2014;35(43):3033–69, 3069a–3069k.
13. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). European Heart Journal. Oxford Academic [Internet]. https://academic.oup.com/eurheartj/article/41/4/543/5556136. Accessed 23 Jun 2020.
14. Delcroix M, Mélot C, Lejeune P, Leeman M, Naeije R. Effects of vasodilators on gas exchange in acute canine embolic pulmonary hypertension. Anesthesiology. 1990;72(1):77–84.

15. Huet Y, Brun-Buisson C, Lemaire F, Teisseire B, Lhoste F, Rapin M. Cardiopulmonary effects of ketanserin infusion in human pulmonary embolism. Am Rev Respir Dis. 1987;135(1):114–7.
16. Lankhaar J-W, Westerhof N, Faes TJC, Marques KMJ, Marcus JT, Postmus PE, et al. Quantification of right ventricular afterload in patients with and without pulmonary hypertension. Am J Physiol Heart Circ Physiol. 2006;291(4):H1731–7.
17. Wells PS, Anderson DR, Rodger M, Stiell I, Dreyer JF, Barnes D, et al. Excluding pulmonary embolism at the bedside without diagnostic imaging: management of patients with suspected pulmonary embolism presenting to the emergency department by using a simple clinical model and d-dimer. Ann Intern Med. 2001;135(2):98–107.
18. Qanadli SD, Hajjam ME, Mesurolle B, Barré O, Bruckert F, Joseph T, et al. Pulmonary embolism detection: prospective evaluation of dual-section helical CT versus selective pulmonary arteriography in 157 patients. Radiology. 2000;217(2):447–55.
19. Value of the Ventilation/Perfusion Scan in Acute Pulmonary Embolism. Results of the prospective investigation of pulmonary embolism diagnosis (PIOPED). JAMA. 1990;263(20):2753–9.
20. Anderson DR, Kahn SR, Rodger MA, Kovacs MJ, Morris T, Hirsch A, et al. Computed tomographic pulmonary angiography vs ventilation-perfusion lung scanning in patients with suspected pulmonary embolism: a randomized controlled trial. JAMA. 2007;298(23):2743–53.
21. Waxman AD, Bajc M, Brown M, Fahey FH, Freeman LM, Haramati LB, et al. Appropriate use criteria for ventilation-perfusion imaging in pulmonary embolism: summary and excerpts. J Nucl Med. 2017;58(5):13N–5N.
22. Bova C, Greco F, Misuraca G, Serafini O, Crocco F, Greco A, et al. Diagnostic utility of echocardiography in patients with suspected pulmonary embolism. Am J Emerg Med. 2003;21(3):180–3.
23. Jay G, Sista Akhilesh K, Ido W, Clive K, Kumbhani Dharam J, Desai Nimesh D, et al. Interventional therapies for acute pulmonary embolism: current status and principles for the development of novel evidence: a scientific statement from the American Heart Association. Circulation. 2019;140(20):e774–801.
24. Wible BC, Buckley JR, Cho KH, Bunte MC, Saucier NA, Borsa JJ. Safety and efficacy of acute pulmonary embolism treated via large-bore aspiration mechanical thrombectomy using the inari flowtriever device. J Vasc Interv Radiol. 2019;30(9):1370–5.
25. Rosenberger P, Shernan SK, Shekar PS, Tuli JK, Weissmüller T, Aranki SF, et al. Acute hemodynamic collapse after induction of general anesthesia for emergent pulmonary embolectomy. Anesth Analg. 2006;102(5):1311–5.
26. Blaise G, Langleben D, Hubert B. Pulmonary arterial hypertension: pathophysiology and anesthetic approach. Anesthesiology. 2003;99(6):1415–32.
27. Layish DT, Tapson VF. Pharmacologic hemodynamic support in massive pulmonary embolism. Chest. 1997;111(1):218–24.
28. Ghignone M, Girling L, Prewitt RM. Volume expansion versus norepinephrine in treatment of a low cardiac output complicating an acute increase in right ventricular afterload in dogs. Anesthesiology. 1984;60(2):132–5.
29. Treschan TA, Peters J. The vasopressin system: physiology and clinical strategies. Anesthesiology. 2006;105(3):599–612; quiz 639–40.
30. Bhat T, Neuman A, Tantary M, Bhat H, Glass D, Mannino W, et al. Inhaled nitric oxide in acute pulmonary embolism: a systematic review. Rev Cardiovasc Med. 2015;16(1):1–8.
31. Webb SAR, Stott S, van Heerden PV. The use of inhaled aerosolized prostacyclin (IAP) in the treatment of pulmonary hypertension secondary to pulmonary embolism. Intensive Care Med. 1996;22(4):353–5.
32. Devcic Z, Kuo WT. Percutaneous pulmonary embolism thrombectomy and thrombolysis: technical tips and tricks. Semin Interv Radiol. 2018;35(2):129–35.
33. Abrams D, Combes A, Brodie D. Extracorporeal membrane oxygenation in cardiopulmonary disease in adults. J Am Coll Cardiol. 2014;63(25 Pt A):2769–78.
34. Zarghouni M, Charles HW, Maldonado TS, Deipolyi AR. Catheter-directed interventions for pulmonary embolism. Cardiovasc Diagn Ther. 2016;6(6):651–61.
35. Matthay MA, Wiener-Kronish JP. Respiratory management after cardiac surgery. Chest. 1989;95(2):424–34.
36. Imanaka H, Miyano H, Takeuchi M, Kumon K, Ando M. Effects of nitric oxide inhalation after pulmonary thromboendarterectomy for chronic pulmonary thromboembolism. Chest. 2000;118(1):39–46.
37. Kramm T, Eberle B, Guth S, Mayer E. Inhaled iloprost to control residual pulmonary hypertension following pulmonary endarterectomy. Eur J Cardiothorac Surg. 2005;28(6):882–8.
38. Moser KM, Metersky ML, Auger WR, Fedullo PF. Resolution of vascular steal after pulmonary thromboendarterectomy. Chest. 1993;104(5):1441–4.

41 Anesthesia for the Patient with Fibrodysplasia Ossificans Progressiva

Max Shilling and Adam Thaler

Learning Points

- FOP is a rare genetic disorder that leads to heterotopic ossification and progressive disability in the affected patient.
- Peri-operative care for the surgical patient with FOP requires a multidisciplinary approach to optimize patient safety and outcomes
- General anesthesia with awake nasotracheal intubation is considered to be standard of care for securing the airway of a patient with FOP
- Steroid administration is critical for the prevention of flare-ups precipitated by surgical stress
- Regional and neuraxial analgesia may be difficult or impossible in the surgical patient with FOP, requiring careful administration of multimodal analgesia to facilitate extubation and discharge

Introduction

Fibrodysplasia ossificans progressiva (FOP) is a rare genetic disorder causing progressive heterotopic ossification of connective tissue such as muscles, tendons, and ligaments, progressively leading to the formation of a heterotopic skeleton [1]. Heterotopic bone formation causes ankylosis of joints throughout the body, progressively leading to loss of mobility and joint function, and severe disability. Any traumatic incident to connective tissue like a fall or invasive medical procedure, or a systemic medical illness such as influenza, has the potential to trigger an episode of muscle swelling and inflammation, known as a flare-up [2]. Rapid ossification with heterotopic bone formation may follow this period of inflammation, leading to progressively worsening disability. Throughout childhood and young adult life, bone formation is episodic, progressive, and extensive, progressively immobilizing all of the joints of the normotopic skeleton, rendering movement largely impossible. Flare-ups tend to be observed in a well-defined spatial pattern, causing extra-articular ankyloses of the joints of the axial and appendicular skeleton, immobilizing the patient in a 'new' skeleton of heterotopic bone [2]. Diagnosis of FOP is usually based on clinical examination and evaluation, which should lead to genetic confirmation. Unfortunately due to the rare nature of the disease, an affected patient may be initially misdiagnosed with a different disorder, leading to a delay in diagnosis. Common differential diagnoses include cancer and fibrosis, which may lead to the inappropriate performance of a biopsy of a lesion of ossification, which can cause detrimental flare-ups in the affected patient [3].

M. Shilling · A. Thaler (✉)
Department of Anesthesiology, Thomas Jefferson University Hospital, Philadelphia, PA, USA
e-mail: max.shilling@jefferson.edu; Adam.thaler@jefferson.edu

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_41

Genetic Basis of Disease

FOP has a prevalence of approximately 1–2/1,000,000. A mutation mapped to the gene ACVR1 on chromosome 2q23–24 has been identified as being responsible for causing FOP [4–6]. The gene encodes instructions for producing the protein activing receptor type-1. This protein is part of the family of bone morphogenetic protein type I receptors, found in many body tissues such as skeletal muscle and cartilage. Autosomal dominant inheritance is observed, but most cases are caused by spontaneous mutation. Approximately 97% of patients with FOP have this recurrent mutation, and 3% of affected individuals have a variant mutation in ACVR1 [6]. The mutated gene causes abnormal activation of ACVR1, which leads to the production of heterotopic ossification of the affected individual's connective tissue. No ethnic, racial, gender, or geographic predilection to FOP has been identified [6]. Patients with classic clinical features of FOP demonstrate great toe malformations and progressive heterotopic ossification in a characteristic anatomic pattern [2]. These patients have been found to carry the same heterozygous mutation in the activation domain of ACVR1. Atypical FOP patients have also been described in the literature. Kaplan et al. formed two classes of these patients with clinical features unusual for FOP, classified as FOP-plus and FOP variants. FOP-plus patients are described as having classic defining features of FOP, plus one or more atypical features. These atypical features may include intraarticular synovial osteochondromatosis of hips, degenerative joint disease of hips, mild cognitive impairment, childhood glaucoma, cerebellar abnormalities, and diffuse cerebral dysfunction, among other features [6]. FOP variants have major variations in one or both of the two classic defining features of FOP. A study of 112 FOP patients demonstrated that 104 were sporadic cases, and 8 were familial cases [2]. Classic FOP was found in 82 sporadic cases and 7 familial cases, while 20 sporadic cases and 1 familial case had atypical disease. Some patients with atypical clinical presentation of FOP were found to have alternate mutations in the ACVR1 gene. The classic missense or in-frame deletion occurs in most patients with FOP-plus, however, some patients with FOP-plus may also have novel mutations explaining their additional features. FOP variant patients were also found to have a novel mutation.

Clinical Features and Management

FOP is an incurable progressive disease, with sporadic or triggered episodes and flare-ups of painful soft tissue swellings. Children born with FOP appear normal at birth, with the exception of a congenital malformation of the great toes [6]. If the diagnosis FOP is suspected, it is critical that all elective surgeries, biopsies, and intramuscular immunizations be delayed until a definitive diagnosis is made, to prevent the precipitation of flare-ups [7]. Progressive episodes of heterotopic ossification occur in specific patterns, usually first manifested as ossification of the dorsal, axial, cranial, and proximal regions of the body. Ventral appendicular, caudal, and distal regions tend to follow. The cervical spine often becomes ankylosed early in life, with fusion of the facet joints between C2 and C7. Misdiagnosis of ossification sites as tumor or fibrosis may lead to attempts at removal. This can result in rapid and progressive ossification and painful flare-ups. Any trauma can produce a flare up of ossification, such as minor soft tissue injury, muscle injury, intramuscular injection for immunization, and injections for dental work. As patients become progressively immobile, they tend to become wheelchair-bound by the end of the second decade of life [6]. It is important to note that the diaphragm, tongue, extra-ocular muscles, and cardiac muscle are all spared from the disease.

Progressive immobility and ankylosis can lead to additional life-threatening manifestations and complications of disease. Malnutrition, weight loss, and dehydration may result from ankyloses of the jaw and inability to open the mouth. Orthotopic ankyloses of the costovertebral joints, in addition to ossification of intercostal and paravertebral muscles is common. One study of 40 FOP patients demonstrated 65% of subjects having radiographic evidence of scoliosis [8]. Progressive heterotopic ossification in the paravertebral musculature, in combination with the

development of kyphoscoliosis, may lead to thoracic insufficiency syndrome (TIS) [6, 7]. Worsening TIS may progress to severe restrictive lung disease, hypoxia, pulmonary hypertension, and right-sided heart failure. Recurrent pneumonia and bronchiectasis is also seen in patients with TIS, due to difficulty with pulmonary toilet. Table 41.1 displays a full range of signs and symptoms which may be seen in the affected patient. Appropriate and timely immunization is critical for prevention of disease such as influenza and pneumonia, which themselves may cause flare-ups or progress to fatal illness. Intramuscular injection, though, must be avoided due to the risk of producing a flare-up. Instead, vaccinations should be administered by alternative routes [7].

Table 41.1 Signs and symptoms of FOP; adapted from Online Mendilian Inheritance in Man [18]

Head and neck	• Sensorineural and/or conductive hearing loss • Jaw fixation • Widely spaced teeth
Pulmonary	• Restrictive lung disease • Thoracic insufficiency syndrome • Respiratory failure
Skull	• Flat, broad mandibular condyles
Spine	• Progressive cervical vertebral spine fusion, with small cervical vertebral bodies • Scoliosis
Limbs	• Painful swellings in tendons, progressive ectopic ossification of tendons and ligaments • Broad femoral neck • Proximal medial tibial osteochondromas • Joint immobility
Hands	• Short thumb • Short first metacarpal • Fifth finger clinodactyly
Feet	• Short hallux, hallux valgus • Malformed first metatarsal[a] • Monophalangism of first metatarsal
Skin, Nails, Hair	• Alopecia
Muscle, Soft Tissues	• Painful swelling in aponeuroses and fasciae • Progressive ectopic ossification of neck, dorsal trunk, proximal limbs, sternocleidomastoid, and masseters
Neurologic	• Asymptomatic hamartoma-like lesions in dorsal medulla and pons • Bulging of dorsal pons • Thickened pontomedullary junction and enlarged medulla • Enlargement of origin of vestibulocochlear nerves • Rarely mental retardation

[a]This classic sign is usually present at birth, and can help with making an early diagnosis of the disorder

At present, there is no definitive medical treatment for FOP. Flare-ups of painful inflammation and ossification have been demonstrated to have an inflammatory component, involving macrophages, lymphocytes, and mast cells in early FOP lesions [9]. Because of this inflammatory and immune component of flare-ups, corticosteroids are indicated as first-line treatment at the beginning of such episodes [7]. A 4-day course of high-dose corticosteroids, equivalent to 2 mg/kg/day of oral prednisone, should be started within the first 24 h of a flare up [7]. Experts recommend that use of corticosteroids be restricted only to extremely early symptomatic treatment of flare-ups affecting major joints, the jaw, and the submandibular area. Additionally, corticosteroids are recommended for prevention of flare-ups following major soft tissue injury, and for the prevention of flare-ups in in elective or emergent surgery. Many flare-ups are extremely painful, and may require oral/topical NSAIDs and/or muscle relaxants. It is recommended to avoid narcotic analgesia whenever possible [7].

As there is no definitive treatment for FOP, affected individuals have a considerably shortened lifespan [10]. In a large review of mortality reports from two large registries of known FOP patients, 60 deaths were reported during a 33 year period. The median age at the time of death for these patients was 40 years. In this review, the two most common causes of death in patients with FOP were cardiorespiratory failure from TIS (54%) and pneumonia (15%).

Anesthetic Management

Pre-admission Evaluation

The patient with FOP may present to surgery for a variety of reasons. For example, affected indi-

viduals may present for a variety of periodontal procedures, including dental rehabilitation, extraction of teeth, and drainage of oral abscesses. As temporomandibular joint ankylosis results in very limited mouth opening, affected individuals often have difficulty with maintaining oral hygiene, necessitating periodontal surgery. Whenever possible, a multi-disciplinary team should be involved in the peri-operative care of the patient with FOP, including an appropriate surgical presence (such as a dentist or an oral and maxillofacial surgeon), an anesthesiologist, and an otolaryngologist [11, 12]. Additional consultation from a pulmonologist or cardiologist may be useful in the patient with significant cardiorespiratory dysfunction. A pre-admission anesthetic assessment prior to the date of surgery is critical in establishing disease course and severity. A thorough history and physical examination should be performed, with particular emphasis on examination of the airway and assessing cardiorespiratory function. Affected individuals may have limited or minimal mouth opening secondary to ankylosis of the temporomandibular joint. Cervical spine involvement, causing limited or absent neck flexion and extension, may further complicate airway management. Room air pulse oximetry can be a useful metric of baseline gas exchange in the patient, and should be performed prior to surgery. Additionally, auscultation of the chest well and precordium can elicit signs of respiratory illness or cardiovascular decompensation. Useful laboratory workup may include a complete blood count and basic metabolic panel. Chronic hypoxemia may cause secondary erythrocytosis, with an increased hemoglobin and hematocrit, while an elevated bicarbonate level may indicate a chronic compensated acid-base disturbance. Additionally, longstanding malnutrition may result in a derangement of sodium, potassium, and chloride, further highlighting the potential relevance of pre-operative lab work.

Intravenous Access

Patients should be encouraged to drink clear liquids up to 2 hrs prior to surgery, to prevent further dehydration from a traditional NPO from midnight approach. Difficulty with obtaining intravenous access should be expected, given that the affected patient may be dehydrated and may have musculoskeletal deformities further complicating anatomical assessment of peripheral veins. Extra care should be taken when securing intravenous access, and the use of ultrasound may be necessary. Although intramuscular injection is contraindicated in affected individuals, intravenous insertion can be well tolerated with the minimization of attempts and tourniquet time, and choosing a superficial vein if possible [7]. The smallest intravenous catheter appropriate for the procedure should be used [7]. Once intravenous access is obtained, administration of an antimuscarinic such as glycopyrrolate should be considered, to reduce airway secretions which may complicate later airway topicalization and intubation.

Airway Management

The patient with FOP presents many risk factors for difficulty with ventilation and intubation. Ankylosis of the temporomandibular joint may produce limited mouth opening and jaw prognathation, while involvement of the cervical spine may severely reduce the patient's ability to flex and extend their neck. Ossification of the strap muscles of the neck can also potentially complicate obtaining emergent front-of-neck access for a surgical airway if needed. Affected individuals may have respiratory compromise and little functional residual capacity, resulting in a shortened time period for desaturation following apnea. When considering the above risks, the recommended standard for airway management in the patient with FOP who requires general anesthesia is an awake nasotracheal intubation with fibreoptic bronchoscopy [7]. It is further recommended that a highly-skilled FOP-aware anesthesiologist be present for all elective intubations [7]. The use of local anesthetic for surgical anesthesia is often not an option for the surgical patient with FOP for a variety of reasons. For example, routine injections of local anesthetic for

dental procedures, specifically the use of mandibular blocks, should not be used due to the potential for rapid ossification of the pterygoid muscles, producing ankylosis of the temporomandibular joint [13]. Any injection of local anesthetic at any body site has the potential to precipitate a disease flare-up. Depending on the severity of disease, the presenting patient may or may not have limited mouth opening. Regardless of the ability to open the mouth, experts recommend that the nasal route for intubation is used, as opposed to orotracheal intubation [7]. Stretching of the pharyngeal and neck muscles, with potential trauma at the temporomandibular joint associated with direct or video laryngoscopy, may precipitate a future flare-up. A large case series describing the anesthetic records of 42 general anesthetics for 30 patients with FOP undergoing dental procedures highlights many of the significant considerations necessary when performing a general anesthetic for the patient with FOP, and recommendations made in this section are largely based on a review of this case series in conjunction with other available case reports in the literature [12]. General anesthesia was administered to all of the patients for their procedures, and in 34 of 42 cases, awake nasotracheal intubation was performed, with one intubation being orotracheal and another patient presenting to surgery with a pre-existing tracheostomy.

Care should be taken when achieving airway topicalization for an awake nasotracheal intubation. It may be difficult or impossible to perform targeted nerve blocks for the purposes of topicalization due to limited mouth opening. Additionally, there is a potential risk of precipitating a disease flare up with the targeted injection of local anesthetic, such as in a transtracheal block. Given these important considerations, utilizing alternative methods for airway topicalization may be preferred. These methods may include 4% lidocaine nebulization in the preoperative holding area, nasopharyngeal airways lubricated with viscous lidocaine, and instillations of 4% lidocaine onto relevant airway structures via bronchoscopic visuliazation. Special attention should also be paid towards calculating the safe dose of local anesthetic prior to airway topicalization, as the patient with FOP may be severely underweight, resulting in a much lower safe dose of local anesthetic. Prior to insertion of a nasopharyngeal airway, it the use of a nasal decongestant agent, such as oxymetazoline or phenylephrine, to dilate the breadth of the nasal passage may be useful to prevent epistaxis and allow for easier passage of a fibreoptic bronchoscope. Epistaxis and subsequent laryngospasm during attempted nasotracheal intubation in the patient with FOP could prove catastrophic, due to potentially difficult or impossible front-of-neck access as a result of ossification in the neck, so every possible effort should be made to prevent this from occurring. Sedative medication may be used cautiously to help facilitate awake nasotracheal intubation, with consideration that the patient with FOP may be very sensitive to small doses of sedative medications. Maintenance of spontaneous respiration is paramount during the procedure, as mask ventilation may prove to be difficult if not impossible, and emergent front-of-neck access may be challenging. In this author's experience, a short-acting benzodiazepine is generally administered (midazolam 1–2 mg) in the pre-operative area. Once in the operating room, ASA standard monitors should be applied, including end-tidal sampling nasal cannula with supplemental oxygen. A low-dose infusion of remifentanil or dexemedetomidine may then be started. If additional sedation is required, careful administration of ketamine may also be considered [7]. An experienced otolaryngologist should be available during airway management, and surgical airway equipment should be immediately available in the operating room [11].

Intraoperative Management

Monitoring

As for any surgical patient, ASA Standard monitors should be applied on presentation to the operating room, with consideration for additional invasive monitoring if the surgical procedure or patient's comorbidities necessitates. Application

of an oscillometric blood pressure cuff is safe in the patient with FOP, but may prove to be difficult due to ankylosis of the upper limbs, so consideration for alternative sites, such as the lower extremities, may be appropriate. Additionally, extra padding should be considered under the cuff to reduce the impact of frequent inflation of the cuff [7].

Positioning

Following successful nasotracheal intubation and administration of general anesthesia, special attention should be focused on ensuring safe patient positioning. Affected patient's joints may be fused in different rigid positions as a product of their disease state and ankylosis, so all pressure points must be padded appropriately, and the neck must be supported [12]. Steep trendelenburg positioning may be needed by the dentist or surgeon in the case of the patient who has a fused cervical spine, so ensuring safe positioning with appropriate padding is critical to ensuring a safe position for the patient while under a general anesthetic [11].

Steroid Administration

The International Clinical Council on FOP & Consultants recommends that steroid prophylaxis be used for dental and surgical procedures, due to the potent anti-inflammatory effects in conjunction with the inflammatory basis triggering FOP flare-ups [7]. Based on this recommendation, the surgical patient should receive methylprednisolone 50 mg IV q6hrs following induction of general anesthesia. Patients should then be continued on a 4 day regimen of oral prednisone per current guidelines once tolerating oral intake [7].

Maintenance Agents

Maintenance of general anesthesia with a volatile or intravenous anesthetic can safely be performed, with particular emphasis on avoiding the administration of muscle relaxation if possible, to prevent the risk of residual neuromuscular block on emergence and extubation. If muscle relaxation is required, use of quantitative neuromuscular monitoring in combination with a novel reversal agent such as sugammadex should be considered, ensuring that appropriate reversal of neuromuscular blockade has been achieved. Administration of succinylcholine should be avoided, as affected patients may be largely immobile, and therefore the risk exists for catastrophic hyperkalemia following administration. The large case series by Kilmartin et al. reports the use of a maintenance anesthetic of sevoflurane in oxygen/air [11]. A review of nine case reports of patients with FOP undergoing general anesthesia report the safe use of several different volatile agents, including sevoflurane, isoflurane, desflurane, and enflurane [14].

Emergence and Extubation

The same precautions which were in place during intubation should be made available during extubation, including the immediate availability of fibre-optic bronchoscopy and surgical airway access. Planning for airway emergencies on tracheal extubation is highlighted by one case report of a patient who required emergent tracheostomy after failed attempts at re-intubation following extubation. (k) Extubation of the trachea should only be attempted once the patient is fully awake and following commands, with objective return of neuromuscular strength documented if a muscle relaxant was administered during the anesthetic.

Patient Disposition

The multidisciplinary team caring for the surgical patient with FOP should have a low threshold to consider post-operative inpatient admission for continued respiratory monitoring and pain management, although this may vary widely depending on the surgical procedure performed.

It is certainly possible, though, to achieve same-day discharge in patients presenting for uncomplicated dental procedures. In the case series by Kilmartin et al. 36 of 42 case were discharged home on the same day as their dental procedure, with no significant postoperative complications encountered [11]. In this case series, reasons for admission were brittle diabetes, a history of malignant hyperthermia, worsening hypoxia post-extubation, concern for development of airway edema. One patient was also admitted due to the presence of multiple medical comorbidities with a history of a difficult airway and tracheostomy [11].

Perioperative Pain Management

Pain management can be challenging in the patient with FOP, especially for those patients who are maintained on outpatient opioid medications. Acetaminophen and nonsteroidal anti-inflammatories should be utilized in all appropriate patients following discussion with the surgical team. Opioid medications should be minimized to avoid post-operative respiratory depression potentially leading to catastrophic respiratory arrest. The use of intravenous ketamine, in an effort to spare opioids, may be considered in appropriate patients [7]. Epidural analgesia for peri-operative analgesia can prove to be difficult if not impossible, due to advanced ossifications at the thoraco-lumbar area. Attempting epidural or spinal analgesia is also relatively contra-indicated in affected patients, due to the risk of precipitating a flare-up [7]. The performance of superficial nerve blockades with local anesthetic has been described in the literature, and this technique may be utilized in appropriate patients for specific surgical procedures, as strict subcutaneous injections have a low potential for the development of heterotopic ossification [15]. Schober et al. reported the successful use of ultrasound-guided ankle block in a 33 year-old woman with advanced FOP presenting with progressive osteomyelitis originating from the fifth digit of her foot [16]. In their report, continuous ultrasound guidance was used to avoid needle contact to muscles, tendons, and bones. Plain bupivacaine 0.5% was injected into the sites of the tibial and deep peroneal nerve sites. This was followed by a strict subcutaneous field block used to anesthetize the remaining three nerves. If additional analgesia is required, the use of patient-controlled analgesia (PCA) may be considered, with the use of supplemental oxygen and careful monitoring of oxygenation and ventilation [7].

Pregnancy and FOP

Report of pregnancy in FOP has occurred infrequently. Muglu et al. published a series of four cases of pregnancy in FOP [17]. Two patients successfully delivered an infant. One patient was a 27-year old woman with classic FOP and complete fusion of the neck, shoulders, elbows, hips, knees, and jaw. She had an emergency caesarean section at 30 weeks gestation under general anesthesia. A second patient was also a 27-year old woman with classic FOP, who as admitted in preterm labor and had an emergency caesarean section. Given the difficulties associated with performing regional anesthesia, as well as potential for ossification in tracheal rings, the use of awake fibreoptic nasotracheal intubation remains the safest option for anesthetic management of the parturient, with a low threshold to keep the patient intubated post-operatively given the risk for post-operative airway edema and difficulty with reintubation [7].

Conclusions

FOP is a rare genetic disease causing progressive heterotopic ossification and disability in the affected patient, ultimately leading to early mortality. The patient with FOP who presents for elective surgery should be seen in advance by a multidisciplinary team, involving the surgical team, anesthesiology, and relevant medical subspecialities. Caution with airway management, and securing the airway via awake nasotracheal intubation is critical. With appropriate precau-

tion and care, it is possible to achieve successful peri-operative outcomes in the surgical patient with FOP.

References

1. Petrie KA, Lee WH, Bullock AN, et al. Novel Mutations in ACVR1 result in atypical features in two fibrodysplasia ossificans progressiva patients. PLoS One. 2009;4(3):e5005.
2. Classic and atypical fibrodysplasia ossificans progressive (FOP) phenotypes are caused by mutations in the bone morphogenetic protein (BMP) type 1 receptor ACVR1.
3. Obamuyide HA, Ogunlade SO. A tumour for which surgery will do more harm than good: a case report of fibrodysplasia ossificans progressiva. Niger Postgrad Med J. 2015;22(1):83–8.
4. Kaplan FS, Glaser DL, Pignolo RJ, et al. A new era for fibrodysplasia ossificans progressiva: a druggable target for the second skeleton. Expert Opin Biol Ther. 2007;7(5):705–12.
5. Shore EM, Xu M, Feldman GJ, et al. A recurrent mutation in the BMP type I receptor ACVR1 causes inherited and sporadic fibrodysplasia ossificans progressiva. Nat Genet. 2006;38(5):525–7.
6. Pignolo RJ, Shore ME, Kaplan FS. Fibrodysplasia ossificans progressiva: clinical and genetic aspects. Orphanet J Rare Dis. 2011;6:80.
7. Kaplan FS, et al. The medical management of fibrodysplasia ossificans progressiva: current treatment considerations. Proc Intl Clin Council FOP. 2019;1:1–111.
8. Shah PB, Zasloff MA, Drummond D, et al. Spinal deformity in patients who have fibrodysplasia ossificans progressiva. J Bone Joint Surg Am. 1994;76(10):1442–50.
9. Kaplan FS, Groppe J, Pignolo RJ, et al. Morphogen receptor genes and Metamorphogenes: skeleton keys to metamorphosis. Ann N Y Acad Sci. 2007;1116:113–33.
10. Kaplan FS, Zasloff MA, Kitterman JA. Early mortality and cardiorespiratory failure in patients with fibrodysplasia ossificans progressiva. J Bone Joint Surg Am. 2010;92(3):686–91.
11. Kilmartin E, Grunwald Z, Kaplan FS, et al. General anesthesia for dental procedures in patients with fibrodysplasia ossificans progressiva: a review of 42 cases in 30 patients. Anesth Analg. 2014;118(2):298–301.
12. Wadenya R, Fulcher M, Grunwald T, et al. A description of two surgical and anesthetic management techniques used for a patient with fibrodysplasia ossificans progressiva. Spec Care Dentist. 2010;30(3):106–9.
13. Nussbaum BL, Grunwald Z, Kaplan FS. Oral and Dental Health Care and Anesthesia for Persons with Fibrodysplasia Ossificans Progressiva. Clinic Rev Bone Miner Metab. 2005;3:239–42.
14. Liu J-X, et al. General anesthesia in fibrodysplasia ossificans progressive: a case report and clinical review. Int J Clin Exp Med. 2014;7(5):1474–9.
15. Lanchoney TF, Cohen RB, Rocke DM, et al. Permanent heterotopic ossification at the injection site after diphtheria-tetanus-pertussis immunizations in children who have fibrodysplasia ossificans progressiva. J Pediatr. 1995;126(5 Pt 1):762–4.
16. Schober P, Krage R, Thone D, et al. Ultrasound-guided ankle block in stone man disease, fibrodysplasia ossificans progressiva. Anesth Analg. 2009;109(3):988–90.
17. Muglu JA, et al. Pregnancy in fibrodysplasia ossificans progressiva. Obstetr Med. 2012;5(1):35–8. https://doi.org/10.1258/om.2011.110042.
18. Online Mendelian Inheritance in Man, OMIM®. Johns Hopkins University, Baltimore, MD. MIM Number: 135100: Last edited 25 September 2017 by O'Neill MJF. https://omim.org/nSynopsis/135100.

42 Paraesophageal Hernia: The Bane of Hiatus Hernia

Nalini Kotekar, Anshul Shenkar,
U. Krishna Chaitanya, and N. Ravishankar

Introduction

Hiatal hernia (HH) was first described by Henry Ingersoll Bowditch in Boston in 1853 and then further classified into three types by the Swedish radiologist Ake Akerlund in 1926.

A hiatal hernia is essentially an enlargement of the space between the diaphragmatic crura, allowing the abdominal viscera to protrude into the mediastinum. Increased intra-abdominal pressure causes a transdiaphragmatic pressure gradient between the abdominal and thoracic cavities at the gastroesophageal junction, which in turn results in weakening of the diaphragmatic hiatus aperture, causing hiatal defects. Chronic cough secondary to chronic obstructive pulmonary disease, pregnancy, chronic constipation and obesity are some of the conditions associated with increased intra-abdominal pressure. An autosomal dominant genetic component as an important cause of HH is gaining momentum [1].

The real incidence of these hernias is not clear because many patients are asymptomatic and HH may be an incidental diagnosis during chest or abdominal imaging for unrelated conditions. Hiatal hernia is a common abnormality in the general population and is predicated to increase in numbers due to an upward trend in the ageing population. Incidence of giant paraesophageal hernia (PEH) is higher in the elderly, possibly as a result of progressive weakening and enlargement of the diaphragmatic hiatus with advancing age. The issues of concern pertain to the associated comorbidities and concomitant polypharmacies, presence of gastroesophageal reflux disease and poor cardiopulmonary reserve caused by the herniation of abdominal contents into the thorax, worsened by kyphoscoliotic changes in the elderly. Large PEH repair presents additional challenges to the surgeon and anaesthesiologist alike.

Classification

Two types of HH have been described—sliding hernia and the paraesophageal hernia [2].

HH are classified into four types [3]:

TYPE 1 "Sliding hernia": The esophagogastric junction (EGJ) herniates above the diaphragm into the mediastinum. The stomach remains in its usual longitudinal alignment and the fundus remains below the EGJ (Fig. 42.1).

N. Kotekar (✉) · U. Krishna Chaitanya
Department of Anesthesiology, JSS Academy of Higher Education and Research, Mysore, India

A. Shenkar
Kamakshi Hospitals, Mysore, India

N. Ravishankar
Department of Surgery, JSS Academy of Higher Education and Research, Mysore, India

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1_42

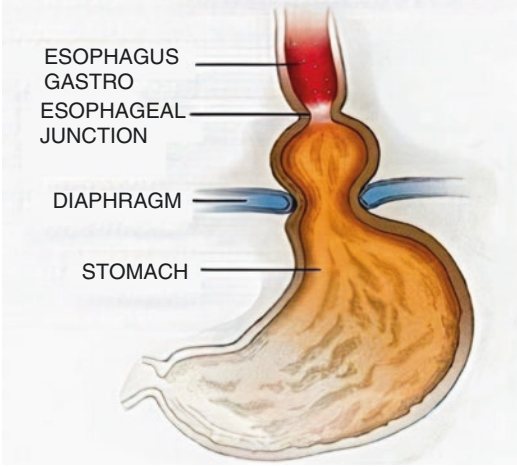


Fig. 42.1 HH type 1: Sliding Hernia

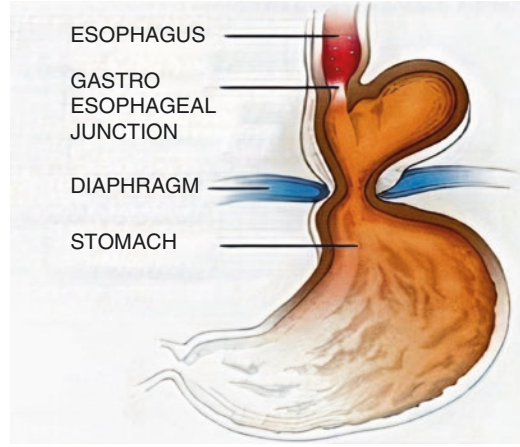


Fig. 42.3 HH type 3

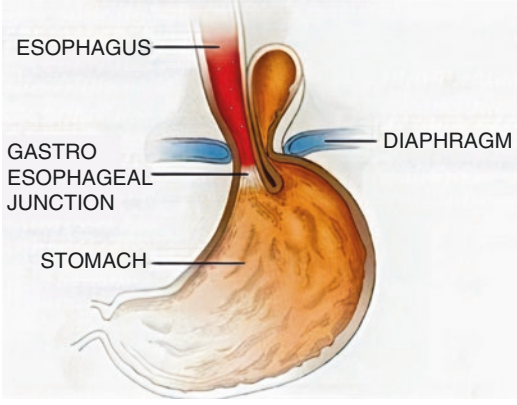


Fig. 42.2 HH type 2: Pure PEH

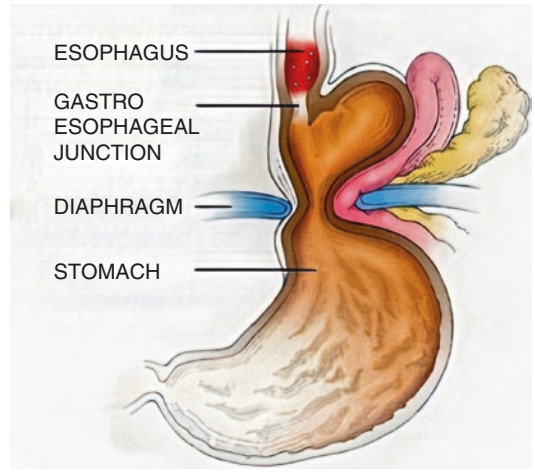


Fig. 42.4 HH type 4

- TYPE 2: A portion of the stomach is herniated into the mediastinum through the diaphragmatic esophageal hiatus alongside the esophagus. The EGJ remains below the hiatus and the stomach rotates in front of the esophagus and herniates into the chest. These are pure PEHs (Fig. 42.2).

TYPE 3: The EGJ is above the hiatus, and a portion of the stomach is folded alongside the esophagus. This hernia is a combination of type 1 and type 2 (Fig. 42.3).

TYPE 4: An intra-abdominal organ other than the stomach is additionally herniated through the hiatus such as omentum, colon or small bowel (Fig. 42.4).

Giant PEH may be defined as type 3 and 4 hernias or may be described as those PEHs that have up to half the stomach in the thorax.

Applied Anatomy and Physiology

The hiatus is the opening in the right diaphragm, through which the esophagus takes a natural path before getting attached to the stomach at the level of T10 thoracic vertebra. Parasympathetic and sympathetic nerves provide innervation to the esophageal parasympathetic input and affects the

peristalsis via the tenth cranial nerve which runs from the medulla through the face and thorax to the abdomen. Both parasympathetic and sympathetic afferent nerves transmit information to the central nervous system via the spinal cord. The neuroanatomic pathways of the esophagus are shared by both the cardiac and respiratory systems, hence it may be difficult to ascertain the organ responsible for syndromes causing chest pain.

Structurally the mucosa, sub-mucosa, muscularis propria and the adventitia make up the four layers of the esophagus. Most of the motor function of the esophagus is carried out by the muscularis propria. In the upper third of the esophagus the muscularis propria is composed of skeletal muscle, whereas in the distal third it is smooth muscle, and in the middle section it is mixed skeletal and smooth muscle. The upper esophageal sphincter (UES) is at the proximal origin of the esophagus where the inferior pharyngeal constrictor joins the cricopharyngeus muscle. UES tone is contracted at rest thereby preventing aspiration of air during normal breathing. The lower esophageal sphincter (LES) is a 2–4 cm length of asymmetric circular smooth muscle situated within the diaphragmatic hiatus. The LES is contracted at rest so as to prevent regurgitation of gastric contents. Peristaltic waves are initiated by the act of swallowing and under vagal control the bolus of food is carried from the pharynx to the stomach in 5–10 s. The bolus of food enters the stomach by the coordinated relaxation of the LES [3].

Drugs frequently used during surgery affect LES tone. Drugs that decrease the LES pressure are the anticholinergics, sodium nitroprusside, dopamine, beta-adrenergic agonists, opioids and tricyclic antidepressants. Metoprolol, anticholinesterases and metoclopramide have been found to increase the LES tone [3].

Clinical Presentation and Epidemiology

Sliding hernia (Type 1) is the most common type of HH (90%) and rarely associated with severe complications [4]. However, these hernias are a risk factor for gastroesophageal reflux disease (GERD) resulting in heartburn, regurgitation, cough or chest pain. If present over a long time, GERD may lead to erosive esophagitis, Barrett esophagus and esophageal carcinoma.

PEH comprise 5–10% of all HH that present in outpatient clinics for surgical repair [5] signifying less common occurrence but an entity with more cause for concern. 90% of PEH cases present as a type 3 hernia with 50% of the stomach herniated into the mediastinum. Type 4 is considered the least prevalent subtype. PEH may be asymptomatic in most patients and can be safely observed and do not require surgery. Surgery is indicated with the appearance of symptoms such as epigastric discomfort, chest pain, dysphagia, post prandial bloating or respiratory symptoms characterised by wheezing, cough, dyspnoea caused by chronic aspiration. Patients may experience heart burn on regurgitation due to gastroesophageal reflux. Symptomatic PEH are at higher risk for progressing to incarceration or ischemia mandating emergency surgery. The lifetime complications of PEH include obstruction, acute dilatation, perforation and mucosal haemorrhage of the stomach [6]. In some patients with PEH, the stomach may turn upon itself resulting in a specific kind of ulceration known as Cameron's erosion which can sometimes contribute to chronic blood loss and anaemia. As more of the stomach moves up into the thorax, respiratory symptoms may predominate secondary to pulmonary compression and reduction in functional vital capacity. Recurrent aspiration pneumonia is an anticipated complication in complicated PEH [7, 8]. Acute life-threatening complications can develop, manifesting as severe chest or epigastric pain, dysphagia and often inability to pass a naso-gastric tube (Borchardt's triad). Obstruction or gastric volvulus with strangulation must be suspected when there is difficulty in passing a naso-gastric tube. This mandates emergency surgical intervention. The mortality rates of emergency surgery in the event of gastric necrosis and/or perforation can be as high as 50%. The estimated mortality rate of acutely symptomatic PEH (type 2, 3, 4) is 16.4% without and 3.2% with an emergent surgical procedure [9, 10]. Though "watchful waiting" has been recommended in asymptomatic patients

with PEH, increasing experience with laparoscopic surgeries has provided good results and has been advocated. Should emergency surgery become necessary, the morbidity and mortality rates increase significantly.

Investigations and Diagnosis

The diagnostic pathway for sliding hernia overlaps with that of GERD [11].

Radiographs may identify soft tissue opacity with or without an air-fluid level within the thorax. A retrocardiac air-filled level on chest X-ray is pathognomonic of PEH. Visceral gas may be seen in cases of intestinal herniation. Loops of bowel may be visualised running in an unusual vertical pattern towards the sac and the transverse colon may be seen in case of a colonic herniation [12].

Contrast studies may be required to assess the size and reducibility of the PEH and to assess the precise location of the GEJ in relation to the esophageal hiatus. Barium is the most frequently used contrast agent. Ionic water-soluble contrast is generally avoided as the patients presenting with acute gastric outlet obstruction are at risk of aspiration pneumonitis [13].

Computed tomography (CT) scan is helpful in patients with suspected complications from a volvulised PEH. Cephalad migration of the GEJ through the hiatus is well perceived on oral contrast enhanced CT images [14].

Esophagogastroduodenoscopy (EGD) allows visual assessment of the mucosa of the esophagus, stomach and duodenum as also the size and type of hernia. Volvulized PEH may be diagnosed by difficulty in reaching the duodenum in case of a large PEH. Gastric viability may also be evaluated in patients requiring emergency surgery for incarcerated hernias. Presence of gastric or esophageal inflammation in EGD may be suggestive of carcinoma. Ulceration of the mucosal folds lining the stomach, also known as Cameron ulcers, caused by extrinsic compression of the diaphragm on the distal neck of a HH may be seen and though asymptomatic, they may present as acute and severe upper gastrointestinal bleeding.

Esophageal manometry helps study abnormal esophageal motility which is common in patients with HH. It may be utilised to demonstrate the level of the diaphragmatic crura, the respiratory inversion point and the placement of the lower esophageal sphincter. Size of the sliding component of HH may be calculated using high resolution motility technology. Esophageal motility study is essential to enable a pH probe to be properly positioned above the LES in patients with sliding HH and GERD [15].

Testing for pH may have little relevance for diagnosing a HH but is critical in identifying the presence of increased esophageal acid exposure in patients with type 1 HH who might benefit from anti-reflux surgery.

Nuclear medicine studies, trans-esophageal echocardiogram and endoscopic ultrasound may diagnose HH but are not routinely used for diagnosis.

The mainstay of evaluation for patients with HH, especially prior to surgical correction, are upper GI endoscopy and barium swallow. The clinical presentation may dictate the choice of the diagnostic technique to be utilised.

Surgical Repair

A number of surgical approaches have been described for GERD and HH. Laparoscopic repair has gained prevalence because of a decrease in perioperative complication and length of hospital stay. When compared to laparotomy or transthoracic approaches, laparoscopic fundoplication surgeries cause significantly less pain, eliminates the need for a tube thoracotomy, minimizes chances of postoperative incisional hernias and provides visualisation for the diagnosis of other intra-abdominal pathologies. Other surgical alternatives include endoluminal, robotic assisted laparoscopic fundoplication, transthoracic and transabdominal approaches. A relatively recent procedure, the Transoral Incisionless Fundoplication (TIF) is a completely endoluminal procedure which can be performed by both medical gastroenterologists

or surgeons and appears to be a safe and effective alternative to more invasive surgical procedures.

Anaesthetic Management of PEH Repair

Pre-operative Evaluation and Preparation

The concept of enhanced recovery (ER) or accelerated recovery following "stress free anaesthesia and surgery" has gained global recognition, specifically in the area of high-risk surgeries. Enhanced recovery protocol includes preoperative, intraoperative and postoperative components and have been shown to facilitate faster return of gut function, reduced complication rate and reduced length of hospital stay. The mechanism for efficacy of ER is an attenuation of the neuroendocrine perioperative stress response and maintenance of organ function, in particular cardiopulmonary function [16].

A thorough history and physical examination should be performed prior to the surgery. One of the core principles of ER is to prepare the patient to be in the best possible physical condition with best possible optimization of chronic illnesses such as but not limited to coronary artery disease, chronic obstructive pulmonary disease, hypertension and diabetes mellitus. Particular attention is needed to check for signs and symptoms of esophageal obstruction, especially those with signs of obstruction such as dysphagia and painful swallowing (odynophagia) which may lead to reduced oral intake and malnutrition resulting in poor outcomes [17]. Patients with severe GERD with aspiration may present with hypersalivation in response to reflux, coughing in supine position, feeling of lump in the throat, laryngitis and asthma like symptoms [18]. It is advisable for patients at high risk for pneumonitis secondary to aspiration, to be prescribed pharmacologic prophylaxis with the H_2 receptor antagonists, and (or) proton pump inhibitors so as to reduce gastric volume, acidity and the likelihood of developing pneumonitis, should they aspirate.

Surgery of the upper abdomen or thorax in itself may place the patients at high risk of major perioperative respiratory complications, such as aspiration pneumonia, atelectasis and respiratory failure, thereby increasing the risk of morbidity and mortality. Hence optimization of pre-existing respiratory disorders following the relevant pulmonary function tests is prudent.

Thoracotomy and selective lung ventilation may be often required for PEH surgeries. Maintaining oxygenation, ventilation and weaning from ventilatory supports maybe more difficult in patients with pulmonary compromise.

Cardiovascular disease has significant implications for patients undergoing major surgeries of the esophagus. Cardiovascular risk may be evaluated with attention to the Revised Cardiac Risk Index (RCRI) and the ACC/AHA guidelines for perioperative cardiovascular evaluation, PEH surgeries which entail significant physiological trespass, hypoxemia, dysrhythmias and pain have a higher risk of cardiovascular complications. Preoperative 12-lead electrocardiogram (ECG) and echocardiography serve as screening tests for coronary vascular disease and provide a baseline for comparison in the event of perioperative cardiac insufficiency. A preoperative chest X-ray may give valuable information about co-existing pulmonary and cardiac disease.

Cessation of Smoking and Alcohol Abuse

Smoking has serious implications on the respiratory, cardiovascular and wound healing physiology. It is linked to increased length of hospital stay and ICU admissions. Hence cessation of smoking for a minimum period of 4 weeks is to be strictly implemented.

Hazardous alcohol usage carries several negative health issues such as poor wound healing, malnutrition, impaired coagulation and arrythmias. Abstinence from alcohol has a positive impact on the length of hospital stay and postoperative pulmonary complications.

Preoperative Nutrition

Preoperative oral nutrition supplementation for 7–10 days has been found to reduce postoperative complications and length of hospital stay in malnourished patients undergoing gastrointestinal surgery.

Correction of Anaemia and Nutritional Disorders

Patients with PEH have an inherent risk of iron deficiency anaemia which is associated with significant postoperative morbidity and mortality. Preoperative correction of anaemia serves to avoid adverse effects of both blood transfusion and anaemia. Elderly and frail patients of PEH become progressively more symptomatic with increased postprandial pain, dysphagia and early satiety, all of which results in these patients modifying their diet and eating suboptimally so as to avoid solid food, leading to unintentional weight loss and malnutrition. Cameron's lesions are found in 29–42% of anaemic patients with PEHs, which show significant resolution of erosions following surgical repair along with resolution of anaemia in 60–70% [19]. In non-emergent PEH repair involving severely anaemic patients, pre optimization of haemoglobin and iron stores are recommended in order to improve outcome including readmissions and length of hospital stay [20].

Hypoalbuminemia is an important indicator of malnutrition and has a relationship with adverse surgical events and poor outcomes [21]. Serum albumin is the most important protein entity of human blood. It binds ions such as calcium, hormones, bilirubin and few medications besides having a role in maintaining the oncotic pressure of blood. Albumin is a 'negative' acute phase protein that decreases in the setting of inflammation and acute illness. Therefore, low albumin in patients presenting for emergent PEH repair may be a reflection of the acute inflammatory response [22, 23]. Preoperative evaluation and correction of nutritional status may decrease adverse postoperative outcomes and have been recommended by both the American (ASPEN) and European (ESPEN) societies for parenteral and enteral nutrtion [24].

Assessment of Aspiration Risk

Patients in need for esophageal surgery, including PEH repair are considered to be at an elevated risk of aspiration and its sequelae and the use of rapid sequence induction techniques is widely used and advocated. HH in particular has been associated with spontaneous aspiration pneumonitis, hence these patients may benefit from longer periods of NPO status. Practice guidelines for preoperative fasting apply to healthy patients and elective surgical procedures. Optimal periods of NPO status in patients with gastroesophageal pathology with severe PEH is yet to be established. A liquid diet for up to 72 h prior to the procedure may help facilitate optimal surgical conditions and decrease aspiration risk.

Thromboprophylaxis and Anticoagulant Management

Thromboprophylaxis is recommended using a risk stratification screening tool such a Caprini score [25] which evaluates the risk of bleeding and juxtaposes this against the risk of venous thromboembolism. The guidelines published by the American Society of Anaesthesia and Pain Medicine stipulate the cessation of P_2Y_{12} inhibitors 7 days prior to high and moderate risk procedures till 12 h post procedure [26] and the international normalized ratio brought to normal values. Warfarin may be restarted the day after surgery. Intravenous heparin has to be avoided 6 h before the procedure and may be restarted 24 h after the procedure. Subcutaneous heparin should be avoided 6 h prior to the procedure and 8 h post procedure. Low molecular weight heparin (LMWH) prophylactic dosing has to be stopped 12 h prior to the procedure and therapeutic dosing 24 h prior to the procedure. LMWH or unfractionated heparin is used for bridging the

patient perioperatively [27] along with the use of compression stockings [28]. Prophylaxis against deep vein thrombosis assumes more importance in PEH repairs because increased abdominal pressure caused by pneumoperitoneum and the steep Trendelenburg position decreases venous return. In patients who have undergone coronary stenting and are receiving anti platelet medications, it is advised to delay the intervention for 1 month in case of bare metal stents and for at least 6 months in drug eluting stents [29, 30].

Perioperative Management

Induction of Anaesthesia

Induction of general anaesthesia and management of the airway of patients undergoing PEH repair is largely dictated by patient factors including cardiopulmonary reserve, hemodynamic and nutritional status at the time of induction and anticipated risk of aspiration pneumonitis. Patients presenting with complications such as obstruction, bleeding, perforation, strangulation, respiratory compromise and gastric volvulus often lack adequate evaluation of cardiopulmonary status and are challenging as a result of unstable hemodynamic status, sepsis, haemorrhage and respiratory distress.

Preoperative airway assessment should aid in establishing a plan for induction of anaesthesia and airway access. A rapid sequence intubation is advocated for patients with PEH. Most anaesthesiologists prefer intravenous induction agents such as propofol, etomidate, thiopentone, or ketamine along with benzodiazepines and opioids. Along with rapidly acting neuromuscular blocking drugs such as succinylcholine or rocuronium, one can achieve smooth induction of anaesthesia and rapid tracheal intubation with the application of cricoid pressure (Sellick manoeuvre). However excessive force applied during the Sellick manoeuvre may complicate airway management by displacing or compressing the airway and insufficient force may fail to accomplish the desired clinical effect. Despite controversies about the effectiveness of the cricoid pressure, it remains the standard of care for patients at risk of pulmonary aspiration universally. The risk of aspiration can be diminished by minimizing the time between loss of consciousness, muscle relaxation and tracheal intubation. Patient positioning plays an important role in aspiration prevention. The head-up or reverse Trendelenburg position is likely to reduce the passive reflux and aspiration of gastric content besides improving pulmonary mechanics, particularly in the obese patient. The head down tilt is often utilized in patients at risk for vomiting during induction.

After induction of general anaesthesia and tracheal intubation, anaesthesia is maintained with a balanced anaesthetic technique with the use of a non-depolarizing muscle relaxant (NDMR), volatile inhalational agents such as isoflurane, sevoflurane or desflurane, intravenous opioids and local anaesthetic agents using epidural catheterization. Nitrous oxide is best avoided especially in long duration laparoscopic PEH repair so as to avoid bowel distension and post-operative nausea and vomiting (PONV). Volatile anaesthetic agents besides providing fine titratable control over anaesthetic depth have the advantage of preconditioning the myocardium against intraoperative ischemic insult, thus affording myocardial protection in these high-risk patients. However high, unmonitored doses of inhalational agents may predispose these patients for hypotension, PONV, cardiac depression, ventilation-perfusion mismatch during lung isolation techniques, inhibition of hypoxic pulmonary vasoconstriction may affect oxygenation. Total intravenous anaesthesia (TIVA) with propofol infusion is an alternative to using inhalational agents. NDMRs facilitate mechanical ventilation and optimize surgical exposure. NDMRs may be reversed with neostigmine and glycopyrrolate or sugammadex, which has superior reversal properties than neostigmine.

Lung Isolation and One Lung Ventilation

Techniques for lung isolation and one lung ventilation (OLV) have facilitated a variety of surgical

approaches to the thoracic esophagus. The routinely used modalities are double lumen endotracheal tubes (DLT) and endobronchial blockers. DLTs allow rapid lung collapse, airway suctioning, ventilation, oxygen insufflation, lung isolation and can be easily placed by an experienced anaesthesiologist. However, owing to their larger size when compared to the single lumen tube (SLT), the DLT may require expertise and more time to insert and more likely to cause trauma. In the context of a difficult airway and increased time required for the DLT placement there may be increased risk of aspiration in PEH patients who are more prone to regurgitate. The left sided DLT is most commonly employed for transthoracic esophageal surgery and positioning is easily accomplished because the left main bronchus is longer than the right. An alternative viable airway access in these patients would be to place bronchial blockers through the SLT with fibre optic guidance. Bronchial blockers offer protection against aspiration and the use of SLT with rapid sequence induction is made easier in difficult airway. The lung collapse scores are equivalent to or better than that of DLTs [31]. Since a majority of these procedures use a left thoracotomy approach, left bronchial blockade is easily achieved due to longer left main bronchus. The shorter length of the right main bronchus may result in suboptimal isolation of the right upper lobe when right lung isolation is required.

Following intubation, the patient is mechanically ventilated using tidal volumes of 6–8 mL/kg of ideal body weight. Application of positive end—expiratory pressure of 5–10 cm of water may be beneficial. Recruitment manoeuvres may be utilized to negate the effects of pneumoperitoneum on pulmonary mechanics [32].

Placement of Esophageal Dilators and Bougies

Following induction of anaesthesia and intubation, the patient is placed in the right lateral decubitus position. The indwelling gastric tube is withdrawn and a large dilator/bougie is inserted into the esophagus, in coordination with the surgeon. The bougie serves to support proper calibration of the fundoplication and prevents creation of an excessively tight wrap [33]. A trained anaesthesia personnel must pass the lubricated bougie atraumatically into the upper esophagus with manual guidance or with the use of a laryngoscope, exercising caution to avoid excessive force or incorrect insertion technique which in turn may cause perforation. The surgeon controls depth advancement of the bougie via laparoscopic view. The bougie is advanced through the esophagogastric junction and left in position until the fundoplication sutures are secured.

Fluid Management

Perioperative fluid requirements should be calculated based on the preoperative deficits, maintenance requirements and ongoing losses. These patients may be relatively hypovolemic because of long preoperative fasts, particularly in patients with history of obstruction superimposed with baseline diminished oral intake. Minimally invasive repairs generally have low fluid requirements because laparoscopic surgeries have decreased insensible losses, goal directed fluid management [34, 35] is recommended for all major elective surgical procedures because both ends of the fluid management spectrum i.e. hypovolemia and hypervolemia may result in increased morbidity involving all major organ systems and compromised wound healing. Over hydration may raise the central venous pressure causing pulmonary and peripheral oedema along with poor healing of anastomosis and prolonged ileus. Under hydration can be detrimental as it may cause hypovolemia, decrease in stroke volume, cardiac output, tissue oxygen delivery and renal hypo perfusion.

The goal of fluid therapy is to provide optimal circulatory volume without over or under hydration and is referred to as “zero balance approach”. Fluid therapy should be measured to account for blood loss and to meet the maintenance requirements, not to treat the hypotension associated with general or epidural anaesthesia which may be better treated with vasoconstrictors. A balanced salt solution is the ideal option for the perioperative period. Normal saline has been

associated with poor outcomes as it has the propensity to cause sodium load, hyperchloremia and metabolic acidosis, hence is not an appropriate choice for fluid therapy [36].

Management of PEH

The key initial step in the management of PEH, if the presentation is acute, is prompt gastric decompression through the placement of a nasogastric tube. After confirmation of the proper placement of the NG tube low intermittent suctioning is done. Anatomic variations created by PEH may make the placement of a gastric tube unsafe before dissection and mobilization of the stomach. In the subset of patients who present with volvulus with complete obstruction at the esophago-gastric junction, upper GI endoscopy allows for decompression and in some cases, reduction of the volvulus. A successful decompression affords relief from pain and vomiting. Decompression should continue for 12–24 h with observation for signs of ischemia. Persistent pain, vomiting and hemodynamic instability may indicate ischemia and the patient must be prepared for surgery.

In patients who are hemodynamically stable and have undergone successful decompression, obstruction needs to be ruled out. Often an obstructing volvulus de-torses or corrects itself within 12–24 h and an upper GI endoscopy assists in assessing the degree of obstruction. A complete obstruction is an indication for urgent repair. Patients without obstruction may be planned for a semi elective repair. The very high-risk patient segment is considered for long term non operative therapy [37].

Surgical Repair of PEH

Surgical therapies for GERD and HH can be achieved via a number of surgical approaches.

1. Open Thoracotomy and Laparotomy
2. Laparoscopic Repair—PEH, Gastropexy, Gastrectomy
3. Robotic PEH Repair

1. Open Thoracotomy and Laparotomy
   Initial surgeries for PEH repair such as Allison, Nissen and Belsey mark IV fundoplication were performed through left thoracotomy. Traditionally, repair of even giant PEHs has been performed through an open laparotomy or left thoracotomy. Thoracotomy offered the benefit of ease of esophageal mobilization, whereas open abdominal approach allowed quick reduction of incarcerated contents and avoided thoracotomy associated morbidity.
2. Laparoscopic Repair of PEH
   Laparoscopic repair is currently the standard surgical option for PEH repair in most academic centres. The minimal access procedure returns the stomach to its intraabdominal position and if volvulus is present, the volvulus and the contents of hernia are reduced following which the sac is resected. Subsequent to hiatal closure, the esophagus is mobilized to achieve adequate intra-abdominal length so as to prevent recurrence and with the stomach fully reduced, the crura are closed and occasionally reinforced with a biologic mesh. The final step is the fundoplication, the superior edge of which is sutured to the hiatus to prevent recurrence. Upper GI endoscopy is performed to evaluate the stomach and the fundoplication.
   This technique offers the advantages of a minimally invasive approach such as considerably less pain, smaller incisions that decrease the occurrence of post-operative incisional hernias and allows visualization of other intra-abdominal pathology. However, laparoscopy has few disadvantages such as poor ergonomics for the surgeon caused by limited motion of the straight laparoscopic instruments and two-dimensional imaging which has been overcome with the advent of robotic surgery.

   – Laparoscopic Gastropexy
   Gastropexy is a procedure which is done in patients with acute PEH with a risk of incarceration. Patients who are at high risk with advanced age, severe co-morbidities, poor nutritional status, metaboli-

cally deranged state with an ongoing inflammatory process at the hiatus prohibiting an optimal repair are best benefitted with the gastropexy procedure. A definitive repair of the hernia may be undertaken after the patient is optimized and resolution of the acute inflammatory insult at a later stage [37].

– Open/Laparoscopic Gastrectomy
Occasionally an acute obstructed PEH may present with ischemia or perforation of the stomach and the extent of morbidity will depend on the site of the pathology. Necrosis of the gastric antrum would be managed with a distal gastrectomy. A sleeve gastrectomy would be required for necrosis at the fundus or greater curvature of the stomach. Extensive or proximal necrosis will necessitate a total gastrectomy with esophagojejunostomy. The choice between an open or laparoscopic approach would be dictated by patient characteristics and the expertise of the surgeon. The laparoscopic approach offers the advantage of visualization of and access to the mediastinum, which is essential for optimal esophageal mobilization. This is important in terms of obtaining 3–4 cm intra-abdominal esophageal length to be able to perform an esophagojejunostomy, should a total gastrectomy be required.

3. Robotic PEH Repair
Robotic surgery is becoming popular in general surgery in terms of overcoming the drawbacks of open and laparoscopic surgery. Robotic assisted surgery provides augmented skills required for endo-wrist movements and ergonomics for the surgeon with the superior backdrop of three-dimensional visualization. Technically demanding procedures such as PEH repair are currently being performed safely using robotics. Comparative studies between robotic and laparoscopic PEH surgeries have pointed to shorter operative times, including docking time and low complication rates with robotic surgeries. However, cost consideration is the major drawback with the robotic platform [38].

Outcomes and Complications

Young asymptomatic patients and older symptomatic patients presenting with symptoms such as aspiration, regurgitation, cough, dysphagia or anaemia have been shown to benefit from PEH repair. The gold standard of PEH repair remains laparoscopic surgery which offers the benefits of patient satisfaction, improvement of symptoms and a recurrence rate comparable to open surgery.

The outcomes in older patients with multiple co morbidities continue to be unpredictable. The complication and mortality rates of emergency procedures for acute PEH, as per early reports, were high. Thus, followed the era of routine repair of PEH for over fifty decades. The indications for surgical management of PEH continues to be a debatable issue. The Borchardt triad (inability to pass a nasogastric tube, epigastric pain and retching without actual food regurgitation) is considered as an absolute indication for emergent surgical intervention [39]. Elderly patients with minimal symptoms in whom PEH is an incidental finding, a "watchful waiting" strategy appears to be a reasonable alternative [40]. An elective repair would be pertinent in cases of aspiration, cough, severe regurgitation, anaemia or dysphagia. These symptoms are often preceded by symptoms of early satiety and post prandial dyspnoea which increases over the years and are attributed to aging. PEH related dyspnoea in the elderly is frequently mistaken to have cardio-pulmonary aetiology.

There have been reports of complications related to laparoscopic fundoplication and carbon dioxide insufflation, such as pneumothorax, pneumomediastinum, emphysema and pneumopericardium. Early diagnosis of pneumothorax may be possible by observing for increasing airway pressures and end-tidal carbon dioxide ($ETCO_2$) and decreasing peripheral oxygen saturation (SpO_2) [41]. Iatrogenic pneumothorax requires immediate intervention. Nitrous oxide

must be discontinued and pneumoperitoneum deflated. Further management protocols include intercostal drain placement, initiation of positive end expiratory pressure (PEEP) and sealing the pleural rent. Insertion of an intercostal drain causes loss of pneumoperitoneum and creates sub optimal conditions for laparoscopic surgery. The use of PEEP as an alternative to chest tube placement proves a superior option in correcting respiratory changes associated with pneumothorax. Initiation of PEEP decreases the pressure gradient between the abdominal and pleural cavities during inspiration and expiration, subsequently inflating the lung. Re-expansion of the lungs with PEEP can serve to mechanically seal the surgically induced tear in the peripheral pleura. Omental plugs placed by the surgeon to seal pleural rent serves as an alternative treatment option [42, 43].

Recurrence of PEH is an anticipated undesirable complication because the esophageal hiatus is subjected to constant diaphragmatic movement with negative pressure from the mediastinum and positive pressure from the abdomen. The decision to place a mesh during the surgical repair is highly selective and is mostly based on intraoperative findings. Biological mesh is usually placed to buttress the repair if the surgeon considers that the repair is done under tension. The use of non-absorbable mesh is linked to complications such as esophageal stricture or mesh erosion into the esophagus or the aorta with catastrophic consequences [44, 45].

Obese patients are at a higher risk of hernia recurrence. Concomitant obesity in previously non obese patients who undergo PEH repair has been shown to increase the failure rate of antireflux surgery [46]. Larger hernias of surface areas greater the 5.6 cm^2 are more prone for recurrence, independent of patient height, weight and BMI. Crural mesh reinforcement may be advocated for large hernia to prevent recurrence [47].

Open conversions are occasionally mandated for reasons such as bleeding, splenic injury or dense adhesions and it is important for the laparoscopic surgeons to be comfortable with an open repair, should conversion become necessary.

Post Operative Management

The patient is started on scheduled analgesics, antiemetics and kept nil per oral on the evening post surgery. Early post-operative dysphagia is common; hence attention should be paid to adequate caloric and nutritional supplementation. An esophagogram might be required on the postoperative day 1 only if there has been an esophageal lengthening procedure, significant pain, dysphagia or emesis following surgery.

Sudden increases in intra-abdominal pressure may predispose the patient to early anatomic failure of the hernia repair. Early post-operative gagging, belching and vomiting may result in anatomic failure and mandates rapid and aggressive therapy. Gastric distension may be potentially dangerous and may be treated easily by placement of a nasogastric tube. All asymptomatic patients are started on a clear liquid diet on the first post-operative day in the morning and advanced to a soft diet by afternoon. Their ability to tolerate a soft diet is an important discharge criterion on post-operative day 2. Patients are instructed to remain on a soft diet for at least 2 weeks following surgery. The anatomic integrity of the repair is routinely assessed at 6–12 months post-surgery with a barium swallow. Further patient symptomatology would dictate additional screening if required subsequently.

Post Operative Pain Mangaement

Pain following laparoscopic anti reflux surgery occurs in more than 20% of patients, and ranges from mild to moderate pain. Multimodal analgesia has been shown to provide optimal pain control. Opioids, local infiltration at laparoscopic port sites, continuous local anaesthetic infusions (especially for large incisions), transversus abdominal plane block and epidural analgesia in case of open abdominal surgery are popular elements of multimodal pain management [48]. Nonsteroidal anti-inflammatory analgesics and Cyclooxygenase type 2 specific inhibitors may be supplemented to augment pain relief.

Pain, beyond that expected in the acute post-operative period, may have a dramatical presentation and may result from complications such as esophageal or gastric perforation, herniated fundoplication, hiatal closure failure or portal thrombosis. Visceral or referred pain may be experienced in the form of shoulder pain resulting from irritation of the phrenic nerve secondary to diaphragmatic distension, residual subdiaphragmatic carbon dioxide and closure of the hiatus.

Persistence of pain beyond the usual recovery period may be felt in the abdomen, chest or shoulder. Some patients may present with odynophagia which may be due to esophagitis, ulceration, oedema or spasm [49]. Other causes include haematoma or infection at site of incision, port site hernia, intra-abdominal abscess, haemorrhage, obstruction or perforation of bowel, pneumothorax or pleural effusion [50]. Surgical injury to the vagal nerve causes a range of post-operative symptoms including pain caused by post prandial gastric distension [51].

A detailed history followed by clinical examination is important in order to identify and manage complications. Investigations such as chest radiography may identify pleural effusion, pneumothorax or recurrent hiatus hernia, computed tomography (CT) can help identify abscess formation, perforation, portal thrombosis or disrupted fundoplication. A small proportion of patients may experience persistent pain despite investigations and appropriate treatment. These patients need to be managed in a specialised pain environment where they have access to medical, physical and psychological treatment modalities.

Transoral Incisionless Fundoplication (TIF)

TIF is an advanced minimally invasive endoscopic procedure that is being performed by medical and surgical gastroenterologists. It aims to restore the integrity of the gastro esophageal valve by creating a 270° esophageal wrap around the distal esophagus, anchored by multiple polypropylene fasteners. Thus, a semi-circular valve is created just beneath the lower esophagus and functions like the LES, creating a strong reflux barrier. This procedure seems to be a technique that fills the 'therapy gap' between medical therapy and the more invasive surgical procedures such as laparoscopic or open antireflux procedures [52].

Paediatric Considerations

HH and PEH in children may be congenital as a result of embryologic abnormalities or genetic predisposition. It may also be acquired following gastroesophageal surgery such as fundoplication. Conservative management in children with HH and gastroesophageal reflux often exhibit high failure rates thereby mandating surgical repair with concomitant fundoplication.

HH in children may be clinically asymptomatic or present with reflux symptoms such as vomiting, aspiration, respiratory and constitutional symptoms including anaemia and failure to thrive. Chest Xray and upper GI endoscopy confirms the diagnosis. Treatment is surgical with the goal of reducing hernia contents, excising the hernia sac, closing the crura and performing an anti-reflux procedure [53].

Conclusion

The management of PEH is challenging as it is predominantly seen in geriatric patients with high comorbidity-polypharmacy scores. Prompt diagnosis requires a high index of suspicion, meticulous history, a focused physical examination, followed by confirmatory investigations. Laparoscopic PEH repair has proven benefits over conventional open surgery technique with regard to length of hospital stay, recovery time and decreased rates of complications. More recently, robotic-assisted surgery for PEH repair has gained popularity as a safe and effective technique with low complication rates, even in older high-risk individuals. In the event of conversion to open surgery, it is important for laparoscopic and robotic surgeons to be comfortable in performing open repair.

References

1. Oleynikov D, Jolley JM. Paraesophageal hernia. Surg Clin North Am. 2015;95:555–65.
2. Gangopadhyay N, Perrone JM, Soper NJ, et al. Outcomes of laparoscopic paraesophageal hernia repair in elderly and high-risk patients. Surgery. 2006;140:491–8.
3. Patti MG, Di Corpo M, Schlottmann F, editors. Foregut surgery: achalasia, gastroesophageal reflux disease and obesity. Cham: Springer International Publishing; 2020. https://doi.org/10.1007/978-3-030-27592-1.
4. Kahrilas PJ, Lin S, Chen J, et al. The effect of hiatus hernia on gastro-esophageal junction pressure. Gut. 1999;44:476–82.
5. Dallemagne B, Kohnen L, Perretta S, et al. Laparoscopic repair of paraesophageal hernia. Long-term follow-up reveals good clinical outcome despite high radiological recurrence rate. Ann Surg. 2011;253:291–6.
6. Tsuboi K, Tsukada K, Nakabayashi T, et al. Paraesophageal hiatus hernia, which has progressed for 8 years: report of a case. Hepato-Gastroenterology. 2002;49:992–4.
7. Low DE, Simchuk EJ. Effect of paraesophageal hernia repair on pulmonary function. Ann Thorac Surg. 2002;74:333–7; discussion 337
8. Awais O, Luketich JD. Management of giant paraesophageal hernia. Minerva Chir. 2009;64:159–68.
9. Sihvo EI, Salo JA, Räsänen JV, et al. Fatal complications of adult paraesophageal hernia: a population-based study. J Thorac Cardiovasc Surg. 2009;137:419–24.
10. Jassim H, Seligman JT, Frelich M, et al. A population-based analysis of emergent versus elective paraesophageal hernia repair using the Nationwide Inpatient Sample. Surg Endosc. 2014;28:3473–8.
11. Kohn GP, Price RR, DeMeester SR, et al. Guidelines for the management of hiatal hernia. Surg Endosc. 2013;27:4409–28.
12. Eren S, Gümüş H, Okur A. A rare cause of intestinal obstruction in the adult: Morgagni's hernia. Hernia. 2003;7:97–9.
13. Morcos SK. Review article: effects of radiographic contrast media on the lung. Br J Radiol. 2003;76:290–5.
14. Eren S, Ciriş F. Diaphragmatic hernia: diagnostic approaches with review of the literature. Eur J Radiol. 2005;54:448–59.
15. Swanstrom LL, Jobe BA, Kinzie LR, et al. Esophageal motility and outcomes following laparoscopic paraesophageal hernia repair and fundoplication. Am J Surg. 1999;177:359–63.
16. Kehlet H. Multimodal approach to control postoperative pathophysiology and rehabilitation. Br J Anaesth. 1997;78:606–17.
17. Sungurtekin H, Sungurtekin U, Balci C, et al. The influence of nutritional status on complications after major intraabdominal surgery. J Am Coll Nutr. 2004;23:227–32.
18. Blank RS, Collins SR, Huffmyer JL, et al. Anesthesia for esophageal surgery. In: Slinger P, editor. Principles and practice of anesthesia for thoracic surgery. Cham: Springer International Publishing; 2011. p. 609–49.
19. Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. Developed in collaboration with the American College of Surgeons, American Society of Anesthesiologists, American Society of Echocardiography, American Society of Nuclear Cardiology, Heart Rhythm Society, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Vascular Medicine Endorsed by the Society of Hospital Medicine. J Nucl Cardiol. 2015;22:162–215.
20. Lebenthal A, Waterford SD, Fisichella PM. Treatment and controversies in paraesophageal hernia repair. Front Surg. 2015;2:13.
21. Meyer CP, Rios-Diaz AJ, Dalela D, et al. The association of hypoalbuminemia with early perioperative outcomes—A comprehensive assessment across 16 major procedures. Am J Surg. 2017;214:871–83.
22. Huhmann MB, August DA. Nutrition support in surgical oncology. Nutr Clin Pract. 2009;24:520–6.
23. Kim S, McClave SA, Martindale RG, et al. Hypoalbuminemia and clinical outcomes: what is the mechanism behind the relationship? Am Surg. 2017;83:1220–7.
24. Clark LN, Helm MC, Higgins R, et al. The impact of preoperative anemia and malnutrition on outcomes in paraesophageal hernia repair. Surg Endosc. 2018;32:4666–72.
25. Bell BR, Bastien PE, Douketis JD, et al. Prevention of venous thromboembolism in the Enhanced Recovery After Surgery (ERAS) setting: an evidence-based review. Can J Anaesth. 2015;62:194–202.
26. Narouze S, Benzon HT, Provenzano D, et al. Interventional Spine and Pain Procedures in Patients on Antiplatelet and Anticoagulant Medications (Second Edition): Guidelines From the American Society of Regional Anesthesia and Pain Medicine, the European Society of Regional Anaesthesia and Pain Therapy, the American Academy of Pain Medicine, the International Neuromodulation Society, the North American Neuromodulation Society, and the World Institute of Pain. Reg Anesth Pain Med. 2018;43:225–62.
27. Schlitzkus LL, Summers JI, Schenarts PJ. Rapid reversal of novel anticoagulant and antiplatelet medications in general surgery emergencies. Surg Clin N Am. 2018;98:1073–80.
28. Khan S, Gatt M, Horgan A, Anderson I, MacFie J. Issues in professional practice: guidelines for implementation of enhanced recovery protocols. 1st

ed. London: Association of Surgeons of Great Britain and Ireland (ASGBI); 2009. p. 1–19.
29. Maggard Gibbons M, Ulloa JG, Macqueen IT, et al. Management of antiplatelet therapy among patients on antiplatelet therapy for coronary or cerebrovascular disease or with prior percutaneous cardiac interventions undergoing elective surgery: a systematic review. Washington, DC: Department of Veterans Affairs (US); 2017.
30. Kazakova T, Hammond B, Talarek C, et al. Anesthetic management for paraesophageal hernia repair. Thorac Surg Clin. 2019;29:447–55.
31. Bussières JS, Somma J, Del Castillo JLC, et al. Bronchial blocker versus left double-lumen endotracheal tube in video-assisted thoracoscopic surgery: a randomized-controlled trial examining time and quality of lung deflation. Can J Anaesth. 2016;63:818–27.
32. Remístico PPJ, Araújo S, de Figueiredo LC, et al. Impact of alveolar recruitment maneuver in the postoperative period of videolaparoscopic bariatric surgery. Rev Bras Anestesiol. 2011;61:163–8, 169–176, 88–94.
33. Jarral OA, Athanasiou T, Hanna GB, et al. Is an intra-esophageal bougie of use during Nissen fundoplication? Interact Cardiovasc Thorac Surg. 2012;14:828–33.
34. Gupta R, Gan TJ. Peri-operative fluid management to enhance recovery. Anaesthesia. 2016;71(Suppl 1):40–5.
35. Manning MW, Dunkman WJ, Miller TE. Perioperative fluid and hemodynamic management within an enhanced recovery pathway. J Surg Oncol. 2017;116:592–600.
36. Sethi AK, Kochhar A, Ahmad Z. Chapter 13: Enhanced recovery after surgery. In: Yearbook of anaesthesiology, vol. 6. New York: Springer; 2017. p. 152–63.
37. Rodriguez HA, Minneman JA, Oh JS, et al. Paraesophageal hernia. In: Renton D, Lim R, Gallo AS, et al., editors. The SAGES manual of acute care surgery. Cham: Springer International Publishing; 2019. p. 219–33.
38. Vasudevan V, Reusche R, Nelson E, et al. Robotic paraesophageal hernia repair: a single-center experience and systematic review. J Robot Surg. 2018;12:81–6.
39. El Khoury R, Ramirez M, Hungness ES, et al. Symptom relief after laparoscopic paraesophageal hernia repair without mesh. J Gastrointest Surg. 2015;19:1938–42.
40. Dahlberg PS, Deschamps C, Miller DL, et al. Laparoscopic repair of large paraesophageal hiatal hernia. Ann Thorac Surg. 2001;72:1125–9.
41. Rajan GR, Foroughi V. Mainstem bronchial obstruction during laparoscopic fundoplication. Anesth Analg. 1999;89:252–4.
42. Singhal T, Balakrishnan S, Hussain A, et al. Management of complications after laparoscopic Nissen's fundoplication: a surgeon's perspective. Ann Surg Innov Res. 2009;3:1.
43. Kaur R, Kohli S, Jain A, et al. Pneumothorax during laparoscopic repair of giant paraesophageal hernia. J Anaesthesiol Clin Pharmacol. 2011;27:373–6.
44. Oelschlager BK, Pellegrini CA, Hunter J, et al. Biologic prosthesis reduces recurrence after laparoscopic paraesophageal hernia repair: a multicenter, prospective, randomized trial. Ann Surg. 2006;244:481–90.
45. Oelschlager BK, Pellegrini CA, Hunter JG, et al. Biologic prosthesis to prevent recurrence after laparoscopic paraesophageal hernia repair: long-term follow-up from a multicenter, prospective, randomized trial. J Am Coll Surg. 2011;213:461–8.
46. Perez AR, Moncure AC, Rattner DW. Obesity adversely affects the outcome of antireflux operations. Surg Endosc. 2001;15:986–9.
47. Braghetto I, Korn O, Csendes A, et al. Postoperative results after laparoscopic approach for treatment of large hiatal hernias: is mesh always needed? Is the addition of an antireflux procedure necessary? Int Surg. 2010;95:80–7.
48. Pirrera B, Alagna V, Lucchi A, et al. Transversus abdominis plane (TAP) block versus thoracic epidural analgesia (TEA) in laparoscopic colon surgery in the ERAS program. Surg Endosc. 2018;32:376–82.
49. Swanstrom L, Wayne R. Spectrum of gastrointestinal symptoms after laparoscopic fundoplication. Am J Surg. 1994;167:538–41.
50. Watson DI, de Beaux AC. Complications of laparoscopic antireflux surgery. Surg Endosc. 2001;15:344–52.
51. Baty V, Rocca P, Fontaumard E. Acute gastric volvulus related to adhesions after laparoscopic fundoplication. Surg Endosc. 2002;16:538.
52. Joseph SJ, Ebstein AMM, Sapp A. Effectiveness of transoral incisionless fundoplication compared to Toupet fundoplication for chronic or refractory gastroesophageal reflux disease: a systematic review protocol. JBI Database System Rev Implement Rep. 2019;17:507–12.
53. Garvey EM, Ostlie DJ. Hiatal and paraesophageal hernia repair in pediatric patients. Semin Pediatr Surg. 2017;26:61–6.

Correction to: Anesthesia for Endoscopic Skull Base Surgery

Paul B. Audu, Mansour Ousmane Mahamane, Marc D. Fisicaro, and Angelo Andonakakis

Correction to: Chapter "Anesthesia for Endoscopic Skull Base Surgery" in: B. G. Goudra et al. (eds.), Anaesthesia for Uncommon and Emerging Procedures, https://doi.org/10.1007/978-3-030-64739-1_3

The author name was inadvertently published as "Monsour Ousmane Mahamane" and the correct name "Mansour Ousmane Mahamane" has been updated in the book.

The updated online version of this chapter can be found at https://doi.org/10.1007/978-3-030-64739-1_3

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*, https://doi.org/10.1007/978-3-030-64739-1_43

Index

B. G. Goudra et al. (eds.), *Anaesthesia for Uncommon and Emerging Procedures*,
https://doi.org/10.1007/978-3-030-64739-1