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63 Anesthesia for Fetal Surgery and Other Fetal Therapies

MARLA B. FERSCHL and MARK D. ROLLINS

KEY POINTS

- Most fetal anomalies are not appropriate for in utero treatment. A condition appropriate for fetal treatment should cause ongoing irreversible harm to the fetus that is mitigable by early treatment before the fetus can tolerate ex utero neonatal intervention.
- A multidisciplinary approach with open communication is essential to the success of each fetal intervention.
- Maternal safety and the principle of "do no harm" should be foremost in determining the most appropriate therapeutic option. A thorough maternal and fetal evaluation and frank discussion of risks and benefits by all team members with the mother is required to determine an appropriate care plan.
- Although open fetal surgery typically requires general anesthesia, most minimally invasive percutaneous techniques can be performed using local anesthesia infiltration or neuraxial anesthesia techniques.
- Randomized controlled clinical trials show improved outcomes with fetoscopic laser photocoagulation of placental vessels to treat twin-to-twin transfusion syndrome and intrauterine open fetal surgery to treat myelomeningocele.
- In addition to anesthetic considerations associated with nonobstetric surgery during pregnancy, fetal surgery requires planning for fetal anesthesia and analgesia, fetal monitoring, uterine relaxation, preparation for emergent events (e.g., fetal bradycardia, maternal hemorrhage), and postoperative tocolysis.
- Membrane separation, preterm premature rupture of membranes, and preterm labor remain the most common causes of morbidity and suboptimal outcome with fetal surgical interventions.
- Further research into optimal anesthetic techniques for various fetal interventions is essential to improve patient outcomes and advance the field of fetal surgery.

Only recently have medical professionals focused on the human fetus as a patient who is able to undergo surgery or medical intervention. This development has been primarily driven by systematic improvements in prenatal diagnosis, imaging technology, and surgical equipment. Although many fetal surgical procedures are available only at highly specialized institutions, some prenatal interventions are considered conventional therapy and have become more widespread. This chapter reviews the unique pathophysiological processes of various fetal and placental conditions amenable to intervention, current outcome data, specific procedural considerations, and perioperative anesthesia management.

Most fetal abnormalities are not appropriate for antenatal intervention and are more amenable to treatment after delivery. However, some anatomic malformations may result in irreversible end-organ damage and would benefit from intervention before birth. This has led to the theory that surgical or procedural correction in utero could allow normal fetal development and might mitigate much of the detrimental pathologic processes observed.[1] Other defects, such as congenital airway obstruction, can be managed intrapartum by keeping the uteroplacental unit intact while the defect is repaired or airway secured, without the urgency that would be associated with attempting similar procedures immediately after birth.

Prerequisite guidelines for performing fetal surgery were initially developed in 1982 at a multidisciplinary meeting with participants from 13 medical centers representing five countries.[2] Over time these criteria have evolved and include: (1) the fetal lesion is accurately diagnosed; (2) the progression and severity of the anomaly is predictable and well understood; (3) other severe associated anomalies that would contraindicate fetal intervention are excluded; (4) the fetal abnormality would lead to fetal demise, irreversible organ damage, or severe postnatal morbidity if left untreated before birth, and intervening before birth would benefit the neonatal outcome; (5) the maternal risk is acceptably low; (6) animal models have demonstrated feasibility of the surgical technique; (7) fetal interventions are performed at specialized multidisciplinary institutions using protocols approved by the center's ethics committees with maternal informed consent; and (8) the patient has access to highly specialized multidisciplinary care including bioethical and psychological counseling.[1-3]

TABLE 63.1 Fetal Conditions Currently Considered for Intervention

Fetal Condition	Therapy Rational	Type	Intervention
Fetal anemia or thrombocytopenia	Prevention of heart failure and fetal hydrops	FIGS-IT	Intrauterine transfusion
Aortic stenosis, intact atrial septum, or pulmonary atresia	Prevention of fetal hydrops, myocardial dysfunction, and hypoplastic left (and right) heart	FIGS-IT	Percutaneous fetal valvuloplasty or septoplasty
Lower urinary tract obstruction	Bladder decompression with reduction in renal dysfunction, pulmonary hypoplasia, oligohydramnios, and limb malformation	FIGS-IT or fetoscopy	Percutaneous vesicoamniotic shunting or fetoscopic posterior urethral valve laser ablation
Twin reversed arterial perfusion	Prevention of high-output cardiac failure in the normal twin by stopping flow to acardiac twin	FIGS-IT or fetoscopy	Image-guided radiofrequency ablation or fetoscopic coagulation of acardiac twin umbilical cord. Percutaneous coiling or ligation of umbilical cord is also used.
Twin-twin transfusion syndrome	Reduction of twin-twin blood flow and prevention of cardiac failure	Fetoscopy	Fetoscopic laser photocoagulation of placental vessels and amnioreduction
Amniotic band syndrome	Prevention of limb loss	Fetoscopy	Fetoscopic band ablation
Congenital diaphragmatic hernia	Prevention of pulmonary hypoplasia	Fetoscopy	Fetoscopic tracheal occlusion
Myelomeningocele	Reduction in hydrocephalus and hindbrain herniation, with reduced spinal cord damage and improved neurologic function	Open or Fetoscopy	Closure of fetal defect through hysterotomy
Sacrococcygeal teratoma	Prevention of high-output cardiac failure, hydrops, and polyhydramnios	FIGS-IT or open	Ablation of tumor vasculature or open fetal tumor debulking
Congenital cystic adenomatoid malformation	Reversal of pulmonary hypoplasia and cardiac failure	FIGS-IT or open	Thoracoamniotic shunting or open surgical resection
Fetal airway compression	Secured open airway and/or circulatory support to prevent respiratory compromise at birth	Open intrapartum	Ex-utero intrapartum therapy (EXIT) that allows fetal stabilization while on uteroplacental circulation

FIGS-IT, Fetal image-guided surgery for intervention or therapy.
Modified from Partridge EA, Flake AW. Maternal-fetal surgery for structural malformations. *Best Pract Res Clin Obstet Gynaecol*. 2012;26:669–682; and Hoagland MA, Chatterjee D. Anesthesia for fetal surgery. *Paediatr Anaesth*. 2017;27:346–357.

All interventions should be preceded by a thorough multidisciplinary team deliberation of the clinical case. Discussions should focus on a comprehensive risk–benefit analysis, and the family should be provided appropriate counseling that includes options for elective termination or continuation of the pregnancy without fetal therapy. Potential risks to the mother should be part of the informed consent, and a detailed maternal preoperative evaluation should be performed to ensure maternal risks are minimal.[4]

The advancement of fetal surgery has benefited from a multidisciplinary approach and establishment of the International Fetal Medicine and Surgery Society to disseminate techniques and outcome data through an international registry.[5] Medical centers offering fetal treatment rely on surgeons and anesthesiologists devoted to the care and counseling of these complex maternal and fetal patients, as well as the expertise of radiologists, perinatologists, geneticists, neonatologists, psychologists, social workers, and numerous support staff. A bioethics committee derived from both the American College of Obstetricians and Gynecologists and the American Academy of Pediatrics has provided guidelines for fetal treatment centers and recommends a comprehensive informed consent and counseling process, maternal-fetal research oversight, use of a multidisciplinary approach, and participation in a collaborative data-sharing fetal therapy network.[6]

Fetal surgery is broadly categorized into three types of interventions: minimally invasive procedures, open procedures, and intrapartum procedures. A summary of conditions considered for fetal intervention with corresponding rationale and recommended treatment is shown in Table 63.1.

Minimally invasive fetal procedures include (1) percutaneous interventions guided by ultrasound, also known as fetal image-guided surgery for intervention or therapy, and (2) fetal endoscopic surgery using small endoscopic instruments inserted percutaneously guided by direct fetoscopic camera view and simultaneous real-time ultrasound imaging. With these minimally invasive approaches, the risks for preterm labor and delivery are reduced compared with those in open procedures that include a hysterotomy. Unlike in open fetal procedures, the mother can safely undergo a vaginal delivery for this and future pregnancies. However, the risk for preterm premature rupture of membrane (PROM) remains significant.[7]

Open fetal procedures involve a maternal laparotomy, a hysterotomy, and the need for intraoperative uterine relaxation. These procedures incur significantly more risk to both the fetus and mother than minimally invasive procedures. These increased risks include preterm PROM, oligohydramnios, preterm labor and delivery, uterine rupture, and fetal mortality.[8,9] Additional maternal and fetal risks include not only the anesthetic risks noted for nonobstetric surgery during pregnancy (see also Chapter 62), but also pulmonary edema, hemorrhage, membrane separation, and chorioamnionitis.[4,8] Cesarean delivery is required after an open fetal procedure and for all future pregnancies owing to the increased risk for uterine dehiscence or rupture at the site of the hysterotomy.

For fetuses with known airway compromise or obstruction, an ex utero intrapartum therapy (EXIT) procedure[10] allows continued fetal support by the intact uteroplacental unit (placental bypass) while the fetal airway is secured or other procedures completed without the concern for postnatal respiratory compromise, hypoxia, and asphyxia. The EXIT procedure has become a widely practiced fetal intervention for a growing list of indications. Congenital high airway obstruction due to laryngeal stenosis, laryngeal web, cystic hygroma, lymphangioma, or cervical teratoma is the most common anatomical indication for an EXIT procedure.[11] Congenital pulmonary lesions and sacral teratomas have also been resected during the EXIT procedure, with resulting normal umbilical cord carbon dioxide and pH values at birth, even when surgical time has exceeded 2.5 hours.[12] Extracorporeal membrane oxygenation (ECMO) can be initiated during an EXIT procedure for a fetus with significant cardiopulmonary disease.[13]

Much of the success of fetal therapy in the past three decades can be attributed to advances in both ultrasonography and magnetic resonance imaging (MRI), which have substantially improved the accuracy of prenatal diagnosis and expanded our understanding of the pathophysiologic factors of various untreated fetal abnormalities. Significant advancements in ultrasonographic transducer hardware and digital signal processing have resulted in better image resolution with more accurate differentiation of abnormal fetal anatomy, wider fields of view, and improvement in the dynamic range for both near-field and far-field signal-to-noise ratio. Use of this improved ultrasonographic imaging as a real-time guide has enabled practitioners to develop and perform various diagnostic tests and fetal therapies more precisely and safely. Examples of fetal ultrasound-guided diagnostic procedures include first-trimester chorionic villus sampling, embryofetoscopy, amniocentesis, umbilical cord sampling, and fetal biopsies.[14] These diagnostic advances allow more accurate prenatal consultation, the ability to intervene at an earlier gestational age (GA), and usually enough time to change the location of antepartum care and the delivery plan if needed. Live ultrasound is typically used to guide all minimally invasive fetal procedures and is also critical to initial portions of open fetal procedures and fetal monitoring.

MRI has undergone technologic improvements that have reduced image acquisition time, decreased motion artifacts, and enhanced image resolution to a point at which fetal MRI is frequently used in conjunction with ultrasound to better detect and evaluate anatomic pathologic processes. Fetal MRI can aid in diagnosis as a complementary technique to ultrasound as it provides a larger field of view that is not obscured by fetal bone artifact, but it is expensive and not available in all centers.[15,16]

In addition to advances in imaging technology, decades of procedural innovations and research have provided the basis for the in utero fetal interventions used clinically today. Initial pioneers in the field of fetal therapy include Sir (Albert) William Liley. In the early 1960s, Liley was the first to successfully treat erythroblastosis fetalis with an intraperitoneal blood transfusion that allowed the transfused red cells to be absorbed into the fetal circulation through the subdiaphragmatic lymphatics and thoracic duct.[17,18] Unfortunately, initial attempts to perform fetal blood transfusion through direct cannulation of the umbilical vessels were unsuccessful until 1981, when a reliable technique that employed fetoscopy was described.[19,20] With improved imaging resolution, the standard technique quickly became direct needle access of the umbilical vessels using ultrasound guidance. In the early 1970s, Liggins administered corticosteroids to the fetus via the maternal circulation to increase surfactant production in preterm fetuses at risk for respiratory distress syndrome.[21] Fetal surgery began in the early 1980s after rigorous research efforts and technical advancements in sheep[22-24] and monkey models.[25] Harrison and colleagues performed the first successful human fetal surgery by creating a vesicostomy in a fetus with a congenital lower urinary tract obstruction (LUTO) resulting in bilateral hydronephrosis.[26] Working with Harrison in the early 1980s, Rosen refined fetal anesthetic techniques in monkeys to improve intraoperative uterine relaxation[25] and clinical outcome before employing them for the first human fetal surgeries. Since the early 1980s, great advances have been made in the development of minimally invasive percutaneous surgical techniques, fetoscopy, and procedural aspects of open fetal surgery with hysterotomy. Fetal therapy has also advanced in its outcome evaluation from published case reports and series to prospective randomized controlled trials.

Fetal surgery is a reasonable therapeutic intervention for certain correctable fetal anomalies with predictable, life-threatening, or serious developmental consequences. With all types of fetal intervention, meticulous planning and a multidisciplinary team approach are critical to a successful outcome. The following sections provide a review and summary of the congenital lesion, outcome data, procedural considerations, and perioperative anesthesia considerations for the various conditions currently amenable to fetal intervention.

Indications, Procedures, and Outcomes

ANEMIA AND INTRAUTERINE TRANSFUSION

The incidence of fetal anemia secondary to rhesus D (RhD) sensitization has decreased since the introduction of RhD immunoglobulin prophylaxis in the late 1960s, to rates of approximately 1 in 1000 pregnancies.[18] However, other red blood cell (RBC) antigens, parvovirus B19 infection, maternal-fetal hemorrhage, and homozygous thalassemia also cause fetal anemia and combine to reach a rate of approximately 6 cases in 1000 live births.[18,27] Although spectral analysis examining bilirubin levels in serial amniotic fluid samples was originally used to detect fetal anemia and determine the timing of therapy, most treatment centers currently rely on noninvasive Doppler studies of the middle cerebral artery (MCA).[27] An increased peak MCA blood flow velocity more than 1.5 multiples of the median is an accurate threshold in detecting moderate-to-severe fetal anemia requiring intervention.[28] The value of this peak velocity threshold may be increased with each serial

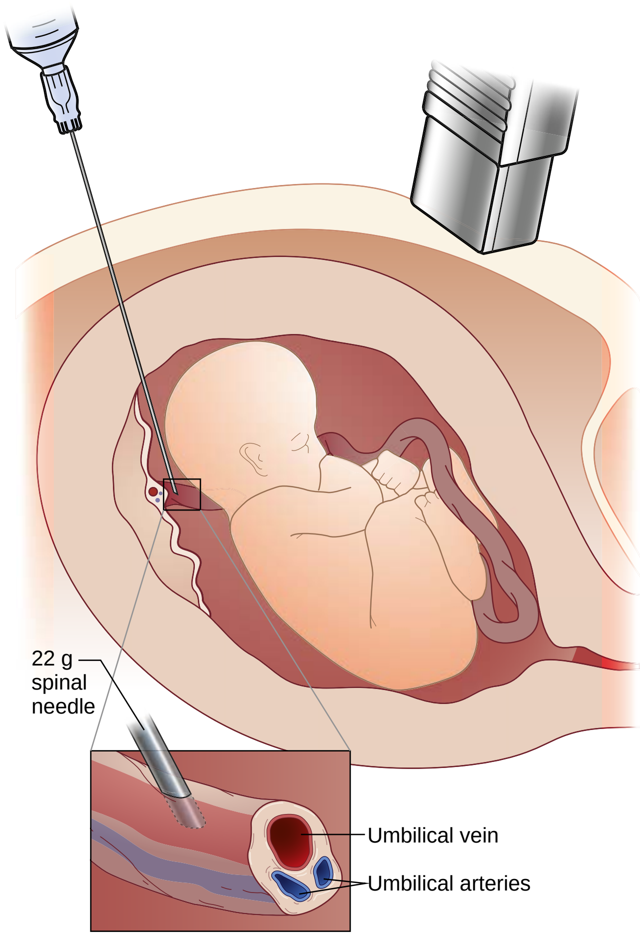

Fig. 63.1 Diagram of cordocentesis procedure used in intrauterine transfusion. Inset window shows tip of 22-gauge spinal needle entering the umbilical vein. (Redrawn from Ralston SJ, Craigo SD. Ultrasound-guided procedures for prenatal diagnosis and therapy. *Obstet Gynecol Clin North Am.* 2004;31:101–123.)

transfusion treatment to decrease the false positive rate. Fetal blood sampling from the umbilical vein just before starting the intrauterine transfusion (IUT) is the gold standard for determining the degree of fetal anemia. IUT is not used before 18 weeks' GA because umbilical vein access is not reliable. For cases requiring earlier intervention, fetal intraperitoneal transfusion of red cells may initially be the intervention of choice.[29]

IUTs are typically performed using local anesthesia and require minimal maternal sedation and analgesia. However, the anesthesiologist should be prepared for an emergent cesarean delivery at any time during the procedure if the fetus is at a viable GA. Using ultrasound image guidance, a 20- or 22-gauge needle is used to access the umbilical vein. The access point is typically near the placental cord insertion to provide stability (Fig. 63.1). Puncture of an umbilical artery rather than the umbilical vein is associated with prolonged bleeding and fetal bradycardia secondary to spasm.[18] Occasionally a free loop of the umbilical cord or intrahepatic portion of the umbilical vein may be used. The umbilical cord has no known pain receptors, but needle access of the intrahepatic portion of the umbilical vein stimulates pain receptors with passage of the needle into the fetus. Fentanyl attenuates the fetal stress response from intrahepatic fetal needle placement.[30] In one study, fetal stress hormone changes with IUT were unrelated to site of needle placement;[31] however, these results are difficult to interpret because hormone levels may be affected by changes due to the underlying fetal anemia and hemodynamic alterations associated with intravascular volume expansion. Given this uncertainty, fentanyl (10-20 μg/kg) is administered intramuscularly to the fetus before use of an intrahepatic approach. There is some evidence to suggest that fetal anesthesia does not alter MCA peak systolic velocity flow patterns following transfusion.[32]

An intramuscular muscle relaxant (e.g., rocuronium 2.5 mg/kg) can be administered to the fetus to decrease the likelihood of fetal movement that could dislodge the needle or sheer the umbilical vein.[33] If a muscle relaxant is administered directly into the umbilical vein the dose of muscle relaxant can be reduced (e.g., rocuronium 1.0 mg/kg). The volume of type O, rhesus (Rh)-negative, irradiated, viral screened, packed RBCs transfused is estimated from the GA, estimated fetal weight, donor unit hemoglobin (Hb), and pretransfusion Hb.[34] The rate of transfusion is typically 5 to 10 mL/min with a target hematocrit of 45% to 55%. Steady intravascular location of the needle tip can be assessed with Doppler imaging throughout the transfusion injection. Periodic sampling is used to guide the final transfusion volume. After IUT therapy, fetal Hb levels decrease approximately 0.3 g/dL/day[35] and multiple repeat IUTs are typically required at 1- to 3-week intervals, depending on the rate of Hb decline.

Perinatal fetal loss rate is approximately 2% per IUT, and transient fetal bradycardia (8%) is a common complication.[27,36] Other complications including emergency cesarean delivery, intrauterine infection, preterm PROM, and preterm delivery occur in approximately 3% of IUT procedures.[37] Although survival rates are significantly less for hydropic fetuses, recent published overall survival rates with IUT typically exceed 95%.[27,37] A long-term outcome study of 291 children (median age of 8.2 years with a range of 2-17 years of age) who underwent IUT during gestation for hemolytic disease found a 4.8% rate of neurodevelopmental impairment, including cerebral palsy (2.1%), severe developmental delay (3.1%), and bilateral deafness (1.0%).[38] Severe fetal hydrops was independently associated with neurodevelopmental impairment.

CONGENITAL HEART DEFECTS

Congenital heart anomalies occur with a frequency of approximately 1/100 live births (see also Chapter 78).[39] Ventricular septal defects are the most common cardiac anomaly.[40] The majority of cardiac heart defects are not amenable to fetal intervention. Ultrasound imaging allows diagnosis of cardiac defects as early as 12 to 16 weeks gestation, but is generally performed at 18 to 22 weeks gestation, when obstetric ultrasound assessments are used to screen for other fetal abnormalities.[41]

The majority of fetal surgical cardiac interventions focus on opening a stenotic valve or enlarging a restricted opening. These include (1) aortic balloon valvuloplasty for treatment of critical aortic stenosis and evolving hypoplastic left heart syndrome (HLHS), (2) atrial septostomy for highly restrictive or intact atrial septum seen in HLHS,

(3) pulmonic valvuloplasty for pulmonary atresia or intact ventricular septum and hypoplastic right ventricles, and (4) pericardiocentesis to treat congenital cardiac tumors or aneurysms.[41-43a] In utero intervention attempts to halt or reverse the morbid effects of the cardiac lesion before irreversible consequences occur. Early childhood mortality from severe cardiac defects, such as HLHS, remains in the range of 25% to 35%.[44,45] Survivors have significant associated abnormalities in neurologic development.[46,47]

The most commonly performed procedure is an aortic valvuloplasty for aortic stenosis with evolving HLHS. Significant aortic stenosis maintains fetal circulation primarily through the low-resistance foramen ovale and diminishes left ventricular development. Selection guidelines for fetal aortic valvuloplasty focus on the presence of significant aortic stenosis, evolving HLHS, and the potential for a technically successful procedure and biventricular postnatal outcome.[48,49] For this procedure,[50] the fetus is ideally positioned with the left chest anterior, and ultrasound is used to guide the percutaneous passage of an 18- or 19-gauge needle cannula through the uterus, through the fetal chest, and into the apex of the left ventricle (Fig. 63.2*A*). Maternal local anesthesia infiltration or neuraxial block is typically used for these procedures, and fetal resuscitation drugs must be readily available. In some cases, general anesthesia may be preferred for uterine relaxation to facilitate an external version to change fetal position and improve cannula trajectory. Before cannula insertion, intramuscular fentanyl and a paralytic agent are administered to the fetus with ultrasound guidance, as detailed in the section on "Fetal Anesthesia, Analgesia, and Pain Perception."[51]

The cannula tip is ideally positioned in the left ventricle, directly in front of the opening of the stenotic aortic valve and aligned with the left ventricular outflow tract. A coronary balloon catheter with guidewire is passed through the cannula into the stenotic valve and positioned in the aortic annulus, where it is inflated and deflated multiple times (see Fig. 63.2*B*). In certain cases, a small laparotomy is used to facilitate improved cannula alignment with the cardiac lesion. Technical success for fetal aortic valvuloplasty is approximately 75% using an angioplasty balloon over a guidewire.[51a] Technical success creates improved left ventricular function, improved aortic and mitral valve development, and birth of a live neonate in 90% of interventions.[52,53] Fetal complication rates from centers in Linz, Austria (n = 24) and Boston (n = 70) for fetal aortic valvuloplasty include: fetal bradycardia (17% and 38%, respectively), pericardial effusion (13% and 14%, respectively), ventricular thrombosis (21% and 15%, respectively), and fetal death (13% and 8%, respectively).[48,54,55] A recent systematic review noted complication rates following fetal aortic valvuloplasty of preterm delivery (16%), neonatal death (16%), bradycardia (52%), and hemopericardium (20%).[43] Approximately 40% of technically successful cases result in aortic regurgitation and minimal subsequent left ventricular growth. Biventricular circulation is present at birth in approximately half of the successful cases.[43a]

In addition to treatment of aortic stenosis, other cardiac anomalies have been treated in utero. Similar surgical techniques are used for atrial septoplasty and pulmonary valvuloplasty.[42] Outcomes from a small series of fetal atrial septostomies are promising; however, the defect created

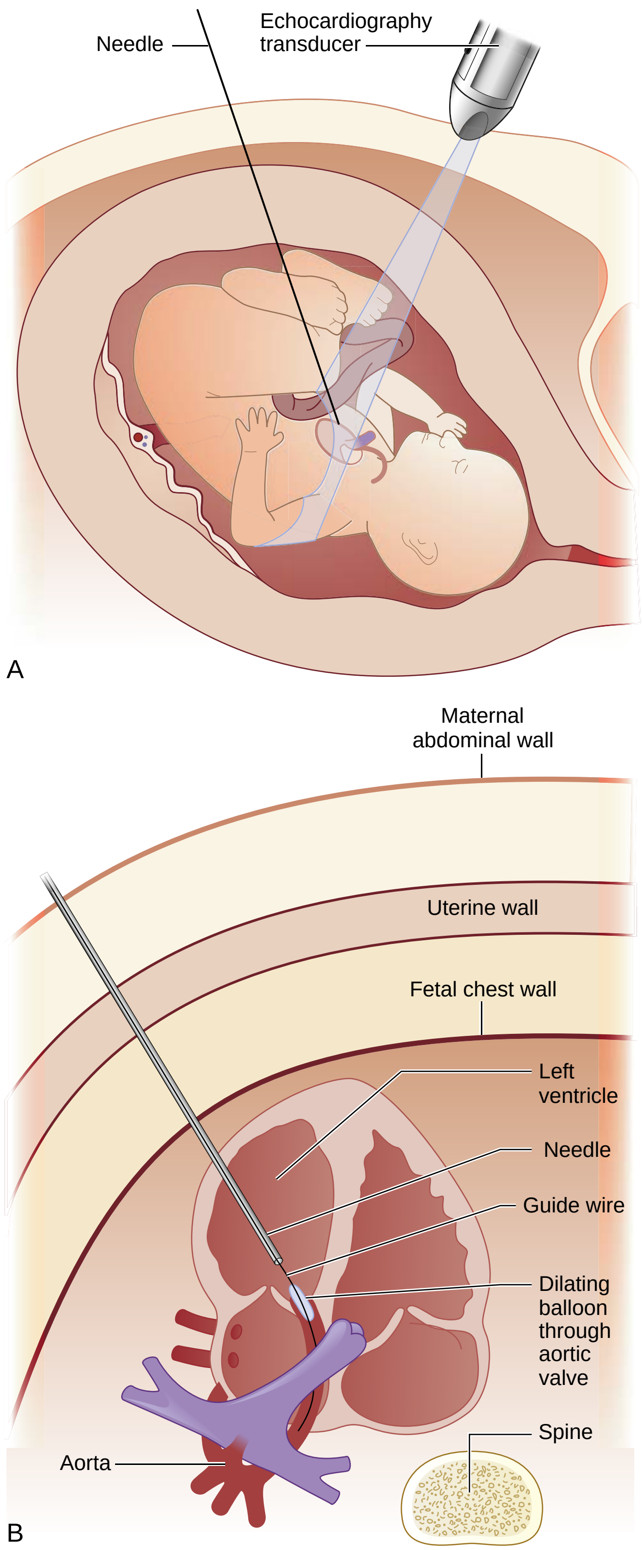

Fig. 63.2 (A) Depiction of ideal fetal position and insertion needle orientation. The fetal left chest is anterior, and the pathway from maternal abdomen entry point to the apex of the left ventricle is unobstructed. (B) This linear cannula course continues from left ventricle apex to the aortic valve. (Redrawn from Tworetzky W, Wilkins-Haug L, Jennings RW, et al. Balloon dilation of severe aortic stenosis in the fetus: potential for prevention of hypoplastic left heart syndrome—candidate selection, technique, and results of successful intervention. *Circulation.* 2004;110:2125–2131; with permission from Lippincott Williams & Wilkins.)

by the balloon dilation tends to close over time unless a stent is placed (which can be difficult and deployment has been successful in only 44%-62% of the time in a small case series).[56] Pulmonary valvuloplasty for pulmonary atresia and prevention of hypoplastic right ventricle was technically successful in 7 of 11 procedures, but long-term outcome data are unavailable.[42,57,58] In utero placement of cardiac pacing has been investigated to treat fetal cardiac arrhythmias unresponsive to conventional management with transplacentally administered antiarrhythmic drugs.[59,60] Unfortunately, these initial attempts have been frequently unsuccessful.

OBSTRUCTIVE UROPATHY

Fetal LUTO affects 2 in 10,000 live births.[61] These obstructions can be bilateral or unilateral and occur at the ureteropelvic junction, at the ureterovesical junction, or at the level of the urethra. If the obstruction is urethral or bilateral, significant developmental consequences occur (Box 63.1). Rates of perinatal mortality in these cases are as high as 90%, and survivors have more than 50% renal impairment.[62,63]

Posterior urethral valves are the most common cause of congenital bilateral hydronephrosis in male fetuses. Urethral obstruction is the most common cause in females, with other possible causes including ectopic ureter, ureterocele, megacystis megaureter, multicystic kidney, or other complex pathologic processes.[63,64] Ultrasound investigations of oligohydramnios resulting from decreased fetal urine output easily detect these uropathies with high sensitivity and specificity. Fetal MRI should be considered in cases of severe oligohydramnios as an additional imaging technique to determine the presence of associated fetal anomalies.[65] Grading systems based on ultrasound imaging of renal diameter to determine the severity of hydronephrosis and assessment of urinary tract dilation are used to determine risk stratification and treatment options.[66] Recently, a classification system for LUTO has been proposed that is based on amniotic fluid index, renal imaging, and fetal urine chemistry.[67] The associated morbidity predicted for each type of uropathy depends on obstruction location, duration, gender, and GA at onset.[68] Preterm delivery allows neonatal urinary tract decompression, but morbidity from pulmonary immaturity prevents early intervention and limits the efficacy of this approach.

Poor prognosis is associated with earlier presentation during gestation, more severe oligohydramnios, associated structural abnormalities, and increased concentrations of fetal urine electrolytes, osmolality, protein, and β_2-microglobulin.[68,69] Each case should be thoroughly investigated to determine whether other anomalies are present and if the fetus is a suitable candidate for intervention. If LUTO is corrected postnatally, 25% to 30% of surviving neonates will require dialysis by age 5.[70]

Placement of an in utero fetal vesicoamniotic shunting (VAS) for in utero treatment of LUTO allows decompression of the fetal bladder and urinary tract into the amniotic cavity. VAS prevents urine accumulation, allows normal bladder emptying and development, improves dysplastic renal histologic conditions, increases amniotic fluid volume, improves lung development, and prevents bladder wall fibrosis in animal models.[71-73] Determination of which human fetuses would benefit from in utero treatment of LUTO remains uncertain.[70,74] Human VAS placement started in the 1980s in an effort to improve renal development and reduce the pulmonary hypoplasia associated with oligohydramnios. These valveless, double-coiled shunts are inserted percutaneously with ultrasonographic guidance and local anesthesia. One coil remains in the urinary bladder and the other in the amniotic cavity. Prior infusion of fluid into the amniotic cavity can aid in proper shunt placement. Complications associated with these shunts include difficult placement, subsequent occlusion, and position migration (malfunction occurs in up to 60% of cases).[75] Fetal and maternal complications include fetal trauma, iatrogenic abdominal wall injury, gastroschisis, amnioperitoneal leaking, preterm PROM, preterm labor and delivery, and infection.[61] Neonatal survival rates after fetal VAS vary in the literature from 40% to 90%, with approximately 50% of survivors having normal renal function.[70,76-78] A meta-analysis of LUTO treatment studies through 2015 noted a perinatal survival advantage with in utero VAS placement compared to standard care (57% vs. 39%), but ultimately there was no difference in renal function or 2-year survival.[70] A multicenter, randomized controlled trial (the Percutaneous Shunting in Lower Urinary Tract Obstruction [PLUTO] trial) compared the perinatal mortality and renal function of fetuses with LUTO treated by either VAS or conservative noninterventional care. The trial was unable to recruit sufficient cases, with only 31 out of 150 desired patients recruited over a 4-year period. Analysis of this smaller enrollment noted a mortality benefit in the fetal treatment group at 28 days, 1 year, and 2 years of age; however substantial morbidity occurred in both groups, leading to only two children with normal renal function at 2 years of age.[79]

Fetal cystoscopy is a recent intervention that allows prenatal visualization of the fetal urethra and ablation of the urethral obstruction. Cystoscopy facilitates diagnosis between LUTO resulting from urethral atresia and posterior urethral valves. This is an important distinction, as urethral atresia is nearly universally lethal and does not improve with VAS placement, while posterior urethral valves are amenable to fetal intervention. Ablation of

BOX 63.1 Developmental Consequences of Fetal Urethral Obstruction

Oligohydramnios

- Potter facies (prominent infraorbital folds)
- Hypoplastic lungs
- Flexion contracture

Hydronephrosis

- Type 4 cystic dysplasia
- Renal failure

Hydroureter and Megacystis

- Abdominal muscle deficiency
- Prune belly

Data from Harrison MR, Filly RA, Parer JT, et al. Management of the fetus with a urinary tract malformation. *JAMA*. 1981;246:635–639.

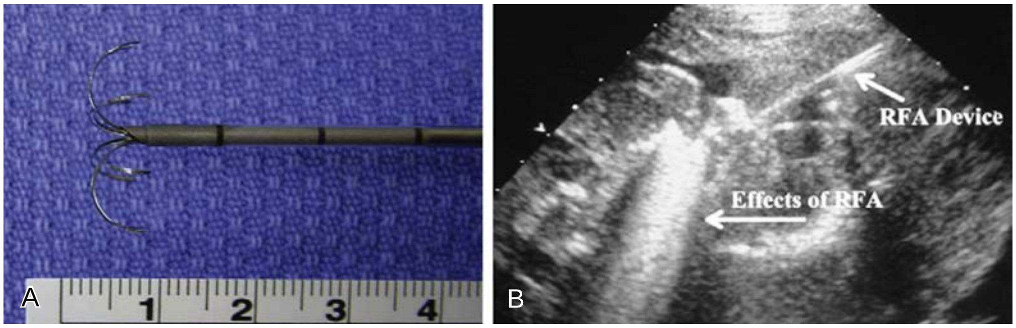

Fig. 63.3 (A) Photograph of a radiofrequency ablation *(RFA)* device with tines deployed. Scale below device in centimeters. (B) Intraoperative ultrasound image shows adequate position of the RFA device (tines deployed), with evidence of effects on the fetal tissues (regional increased echogenicity) as energy is applied. (Figures reproduced with permission from Hopkins LM, Feldstein VA. The use of ultrasound in fetal surgery. *Clin Perinatol.* 2009;36:255–272.)

posterior urethral valves may increase survival compared with expectant management. A case series[80] and retrospective case control study[81] demonstrated that fetoscopic laser ablation for posterior urethral valves can achieve bladder decompression and amniotic fluid normalization. In addition, fetal cystoscopy may improve 6-month survival in severe LUTO compared to no fetal intervention and result in improved renal function at birth when compared to treatment with VAS.[81] Future prospective trials are necessary to validate these initial retrospective results.

Selective fetal intervention with shunting or cystoscopy for LUTO restores amniotic fluid volume, prevents pulmonary hypoplasia, and improves perinatal mortality. However, the effects on medium-term and long-term renal function, neurologic function, bladder function, and other morbidities remain unclear and additional clinical research is needed.[74,82]

Twin Reversed Arterial Perfusion Sequence

Twin reversed arterial perfusion (TRAP) sequence is an abnormality of monozygotic twins that affects approximately 1 in 35,000 pregnancies, 1 in 100 monozygotic twin gestations, and 1 in 30 triplet gestations.[83] In this condition, one of the monozygotic twins has an absent or nonfunctioning heart and no connection to the placenta. The nonviable twin is perfused with retrograde blood flow from the other twin through vascular anastomoses. Blood returns to the normal twin by anastomoses that bypass the placenta. The inadequate perfusion of the recipient twin (primarily occurring retrograde through the umbilical artery) results in a lethal set of anomalies that include acardia and acephalus. Because the normal or "pump" twin generates blood flow for both itself and the nonviable twin, it is at risk for high-output congestive heart failure, hydrops fetalis, and preterm birth secondary to the increased uterine volume from polyhydramnios and increased size of the hydropic nonviable twin.[84,85] If untreated, TRAP sequence is associated with a 35% to 55% risk for intrauterine death of the normal pump twin, with survivors having an average GA of only 29 weeks.[86,87] Diagnosis is confirmed by reverse flow to the nonviable twin via the umbilical artery on ultrasound. The objective of fetal therapy is to disrupt the vascular communication between the two twins in an effort to prevent further cardiac failure in the pump twin. Successful treatment of TRAP sequence results in cessation of flow in the recipient twin's umbilical artery and the death of the nonviable fetus.

Several in utero approaches can accomplish these goals. Ultrasound-guided umbilical cord coagulation using laser, radiofrequency, or bipolar techniques, fetoscopic laser coagulation of placental anastomoses, and percutaneous intrafetal laser or radiofrequency ablation of the acardiac twin's umbilical cord base appear to be the most viable therapeutic options (Fig. 63.3).[88-90] Additional interventions include selective delivery of the nonviable fetus by hysterotomy, umbilical cord ligation, cord transection, and cord coagulation using coils or other thrombogenic material. Ablative techniques are likely superior to cord ligation or occlusion techniques.[88,91] A multicenter retrospective review of 98 TRAP sequence cases treated with radiofrequency ablation noted survival rates of 80% and a median GA at delivery of 37 weeks.[89] Although it is difficult to determine the optimal timing and treatment option, the therapeutic benefit of ablative intervention as early as 12 weeks GA has been demonstrated, as significant cardiac failure and death may occur in up to a third of pump twins if therapy is delayed until after 16 weeks gestation.[88,91,92] The most common complications following TRAP treatment include preterm PROM, preterm delivery, and intrauterine fetal demise.

Minimally invasive procedures to treat TRAP typically only require infiltration of local anesthesia at the percutaneous insertion site of the fetoscope or ablative device, although neuraxial anesthesia can also be used. Ultrasound guidance and assessment is critical for all of these therapies, and procedure success is confirmed by absence of flow to the nonviable acardiac twin at the end of the procedure and again approximately 12 to 24 hours later.

TWIN-TO-TWIN TRANSFUSION SYNDROME

Monochorionic twins share the same placenta and typically have intertwin vascular connections that create shared blood flow between the two fetuses. A significant number of these chorionic vascular anastomoses can result in unequal placental blood flow between the two monochorionic twins that can lead to twin-to-twin transfusion syndrome (TTTS). The occurrence of TTTS is approximately 1 to 3/10,000 births.[93] Monochorionic twinning occurs in approximately 20% to 25% of twin pregnancies, with TTTS complicating about 10% of these monochorionic gestations.[93-95] TTTS

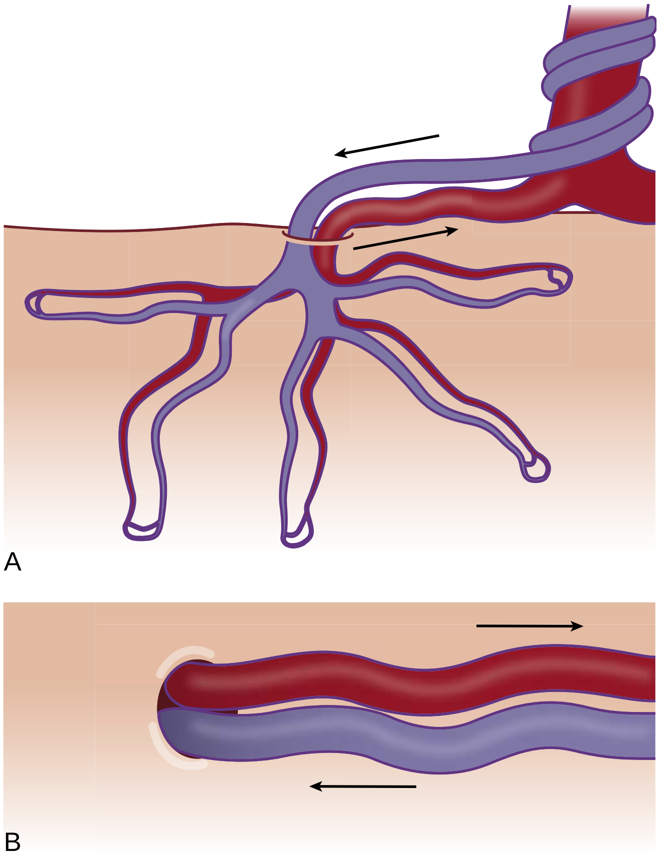

Fig. 63.4 (A) Normal placenta angioarchitecture (cotyledon). (B) Superficial view of bidirectional flow into and out of a cotyledon. (Redrawn from Rand L, Lee H. Complicated monochorionic twin pregnancies: updates in fetal diagnosis and treatment. *Clin Perinatol.* 2009;36:417–430.)

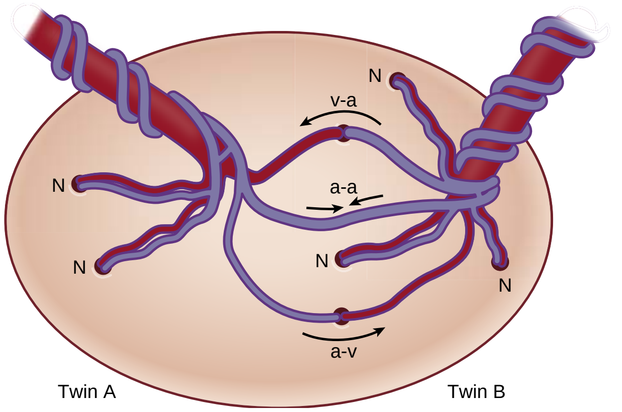

Fig. 63.5 Depiction of various types of vascular anastomoses present in monochorionic placentas. *a-a,* Arterioarterial anastomosis; *a-v,* arteriovenous anastomosis; *N,* normal angioarchitecture (cotyledon); *v-a,* venoarterial anastomosis. (Modified with permission from Simpson LL. Twin-twin transfusion syndrome. *Am J Obstet Gynecol.* 2013;208:3–18.)

usually manifests after the first trimester and is typically recognized at midgestation.[94,96]

Normally, umbilical arteries carry deoxygenated blood to the surface of the placenta, where gases and nutrients are exchanged with the maternal circulation. The returning venous blood flow is "paired" with the arterial flow, and the two components lie next to each other (Fig. 63.4). This fetal-placental vascular configuration (cotyledon) represents normal anatomy. A variety of abnormal unidirectional and imbalanced vascular connections are present in TTTS (Fig. 63.5). In TTTS, a branch of an umbilical artery descends into the placenta and cotyledon, but instead of connecting with a paired vein, it connects with a vein that brings blood to the other twin, and this results in an arteriovenous anastomosis between the two fetuses.[94,96] Although some inter-twin arteriovenous vascular architecture is found in 90% to 95% of all monochorionic twins, the shared blood flow is balanced by the presence of arterioarterial and venovenous bidirectional connections, which are found in 85% to 90% and 15% to 20% of monochorionic twin placentas, respectively.[94,97,98] The presence of arterioarterial connections is viewed as protective by allowing the overall resistance and blood flow to equalize between the twins and is associated with a significant reduction in TTTS.[99]

The complex pathophysiology of TTTS is dynamic and secondary to a variety of humoral, biochemical, hemodynamic, and functional changes in the two fetuses.[94] The increased blood flow to the recipient twin leads to polycythemia, polyuria, and polyhydramnios and can cause hypertrophic cardiomyopathy, hydrops fetalis, and fetal death. The donor twin (often described as the "stuck" or "pump" twin) is typically hypovolemic, growth-restricted, confined against the endometrium in an oligohydramniotic sac. This twin is primarily at risk for renal failure, cardiac failure, and hydrops fetalis secondary to the high cardiac output state.

The diagnosis of TTTS requires (1) a monochorionic diamniotic pregnancy and (2) a significant discrepancy in amniotic fluid volumes with ultrasound measurements of the maximal vertical pocket (MVP) of less than 2 cm in the oligohydramniotic twin and the MVP greater than 8 cm in the polyhydramniotic twin.[94,100] Twin size discordance and the presence of intrauterine growth restriction are often present in TTTS, but are not considered necessary to confirm the diagnosis. Although a variety of staging systems exist for determining the severity of TTTS, the most commonly used is the Quintero staging system (Table 63.2), which is based on ultrasound findings.[101,102] The progression of hypertrophic cardiomyopathy in the fetal recipient is detailed in a scoring system presented by Rychik and colleagues utilizing fetal echocardiography[103,104] that provides a more detailed assessment of TTTS severity when combined with the Quintero staging system.[95]

Fetuses with TTTS are at risk for preterm PROM, preterm delivery, and neurologic injury with white-matter lesions and long-term disability.[105] Neurodevelopmental impairment is associated with a low GA at birth.[106-108] Although outcome data stratified for the advanced stages of TTTS are limited, a higher mortality rate is likely associated with more advanced progression of disease.[100,109] TTTS treatment at stage I has an 85% survival rate, while higher-staged TTTS can increase to greater than 80% mortality if untreated.[93,110]

Several therapeutic management techniques have been developed to treat TTTS. Amnioreduction can help control polyhydramnios and thereby reduce the risk for both preterm labor and maternal respiratory distress. Also, placental blood flow may improve by decreasing amniotic hydrostatic

TABLE 63.2 Stages of Twin-Twin Transfusion Syndrome

Stage	Ultrasound Findings
I	Amniotic Fluid: Oligohydramnios in donor twin sac with MVP < 2 cm and polyhydramnios in recipient twin sac with MVP > 8 cm
II	Fetal Bladder: Stage I criteria AND no visualization of donor twin bladder with over 1 h of ultrasound observation
III	Doppler Flow: Stage II criteria AND (1) absent or reversed umbilical artery end-diastolic flow, (2) reversed ductus venosus a-wave flow, OR (3) pulsatile flow in the umbilical vein
IV	Fetal Hydrops: Either stage I or stage II criteria AND fetal hydrops in either twin
V	Fetal Demise: Fetal demise in either or both twins as assessed by absent fetal cardiac activity

MVP, Maximal vertical pocket.
Staging data based on criteria from Quintero RA, Morales WJ, Allen MH, et al. Staging of twin-twin transfusion syndrome. *J Perinatol*. 1999;19:550–555.

pressure on the placental vasculature. Serial amnioreductions have been used to treat TTTS for more than 25 years by improving placental perfusion and decreasing the rate of preterm deliveries.[111] A retrospective review of 223 twin sets with TTTS found that use of amnioreduction resulted in an overall birth survival rate of 78%, with survival rates of 65% for recipient twins and 55% for donor twins at 1 month of age.[112] Another review of 112 TTTS cases reported a 61% perinatal survival rate with use of amnioreduction.[113]

Use of an ultrasound-guided needle to create a surgical septostomy was hypothesized to improve TTTS outcome by equalizing the amniotic pressure between the two fetal sacs. In a prospective randomized trial comparing serial amnioreduction to septostomy, no survival difference was found between the techniques.[114] Septostomy is rarely used now for TTTS treatment because it offers no outcome advantage, and the creation of a single amniotic sac can increase the risk for umbilical cord entanglement. Selective feticide with the goal of improving the chance for survival of the other twin is accomplished using techniques described previously in the section on TRAP sequence. This option is typically used only for the most severe cases of TTTS.

Selective fetoscopic laser photocoagulation (SFLP) of the vascular anastomoses between the two twins is the best therapeutic approach for treating TTTS (stages II-IV) between 18 and 26 weeks gestation.[94,95,115] By detailed fetal ultrasound examination, the location of the placenta, cord insertions, and fetal orientation and anatomy are confirmed before the start of the procedure. Local anesthesia infiltration with monitored anesthesia care is a common anesthetic technique, though neuraxial anesthesia can also be used. Using ultrasound guidance, a 3-mm trocar or cannula is inserted percutaneously over a wire into the recipient twin's amniotic sac and directed perpendicular to the longitudinal axis of the donor twin.[115] The fetoscope is inserted into the trocar sheath and the laser fiber bundle passed into the fetoscope guide. Vessels that cross the membrane dividing the amniotic sacs are visualized and Doppler imaging can be used to confirm flow magnitude and direction. The abnormal connecting vessels are selectively laser coagulated, with an effort to spare the normal cotyledons.[7,96] Ideally this delineates two separate placental regions with each supplying an individual fetus. After laser ablation, amnioreduction is also performed in an effort to decrease the risk for preterm labor. Nonselective laser ablation of crossing vessels is typically avoided because it is associated with more frequent rates of intrauterine fetal demise and is likely to unnecessarily ablate some normal placental vessels.[101,115] Ablation of all abnormal connecting vasculature is not necessary for the procedure to be successful.[116] Some practitioners advocate use of a sequential technique when coagulating the various types of abnormal anastomoses in an effort to create a net flux of blood from the recipient to the donor and thereby reduce the chance for hemodynamic compromise and hypotension during the procedure in the donor twin.[117] Initially, superficial arteriovenous anastomoses that contain a donor artery are ablated, then arteriovenous anastomoses with a recipient artery, then the arterioarterial anastomoses, and finally ablation is performed at the venovenous anastomoses. A prospective multicenter trial comparing use of sequential SFLP to nonsequenced SFLP found that use of sequential SFLP significantly improved the 30-day survival of both twins and decreased fetal demise.[118,119] However, use of this sequential technique is associated with longer operative times and increased case difficulty, particularly with a placenta located on the anterior uterine wall. A recent modification of SFLP called the “Solomon technique” was created to reduce recurrent TTTS.[120] In the Solomon technique, the entire vascular equator is coagulated following the coagulation of visible vessels, in order to reduce residual anastomoses. A randomized controlled trial comparing SFLP to the Solomon technique trial noted that the Solomon technique reduces the risk of recurrence of TTTS or twin-anemia polycythemia sequence following initial treatment, but no difference in 2-year survival without neurodevelopmental disability was found.[121,122]

A 2004 randomized multicenter trial compared SFLP therapy to amnioreduction for treatment of severe TTTS diagnosed between 15 and 26 weeks gestation.[123] Rates of at least one twin survival were more frequent in the laser treatment group at both 28 days (76% vs. 56%, $P < .01$) and 6 months of life (76% vs. 51%, $P < .01$). In addition, neurologic outcomes were better in the laser treatment group. A large subgroup of survivors from this trial was followed prospectively for 6 years. No additional change in either survival rate or long-term neurologic outcome was found in comparison to the original 6-month data.[124] This conclusion was echoed in a 2014 Cochrane review of laser treatment for TTTS.[110] More recent work has suggested that early intervention in stage I TTTS may be beneficial compared to expectant management.[125]

Although recent SFLP treatment studies of TTTS studies suggests a greater than 60% dual survival rate and near 90% survival of at least one twin,[126] long-term neurologic outcome in TTTS survivors who underwent SFLP remains unclear, with rates of major neurologic abnormalities in survivors ranging from 3% to 25%.[124,127] A recent review of 9 studies examining neurodevelopmental outcomes at 24 months in patients who underwent laser therapy found a mean rate of neurological injury of 14%. The mean rate of cognitive impairment was 8%, 11% for motor delay, 17%

for communication delay, and 6% for cerebral palsy.[105] Neonatal cerebral lesions correlate with neurodevelopmental impairment at 2 years of age.[128]

The most common complication of SFLP is preterm PROM with subsequent preterm labor and delivery. Preterm PROM rates vary widely across studies, but have been reported to occur in 12% to 30% of SFLP cases for TTTS with a rate of preterm labor and delivery before 32 weeks gestation of approximately 30%.[94,95] Other possible complications include placental abruption, need for a second SFLP procedure, placement of the trocar through the placenta, hemorrhage, chorioamnionitis, and possible membrane perforation resulting in limb entrapment and ischemia.[94,95]

In conclusion, treatment of TTTS with SFLP results in better outcomes compared to amnioreduction alone.[126] Additional research is needed to determine optimal timing, further technique refinement, and long-term neurologic outcome for the treatment of TTTS with SFLP.

AMNIOTIC BAND SYNDROME

Amniotic band syndrome (ABS) includes a wide variety of fetal anomalies associated with fibrous bands that entangle or constrict various parts of the fetus or umbilical cord in utero (Fig. 63.6). The resulting malformations include limb and digit amputations, craniofacial abnormalities, visceral defects, and body wall defects. The incidence is approximately 1 in 3000 to 1 in 15,000 live births.[129] The primary cause and pathogenesis of ABS remains unknown, but these defects appear secondary to either a vascular insult or other cause of abnormal perfusion to the affected area.[130] Theories behind the cause of ABS include a primary defect in embryonic development, an early amniotic membrane rupture resulting in the creation of amniochorionic bands, or a vascular disruption early in pregnancy.[131]

Diagnosis is determined by findings on ultrasound imaging consistent with characteristic fetal anomalies of the involved anatomy. Visualization of the bands themselves is not a necessary component of the diagnosis.[132] Fetal MRI can aid in diagnosis as a complementary technique to ultrasound, but the efficacy of its use is currently limited to case reports and a small case series.[133] The progression of morbid conditions from each case of ABS is difficult to predict. In cases of limb entrapment, increasing band constriction decreases both venous and arterial flow. This decreased perfusion leads to limb edema and can eventually result in amputation distal to the constriction. In an otherwise normal fetus, use of fetoscopic-guided sectioning of the band with a laser can restore distal blood flow and may improve functional outcome in some cases.[131] Efficacy of the technique is based on review of a small number of cases in the literature, which range from 50% to 80% of limb form and function preservation provided that some arterial flow to the affected limb is present pre-intervention.[134,135] Single limb involvement is also associated with a more favorable surgical outcome compared to fetuses with multiple limb involvement.[135] Interestingly, the rate of PROM in these procedures is higher than other fetoscopic procedures.[129,131] ABS can also be an iatrogenic complication following minimally invasive fetal procedures in monochorionic diamniotic twins, and should be evaluated for especially if known chorioamnion separation or septostomy occurs.[136]

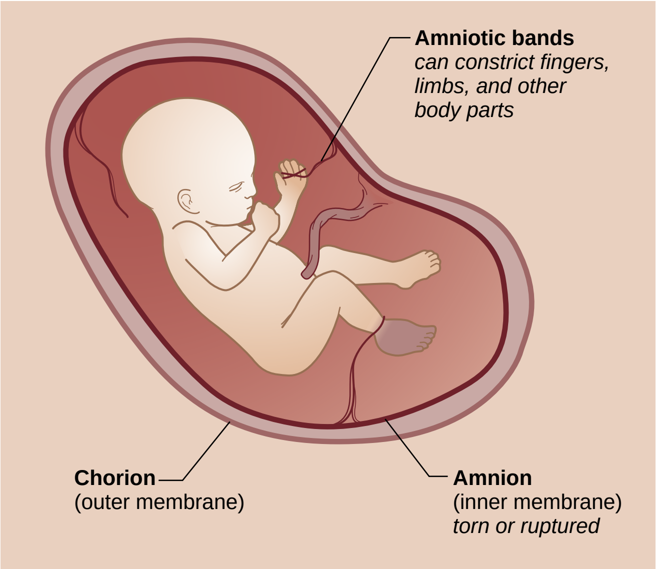

Fig. 63.6 Depiction of amniotic band syndrome. The amnion membrane can become wrapped around various fetal parts (e.g., digits, limbs, neck) and result in amputations or deformities. (Redrawn from Graves CE, Harrison MR, Padilla BE. Minimally invasive fetal surgery. *Clin Perinatol.* 2017;44(4):729–751.)

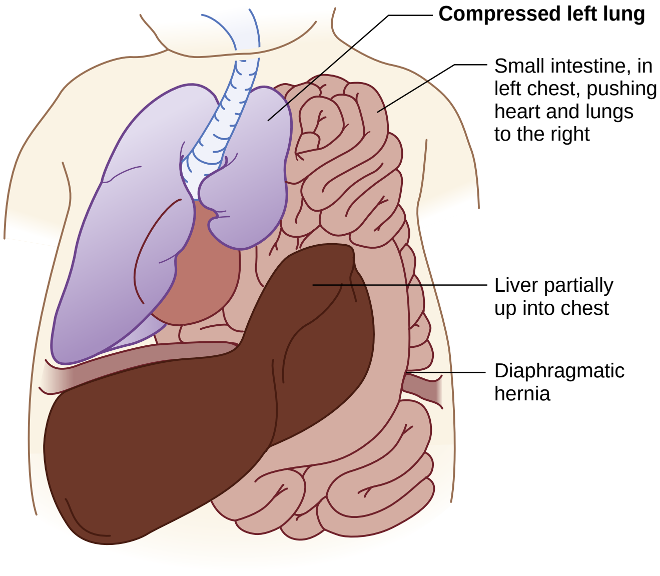

Fig. 63.7 Depiction of congenital diaphragmatic hernia. A defect in the fetal diaphragm allows abdominal contents (e.g., intestines, liver) to enter the thoracic cavity, compress the heart, and prevent lung growth and maturation. (Redrawn from Graves CE, Harrison MR, Padilla BE. Minimally invasive fetal surgery. *Clin Perinatol.* 2017;44(4):729–751.)

CONGENITAL DIAPHRAGMATIC HERNIA

Approximately 1 in 2500 newborn infants has a congenital diaphragmatic hernia (CDH).[137] During early gestation, abdominal contents herniate into the thoracic cavity and compress the fetal lungs (Fig. 63.7). This results in significant neonatal morbidity and mortality from pulmonary hypoplasia, respiratory insufficiency, and pulmonary hypertension. CDH survival rates when ECMO is not required have improved to greater than 70% over the past 25 years at tertiary care centers.[138,139] These highly specialized centers offer care that includes early intubation, surfactant administration, ventilation techniques to minimize lung trauma, surgical closure of the defect, and ECMO therapy. Mortality rates vary greatly with the severity of pulmonary hypertension and respiratory dysfunction.[140,141] If ECMO is required, survival rates vary between 50% and 80%.[139] Fetal intervention for CDH aims to improve fetal lung development and prevent the morbidity of pulmonary hypoplasia.

In utero repair of diaphragmatic hernia in lamb models reversed both the parenchymal hypoplasia and pulmonary vascular changes associated with CDH.[23] Initial human in utero intervention focused on open repair of the fetal diaphragm with limited success.[142,143] However, these initial interventions advanced fetal surgery techniques and paved the way for a minimally invasive approach to CDH intervention.

Initial open intervention experience found that a fetal abdominal patch was necessary to accommodate the added abdominal viscera without increasing intraabdominal pressure and compromise of ductus venosus blood flow. These early open interventions also determined that in utero reduction of the herniated liver compromised umbilical circulation and significantly increased fetal mortality. Additionally, the advantage of opening the uterus with a stapling device to ensure effective hemostasis was demonstrated. However, adequate control of postoperative uterine tone remained a substantial problem. In a prospective clinical trial sponsored by the National Institutes of Health, in utero CDH treatment using an open technique for fetuses without herniation of the liver into the thorax did not improve neonatal survival compared with standard postnatal treatment.[144]

After these efforts, tracheal occlusion was advanced as a less-invasive strategy for treating fetal CDH and improving lung development. Fetal lungs secrete over 100 mL/kg/day of fluid that exits the trachea and mouth into the amniotic cavity. In fetal lamb models, tracheal occlusion restricts the normal outflow of the fetal lung fluid and provides an increase in pulmonary hydrostatic pressure. This increased pressure pushes the viscera out of the thorax, promotes expansion of the hypoplastic lung, and thereby improves lung growth and development.[145,146] Fetal reversible tracheal occlusion[147-149] has replaced primary repair in utero for the treatment of CDH. Initially, a tracheal foam plug was inserted in the fetal airway during open surgery, but it failed to provide adequate occlusion.[150] Later, metallic hemoclips were placed around the trachea after meticulous neck dissection.[150] Unfortunately, survival with this initial open tracheal occlusion procedure was poor (15%) and lower than survival in CDH fetuses receiving postnatal standard treatment (38%).[151]

Subsequently, minimally invasive fetal endoscopic surgical techniques replaced the open technique for placement of the clips. These procedures are performed with local or neuraxial maternal anesthesia and the administration of fetal anesthesia by intramuscular injection. A variety of occlusive devices, including cuffs, plugs, valves, and balloons, were attempted at various medical centers.[152] Currently, percutaneous endoscopic endotracheal intubation is used to place a small detachable occlusive balloon in the fetal trachea.[149] With initial procedures the balloon was left in place until delivery (see discussion on EXIT procedures), but currently, it is deflated and removed before term with a second fetal endoscopy.[153] The balloon removal may improve type II pneumocyte function, increase surfactant production, and allow a vaginal delivery when appropriate.[152]

TABLE 63.3 Postnatal Survival in Fetuses With Left-Sided Congenital Diaphragmatic Hernia and Intrathoracic Liver Herniation Based on Fetal Lung to Head Ratio

	POSTNATAL MANAGEMENT		FETOSCOPIC TRACHEAL OCCLUSION	
LHR (mm)	**Fetuses *n***	**Survival *n* (%)**	**Fetuses *n***	**Survival *n* (%)**
0.4-0.5	2	0	6	1 (16.7)
0.6-0.7	6	0	13	8 (61.5)
0.8-0.9	19	3 (15.8)	9	7 (77.8)
1.0-1.1	23	14 (60.8)		
1.2-1.3	19	13 (68.4)		
1.4-1.5	11	8 (72.7)		
≥1.6	6	5 (83.3)		
Total	86	43 (50)	28	16 (57.1)

LHR, Lung area-to-head circumference ratio.
Modified from Jani JC, Nicolaides KH, Gratacos E, et al. Fetal lung-to-head ratio in the prediction of survival in severe left-sided diaphragmatic hernia treated by fetal endoscopic tracheal occlusion (FETO). *Am J Obstet Gynecol*. 2006;195:1646–1650.

Use of ultrasound imaging to determine the ratio of fetal lung area to head circumference (LHR) and the presence of thoracic liver herniation ("liver up" vs. "liver down") are historically the most reliable prognostic indicators of fetal CDH outcome.[152,154,155] Evaluation of survival in fetuses with left-sided CDH and intrathoracic liver herniation managed postnatally noted no survival with an LHR of 0.7 or less and a survival rate of 72.7% or greater with an LHR of 1.4 or greater (Table 63.3).[154] The LHR increases exponentially with GA and is less useful after 28 weeks gestation.[156] The Antenatal CDH Registry Group normalized the LHR to GA by creating an observed to expected LHR (o/e LHR)[157] that correlates well with survival rate (Fig. 63.8).[158,159] More recently, fetal MRI measurement of observed to expected total fetal lung volume (o/e TFLV) correlates well with neonatal survival in fetuses with isolated CDH as an assessment of pulmonary hypoplasia.[160,161] In addition to presence of liver herniation, use of a 25% threshold with o/e LHR and o/e TFLV appear to perform the best as predictors of survival with CDH.[159]

A prospective randomized trial (1999-2001) evaluated fetal endoscopic tracheal occlusion (FETO) for prenatal treatment of CDH using both clip and balloon occlusion techniques.[162] Inclusion criteria included a 22- to 28-week GA, left-sided thoracic liver herniation, and an LHR of less than 1.4. The trial was closed early, and no benefit in survival or reduction in 90-day morbidity was found with prenatal treatment (n = 11) compared with control (n = 13) (survival rates of 73% vs. 77%). Additionally, rates of PROM and preterm delivery were more frequent in the fetal intervention group, with 100% of the fetoscopic intervention group having PROM.[162] The inclusion of fetuses with an LHR of up to 1.4 may have decreased the ability to determine a significant difference, because many of these fetuses were likely to survive with standard postnatal tertiary medical care (see Table 63.3).

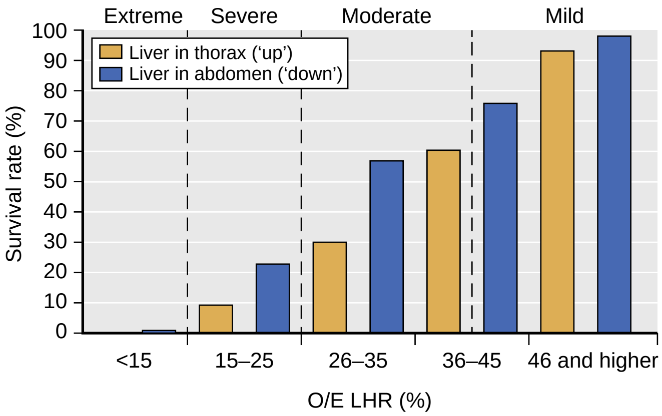

Fig. 63.8 Survival rates of fetuses with isolated left-sided congenital diaphragmatic hernia, depending on measurement of the observed to expected lung area to head circumference ratio *(O/E LHR)* and position of the liver. (Redrawn from Deprest JA, Nicolaides K, Gratacos E. Fetal surgery for congenital diaphragmatic hernia is back from never gone. *Fetal Diagn Ther.* 2011;29:6–17.)

Three European medical centers and the FETO task force began a collaboration for treatment of severe cases of CDH with a high risk for mortality (LHR < 1.0 and liver herniation into the hemithorax).[157,163] Because of concern for tracheal damage by very early tracheal balloon placement,[164] the tracheal balloon was placed at 26 to 28 weeks gestation and removed around 34 weeks gestation. Data from FETO task force cases through 2008 ($n = 210$, mean GA of placement at 27 weeks, LHR < 1.0, and primarily left-sided CDH) were compared with historic postnatal treatment controls (1995-2004). Use of prenatal reversible tracheal occlusion significantly improved the survival rate (47% vs. 20% in historic controls), and delivery occurred at a median GA of 35 weeks.[163] In addition, mean operating time was minimal (<10 minutes) and more than 95% of procedures were successful on the first attempt. Some of the survival benefit with in utero treatment may represent selection bias as well as improvement in both technique and neonatal care over time.

A 2016 metaanalysis of all studies comparing survival outcome between FETO and a contemporary control group found fetal intervention improved survival in patients with isolated CDH and a LHR ≤ 1.0. Fifty-one of 110 fetuses (46.3%) who had undergone FETO survived to discharge, compared with 6 of 101 (5.9%) in the control group.[165] Another recent study suggests that patients undergoing FETO for severe isolated CDH have morbidity outcomes similar to those fetuses with moderate lung hypoplasia.[166] Although FETO improves lung growth, and decreases need for ECMO, left heart hypoplasia may persist until after the postnatal CDH repair.[167]

A multicenter randomized Tracheal Occlusion to Accelerate Lung growth trial is ongoing (http://www.totaltrial.eu).[168] It compares postnatal management to both late (30-32 weeks gestation) FETO intervention for moderate lung hypoplasia and earlier FETO intervention (27-30 weeks gestation) for severe lung hypoplasia. This trial uses o/e LHR criteria, and balloon occlusion removal is planned for 34 weeks gestation, with postnatal management standardized by a consensus protocol. Long-term outcome data on pulmonary and neurologic development are needed to better determine if and when FETO should be offered for individual cases of severe CDH. New data suggest that prenatal administration of sildenafil may further reduce neonatal pulmonary hypertension, with or without invasive fetal surgery.[149]

MYELOMENINGOCELE

Spina bifida includes all defects with incomplete neural tube closure. Myelomeningocele (MMC) is the most common type of spina bifida and results in exposure of the meninges and spinal cord through a congenital defect in the vertebrae and overlying tissues. MMC occurs during the third and fourth weeks of gestation with incomplete embryonic neural plate development. Folate supplementation in the maternal diet has decreased the rate of MMC by nearly 50%, but the benefit reached a plateau without eliminating the disorder and MMC remains at a rate of approximately 1 in 3000 live births.[169,170] Improved prenatal screening with α-fetoprotein measurement and ultrasonography allows the possibility of pregnancy termination, and it is estimated that 25% to 40% of MMC pregnancies are terminated. MMC can result in lifelong morbidity and disability, including loss of motor and sensory function based on lesion level, bowel and bladder dysfunction, sexual dysfunction, hydrocephalus, Arnold-Chiari type II malformation, tethered cord, and impaired cognition.[169,171] If uncorrected in utero, surgical closure of the spinal defect must be performed within a few days after birth. Children with lumbosacral MMC defects often require ventriculoperitoneal shunting for hydrocephalus.[172] Even with successful shunting, complications of central hypoventilation, vocal cord dysfunction, and swallowing difficulties can persist because of an associated Arnold-Chiari malformation.[173] The mean intelligence quotient in patients with MMC who underwent ventriculoperitoneal shunting is 80 (low normal)[174] and decreased compared to those who do not require a shunt.[175] Neonates with spina bifida have a 14% mortality rate by 5 years of age and a 35% mortality rate in those with known brainstem dysfunction and Arnold Chiari type II malformation.[169]

The cause of MMC remains unknown. The abnormalities and deficits of MMC are hypothesized to be the result of two separate mechanisms. The primary cause is anatomic malformation with abnormal development of the spinal cord and associated tissues. Secondary damage is likely created by exposure of these open neural elements to the amniotic fluid and direct trauma. Consequently, the ability to close the defect in utero and isolate the neural tissue from contact with the intrauterine environment has the potential to improve outcome in contrast to delaying closure until after birth.

This hypothesis has been supported by animal models that found improved neonatal neurologic function with fetal closure of the defect in utero.[176-179] Ultrasound assessment demonstrates that central and peripheral neurologic injury is progressive during gestation.[180,181] Motor deficits and cognitive dysfunction are correlated with lesion level and higher levels are associated with a greater degree of morbidity.[177] Improved motor function has been observed at 2 years of age in children with MMC who underwent cesarean delivery before labor onset compared to those delivered vaginally or by cesarean delivery after onset of labor.[169,182] Therefore, women with fetuses with MMC and planned postnatal repair typically undergo cesarean delivery before onset of labor or rupture of membranes in an effort to minimize any additional injury to the open neural elements.

The rationale for fetal intervention for MMC is to improve functionality and quality of life. Prenatal repair for MMC is most commonly performed with an open fetal surgery technique requiring both maternal laparotomy and hysterotomy, although a few centers have started performing the repair with an endoscopic fetal technique. Considerations for anesthesiologists involved in open MMC repair (see section on "Management of Open Procedure") include participating in comprehensive, multidisciplinary, preoperative maternal evaluation and counseling; preparing for potential intraoperative hemorrhage; planning an anesthetic that provides profound uterine relaxation; administering analgesia and muscle relaxant directly to the fetus; monitoring the need for potential fetal resuscitation or urgent delivery; and managing maternal analgesia and postoperative uterine and fetal monitoring.[183]

MMC in utero surgery typically occurs between 19 and 26 weeks gestation. Initial human studies found that in utero repair reversed the hindbrain herniation of the Arnold-Chiari II malformation and decreased the requirement for ventriculoperitoneal shunt placement before 1 year of age.[184] In addition, a 1999 series of 10 fetuses undergoing in utero MMC closure at 22 to 25 weeks gestation found improved lower extremity function among 6 out of 9 fetuses compared with expected function based on the level of lesion, with one fetal death at 25 weeks gestation from preterm delivery and associated respiratory insufficiency.[185] A randomized, prospective clinical trial completed between 2003 and 2010 at three U.S. medical centers examined the risks, benefits, and outcomes of open in utero repair for MMC compared with standard postnatal repair among 183 patients.[186] Open fetal repair reduced the need for ventriculoperitoneal shunting, decreased hindbrain herniation, and improved lower extremity motor function at 30 months of age. However, prenatal repair significantly increased the risk for various fetal and maternal complications,[8,186] including spontaneous membrane rupture, partial or complete uterine dehiscence, and preterm birth with increased risk for respiratory distress syndrome (Table 63.4). Two perinatal deaths occurred in each group. A 30-month follow-up study demonstrated that patients undergoing fetal surgery were more likely to have a level of function 2 or more levels better than expected (26.4% vs. 11.4%), to be able to walk independently (44.8% vs. 23.9%, $P = .004$), to perform better on the Bayley Mental Development Index, and to have improved Peabody Developmental Motor Scale.[187,188] Long-term outcomes from this trial are still ongoing, but a pretrial cohort of 54 patients undergoing fetal MMC repair reported improved functional and behavioral outcomes at age 10 years, especially among children who did not require ventriculoperitoneal shunting.[189]

Results of this trial should not be generalized to patients outside the inclusion criteria of the study and should be considered only at medical centers that can develop a practice with significant volume and depth of resources.[190] It is recommended that this procedure be offered only at medical facilities with the expertise, multidisciplinary teams, services, and facilities to provide the intensive care required for these patients, while maintaining rigorous patient selection.[191]

TABLE 63.4 Maternal Complications for Management of Myelomeningocele Study Trial Patients

	Prenatal ($n = 91$)	Postnatal ($n = 92$)	P
MATERNAL OUTCOMES			
Chorioamniotic membrane separation	30 (33%)	0	<.0001
Pulmonary edema	5 (6%)	0	.03
Oligohydramnios	19 (20%)	3 (3%)	<.001
Placental abruption	6 (7%)	0	.01
Spontaneous rupture of membranes	40 (44%)	7 (8%)	<.0001
Spontaneous labor	39 (43%)	13 (14%)	<.0001
Maternal blood transfusion at delivery	8 (9%)	1 (1%)	.02
Hysterotomy site thin, or partial or complete dehiscence noted at delivery	31 (35%)	N/A	N/A
Mean gestational age at birth (weeks)	34.0 ± 3.0	37.3 ± 1.1	<.0001

The table lists maternal complications that were significantly different ($P < .05$) between the prenatal and postnatal repair groups in the Management of Myelomeningocele Study (MOMS) following complete cohort analysis of 183 patients. Other outcomes were evaluated, but only those that were different between the two groups are included. Data for each group are shown as both an absolute number and as a percentage.

Modified from Johnson MP, Bennett KA, Rand L, et al. The Management of Myelomeningocele Study: obstetrical outcomes and risk factors for obstetrical complications following prenatal surgery. *Am J Obstet Gynecol*. 2016;215:778.e1–e9.

With improvement in surgical technique, and feasibility demonstrated in animal studies,[192] endoscopic MMC repair is increasingly practiced. In theory, a minimally invasive approach may reduce maternal complications and obviate the need for maternal cesarean delivery.[193] A phase I clinical trial of percutaneous endoscopic repair ($n = 10$) using a biocellular patch over the defect followed by skin closure revealed improved hindbrain herniation and motor function, however preterm delivery was significant with the mean gestational birth age being 32 weeks.[194] In addition, 2 of 10 procedures were aborted due to loss of uterine access, preterm PROM occurred in all 10 cases, and 1 fetus and 1 neonate died. Outcomes have improved with evolution of the fetoscopic repair technique to include a maternal laparotomy and exteriorization of the uterus prior to insertion of the fetoscope ports.[193,195] After port placement, a portion of amniotic fluid is withdrawn and carbon dioxide is insufflated. A retrospective cohort trial of 28 patients undergoing fetoscopic MMC repair (22 fetoscopic, 4 conversion to hysterotomy, 2 abandoned) noted a mean delivery at 39 weeks gestation with a standardized surgical approach ($n = 10$) using a two-port technique and a preterm PROM rate between 10% and 30%.[193] Of the 22 patients who underwent a fetoscopic repair, 50% delivered vaginally. Recently a method using partial amniotic carbon dioxide insufflation without pre-removal of amniotic fluid has been described and successfully used in MMC repair.[196]

A 2017 metaanalysis of 11 studies examining fetal MMC repair found no difference in mortality or need for ventriculoperitoneal shunt among fetal patients treated with an open or endoscopic technique.[9] Patients treated with a percutaneous fetoscopic technique had a higher PROM rate (91% vs. 36%), a higher risk of preterm delivery (96% vs. 81%), and a higher rate of cerebral spinal fluid leakage from the MMC repair site (30% vs. 7%). Fetal repair via a fetoscopic approach following maternal laparotomy had a lower rate of premature birth. Uterine dehiscence was higher in the open surgical group (11% vs. 0%). The authors concluded that a fetoscopic technique is a promising, though not yet perfected, technique for fetal MMC repair.[9] Minimally invasive endoscopic repair of MMC should still be considered an experimental treatment given the steep learning curve and lack of long-term outcome data.[7]

SACROCOCCYGEAL TERATOMA

The incidence of sacrococcygeal teratoma (SCT) is approximately 1 in 15,000 to 40,000 live births.[197] These teratomas are typically diagnosed by ultrasound in the second trimester of pregnancy and may grow rapidly (>150 cm^3/week), with some reaching sizes of 1000 cm^3 or more.[198] The larger tumors create a significant arteriovenous shunt and low resistance state and lead to the development of high-output cardiac failure, polyhydramnios, placentomegaly, and hydrops fetalis.[199] In addition, rapidly growing tumors may rupture and hemorrhage. Perinatal mortality varies greatly in different published series, ranging from 16% to 63%.[200] In addition, fetuses with SCT are at risk for preterm birth, intrapartum dystocia, tumor rupture with hemorrhage, and urinary obstruction. Cesarean delivery is frequently required.

Tumor staging is based on criteria from the American Academy of Pediatrics Surgical Section as detailed by Altman (Fig. 63.9).[201] Based on the external location, stage I tumors are suitable for fetal intervention whereas stage IV tumors are entirely internal and not considered appropriate for fetal resection.[198] Fetal MRI can assist in tumor size, location, and staging. A tumor volume to fetal weight ratio greater than 0.1 cm^3/g prior to 24 weeks gestation is predictive of poor fetal outcome.[202]

Fetuses diagnosed with SCT before 30 weeks gestation or with rapidly growing tumors have a poor prognosis (<7% survival), but may benefit from in utero intervention.[203] Radiofrequency ablation, embolization, thermocoagulation of the tumor or vascular supply, and cyst drainage have been employed to treat SCT in utero and prevent hydrops fetalis, but the benefit remains unclear.[127,203]

A review of minimally invasive fetal intervention for SCT in 34 patients from 1980 to 2013 demonstrated an overall survival rate of 44% with mean delivery at 29.7 ± 4.0 weeks.[199] Preexisting hydrops led to a worse outcome, with only 30% survival (6/20) in this cohort. A subsequent review of 33 patients examined the effectiveness of different techniques, comparing interstitial tumor ablation (n = 22) to targeting the feeding vessels of the tumor (n = 11).[127] Fetuses undergoing vascular ablation seemed to have a survival advantage over the interstitial ablation group (63.6% vs. 40.9%), which the authors suggested may be because interstitial ablation often led to tumor necrosis and subsequent hemorrhage.

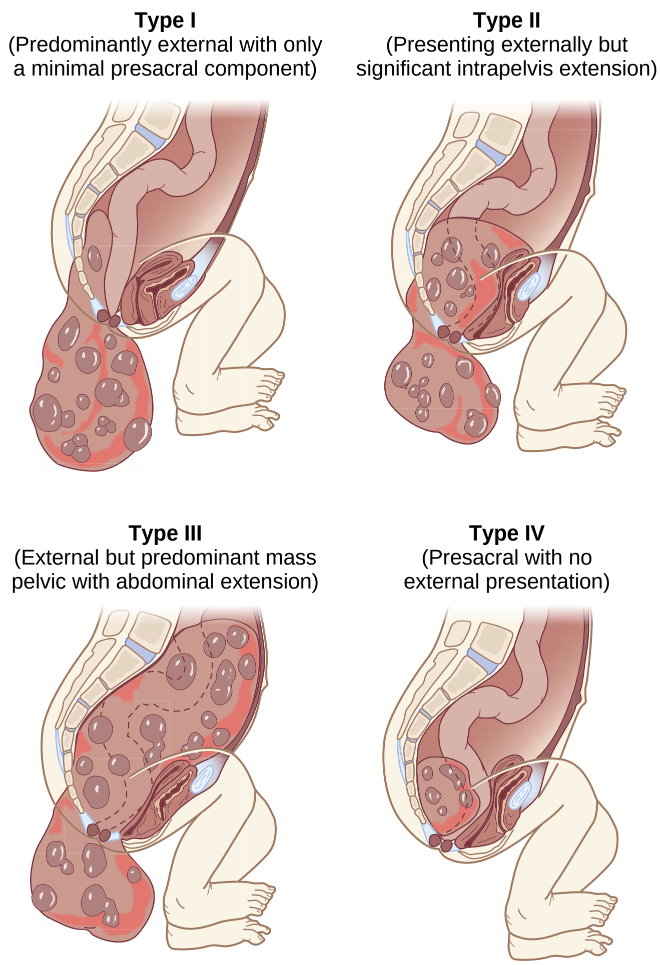

Fig. 63.9 Sacrococcygeal tumors are classified according to their location. Type I tumors are predominantly external (sacrococcygeal) with minimal presacral component; type II tumors present externally but have a significant intrapelvic extension; type III tumors are present externally but the predominant mass is pelvic and extends into the abdomen; type IV tumors are presacral with no external presentation. (Redrawn from Altman RP, Randolph JG, Lilly JR. Sacrococcygeal teratoma: American Academy of Pediatrics Surgical Section Survey-1973. *J Pediatr Surg*. 1974;9:389–398.)

SCTs have been resected in utero (Fig. 63.10) with successful outcomes, but the optimal timing and criteria for fetal intervention is uncertain.[12,198,199,204] Fetal teratoma resection has a high risk for fetal hemorrhage; consequently, intraoperative placement of a venous catheter in a fetal hand, leg, or umbilical cord vein is important for the ability to transfuse compatible blood and crystalloid or rapidly administer resuscitation drugs.

In certain cases, fetal SCT may lead to maternal mirror syndrome, in which maternal physiology mimics the abnormal circulatory physiology of the hydropic fetus.[205] The mother develops hypertension with increased peripheral and pulmonary edema from a hyperdynamic state. Mirror syndrome is a form of severe preeclampsia that may develop in association with fetal hydrops and in most cases necessitates delivery,[206] although platelet levels and liver enzymes typically remain in normal ranges. Maternal mirror syndrome does not normally resolve immediately with correction of the fetal pathophysiology and can result in life-threatening maternal complications.[205,207]

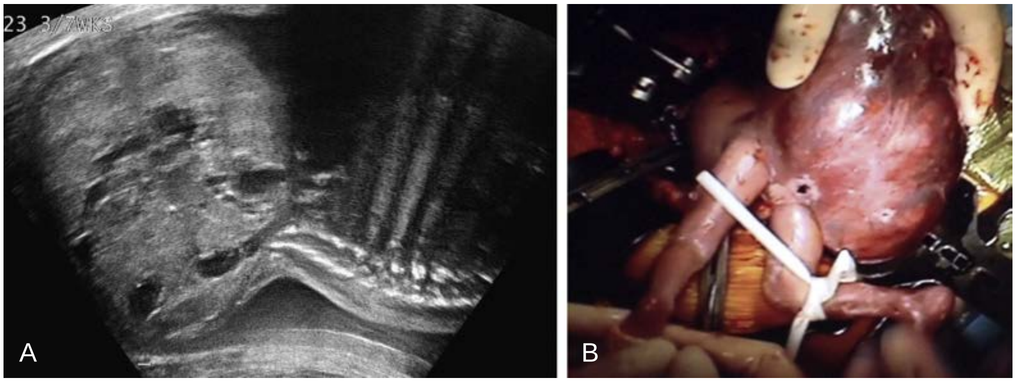

Fig. 63.10 (A) Ultrasound image of fetus with sacrococcygeal teratoma (SCT). Note sacral origin of mass. (B) Fetus with SCT undergoing in utero mass resection. Note tourniquet on left leg placed momentarily before intravenous catheter placement in saphenous vein. (Courtesy Dr. Anita Moon-Grady, Department of Pediatrics, University of California, San Francisco, CA.)

TABLE 63.5 Pathological Classifications and Features of Congenital Pulmonary Airway Malformations

Stocker Classification	Type 0	Type 1	Type 2	Type 3	Type 4
Location	Tracheobronchial	Bronchial/bronchiolar	Bronchiolar	Bronchiolar/alveolar	Distal acinar
Frequency	1%-3%	>65%	10%-15%	5%-8%	10%-15%
Maximal cyst size (cm)	0.5	10.0	2.5	1.5	7
Muscular wall thickness of cysts (μm)	100-500	100-300	50-100	0-50	25-100
Mucous cells	Present	Present in 33% of cases	Absent	Absent	Absent
Cartilage	Present	Present in 5-10% of cases	Absent	Absent	Rare
Skeletal muscle	Absent	Absent	Present in 5% of cases	Absent	Absent
Lobar involvement	All lobes	One lobe in 95% of cases	Usually one lobe	Entire lobe or lung	Usually one lobe
Malignancy risk	No	Bronchioloalveolar carcinoma	No	No	Pleuropulmonary blastoma
Langston classification	Acinar dysplasia	Large-cyst	Small-cyst	Hyperplasia solid/ adenomatoid	
Original CCAM typing		Type I	Type II	Type III	

CCAM, Congenital cystic adenomatoid malformation.

Modified from tables in David M, Lamas-Pinheiro P, Henriques-Coelho T. Prenatal and postnatal management of congenital pulmonary airway malformation. *Neonatology* 2016;110:101–115; and Fowler DJ, Gould SJ. The pathology of congenital lung lesions. *Semin Pediat Surg*. 2015;24:176–182.

CONGENITAL PULMONARY LESIONS

Congenital pulmonary airway malformations (CPAMs), historically known as congenital cystic adenomatoid malformations, are typically benign nonfunctioning pulmonary tumors composed of cystic and solid components normally contained within a single lung lobe.[208] These fetal lesions complicate approximately 1 in 25,000 to 35,000 live births.[209] Other possible fetal abnormalities that require differentiation include bronchopulmonary sequestration, bronchogenic cysts, congenital lobar emphysema, neurogenic cysts, peripheral bronchial atresia, and CDH.[210] CPAM includes five subtypes (Table 63.5) that are based on the presumed tumor development site.[211] Prenatal ultrasonography categorizes lesions as macrocystic (cysts > 5 mm in diameter) or microcystic (cysts < 5 mm in diameter), with microcystic lesions having a more solid or echogenic image.[212] Typically, small lesions regress in the third trimester and can be surgically resected after birth or managed conservatively without surgical intervention.[213] Large lesions can compress the great vessels, create pulmonary hypoplasia, and cause cardiac compression and mediastinal shift that often results in hydrops fetalis. Prognosis depends primarily on size and growth characteristics of the CPAM rather than lesion type.[214] To normalize tumor volume to fetal size, ultrasound measurement of CPAM volume to fetal head circumference ratio (CVR) was evaluated as a predictor of hydrops fetalis and other postnatal outcomes.[214-216] CVR is calculated from the volume of an ellipse using the formula (length × height × width × 0.52)(cm^3)/fetal head circumference (cm).[217] Based on retrospective data from 71 fetuses, a CVR less than 0.56 predicts no adverse postnatal outcome (100% negative predictive value), whereas a CVR greater than 0.56 had a positive predictive value for adverse postnatal outcome of 33%.[215] In addition, a CVR greater than 1.6 is associated with greater risk for hydrops fetalis.[214-216] A recent retrospective analysis of a series of 24 fetuses with a CVR greater than 1.6 found that an abnormal echocardiogram with hydrops was a significant predictor of mortality and need for fetal intervention.[218]

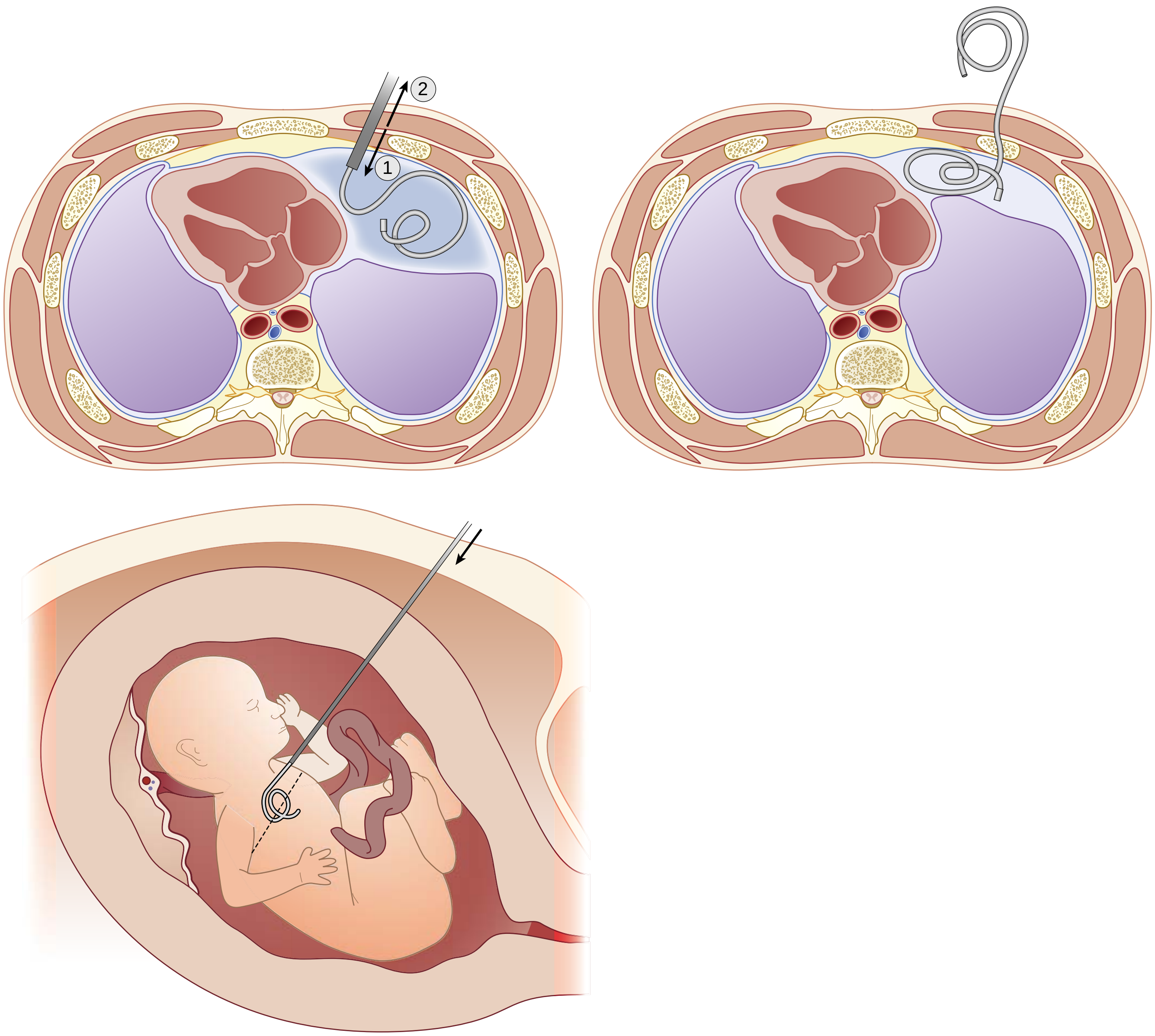

Fig. 63.11 Thoracic shunt insertion (*top left* and *right*) and deployment *(bottom left)*. (From van Mieghem T, Baud D, Devlieger R, et al. Minimally invasive fetal therapy. *Best Pract Res Clin Obstet Gynaecol.* 2012;26:711–725.)

Some lesions regress and leave minimal impact, whereas others grow in size. Patients with CPAM tumors associated with hydrops fetalis have a survival rate of less than 5% without intervention, and early delivery or fetal treatment is indicated in these cases.[219,220] Administration of maternal betamethasone may improve survival in patients with high-risk CPAM.[220,221] Large macrocystic lesions or large pleural effusions can be decompressed in utero by placement of shunt catheters between the cysts and the amniotic cavity (Fig. 63.11). Use of fetal analgesics and muscle relaxants delivered intramuscularly with ultrasound guidance may decrease the fetal stress response and prevent fetal movement during critical portions of the procedure. Shunt placement can prevent or reverse hydrops formation, with definitive resection deferred until after birth.[222] In a retrospective analysis of 75 fetuses undergoing shunt placement for pleural effusion or a macrocystic lung lesion,[223] shunt placement resulted in a decrease in macrocystic lung lesion volume by 55 ± 21% and complete or partial resolution of the pleural effusion in 29% and 71% of fetuses respectively. Hydrops resolved in 83% of fetuses following intervention. Overall neonatal survival was 68%, and correlated with hydrops resolution, GA at birth, a unilateral pleural effusion, and percent reduction in lesion size.[223] Another retrospective study noted a 59% survival rate for fetuses with hydrothorax treated with thoracoamniotic shunts, though repeat procedures were often necessary.[224] In some CPAM lesions, shunts are ineffective because cysts are not in communication with each other, shunts malfunction, or they become displaced. In addition, shunt placement can cause fetal hemorrhage, preterm PROM, or chorioamnionitis.[210] Thoracoamniotic shunt placement has also successfully decompressed large congenital pleural effusions caused by fetal chylothorax that otherwise would result in hydrops fetalis, pulmonary compression, and fetal or neonatal death.[225,226]

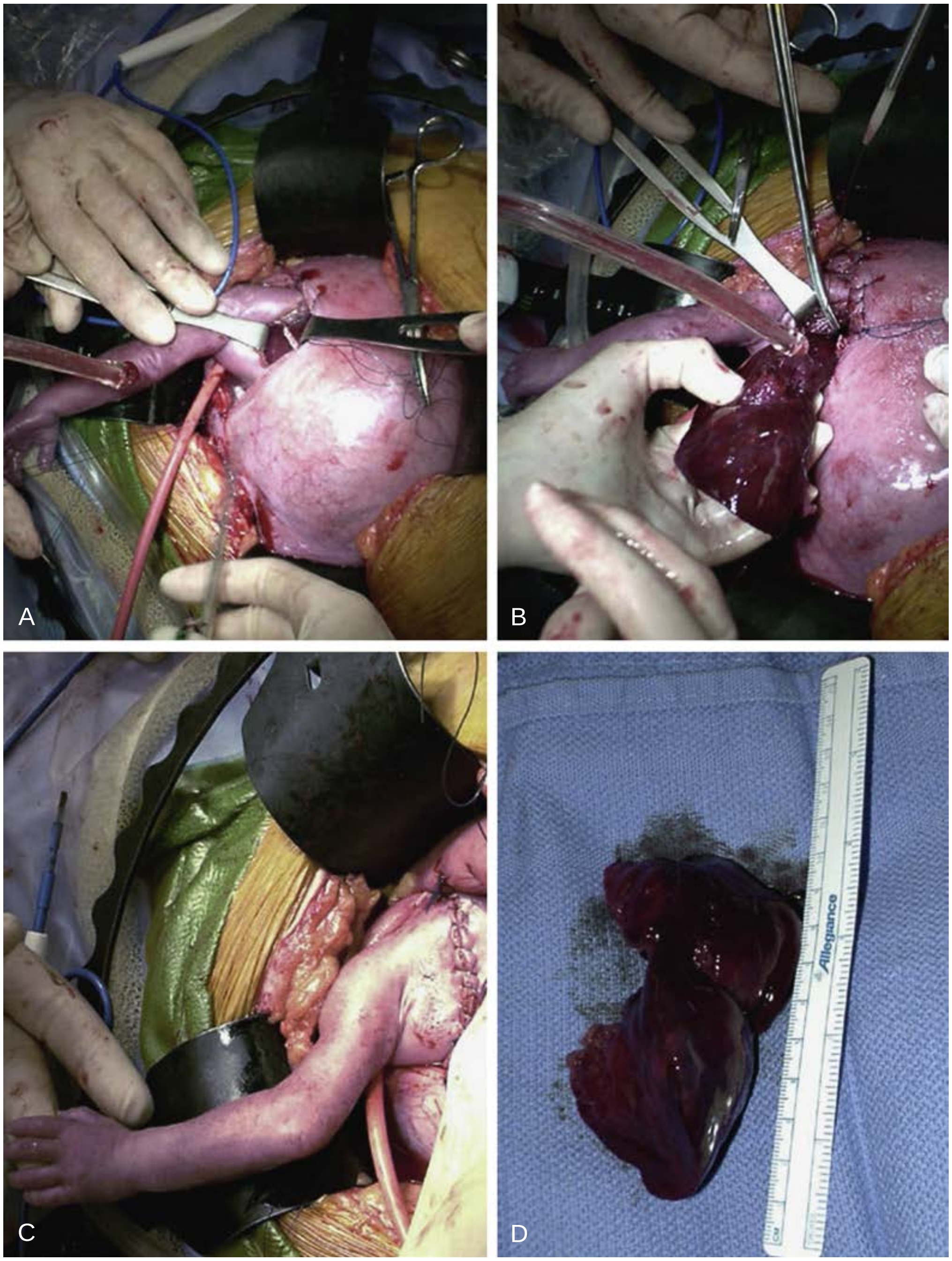

Fig. 63.12 (A) Open resection of fetal congenital pulmonary airway malformation (CPAM) with fetal thoracotomy shown. (B) Resected CPAM mass. (C) Primary closure of fetal thoracotomy. (D) Pathologic specimen of resected CPAM mass. (Courtesy Dr. Anita Moon-Grady, University of California, San Francisco Fetal Treatment Center, San Francisco, CA.)

Some solid or mixed solid/cystic CPAMs inappropriate for shunting can be resected with open fetal lobectomy (Fig. 63.12). Similar to open SCT resection, potential exists for significant fetal hemorrhage and need for in utero fetal resuscitation. Open resection of CPAM lesions associated with hydrops fetalis has resulted in a 30-day postnatal survival rate of 50% to 60%, with tumor resection allowing for compensatory lung growth and resolution of hydrops fetalis.[227]

In some instances, use of an EXIT procedure with fetal thoracotomy, mass resection, and a secured airway before delivery has been a successful approach for tumors with persistent mediastinal compression.[228,229] In a series of nine fetuses with large lung masses (CVR 1.9-3.6 at term) who underwent an EXIT-to-resection procedure, all procedures were successful, with no significant operative complications.[228]

Preoperative Assessment and Counseling

Many considerations for perioperative management of women undergoing maternal-fetal surgery are analogous to those for nonobstetric surgery during pregnancy. Maternal safety is the primary focus when determining a plan that will optimize fetal outcome. All members of the multidisciplinary team should be actively involved in maternal counseling, patient assessment, and perioperative planning. Optimum functioning of a fetal treatment program requires effective communication among the members of a multidisciplinary team, including surgeons, ultrasonographers, maternal fetal medicine physicians, anesthesiologists, nurses, genetic counselors, and social workers. Regularly scheduled multidisciplinary care meetings help ensure coordination of a complete and appropriate perioperative plan, ensure availability of the necessary equipment and personnel at the time of the procedure, and maximize the chance for optimal outcomes for both the mother and fetus. Participation of the anesthesiologist is critical for preoperative maternal assessment to determine whether maternal risk is acceptably low for potential fetal benefit. An understanding of the physiologic changes of pregnancy (for details, see Chapter 62) and their effects on anesthetic management is necessary for appropriate perioperative planning and risk assessment.

Maternal counseling regarding risks and benefits of the procedure should be thorough, unbiased, and convey the most recent outcome and complication data about the planned intervention. For nonurgent procedures, counseling is typically a multi-day process. The team must review the specific condition's natural history, diagnostic limitations, and whether associated anomalies are detected.[230] Discussions should focus on specific implications to the mother, the pregnancy, the fetus, postnatal care, future pregnancies, intermediate and long-term outcomes, and possible adverse outcomes.[6] Patient discussions also should include alternative options such as nonintervention or pregnancy termination if applicable. To provide uniform counseling, all providers should advise the patient regarding information specific to their discipline, but be aware of the general risks and benefits of the fetal process and the proposed procedure (see prior section on "Indications, Procedures, and Outcomes"). Distinctions should be made between interventions that are evidence based, and those that are innovative or experimental. Mothers should be informed about the planned timing and method of delivery, future reproductive implications, and the risk for uterine rupture and need for cesarean delivery with this and all future pregnancies if a hysterotomy is planned. Fertility does not appear to be affected by open fetal surgery, but the risk for uterine rupture or dehiscence before delivery is significant and comparable or even greater than that associated with a prior cesarean delivery performed with a classic incision.[231]

In some situations, consultation with a palliative care provider, clergy, or ethicist may be helpful. In addition, the sequence of events should be outlined in detail so that all questions can be answered. In most circumstances, it is important that the partner or other supporting individuals be included in the counseling process to ensure they have an understanding of the rationale behind the treatment decisions. However, the wishes of the mother assume ultimate priority during pregnancy. Thorough counseling regarding fetuses with pediatric surgical disorders reduces parental anxiety.[232,233] Most mothers prefer specific realistic information provided in an empathetic manner, no matter how dire, and want to be allowed to hope for the best possible outcome.[234] If the fetus is of viable GA, additional counseling is required about the mother's wishes for possible emergent delivery and neonatal resuscitation in the event of unplanned fetal distress unresponsive to in utero treatment. Finally, the fetal intervention should not proceed until the patient has had adequate time to carefully consider all the information and given informed consent.

Intraoperative Management and Considerations

Unlike most surgical procedures performed during pregnancy in which the fetus is merely a bystander (e.g., maternal appendectomy), fetal surgery involves two surgical patients. Consequently, in addition to maternal considerations for anesthetic administration during pregnancy, it is essential to understand the impact of surgery and anesthetic administration on fetal physiology, methods for fetal analgesia and anesthesia, techniques for fetal monitoring, intraoperative anesthetic management, and postoperative care for both mother and fetus.

FETAL PHYSIOLOGY AND MONITORING

During fetal surgery, procedural and pharmacologic interventions can adversely affect fetal physiology by altering uteroplacental or fetoplacental circulation and gas exchange. Appropriate fetal monitoring facilitates early intervention. In addition to the physiologic effects of medications administered to the mother or fetus, a detailed knowledge of both maternal physiology of pregnancy, and fetal cardiovascular, neurologic, and placental physiology provides the basis for optimal fetal care. Uteroplacental and fetoplacental physiology, including uterine perfusion, placental gas exchange, and drug transfer are detailed in Chapter 62, which also discusses the effects of maternal positioning, maternal neuraxial anesthesia, and administration of general anesthesia on the uteroplacental unit.

Fetal cardiac output depends primarily on heart rate.[235] Compared to a neonate, the contractility of the fetal myocardium is decreased secondary to decreased myofibrillar density and it is intolerant of hypocalcemia because of an immature calcium regulatory system.[236] Fetal myocardium is also less compliant than adult myocardium, near the peak of the Frank–Starling ventricular function curve, and fluid-filled lungs also inhibit additional ventricular filling.[236,237] Consequently, modest changes in preload have minimal effect on cardiac output. The normal fetal cardiac output (sum of right and left ventricular output) is in the range of 425 to 550 mL/min/kg throughout gestation.[235]

Fetal blood volume increases during gestation, and approximately twothirds of the fetal-placental blood volume resides within the placenta and the placenta receives about 40% of the fetal cardiac output.[238,239] During the second trimester, fetal blood volume is estimated to be approximately 110 to 160 mL/kg of fetal body weight.[240] After midgestation, fetal blood volume can be estimated based on GA using the equation, estimated fetal blood volume (mL) = $11.2 \times \text{GA} - 209.4$.[241] In the developing fetus, hemoglobin F is the

TABLE 63.6 Coagulation Screening Tests in Fetuses and Full-Term Newborns

	GESTATIONAL AGE (WEEKS)			
Test*	19-23	24-29	30-38	Newborns
PT (s)	32.5 (19-45)	32.2 (19-44)	22.6 (16-30)	16.7 (12-24)
PT (INR)	6.4 (1.7-11.1)	6.2 (2.1-10.6)	3.0 (1.5-5.0)	1.7 (0.9-2.7)
aPTT (s)	169 (83-250)	154.0 (87-210)	104.8 (76-128)	44.3 (35-52)
TCT (s)	34.2 (24-44)	26.2 (24-28)	21.4 (17-23)	20.4 (15-25)

*Normal values for coagulation tests determined from umbilical cord sampling. Values are the mean, followed in parentheses by the lower and upper boundaries, including 95% of the population studied.

aPTT, Activated partial prothrombin time; *INR,* International normalized ratio; *PT*, Prothrombin time; *s*, Seconds; *TCT,* Thrombin clotting time.

Modified from Reverdiau-Moalic P, Delahousse B, Body G, et al. Evolution of blood coagulation activators and inhibitors in the healthy human fetus. *Blood*. 1996;88:900–906.

primary oxygen carrier. Beginning at 32 weeks' gestation there is a gradual shift toward adult hemoglobin synthesis.[242] Mean fetal Hb levels increase linearly from 11 g/dL at 17 weeks gestation to 18 g/dL in a term neonate.[243,244]

Fetal lung epithelium produces more than 100 mL/kg/day of fluid that fills the lungs and facilitates appropriate pulmonary growth and development. Excess lung fluid exits the trachea and is either swallowed or flows into the amniotic fluid. Although fetal hepatic enzymes are less functional than those of adults, most drugs still undergo metabolism and the umbilical circulation provides initial hepatic metabolism (first-pass metabolism) before medications reach the fetal brain or heart. Although fetal liver function is immature, coagulation factors are synthesized independent of the maternal circulation and do not cross the placenta. The serum concentrations of these factors increase with GA (Table 63.6),[245] but fetal clot formation in response to tissue injury is decreased in contrast to that in adults throughout gestation and the first 6 months of life.[246] Platelets first appear at 5 weeks gestation and increase in number with time, reaching a mean of 150×10^9/L by the end of the first trimester of pregnancy and values reaching normal adult range by 22 weeks gestation.[247]

During open procedures, the fetal circulation and flow distribution can be severely impaired by fetal manipulation or direct compression of the umbilical cord, inferior vena cava, or mediastinum. Increased uterine activity, maternal hypotension, and significant maternal hypocarbia can all decrease uteroplacental perfusion. Fetal heart rate (FHR) monitoring is important during both minimally invasive and open procedures. During IUT, the transfusion needle can lacerate umbilical vessels with unanticipated fetal movement, and use of laser therapy for TTTS can disrupt surface placental vessels critical to fetal blood flow. During labor, FHR monitoring with external Doppler or a fetal scalp electrode is commonly employed to assess fetal well-being, but during fetal procedures, echocardiography, pulse oximetry, and ultrasound imaging of umbilical artery flow are the primary methods for fetal assessment. After exposure of the fetal head during an EXIT procedure, placement of an Hb saturation monitor and insertion of a fetal scalp electrode have both been used successfully for FHR monitoring.[11,248] It remains unclear whether fetal oximetry or heart rate monitoring is more sensitive to decreased umbilical-fetal blood flow. In a fetal lamb model examining the effects of umbilical cord compression, Hb desaturation was detected by fetal pulse oximetry before the onset of bradycardia.[249] However, FHR deceleration has been shown to precede fetal Hb desaturation with use of fetal pulse oximetry monitoring during labor.[250]

Intraoperative ultrasonography allows imaging of FHR, cardiac contractility, and cardiac filling, as well as Doppler assessment of flow in the ductus arteriosus and umbilical artery flow. Both absent and reversed umbilical artery diastolic flow are associated with increased perinatal morbidity and mortality.[251] In many cases, ultrasonography assessment of fetal well-being can be only intermittent. This is because ultrasonography may be periodically required to guide the intervention or the probe placement can interfere with the surgical procedure.

When intraoperative monitoring detects depression of fetal hemodynamics, steps should promptly be undertaken to improve uterine perfusion, ensure the uteroplacental interface is intact, and relieve any compression of the umbilical cord or placenta. These steps may include administration of medications to increase maternal blood pressure, cardiac output, and uterine relaxation. In some cases, administration of resuscitation medications directly to the fetus may be needed, or if previously determined to be viable ex utero fetal resuscitation may be necessary.

In utero, the fetus is unable to thermoregulate and depends on maternal body temperature secondary to placental circulation and surrounding amniotic fluid. Induction of general anesthesia, surgical exposure, and hysterotomy can reduce fetal temperature dramatically both directly and secondarily if maternal core temperature drops significantly. Fetal sheep studies demonstrate the fetus is unable to generate heat through thermogenesis[252] and decreases in sheep fetal temperature can lead to tachycardia and hypertension in utero. In contrast, human reports associate maternal/fetal hypothermia with fetal bradycardia.[253,254] Consequently, maintenance of maternal euthermia with use of forced air warming likely improves fetal well-being during minimally invasive procedures. During open fetal surgery, use of warmed fluid for intrauterine irrigation and monitoring of both maternal core and amniotic fluid temperatures are also important.

FETAL ANESTHESIA, ANALGESIA, AND PAIN PERCEPTION

The capability of the fetus to perceive pain remains controversial. The fetus exhibits pituitary-adrenal, sympathoadrenal, and circulatory stress responses to noxious stimuli as early as 16 to 18 weeks gestation.[255-258] Although invasive fetal procedures elicit a stress response,[30,259,260] this response is mediated at the level of the spinal cord, brainstem, and/or basal ganglia and does not necessarily correlate with conscious cortical perception of pain.[261] Administration of opioids in preterm neonates blunts hormonal responses to surgery, including changes in plasma adrenaline, noradrenaline, glucagon, aldosterone, corticosterone, glucose, and lactate.[262] Providing adequate anesthesia and analgesia is associated with both attenuation of the deleterious effects and improved outcomes.[259] Stress responses secondary to invasive fetal procedures are blunted with opioid administration,[30] but reduction of plasma stress hormone levels is not necessarily evidence of adequate analgesia.[261]

Pressure, temperature, and vibration sensory nerve terminals develop in human skin between 6 and 10 weeks gestation.[263] Skin nerve terminals required for peripheral sensory nociception likely develop between 10 and 17 weeks gestation.[264] Noxious stimuli follow a reflex arc of afferent fibers that synapse on spinal cord interneurons, which then synapse with motor neurons. A fetus can reflexively withdraw from a noxious stimulus by 19 weeks GA without input from the cerebral cortex.[265,266]

The perception of pain requires not only intact neural pathways from the periphery to the primary sensory cortex, but also higher cortical structures.[266] Thalamocortical circuits, thalamic pain fibers likely reach the somatosensory cortex at 24 to 30 weeks gestation.[258,266] Thalamic projections reach the visual subplate at 20 to 22 weeks,[267] the visual cortex at 23 to 27 weeks,[268] and the auditory cortical plate at about 26 to 28 weeks gestation.[269] However, fetuses are unlikely to experience pain before 24 weeks gestation because the cortex requires additional growth, remodeling, and development to establish the extensive neural network of pathways to other central nervous system structures.

This timeline is supported by electroencephalographic (EEG) studies. Cortical EEG activity is present only 2% of the time in fetuses at 24 weeks gestation and increases to being present 80% of the time with EEG patterns becoming more distinct by 34 weeks gestation.[270]

Both the long-term impact of untreated fetal stress and the timing of fetal pain perception remain unknown. Given this uncertainty and the more than 35-year history of safe anesthetic administration in neonates and fetuses undergoing invasive procedures,[271-273] analgesia should be provided during fetal surgery.[258,274] In addition to blunting pain, administration of fetal analgesia helps to prevent fetal movement and inhibit the circulatory stress response.

Opioid analgesics can be transferred to the fetus by maternal administration or direct fetal intramuscular or intravenous umbilical cord administration using ultrasound guidance. For most invasive procedures causing noxious fetal stimulation, fetal intramuscular administration of fentanyl 10 to 20 μg/kg (or other opioid in equivalent dosing) is used to provide analgesia immediately before the intervention.[30,183,258] This can be achieved percutaneously using ultrasound guidance or under direct vision when a hysterotomy is performed. Some physicians administer prophylactic intramuscular atropine 20 μg/kg with opioids to minimize the risk for fetal bradycardia.[275,276] Fetal movement can be prevented by intramuscular or umbilical vessel administration of a muscle relaxant such as rocuronium (intramuscular 2.5 mg/kg or intravenous 1.0 mg/kg) or vecuronium (intramuscular 0.25 mg/kg or intravenous 0.1 mg/kg) using ultrasound guidance.[183,258] The onset of fetal paralysis varies with the specific drug and dose, but typically occurs in 2 to 5 minutes, with an approximate duration of 1 to 2 hours.[277] In many instances, opioid, anticholinergic, and muscle relaxant are combined in a single injection. Maternal administration and placental transfer of intravenous remifentanil provides adequate fetal immobility during fetoscopic interventions that involve only the umbilical cord or placenta.[278]

For open fetal procedures, placental transfer of maternally administered general anesthesia with volatile anesthetics provides fetal anesthesia. These anesthetics readily transfer across the placenta, with fetal concentration and the fetal-to-maternal (F/M) ratio depending on both the maternal inspired anesthetic concentration and the duration of maternal anesthetic administration. In human studies of anesthetic levels at the time of cesarean delivery (~10-minute duration of general anesthesia), isoflurane has an F/M ratio of approximately 0.7.[279] Although placental transfer of desflurane and sevoflurane may be similar, published human F/M data are not currently available in the literature. Nitrous oxide has an F/M ratio of 0.83 after only 3 minutes of administration.[280]

High levels of volatile anesthetic can depress fetal myocardium and lead to increasing fetal acidosis.[281] In animal models, volatile anesthetic concentrations often employed for uterine relaxation (>2 minimum alveolar concentration [MAC]) lead to significant reductions in maternal cardiac output with associated decrease in uterine perfusion up to 30%.[282] A retrospective analysis of echocardiographic data from clinical cases of open fetal surgery and EXIT procedures reveals a moderate-to-severe left ventricular systolic fetal cardiac dysfunction with use of high concentrations of desflurane.[283] In addition, case reports have described epileptiform EEG activity and generalized tonic-clonic seizures in both adults and children exposed to high levels of sevoflurane.[284] Seizure activity has also been attributed to high-dose sevoflurane during an open fetal procedure.[285] Therefore, high concentrations of volatile anesthetic administration, while useful for maternal uterine relaxation, may not be the optimal anesthetic for the fetus despite years of successful use. Consequently, a reduced level of volatile anesthetic (1.0-1.5 MAC) is combined with remifentanil and propofol infusions for open fetal surgery at some institutions.[283,286] Remifentanil has significant placental transfer and prevents fetal movement during TTTS laser photocoagulation therapy.[278,287] Some prefer to administer maternal remifentanil and nitroglycerin as part of the anesthetic for open fetal or EXIT procedures to decrease the amount of volatile anesthetic.[275,278,288] Currently, no evidence indicates that any one anesthetic method provides an improved fetal or maternal outcome as long as appropriate uterine quiescence is maintained.

Anesthetic neurotoxicity of the developing brain is a concern for all providers administering anesthetic agents for fetal procedures. In animal models, anesthetics affect neonatal brain development and create histologic changes, as well as learning and memory deficits.[289,290] Recent nonhuman primate studies found repeated exposures to clinically-relevant concentrations of sevoflurane during infancy resulted in neurocognitive impairment and behavioral changes at 1 to 2 years of age.[291,292] However, specific long-term effects of anesthetics on human brain function in neonates or fetuses are currently inconclusive. Two prospective trials examining the effect of a short anesthetic exposure have suggested no long-term neurodevelopmental consequences.[293-295] In 2016, the U.S. Food and Drug Administration advisory committee issued a warning that "repeated or lengthy use of general anesthetic and sedation drugs during surgeries or procedures in children younger than 3 years or in pregnant women during their third trimester may affect the development of children's brains."[296]

Limited data about anesthetic exposure in the fetal population exists. One study looked retrospectively at the use of general anesthesia for cesarean section and the incidence of learning disabilities at age 5 and found no correlation.[297] To date, no studies have examined the neurocognitive consequences of midgestation fetal anesthesia. No general anesthetic agent is known to be superior to another, and whether exposure to general anesthetics during gestation compared to the neonatal period is more beneficial or harmful is unknown. In an effort to systematically collect current data, an international registry has been established for the purpose of assessing the long-term neurodevelopmental outcomes of fetal surgery patients (Clinical Trials.gov identifier NCT02591745).[298] In addition, whether in utero exposure to anesthetic drugs compared with postnatal exposure has any effect on neurocognitive outcome is not known and makes data collection and analysis challenging, as many patients undergoing fetal procedures are re-exposed to general anesthesia during infancy and childhood.[299]

MANAGEMENT OF MINIMALLY INVASIVE PROCEDURES

The same considerations that apply to nonobstetric surgery during pregnancy should be followed for fetal procedures. For most fetal image-guided surgery procedures (see Table 63.1), use of monitored anesthetic care with local anesthesia infiltration into the superficial tissues and abdominal wall provides an adequate level of maternal comfort. Administration of additional opioid, benzodiazepine, or other anesthetic agent can be used for maternal analgesia and anxiolysis. Use of supplemental anesthetic drugs will also decrease the likelihood of fetal movement via placental transfer. Local anesthetic infiltration can also be used for fetoscopic procedures, which typically employ endoscope trocars that are only 2 to 5 mm in diameter.[300] Neuraxial techniques can be beneficial and preferable when multiple insertion sites are required; maternal immobility must be ensured; a mini-laparotomy must be performed; or concern exists about adequate patient comfort or cooperation during the procedure. General anesthesia is rarely necessary for percutaneous procedures unless placental location and fetal orientation present potential technical difficulty or uterine exteriorization is needed, as is the case with fetoscopic MMC repair.[301]

Although maternal intravenous fluid administration should be guided by standard intraoperative requirements, use of significant amounts of pressurized uterine crystalloid irrigation into the amniotic cavity during fetoscopic surgery should be avoided because it has resulted in maternal pulmonary edema.[302]

In cases of IUT, cord blood sampling, or thoracic shunt placement, fetal movement may displace the needle or catheter and result in trauma, bleeding, or compromise of the umbilical circulation. In one study of fetoscopic surgery, maternal administration of remifentanil (0.1 μg/kg/min) reduced fetal movement and improved operating conditions compared with maternal administration of diazepam.[278] Although maternally administered opioids and benzodiazepines can reduce fetal motion,[123] they do not guarantee immobility for procedures directly involving the fetus. Fetal immobility can be safely achieved with direct fetal intramuscular or umbilical venous administration of muscle relaxant. For invasive fetal procedures that involve potentially noxious stimulation to the fetus, such as shunt placement, endoscopic MMC repair, or fetal cardiac interventions, an opioid should be administered to the fetus (e.g., intramuscular fentanyl 10-20 μg/kg). When general anesthesia is employed, placental transfer of a volatile anesthetic provides significant fetal anesthesia and decreases fetal movement, but supplemental opioids should also be administered if fetal analgesia is required.

Weight-based unit doses of atropine (20 μg/kg) and epinephrine (10 μg/kg) should be immediately available in individually labeled syringes for direct fetal administration by the surgeon under ultrasonography guidance. These medications require sterile transfer to the surgical field preoperatively, meticulous labeling, and accurate dosing before commencement of the procedure. The surgeon can administer the indicated medication by a variety of routes (intramuscular, intravenous, or intracardiac) depending on the procedure and urgency of the situation. If gestational development is compatible with extrauterine life, the obstetric team should be prepared to perform an emergency cesarean delivery if fetal bradycardia persists despite efforts to resuscitate in utero. The anesthesiologist should be prepared to emergently provide maternal general anesthesia and assist with neonatal resuscitation.

MANAGEMENT OF OPEN PROCEDURES

Although most women undergo cesarean delivery with neuraxial anesthesia, general anesthesia is primarily employed for fetal surgery requiring a hysterotomy. Unlike minimally invasive fetal procedures, open fetal surgery requires profound uterine relaxation and often entails additional fetal monitoring beyond intermittent ultrasonography. Open surgery involves more surgical stimulation, hemodynamic perturbation, and risk for fetal compromise and requires direct administration of drugs to the fetus. Compared to minimally invasive procedures, open fetal procedures present greater risk to the mother. The anesthesiologist and other team members should be prepared for significant maternal and fetal blood loss, the need for maternal and fetal resuscitation, and possible emergent delivery. A volatile anesthetic is commonly administered to provide maternal and fetal anesthesia, as well as uterine relaxation, which may require a concentration of more than 2 MAC.[303] In an effort to decrease the fetal cardiac dysfunction and abnormal umbilical artery flow associated with high levels of volatile anesthetics, more recent techniques combine 1

BOX 63.2 Perioperative Considerations for Open Fetal Surgery*

Preoperative

- Complete maternal history and physical examination
- Complete fetal workup to exclude other anomalies
- Imaging studies to determine fetal lesion and placental location and estimated weight
- Maternal counseling by multidisciplinary team and presurgical team meeting
- Planning for emergent delivery depending on viability
- High lumbar epidural placement for postoperative analgesia with test dose before use
- Prophylactic premedications: nonparticulate antacid (aspiration) and rectal indomethacin (tocolysis)
- Blood products typed and crossmatched for potential maternal and fetal transfusion; fetal blood should be type O-negative, leukocyte depleted, irradiated, cytomegalovirus negative, and crossmatched against the mother
- Transfer of weight-based fetal resuscitation drugs to scrub nurse in unit doses
- Sequential compression devices on lower extremities for thrombosis prophylaxis
- Initiation of forced air warmer to maintain maternal normothermia following induction

Intraoperative

- Left uterine displacement and standard monitors
- Fetal assessment prior to maternal induction
- Preoxygenation for 3 min before induction
- Rapid sequence induction and intubation
- Maintain maternal FiO_2 greater than 50% and end-tidal carbon dioxide 28-32 mm Hg
- Ultrasonography examination to determine fetal position and placental location
- Urinary catheter placed; additional large-bore intravenous access obtained; possible arterial line
- Prophylactic antibiotics administered
- Maternal blood pressure maintained with IV phenylephrine, ephedrine, and/or glycopyrrolate; typical goal is to maintain mean arterial pressure within 10% of preinduction baseline with appropriate heart rate
- After skin incision, increased concentrations of volatile anesthetic (2-3 MAC) started to obtain uterine relaxation; alternatively, volatile anesthetic (1.0-1.5 MAC) may be combined with IV propofol and remifentanil
- Consider increasing vapor or adding IV nitroglycerin if uterine tone remains increased
- Placement of fetal monitors if needed (e.g., fetal pulse oximeter, intrauterine temperature probe)
- IM fetal administration of opioid and neuromuscular blocking agent; an anticholinergic also may be administered with the opioid
- Placement of fetal IV access device if significant fetal blood loss anticipated
- External irrigation of fetus with warmed saline as needed
- Crystalloid restriction to less than 2 L to reduce risk for maternal pulmonary edema; consider colloid administration
- IV loading dose of magnesium sulfate once uterine closure begins
- Discontinue volatile agents once magnesium sulfate load is complete
- Activate epidural for postoperative analgesia
- Administer maternal anesthetics as needed
- Monitor maternal neuromuscular blockade carefully because of possible prolongation from magnesium sulfate
- Extubate trachea when patient is fully awake

Early Postoperative Considerations

- Complete postoperative debrief
- Continue tocolytic therapy
- Patient-controlled epidural analgesia
- Monitor uterine activity and fetal heart rate
- Ongoing periodic fetal evaluation

*This summary may need to be modified depending on the type of open fetal surgery and patient comorbidities.
FiO_2, Fraction of inspired oxygen; *IM,* Intramuscular; *IV,* Intravenous; *MAC,* Minimum alveolar concentration.
Modified from Ferschl M, Ball R, Lee H, et al. Anesthesia for in utero repair of myelomeningocele. *Anesthesiology.* 2013;118:1211–1223.

to 1.5 MAC of volatile anesthetic with infusions of remifentanil and propofol.[283,286,304] The perioperative considerations for open fetal surgery are detailed in Box 63.2.

Weight-based unit doses of medications for fetal analgesia and muscle relaxation as previously detailed in the section on "Fetal Anesthesia, Analgesia, and Pain Perception" should be available for administration by the surgical team. In addition, resuscitation medications (atropine 20 μg/kg, epinephrine 10 μg/kg, and crystalloid 10 mL/kg) should be prepared preoperatively in sterile weight-based unit doses for emergent treatment of intraoperative fetal hemodynamic compromise. Crossmatched blood should be available for maternal transfusion. For procedures with a high risk of fetal hemorrhage, appropriate blood for fetal transfusion (i.e., O-negative, cytomegalovirus-negative, irradiated, leukocyte-depleted, maternally crossmatched) should be readily available.

Uterine tocolytics (i.e., indomethacin) should be administered to the mother preoperatively. An epidural catheter is placed preoperatively for administration of postoperative analgesia. FHR is assessed and baseline cardiac echocardiography and ultrasound imaging of umbilical cord flow characteristics are performed before anesthetic induction and are intermittently reevaluated throughout the initial period of anesthetic administration to assess the effect of the maternal positioning, anesthetic administration, and any maternal hemodynamic changes on the fetus. Absent or reversed umbilical artery diastolic flow intraoperatively may be an early sign of fetal distress.[304] Additional monitoring sites include fetal cardiac systolic function and flow across the ductus arteriosus.[283,305,306] The gravid uterus is displaced leftward and general anesthesia is induced with a rapid sequence technique identical to patients undergoing nonobstetric surgery during pregnancy.

After anesthetic induction and before maternal skin incision, conventional concentrations of anesthetics are administered to the mother. Ventilation is controlled to maintain eucapnia (end-tidal carbon dioxide levels of 28-32 mm Hg). Fetal condition and fetal and placental locations are reassessed by ultrasound. If an intraarterial catheter is not placed, a maternal arm is positioned to remain accessible in case unexpected invasive pressure monitoring is required (e.g., maternal hemodynamic instability). A large-bore venous catheter is placed for treatment of unexpected significant hemorrhage. Intravenous fluids administered to the mother are minimized (<2 L) to decrease the risk for perioperative pulmonary edema associated with the use of tocolytics, such as magnesium sulfate or administration of large doses of nitroglycerine during fetal surgery.[307] Some fetal surgery teams are more restrictive with intraoperative fluid administration (<500 mL), but no clinical trials have demonstrated benefit of severe intravenous fluid restriction in this setting.

Typical maternal hemodynamic goals include maintaining systolic arterial blood pressure within 10% of baseline values and mean arterial pressure greater than 65 mm Hg with appropriate maternal heart rate. Phenylephrine administration can be used to treat maternal hypotension with minimal changes in the fetal acid-base status.[308] Bolus administration of ephedrine or glycopyrrolate can assist in maintaining maternal heart rate and cardiac output.[309] Administration of a nondepolarizing muscle relaxant is usually unnecessary but may be used to improve operative conditions. If it is used, appropriate neuromuscular monitoring should be employed to carefully assess neuromuscular function with appropriate reversal of blockade before tracheal extubation, particularly with administration of magnesium sulfate, which potentiates neuromuscular blockade.

Before skin incision, the inspired concentration of volatile anesthetic is increased, and before uterine incision, the volatile anesthetic end-tidal concentration is further increased (≥ 2 MAC) to provide profound uterine relaxation. If uterine relaxation is assessed to be inadequate by appearance of contractions or palpation, administration of additional volatile agent (up to 3 MAC) or intravenous nitroglycerin as an infusion or in small boluses (50-200 µg) is useful to decrease uterine tone.[183]

An alternative technique, as mentioned earlier, relies on supplemental intravenous anesthesia. Administration of intravenous propofol and/or remifentanil with volatile anesthetic at 1.5 MAC may prevent fetal ventricular dysfunction as well as improve maternal hemodynamics, uterine blood flow, and fetal acid-base status, while reducing fetal exposure to high levels of volatile agents and providing adequate uterine relaxation.[283,286] A sheep model of this anesthetic regimen notes significantly lower fetal plasma concentrations of propofol compared to maternal concentrations.[288] Remifentanil pharmacokinetics in midgestation during fetal surgery have been shown to be similar to the general population,[310] and remifentanil is known to readily cross from maternal to fetal circulation.[287]

For rare patients with contraindications to volatile anesthetics (e.g., malignant hyperthermia), a neuraxial technique in conjunction with intravenous administration of nitroglycerin in doses up to 20 µg/kg/min has been used successfully for an EXIT procedure.[288] This technique may increase the risk for maternal pulmonary edema secondary to the large doses of nitroglycerin and therefore should be reserved for cases with a particular need. Currently, no specific anesthetic technique demonstrates significant improvement in fetal outcome.

Periodic ultrasonography is used to assess FHR and fetal cardiac function. In some open fetal procedures, pulse oximetry or additional direct fetal monitoring can be employed after the hysterotomy is performed, as previously discussed in the section on fetal physiology and monitoring. Rarely, when uncertainty exists regarding fetal condition, umbilical cord blood gas measurements can be obtained. As described in the prior section on fetal anesthesia, analgesia, and pain perception, an opioid and a muscle relaxant can be administered to the fetus intramuscularly either before uterine incision with ultrasound guidance or under direct vision after uterine incision. Intramuscular atropine also can be administered concurrently to reduce opioid-induced fetal bradycardia.

After uterine exposure and ultrasound placental mapping, a small hysterotomy is created away from the placenta. A stapling device with absorbable lactomer staples is used to extend the incision. The staples prevent hemorrhage from the relaxed uterus and seal the amniotic membranes to the uterine endometrium. Uterine blood loss can be rapid and difficult to estimate. Vigilant observation of the surgical field, close communication with the surgeon, and careful maternal monitoring are essential to avoid occult hemorrhage. Lost amniotic fluid is replaced with warmed crystalloid to bathe the exposed fetus. Intrauterine temperature is closely monitored to prevent hypothermia and associated fetal circulatory compromise.[253,254]

For fetal mass resections or other open procedures with high risk for significant fetal blood loss, an intravenous catheter should be placed in a fetal limb for blood and fluid administration by the anesthesiologist. All blood or fluids transfused to the fetus should be warmed. In urgent situations, fluids can be transfused directly into the umbilical vein through catheter access obtained in the operative field if a fetal peripheral intravenous line is not available.

In the rare event of maternal hemodynamic collapse, if maternal resuscitation has been unsuccessful in restoring adequate maternal hemodynamics after 4 minutes, the fetus should be delivered emergently to relieve aortocaval compression, improve maternal resuscitation efforts, and increase the chance for maternal survival.[311] A neonatologist and neonatal resuscitation team should be readily available in case of emergency delivery. Newborn resuscitation should proceed according to the current recommended guidelines.[312]

After completion of the fetal procedure, an initial loading dose of intravenous magnesium sulfate (4-6 g) is typically administered over 20 minutes during uterine closure to prevent uterine contractions.[313] After the bolus, an intravenous infusion of magnesium sulfate (1-2 g/h) is initiated to maintain uterine quiescence into the postoperative period. The inspired concentration of volatile anesthetic is significantly decreased or discontinued after the magnesium sulfate bolus is complete. After an epidural test dose, epidural anesthesia is initiated. Maternal anesthesia is maintained with epidural anesthesia and supplemented by administration of intravenous opioid, inhaled anesthetics, and/or intravenous propofol. The mother's trachea is extubated after she awakens and after confirming adequate neuromuscular recovery and hemodynamic stability.

Postoperative Management and Considerations

In addition to postoperative concerns associated with a cesarean delivery (i.e., pain management, prevention of venous thromboembolism, monitoring for hemorrhage, avoiding wound infection), postoperative care of patients undergoing fetal surgery also focuses on tocolysis and fetal monitoring. For minimally invasive procedures such as cordocentesis or IUT, tocolysis is typically not required. For more invasive percutaneous procedures (e.g., shunt placement, fetoscopic techniques), preoperative prophylactic tocolytic agents such as indomethacin may be administered. Additional tocolytic drugs are rarely required in the postoperative period.

After open fetal surgery, patients frequently experience early uterine contractions and require continuous uterine monitoring for 2 or 3 days. Management of postoperative preterm labor after fetal surgery is a challenge and has led to significant fetal morbidity from preterm delivery. Magnesium sulfate infusions initiated intraoperatively are continued for approximately 24 hours or more postoperatively. Additional tocolytic agents (e.g., indomethacin, terbutaline, nifedipine) are often necessary. Administration of indomethacin requires periodic fetal echocardiography monitoring because premature closure of the ductus arteriosus is a known complication of therapy. In Europe, atosiban, an oxytocin receptor antagonist, has been shown to provide efficacious tocolysis following open fetal MMC repair with less maternal side effects.[314] Atosiban is currently not available for use in the United States.

The fetus is evaluated postoperatively by ultrasonography. Continuous FHR monitoring is used in the postoperative period. The duration of monitoring is based on GA and fetal condition. Potential fetal morbidities includes infection, heart failure, intracranial hemorrhage, oligohydramnios, and fetal demise. If maternal pulmonary edema is suspected, a chest radiograph should be obtained and critical care admission may be required.

For minimally invasive procedures, satisfactory postoperative analgesia is typically achieved by administration of oral opioid-based pain medications and acetaminophen. For open procedures, postoperative epidural analgesia can initially be provided for a day or two using a dilute solution of local anesthetic and opioid. Intravenous opioids administered with a patient-controlled device can be used in place of an epidural or after the epidural is discontinued. Use of opioids can decrease FHR variability[315] and create some difficulty in FHR tracing interpretation. Inadequate postoperative pain control can increase plasma oxytocin levels and increase the risk for preterm labor.[316]

After open fetal procedures, patients are at high risk for PROM, preterm labor, infection, and uterine rupture.[4] In addition to these risks, periodic assessment of fetal well-being, growth, and integrity of the pregnancy necessitate the mother remain near the fetal treatment institution for the first few weeks after the procedure. The possibility of preterm delivery may necessitate a course of steroids to improve fetal lung maturity. After open procedures, cesarean delivery is often planned for 37 weeks gestation but may be required earlier with the onset of preterm labor. The recent hysterotomy increases the chance for uterine rupture and associated need for emergent cesarean delivery.[317]

Management of Ex Utero Intrapartum Treatment Procedure

Although the initial purpose of the EXIT procedure was to provide a controlled and stable means to remove the tracheal occlusive device previously placed in the fetal airway for in utero treatment of CDH, the EXIT procedure has expanded into a technique used for a variety of other fetal disorders (Table 63.7).[10,12,275,286,318] The EXIT procedure allows the fetus to remain supported by the placental unit with adequate oxygenation and perfusion while airway, surgical repair, and resuscitation interventions are performed in a controlled manner. The procedure has been used successfully to treat fetuses requiring intrathoracic mass resection, as a bridge to ECMO, and in separation of conjoined twins.

TABLE 63.7 Indications for the Ex Utero Intrapartum Therapy Procedure

Procedure	Reason	Fetal Malformation
EXIT-to-Airway	Intrinsic compression	Congenital high airway obstruction syndrome Laryngeal atresia/stenosis Tracheal atresia/stenosis Laryngeal web/cyst
	Extrinsic compression	Cervical teratoma Cystic hygroma Epulis Goiter Hemangioma Lymphangioma Neuroblastoma
	Iatrogenic	Removal of tracheal occlusive device placed to treat CDH
	Craniofacial	Severe micrognathia Severe retrognathia
EXIT-to-Resection	Intrathoracic airway compromise or Mediastinal compression	Bronchogenic cysts Bronchopulmonary sequestration Congenital pulmonary airway malformation Mediastinal mass Thoracic tumor
EXIT-to-ECMO	Cardiopulmonary compromise	Aortic stenosis with intact/restrictive atrial septum CDH with severe pulmonary compromise Hypoplastic left heart syndrome with intact/restrictive atrial septum
EXIT-to-Separation	Prolonged surgical compromise	Conjoined twins

CDH, Congenital diaphragmatic hernia.
Modified from Hoagland MA, Chatterjee D. Anesthesia for fetal surgery. *Paediatr Aneasth*. 2017;27:346–357.

The primary goals of the EXIT procedure are to maintain a prolonged state of uterine relaxation, delay placental separation, and sustain placental-fetal perfusion. Similar to open fetal surgery, EXIT procedures are frequently performed under general anesthesia, employing high concentrations (≥2 MAC) of volatile anesthetic to ensure uterine relaxation. Neuraxial anesthesia in combination with remifentanil and nitroglycerin has been used successfully.[288,319-321] Multiple reviews of the anesthesia, surgical, and obstetric considerations for the EXIT procedure have been published.[10,11,275,286,322] The overall preoperative and intraoperative approach for anesthetic management is similar to that previously described for the preoperative and intraoperative portions of open fetal surgery (see Box 63.2).

The primary difference occurs after delivery of the fetus, when uterine relaxation is no longer required. Thus, after delivery of the neonate, anesthetic management becomes similar to management of a cesarean delivery under general anesthesia.

A detailed multidisciplinary meeting is extremely valuable before the start of the EXIT procedure. It is essential to ensure that all required supplies for fetal monitoring; airway management; maternal, fetal, and newborn resuscitation; and postdelivery care are obtained before entering the operating room. In many situations, the case may present urgently, and having a predetermined checklist and cart with needed EXIT supplies can be extremely useful. In addition to fetal ultrasonography, a pulse oximeter is frequently used to monitor the fetus and can assist with confirmation of a secured airway in addition to capnography. Similar to open fetal surgery, weight-based doses of atropine, epinephrine, and calcium are prepared for possible emergency fetal resuscitation. A sterile fetal ventilation circuit with an air/O_2 source and manometer is prepared in addition to multiple sizes of endotracheal tubes, and laryngoscopes, and blades for fetal tracheal intubation. Both rigid and flexible neonatal bronchoscopes are also useful. Sterile tourniquets, intravenous catheters, crystalloid, and blood (i.e., O-negative, CMV-negative, leukocyte depleted, maternally crossmatched) should be available for fetal venous access and volume replacement.

Anesthetic considerations for the mother are similar to those for open fetal surgery (see Box 63.2). They include possible placement of a preoperative epidural catheter for postoperative analgesia, large-bore intravenous access, invasive monitoring readily available or placement of an intraarterial catheter, uterotonic drugs after delivery of the placenta, and crossmatched maternal blood in the operating room. Anesthetic induction and tracheal intubation are similar to general anesthetic techniques employed for cesarean delivery. Maintenance of appropriate maternal hemodynamics is critical to ensure adequate fetal perfusion. Similar to techniques used for open fetal surgery, high concentrations of a volatile anesthetic (≥2 MAC) with or without intravenous administration of nitroglycerin bolus doses (100-250 μg) or as an infusion (1-10 μg/kg/min) may be required for adequate uterine relaxation. Fetal anesthesia from transplacental transfer of maternal volatile anesthetic can be supplemented with fetal intramuscular administration of an opioid (e.g., fentanyl 5-15 μg/kg or morphine 0.1 mg/kg) and a paralytic agent (rocuronium 2.5 mg/kg or vecuronium 0.3 mg/kg). Sometimes intramuscular atropine (20 μg/kg) is administered to prevent fetal bradycardia. The intramuscular fetal anesthetic drugs can be administered either before uterine incision using ultrasound guidance or under direct vision after performing the hysterotomy. There is significant variation in fetal serum fentanyl concentrations based on umbilical cord blood sampling during EXIT procedures.[323] It is likely that significant variability also may exist with fetal serum concentrations of muscle relaxants and other agents administered to the fetus, making their pharmacologic actions less predictable.

An alternative anesthetic approach uses maternal neuraxial anesthesia combined with intravenous administration of nitroglycerin in an effort to avoid many of the risks

Fig. 63.13 During an ex utero intrapartum therapy procedure, the head and upper torso of a fetus with a neck mass are delivered and the airway secured using direct laryngoscopy. (Courtesy Dr. Anita Moon-Grady, University of California, San Francisco Fetal Treatment Center, San Francisco, CA.)

associated with administration of general anesthesia as previously described.[288,319-321] Significant doses of intravenous nitroglycerin (1-10 μg/kg/min) are often required to achieve uterine relaxation. Although nitroglycerin crosses the placenta, there are minimal fetal effects because a significant amount is metabolized at the placental interface.[288,320] Invasive monitoring with a maternal intraarterial catheter is recommended when prolonged use of nitroglycerin is planned, and the patient should be monitored for onset of pulmonary edema. Some practitioners have also added a remifentanil infusion (0.1-0.3 mcg/kg/min) to the anesthetic regimen. Intravenous remifentanil administered to the mother rapidly crosses the placenta,[287] and has been reported to provide adequate fetal immobilization.[319,321] No prospective clinical trials have been conducted to determine the best anesthetic technique for the EXIT procedure.

After assessment of appropriate uterine relaxation, the placental border is determined by ultrasonography. A small initial hysterotomy is extended outside the placental border with a stapling device to prevent excessive blood loss. If the EXIT procedure is performed to facilitate fetal intubation or neck mass resection, only the fetal head and shoulders are initially delivered (Fig. 63.13). For more extensive procedures requiring access to the thorax or other anatomic locations, the entire body may be delivered.

Before hysterotomy, the fetus is monitored with echocardiography and ultrasonographic evaluation of umbilical cord flow. After hysterotomy, a pulse oximeter probe is placed on the fetal hand and shielded from ambient light. Warmed crystalloid fluids are irrigated continuously in the uterine cavity to maintain fetal temperature and prevent placental separation or spasm of umbilical vessels. Care should also be taken to avoid inadvertent compression or unnecessary manipulation of the umbilical cord, which could lead to vascular reactivity and decreased flow.

Depending on the indication, the duration of an EXIT procedure ranges from a few minutes (e.g., intubation) to several hours (intrathoracic mass resection, neck mass resection with tracheostomy, or ECMO cannulation).

Anesthetic techniques have successfully provided safe maternal and fetal anesthesia with uterine relaxation and uteroplacental stability over several hours.[324] Before ventilation of the fetal lungs, fetal oxyhemoglobin saturation is typically 40% to 70%.[325] After initiating ventilation of the fetal lungs, oxyhemoglobin saturation should increase significantly to above 90%. When fetal lung ventilation fails to result in an appropriate increase in oxyhemoglobin saturation despite appropriate endotracheal intubation, this represents an indication for ECMO initiation before clamping the umbilical cord and fetal delivery.[326] Capnography is beneficial in confirming correct placement of the endotracheal tube. If needed, pulmonary surfactant may be administered once the endotracheal tube is placed. Transporting the neonate to the intensive care area for further care requires significant vigilance to ensure the critical, tentative airway remains secured.

Once the fetus is delivered, the inspired concentration of the volatile agent is significantly decreased and the nitroglycerin infusion is stopped to allow the uterus to contract and diminish the risk for maternal hemorrhage.[327,328] Use of a combination of volatile anesthetics (≤0.5 MAC), nitrous oxide, propofol, and/or an opioid can maintain adequate anesthesia while allowing uterine tone to improve. Oxytocin is routinely administered and additional uterotonic drugs are also provided when necessary, as detailed in Chapter 62. Once the patient is hemodynamically stable with appropriate uterine tone, epidural analgesia may be initiated. The trachea is extubated once the mother is fully awake.

Conclusions and Future Considerations

Establishment of organized, multidisciplinary, and comprehensive fetal intervention programs at a variety of academic centers is critical to improving patient outcomes with innovative surgical techniques, refining diagnostic and treatment strategies, and initiating clinical trials powered to address long-term neonatal outcomes and associated maternal and neonatal morbidity. Advancement of surgical techniques and prenatal diagnostic and management strategies is likely to decrease both maternal and fetal risk and allow safe intervention for additional congenital anomalies and treatment of less severe abnormalities. In addition, in utero stem cell and gene therapy research may lead to novel fetal treatments that allow normal development despite the presence of a congenital anomaly.[329-331] Improvements in managing preterm labor and delivery would greatly improve outcomes in fetal therapy. Preterm birth is associated with morbidities such as respiratory distress syndrome, necrotizing enterocolitis, and intraventricular hemorrhage that all have long-term impact on the child and carry substantial cost.[332] Artificial placental units employing extracorporeal support of the preterm neonate with continuous fluid exchange are novel therapies currently being tested in animals.[333]

Fetal surgery is a relatively new and rapidly evolving area of clinical medicine. In utero treatment raises complex and difficult ethical, social, and legal issues that go far beyond that of most adult or pediatric surgical interventions and include questions regarding maternal rights, access to care, and the option for pregnancy termination.[334,335] Evaluation of each new therapy or change in treatment strategy should be conducted in multicenter clinical trials only after appropriate translational research and animal studies are completed and demonstrate a potential benefit. This transition from innovative breakthrough, to randomized clinical trial, to standard care must be managed in a responsible and ethical framework.

In addition, in utero treatment outcomes from new institutions with minimal experience and intervention for patients outside the strict inclusion criteria of clinical trials are likely to result in less favorable results with increased morbidity compared with the outcomes demonstrated at more established fetal treatment centers participating in the clinical trials.[336] To address these concerns, a bioethics committee from the American College of Obstetricians and Gynecologists and the American Academy of Pediatrics provided recommendations for centers offering fetal therapy.[6] Their recommendations included a thorough informed consent process, appropriate institutional research safeguards, involvement of a multidisciplinary team, and the need for open collaborative research networks. Although this approach has high financial costs, thorough basic science and translational and clinical research in fetal therapy is essential to appropriately manage the unique risks and benefits of future innovations. Appropriate patient selection (both maternal and fetal) and timing of the intervention also need to be better established in many of the procedures.

The principal of *primum non nocere* argues that until a therapy is appropriately tested in animal models, it is unethical to pursue in human trials.[337] Advances in fetal surgery not only require determination of fetal benefit but also must be powered to appropriately evaluate additional fetal and maternal morbidity.[338] Only the results of animal research and descriptive summaries of clinical series currently guide the majority of clinical anesthetic care for fetal surgery. Further rigorous research is needed to determine optimal anesthetic techniques, ensure maternal and fetal cardiovascular stability, improve our understanding of anesthetic exposure and neurocognitive deficits, assess the impact of anesthetic management strategies on uterine tone and uteroplacental perfusion, and to improve our ability to determine the adequacy of fetal anesthesia to produce immobility and block the fetal stress response.[276,339]

Areas of clinical growth include programs for anesthesia training in fetal treatment and the development of standard guidelines for fetal anesthesia and perioperative care of these unique procedures. Fetal treatment is a relatively new, rapidly evolving field of clinical medicine that holds great promise for treating morbid conditions and improving quality of life over the entire lifetime of the patient. Equally significant are the research efforts, technologic advancements, and ethical standards that must be supported to achieve these goals.

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64 *Anesthesia for Orthopedic Surgery*

CHRISTOPH H. KINDLER, OLEG V. EVGENOV, LANE C. CRAWFORD, RAFAEL VAZQUEZ, JASON M. LEWIS, and ALA NOZARI

KEY POINTS

- Degenerative joint disease is the foremost medical condition leading to operations in the United States. With continued population growth and an increasing percentage of older people, a fivefold increase in the demand for hip and knee arthroplasty and spine procedures is projected by 2030.
- Many orthopedic operations including total joint arthroplasties and spine surgeries are classified as intermediate surgical risk, with 30-day cardiac death or myocardial infarction occurring with an incidence of 1% to 5%. Since preoperative cardiac risk evaluation is often inconclusive in high-risk patients with limited mobility, a higher level of monitoring and perioperative troponin measurements should be considered to assess for perioperative cardiac events.
- Comprehensive preoperative geriatric assessment is increasingly used in the perioperative care of older patients who may have multiple comorbid conditions and who have suffered fragility fractures. Prehabilitation programs can be useful in these patients to reduce frailty and improve surgical outcome.
- Fractures of the proximal femur following falls are common in older patients and are associated with high morbidity and mortality. Early surgery (<24 hours) has been associated with reduced pain and length of hospital stay. Patients with significant medical comorbidities that delay surgery for more than 4 days have a higher mortality.
- As compared to the lateral position, beach chair position offers superior surgical exposure and access for most shoulder surgeries, less distortion of muscle anatomy, and less tension on the brachial plexus. Cerebral perfusion pressure can decrease by 15% in sitting patients under general anesthesia, and in patients with cerebrovascular disease detrimental decrease in cerebral blood flow can occur if the systemic pressure is not carefully monitored and maintained. The role of the sitting position on postoperative neurologic outcome remains, however, controversial.
- The most common complications after total hip arthroplasty and total knee arthroplasty are cardiac events, pulmonary embolism, pneumonia and respiratory failure, and infections. Older patients with major comorbidities including cardiac disease, pulmonary disease, and diabetes should have a complete preoperative medical evaluation.
- Cemented fixation of the femoral prosthesis can be complicated by the bone-cement implantation syndrome, resulting in intraoperative hypotension, hypoxia, or even cardiac arrest. Invasive hemodynamic monitoring with an arterial catheter and possibly also a central venous catheter should be considered. Treatment with a potent inotropic agent such as epinephrine may be required. Pulsatile lavage of the femoral canal and drilling a vent hole in the femur before prosthesis insertion can also ameliorate the hemodynamic consequences of this devastating complication.
- Correction of spinal deformities can be associated with large intraoperative blood loss, and measures to minimize blood transfusion should be considered. Deliberate controlled hypotension has been employed but must be used with caution in older adults, those with cardiovascular disease, or those at risk for ischemic complications and postoperative vision loss. Antifibrinolytic agents may be considered to limit blood loss but should be avoided in patients with a history of thromboembolic events, coronary stents, or renal impairment.
- Intraoperative neurophysiologic monitoring is increasingly employed for spine surgeries and is currently recommended for procedures with increased risk for spinal cord injury including correction of spine deformities, resection of intramural tumors, unstable spine trauma, Chiari malformation, spinal cord vascular malformations, as well as those with risk for root damage and in patients with significant risk for compression neuropathies.
- Perioperative visual loss after spine surgery can be caused by anterior or posterior ischemic optic neuropathy, retinal ischemia, cortical blindness, or posterior reversible encephalopathy. Direct pressure on the eye should be avoided and patients should be positioned so that the head is level with or higher than the heart. The patient's head should be maintained in a neutral forward position without significant neck flexion, extension, lateral flexion, or rotation. Staged spine surgery procedures can reduce the risk of perioperative visual loss and should be considered in high-risk patients.

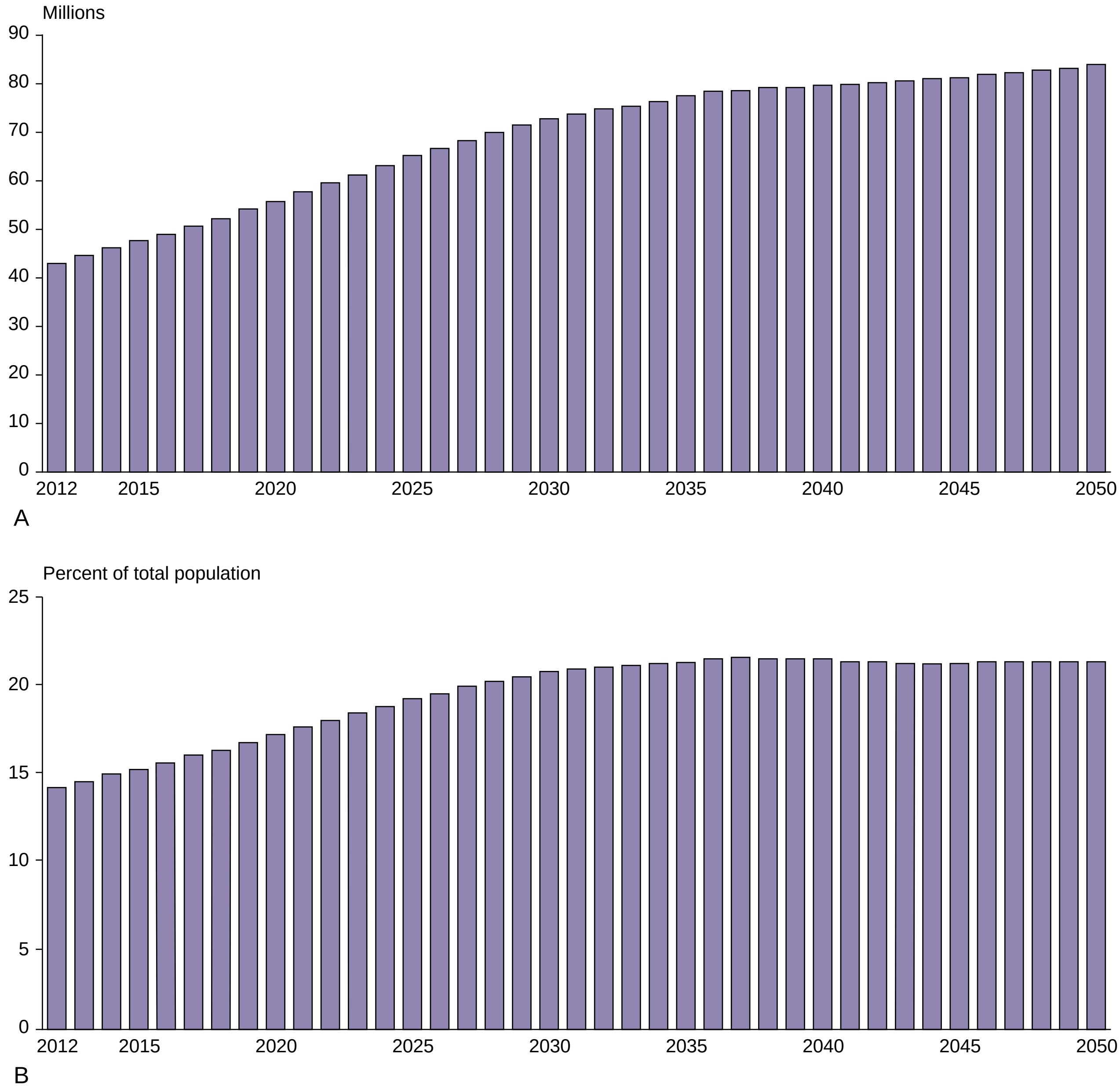

Fig. 64.1 Population aged ≥65 years for the United States 2012 to 2050 in millions (A) and percent of total population (B). (With permission from United States Census Bureau. Ortman JM, Velkoff VA, Hogan H. An aging nation: The older population in the United States; May 2014. https://www.census.gov/library/publications/2014/demo/p25-1140.html.)

Preoperative Evaluation

EPIDEMIOLOGY AND DEMOGRAPHICS OF ORTHOPEDIC SURGERY

Orthopedic operations represent the most frequently performed procedures in U.S. hospitals. Arthroplasty of the knee was the single operation performed most often during U.S. hospital stays in the year 2012, amounting to 700,100 operating room procedures (223 per 100,000 population). Hip replacement surgery with 468,000 operations (149 per 100,000 population) was the fourth most frequent operation and spinal fusion, with 450,900 operations (144 per 100,000 population), the fifth.[1]

These statistics highlight the magnitude of degenerative joint disease, or osteoarthritis (OA), as the foremost medical condition leading to operations in U.S. hospitals. OA is the most common form of arthritis, affecting over 54 million U.S. adults according to 2018 data (78 million U.S. adults are expected to be affected in the year 2045).[2] The lifetime risk of developing OA of the knee is about 46%, and that of the hip is 25% according to the Johnston County Osteoarthritis Project.[3,4]

With age as a prominent risk factor for developing osteoarthritis and with an increasing percentage of elderly people in general, termed population aging (we are expecting 83.7 million US citizens older than 65 years in 2050, almost double the 2012 estimate of 43.1 million for that age group) (Fig. 64.1A and B),[5] the demand for primary total knee arthroplasty is projected to increase by the year 2030 by approximately 5-fold, amounting to 3.4 million surgeries expected to be performed annually in the US (Fig. 64.2A and B).[6,7]

Given the increasing number of patients and volume-based need for orthopedic surgery, every anesthesiologist will sooner

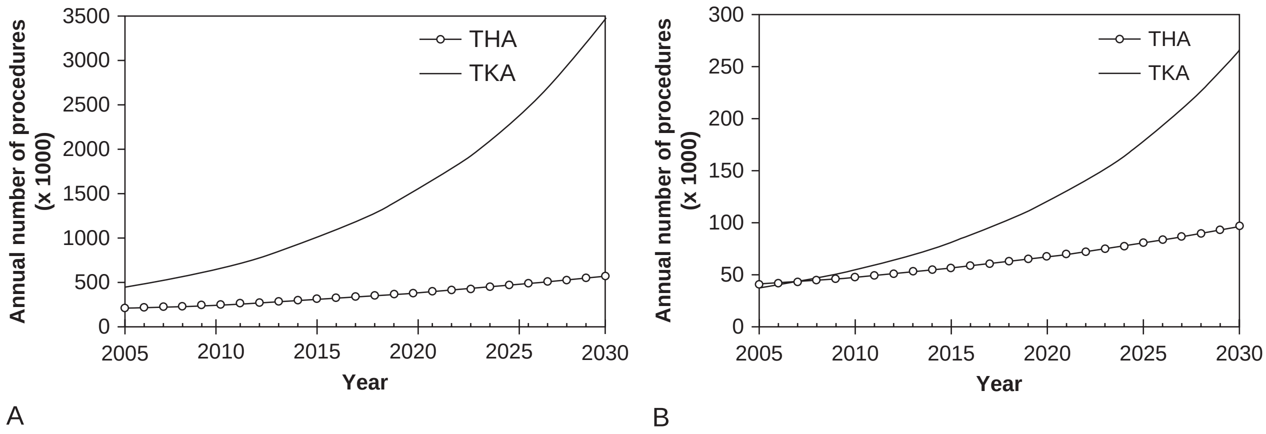

Fig. 64.2 The projected numbers of primary (A) and revision (B) total hip arthroplasties *(THA)* and total knee arthroplasties *(TKA)* in the United States **from 2005 to 2030.** (With permission from Kurtz S, Ong K, Lau E, et al. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am*. 2007;89(4):780–785.)

or later become an orthopedic anesthesiologist. Population aging with the corresponding low support ratio (defined by the number of workers divided by retirees) will also inevitably cause political and financial pressures on public healthcare systems.[8] In particular, financial pressures will certainly intensify and be passed on to orthopedic surgery and anesthesia with its age-related increase in frequency and volume.

It is not surprising that in 2013 the OA-attributable medical costs in the United States were estimated to be $140 billion, with the total medical expenditures and earning losses as high as $304 billion.[9] When conservative therapy including physical activity with muscle strengthening, flexibility and balance exercises, weight control, pain medications, and other personal coping strategies fail to control the symptoms of OA, joint replacement surgery is often the last option for patients suffering from OA to relieve pain and regain mobility.

Using the traditional accounting method, the total cost per hip replacement was recently estimated to be 22,000 to 27,000 USD,[10,11] and for the total cost per knee replacement, 29,500 USD.[11] It is, therefore, not surprising that OA is among the most expensive medical conditions to treat when joint replacement surgery is required. In fact, OA was, following septicemia, the second most expensive health condition treated at U.S. hospitals in 2013. In that year, OA accounted for $16.5 billion, or 4.3% of the combined costs of all U.S. hospitalizations. OA was also the most expensive condition for which privately insured patients were hospitalized, accounting for over $6.2 billion in hospital costs and amounting to 3.6% of the combined costs for all private hospitalizations.[12]

In the past, there was a natural reluctance to perform total joint arthroplasties on very old patients. Older studies reported not only limited evidence of favorable pain and functional outcome of these procedures in patients aged 80 years or older, but also higher rates of complications and mortality.[13-18] Some of these studies were undersized, only used a descriptive or retrospective design, and were also challenged by case-control or prospective community-based studies that failed to report higher complication rates in older age groups.[19-21] The main conclusion of these authors was that with increased life expectancy and elective surgery improving the quality of life, age alone is no longer a factor that affects the outcome of total joint arthroplasty and should, therefore, not be a limitation when deciding who should receive this surgery. Over the past 20 years, arthroplasties in octogenarians and even nonagenarians have become routine procedures in many orthopedic institutions. Nevertheless, a recent study including 7569 patients reported a greater risk of perioperative mortality (relative risk [RR] 3.69; confidence interval [CI], 1.37-9.93), pneumonia, and urinary tract infection in patients 80 years of age or older undergoing aseptic revision total hip arthroplasty (THA).[22] This same study also found general anesthesia compared with epidural, spinal, regional, or monitored anesthesia care to be an independent risk factor for serious adverse events in these patients (RR 1.90; 95% CI, 1.29-2.79).

Considering this enormous financial expenditure combined with the increased age and accompanying comorbidities of the orthopedic patients, anesthesiologists must be highly skilled and apply their utmost vigilance when planning the anesthetic course, including counseling the patient, identifying at-risk patients, and selecting appropriate perioperative anesthetic management and postoperative care.

CARDIOVASCULAR COMORBIDITIES

Coronary Artery Disease

With regard to cardiac risk, surgical interventions can be broadly divided into low-risk, intermediate-risk, and high-risk groups with estimated 30-day cardiac events (cardiac death and myocardial infarction) of less than 1%, 1% to 5%, and more than 5%, respectively.[23] The vast majority of orthopedic operations, such as total joint arthroplasties and spine surgery, are considered and classified as an intermediate surgical risk with 30-day cardiac death or myocardial infarction occurring in 1% to 5% of patients. In fact, most studies have reported a primarily perioperative, acute myocardial infarction rate after hip or knee arthroplasty of 0.3% to 1.8%.[24-26] A recent study defining the intrinsic cardiac risk of a single specified operation rather than groups of operations to improve upon current preoperative cardiac-risk assessment strategies also considered THA as an intermediate intrinsic cardiac risk with an odds ratio (OR) of 0.95 (95% CI, 0.83-1.08) relative to the statistically estimated average procedure.[27] Another interesting study, using

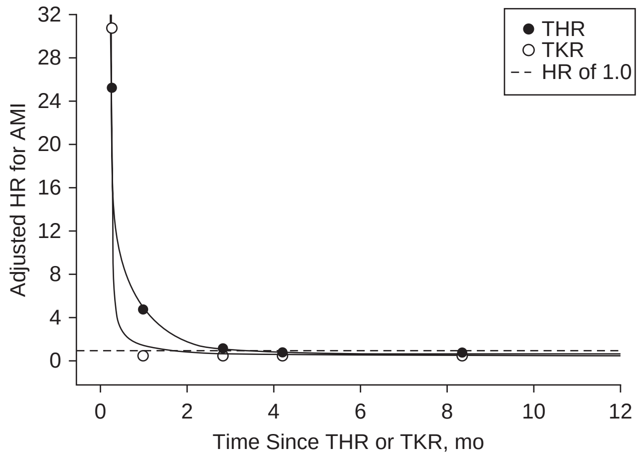

Fig. 64.3 Adjusted hazard ratios *(HR)* for acute myocardial infarction *(AMI)* in patients undergoing total hip replacement *(THR)* and total knee replacement *(TKR)* with respect to time since the operation (mo = months). (With permission from Lalmohamed A, Vestergaard P, Klop C, et al. Timing of acute myocardial infarction in patients undergoing total hip or knee replacement: a nationwide cohort study. *Arch Intern Med.* 2012;172(16):1229–1235.)

matched controls not undergoing surgery, demonstrated an increased risk of acute myocardial infarction during the first 2 weeks after total hip replacement (25-fold) and after total knee replacement (31-fold). The association of an increased cardiac risk and surgery was strongest in patients 80 years of age or older. Interestingly, the risk of acute myocardial infarction decreases significantly after 2 weeks, although it remains elevated during the first 6 weeks for total hip replacement patients (Fig. 64.3).[28]

Over the last 40 years, several indices and scores were developed to better determine perioperative cardiac risk.[29] The first was introduced in 1977 by Lee Goldman.[30] The most widely used of these risk indices today remains the Revised Cardiac Risk Index (RCRI).[31] More recently, a new perioperative risk index known as the Gupta score was proposed using a new model and an up-to-date and simplified approach, which is also available as a risk calculator on the Internet.[32] It was validated on a cohort of more than 400,000 patients of the National Surgical Quality Improvement Program database and uses the American Society of Anesthesiologists (ASA) classification system, dependent functional status, age, abnormal creatinine, and type of surgery as main factors associated with cardiac risk after surgery. In this study, the adjusted OR for myocardial infarction or cardiac arrest was estimated to be 2.22 (95% CI, 1.55-3.17) for orthopedic surgery and 1.24 (95% CI, 0.38-4.00) for spine surgery, compared with an OR of 4.96 for aortic surgery. With a growing geriatric population and an increase in elective noncardiac surgeries in these patients, the necessity of having accurate estimations of the cardiac risk for geriatric patients becomes obvious. For this reason, the new geriatric-sensitive perioperative cardiac risk index (GSCRI), derived solely from geriatric data, was developed in 2017.[33] The GSCRI model contains a total of seven variables, where the main three statistically important variables associated with cardiac risk in the older adult were stroke history, ASA class, and surgical category. Compared to the Gupta score, the GSCRI model considers heart failure, stroke history, and diabetes mellitus status as additional variables. The GSCRI has been shown to be a significantly better predictor of cardiac risk in geriatric patients undergoing noncardiac surgery compared to the Gupta score and RCRI. In the GSCRI, the OR for myocardial infarction or cardiac arrest in orthopedic patients (OR, 2.99; 95% CI, 2.22-4.02) was higher than in the other two indices. The underestimated cardiac risk in geriatric patients resulting from these scores is likely due to estimates that were derived from a younger population.[33]

During the last few years, the focus of cardiac risk has somewhat changed, and perioperative myocardial injury (PMI) has gained increased importance as an additional risk factor for postoperative cardiac events.[34,35] High-sensitivity cardiac troponin assays have been introduced as an important biomarker in routine clinical care. Such novel biomarkers can detect patients at risk beyond established risk scores, and the measurement of these troponins allows for detection of acute cardiomyocyte injury during the perioperative period.[35] PMI is mainly defined by a perioperative increase of absolute or relative troponin values using delta or maximum postoperative values. Despite the current lack of a clear and uniform international definition for PMI, this entity has recently been identified as an important, yet often undetected, complication of noncardiac surgery that is strongly associated with 30-day mortality.[34,36,37] In the most recent study on PMI, Puelacher and coauthors defined PMI as an absolute increase in high-sensitivity cardiac troponin of 14 ng/L or greater from preoperative to postoperative measurements in high-risk patients 65 years or older or in patients 45 years or older with a history of preexisting coronary artery disease, peripheral artery disease, or stroke.[38] In their study population of over 2000 patients, they found an incidence of PMI in orthopedic patients undergoing an intermediate-risk surgical procedure (e.g., total hip or knee replacement) of 20% and for spinal surgery an incidence of PMI of 15% (Table 64.1). With PMI being associated with an overall substantial 30-day mortality as high as 9% and 1-year mortality as high as 22%, recommendations have already been published for screening high-risk patients for PMI.[39] The Canadian Cardiovascular Society Guidelines on perioperative cardiac risk assessment and management of patients undergoing noncardiac surgery already explicitly recommend obtaining daily troponin measurements for 48 to 72 hours after noncardiac surgery in high-risk patients.[40] These perioperative troponin measurements may be particularly useful in high-risk orthopedic patients, since the preoperative cardiac risk evaluation is often inconclusive due to the limited mobility in these patients.

Other Cardiac Comorbidities

Coronary artery disease is probably the single most important cardiac risk factor in orthopedic patients. However, other cardiac diseases such as valvular heart disease or pulmonary hypertension are also important to detect and assess during the preoperative evaluation. Pulmonary hypertension is particularly important in orthopedic patients. In light of the effect of a potentially increased intrathoracic pressure on right heart diastolic function during certain procedures and positioning, the increased risk of venous thromboembolism and the risk of pulmonary embolism of intramedullary contents including fat, bone debris, and cement possibly exacerbating and worsening preexisting right heart strain need to be considered.

TABLE 64.1 Incidence of Perioperative Myocardial Injury in Patients with Increased Cardiovascular Risk (Patients Aged ≥65 Years or Patients with Preexisting Coronary Artery Disease, Peripheral Artery Disease, or Stroke)

		ESC/ESA SURGICAL RISK		
	Incidence of PMI [95% CI]	**<1%**	**1-5%**	**>5%**
All surgical specialties	16% [14-17] (397/2546)	9% [9-13] (79/833)	17% [19-23] (248/1432)	25% [28-39] (70/281)
Orthopedic	16% [12-20] (50/315)	10% [6-18] (12/115)	20% [15-26] (36/183)	12% [2-36] (2/17)
Trauma	18% [15-22] (83/455)	12% [8-17] (22/188)	23% [19-29] (61/260)	0% [0-41] (0/7)
Spinal	15% [11-19] (55/372)	19% [6-44] (3/16)	15% [11-19] (52/356)	0% [0] (0/0)

CI, confidence interval; *ESA*, European Society of Anaesthesiology; *ESC*, European Society of Cardiology; *PMI*, perioperative myocardial injury.
From Puelacher C, Lurati Buse G, Seeberger D, et al. Perioperative myocardial injury after non-cardiac surgery. *Circulation.* 2018;137:1221–1232.

Pulmonary hypertension is hemodynamically defined as a resting mean pulmonary arterial pressure of 25 mm Hg or greater and is classified into five groups: (1) patients with primary pulmonary arterial hypertension, (2) patients with pulmonary hypertension due to left heart disease, (3) patients with pulmonary hypertension due to chronic lung disease and/or hypoxia, (4) patients with chronic thromboembolic pulmonary hypertension, and (5) patients with unclear, mixed, or multifactorial reasons for pulmonary hypertension.[41] A number of retrospective studies reported the considerable risk of morbidity and mortality in patients with pulmonary hypertension undergoing noncardiac surgery with mortality ranging from 3.5% to 18%.[42,43] Major or emergency surgery, long procedure (more than 3 hours), high ASA class score, concomitant cardiovascular disease, poor exercise tolerance, higher preoperative pulmonary artery pressure, and the diagnosis of primary arterial hypertension have all been associated with adverse outcomes in these patients.[43,44] Ramakrishna and associates retrospectively identified 146 patients with pulmonary hypertension undergoing various noncardiac surgical interventions and reported a mortality rate of 7%. When the authors stratified risk by type of surgery, they found that 17% of patients undergoing low-risk surgical procedures experienced morbidity compared with 48% of those undergoing orthopedic surgery. This suggests that patients with pulmonary hypertension undergoing orthopedic surgery represent an especially vulnerable group.[45] Other authors examined 1359 patients with pulmonary hypertension undergoing THA and 2184 patients with pulmonary hypertension undergoing TKA. In-hospital mortality rates among patients with pulmonary hypertension increased by a factor of 3.72 (95% CI, 2.13-6.39) for the cohort undergoing hip arthroplasty compared with controls and by a factor of 4.55 (95% CI, 2.16-9.39) in patients undergoing TKA.[44] The highest rate of in-hospital mortality with 5% was reported in patients with primary pulmonary hypertension undergoing hip arthroplasty.

A thorough clinical examination of a patient with pulmonary hypertension should focus on the nature of symptom progression, exercise tolerance, signs of right ventricle failure, heart rate, blood pressure, electrocardiogram (ECG), chest radiography and biomarkers (B-type natriuretic peptide and high-sensitivity cardiac troponins). Further investigations may include arterial blood gases, echocardiography with estimation of pulmonary artery pressure, computed tomography (CT), coronary angiography, or even advanced and invasive hemodynamic measurements of pulmonary artery pressures and cardiac output depending on the severity of the disease.[42] Mortality of these surgical procedures can be reduced with careful planning, ideally in tertiary nationally designated pulmonary hypertension centers with close preoperative, intraoperative, and postoperative hemodynamic monitoring to prevent a pulmonary hypertension crisis.

Finally, it is important to also consider the noncardiac risks in the orthopedic population. At the moment, there is a lack of data on how noncardiac risk factors such as preoperative mental status, level of dependency, anemia, extreme low or high body weight, pulmonary risk factors, and immune status interact with the cardiovascular risk factors described earlier and how they impact the outcome of orthopedic surgery. There is a need for more general risk scores that can predict the outcome and mortality from noncardiac causes.[23] Therefore, in geriatric orthopedic patients it might be beneficial to obtain a more comprehensive estimation of a patient's functional reserves during the preoperative evaluation. This would also include noncardiac risk factors, rather than focusing on single-organ function and biomarkers alone. Too many healthcare systems are still organized around single-system illnesses. Today, frailty is increasingly recognized as an age-associated, multidimensional syndrome and a unique domain of health status that can be a valid marker of decreased reserves and of resulting perioperative vulnerability and unfavorable postoperative outcome in older patients.[46,47]

FRAILTY

It has long been known that older patients are at increased risk for postoperative complications, possibly due to reduced physiologic reserves to withstand an operation. Linda Fried was the first to use a validated scoring system to define this vulnerability (or frailty) in a more standardized manner and found that such preoperative characterization of frailty using five domains (weight loss, decreased grip strength, exhaustion, low physical activity, and slowed walking speed) could predict surgical outcomes such as postoperative complications, length of hospital stay, and discharge to a skilled- or assisted-living facility. Her frailty score also augmented other risk-assessment models such as the ASA score, the RCRI, or the Eagle's cardiac risk index.[46] Since the first description of this frailty concept in surgical patients, many additional frailty scores and scales including a vast diversity of variables have been proposed in the literature.

In orthopedic surgery, the Clinical Frailty Scale,[48] the FRAIL scale,[48] the modified Frailty Index (mFI),[49] the Groningen Frailty Indicator (GFI) questionnaire,[50] and the Frailty Phenotype and Frailty Index have all been used.[51] Flexman and associates showed in 52,671 patients that approximately 4% of the spine surgery population is frail and that the mFI independently predicted major postoperative complications (unadjusted odds ratio 1.58), prolonged length of stay (unadjusted odds ratio 1.89), discharge to a higher level of care (unadjusted odds ratio 2.29), and 30-day mortality (unadjusted odds ratio 2.05 for every 0.1 increase in frailty score) in patients undergoing surgery for degenerative spine disease.[49] In another study to assess feasibility and validity of the GFI questionnaire in patients undergoing total hip or knee arthroplasties, the authors reported that 33% of patients with hip OA and 24% of patients with knee OA were frail.[50] All studies examining frailty in elderly orthopedic patients reported a significant association with adverse postoperative outcomes such as surgical complications, hospital length of stay, discharge to post-acute institutional care, and readmission rate within 30 days.[48,51]

It has to be pointed out that frailty scales should be accompanied by a thorough clinical examination and comprehensive geriatric assessment including examining the burden of comorbidity, polypharmacy, physical function, psychological status, nutrition, risk of postoperative delirium, and social support to add further insights into the actual risk and the patient's real expectations.[52-54] Well-crafted comprehensive geriatric assessments can be a more powerful predictor of perioperative risk than the ASA score.[55] A study in older patients with a mean age of 78 years examining the prediction of postoperative morbidity and mortality using a comprehensive geriatric assessment reported a significantly higher risk for postoperative death or post-discharge institutionalization for orthopedic surgery compared with abdominal, thoracic, or other surgeries.[52] As such, the value of a comprehensive geriatric assessment has been particularly recognized as a promising system of care for complex older patients who have suffered fragility fractures.[56]

While frailty is increasingly acknowledged as a marker of functional decline, it remains a potentially modifiable risk factor. As such, preoperative rehabilitation programs have been introduced into clinical practice with the idea to reduce frailty and thereby improve surgical outcome. However, today the results of such prehabilitation programs remain controversial.[57-59]

NEUROLOGIC COMORBIDITIES

Stroke is a feared and devastating complication in the perioperative period and is associated with a high rate of morbidity and mortality.[60,61] Large studies have identified a rate of 0.2% for perioperative stroke following total joint arthroplasty, the incidence doubling to 0.4% in patients aged 75 years or older.[60,62] Mortazavi and associates reported advanced age, a history of cerebrovascular, coronary artery, atherosclerotic or cardiac valvular disease, atrial fibrillation or other intraoperative arrhythmias, urgent surgery, and general anesthesia as independent risk factors for stroke in patients undergoing total joint arthroplasties.[60] Compared with matched control subjects not undergoing surgery, Lalmohamed and associates reported a 4.7-fold increased risk of ischemic stroke and a 4.4-fold increased risk for hemorrhagic stroke during the first 2 weeks after THA. The risk remained significantly elevated for at least 6 weeks for ischemic stroke and 12 weeks for hemorrhagic stroke.[63] Since previous strokes represent a significant risk factor, a thorough evaluation of patients with neurologic diseases undergoing surgery can reduce perioperative morbidity and mortality.[64]

Postoperative delirium is recognized as the most common surgical complication in older adults, occurring in 5% to 50% of older patients after surgery. It is associated with major postoperative complications, including postoperative cognitive dysfunction and even death.[65] The main risk factors for postoperative delirium are well established and include among others age of 65 years or older chronic cognitive decline or dementia, poor vision or hearing, severe illness, and the presence of infection. In order to successfully prevent, predict, and manage postoperative delirium, different delirium risk scores were developed of which two were validated in orthopedic surgical patients.[66] Kalisvaart and associates implemented and validated a medical risk factor model in 603 hip surgery patients aged 70 years or older containing four factors: cognitive function at admission, visual impairment, acute physiologic and chronic health status, and blood urea nitrogen (BUN) to creatinine ratio.[67] One point was assigned for each of the four risk factors present, resulting in three groups: a low-, an intermediate-, and a high-risk group with incidences of delirium of 3.8%, 11.1%, and 37.1%, respectively. Cognitive impairment and age were the most important risk factors for delirium in this population of hip surgery patients. Postoperative delirium was four times as frequent in acute hip fracture patients as in elective hip replacement patients. Another study in elective hip or knee arthroplasty patients suggested the use of the Delirium Elderly At-Risk (DEAR) assessment, which incorporates the following risk factors: age, visual or hearing impairment, dependence in more than one activity of daily living, a low mini-mental state score on admission or a previous episode of postoperative delirium, and benzodiazepine or alcohol abuse.[68] A score of two or more using this tool was associated with a greatly increased risk of delirium. Logistic regression models showed the strongest associations of substance abuse and cognitive impairment with the development of postoperative delirium. In a prospective matched controlled cohort study, Kat and colleagues showed that the risk of dementia or mild cognitive impairment at 30 months follow-up is almost doubled in hip surgery patients aged 70 years or older with postoperative delirium compared with at-risk patients without delirium.[69] In addition, a recent study reported poor performance on a preoperative cognitive screening test in older patients undergoing hip or knee arthroplasties as a predictor of postoperative complications such as the development of postoperative delirium, a longer hospital stay, and a lower likelihood to return home in good health upon hospital discharge.[70] Postoperative delirium is also common after spine surgery in older adults and is also associated with increased length of stay, increased costs, and decreased odds of discharge to home.[71] All these studies clearly show the importance of incorporating the assessment of risk of delirium in the preoperative evaluation of elderly orthopedic patients.

THROMBOEMBOLIC DISEASE

Thromboembolic complications remain one of the leading causes of morbidity and mortality after orthopedic surgery. Antithrombotic guidelines are continuously updated and published by the American College of Chest Physicians (ACCP).[72] A systematic review and meta-analysis including 7 million pooled total joint arthroplasty patients found that cardiovascular disease, previous history of venous thromboembolism, neurologic disease, and ASA score were significant and independent risk factors for venous thromboembolism after joint arthroplasties.[73] Two large studies published after the last update of the ACCP guidelines suggested aspirin to be an effective, safe, convenient, and inexpensive alternative to low-molecular weight heparin or to rivaroxaban for extended thromboprophylaxis after joint arthroplasties.[74,75] In an evolving field with many new anticoagulation drugs available, accurate risk stratification would be helpful for physicians as well as patients. While the widely-used Caprini score risk assessment model for thromboembolic disease in the general surgical population failed to provide clinically useful risk stratification information in total joint arthroplasty patients,[76] a more individualized risk model improved the efficacy of preventing venous thromboembolism in these patients.[77] In spine surgery, venous thromboembolism prophylaxis remains even more controversial. An algorithmic approach to this problem was recently published to establish a more specific venous thromboembolism prophylaxis risk/benefit score for spinal surgery.[78]

With the increased use of percutaneous coronary interventions and other vascular stents, and the widespread use of oral anticoagulant drugs for atrial fibrillation or peripheral vascular disease, anesthesiologists are commonly involved in the perioperative management of patients with antiplatelet or anticoagulation therapy.[79] Moreover, a growing number of antiplatelet and anticoagulation therapies, including the non-vitamin K oral anticoagulants (novel or direct oral anticoagulants),[80-82] with unique pharmacodynamic and pharmacokinetic properties complicates the perioperative management of these patients. The timing of discontinuation and postoperative restart of antithrombotic or anticoagulant therapy must be carefully planned and should always be evaluated against the risks of bleeding and cardiac events. An interdisciplinary approach to the perioperative coagulation management involving the surgeons, anesthesiologists, cardiologists, and hematologists may sometimes be required. Patient-specific factors (e.g., age, renal function, vascular and cardiac comorbidities) as well as the surgical factors (urgency, type, risk of bleeding) must be carefully evaluated for individualized risk assessment.[79]

For this reason, we provide only a summary of current antiplatelet and anticoagulant drugs (Tables 64.2 and 64.3). In general, arthroplasties are considered as having a moderate risk of bleeding, whereas vertebrospinal surgery is associated with a high risk of bleeding.[81] In a brief and simplified summary for both types of operations, it is recommended that aspirin should be discontinued 5 days before surgery and until 7 days after surgery in patients with a low- to moderate cardiovascular risk (e.g., in patients taking aspirin as a primary prophylaxis). In patients with a high cardiovascular risk (e.g., patients with known coronary artery disease but an acute coronary syndrome >12 months preoperatively, drug-eluting stent >6 months, bare-metal stent >1 month, cardiac bypass surgery >6 weeks), aspirin can be continued during arthroplasty surgery. However, additional antiplatelet drugs should be discontinued according to their pharmacology and the renal function of the patient. For vertebrospinal surgery, it is advised that both drugs of a dual antiplatelet therapy are adequately stopped. Elective orthopedic surgery is not recommended without optimization in patients with a very high cardiovascular risk (acute coronary syndrome <12 months preoperatively, drug-eluting stent <6 months, bare-metal stent <1 month, cardiac bypass surgery <6 weeks, cerebrovascular accident <4 weeks); such surgery should be delayed when possible.[81,83-85]

TABLE 64.2 Summary of the Characteristics of Currently Available Antiplatelet Drugs

	Aspirin	Clopidogrel	Prasugrel	Ticagrelor	Cangrelor	Abciximab	Eptifibatide	Tirofiban
Route of administration	Oral once daily	Oral once daily, (iv under investigation)	Oral once daily	Oral twice daily	iv	iv	iv	iv
Bioavailability	68%	50%	80%	36%				
Plasma peak level	30-40 min	1 h	30 min	1.5 h	Seconds	Dose dependent	Dose dependent	Dose dependent
Time to plasma steady state		2-8 h	30 min-4 h	30 min-2 h	Seconds	Initial bolus and continuous application	Initial bolus and continuous application 4-6 h	Initial bolus and continuous application 10 min
Plasma half-life	15-30 min	8 h	7 h	7 h	2-5 min	10-15 min	2.5 h	2 h
Plasma protein-binding	Strong	Strong	Strong	Strong				
Time from last dose to offset	7-10 days	7-10 days	7-10 days	5 days	60 min	12 h	2-4 h	2-4 h
Reversibility of platelet inhibition	No	No	No	Yes	Yes	Yes	Yes	Yes
Recommended period of discontinuation prior to surgical intervention	0-5 days	7 days	10 days	7 days	1-6 h	48 h	8 h	8 h

iv, intravenous.
From Koenig-Oberhuber V, Filipovic M. New antiplatelet drugs and new oral anticoagulants. *Br J Anaesth*. 2016;117(suppl 2):ii74–ii84.

TABLE 64.3 Summary of the Characteristics of Currently Available Anticoagulant Drugs

	ORAL					PARENTERAL				
	Warfarin	**Dabigatran**	**Apixaban**	**Edoxaban**	**Rivaroxaban**	**UFH (sc/iv)**	**LMWH (sc)**	**Fondaparinux (sc)**	**Argatroban (iv)**	**Bivalirudin (iv)**
Mechanism of action	Vitamin K antagonist	Direct inhibition IIa	Direct inhibition Xa	Direct inhibition Xa	Direct inhibition Xa	Direct inhibition Xa=IIa	Direct inhibition Xa>IIa	Direct inhibition Xa	Direct inhibition IIa	Direct inhibition IIa
Bioavailability	80%	6%	66%	62%	80%	30%	90%	100%	100%	100%
Plasma half-life	20-60 h	12-14 h	8-15 h	10-14 h	7-10 h	1 h	4 h	17 h	50 min	24 min
Duration of action from last dose	48-96 h	48 h	24 h	24 h	24 h	Dose dependant (sc)	Dose dependant	48-96 h	2-4 h	1 h
Peak plasma level	Variable	2 h	2.5-4 h	1-2 h	1-3 h	4 h (sc)	3 h	2 h		0.25-2 h
Elimination	Metabolism	80% renal	25% renal	50% renal	50% renal, 50% hepatic	Reticuloendothelial system	Hepatic metabolism, renal excretion 10%	Renal	65% feces, 22% urine	20% renal
Drug interaction	CYP2C9, CYP3A4, CYP1A2	P-glycoprotein inhibitors	CYP3Y4, P-glycoprotein inhibitors	P-glycoprotein inhibitors	Strong CYP3A4 inhibitors or inducers and P-glycoprotein inhibitors					

iv, intravenous; *LMWH,* low molecular weight heparins; *sc,* subcutaneous; *UFH,* unfractionated heparin.
From Koenig-Oberhuber V, Filipovic M. New antiplatelet drugs and new oral anticoagulants. *Br J Anaesth.* 2016;117(suppl 2):ii74–ii84.

Similar to patients on antiplatelet therapy, the management of patients under direct oral anticoagulant drugs or vitamin K antagonists also requires consideration of the individual risk of thromboembolic events balanced against the bleeding risk of surgery. Appropriate use of direct oral anticoagulants is particularly important with respect to regional anesthesia in orthopedic patients.[86] The recommendations of the timing of the preoperative interruption of such treatment is somewhat different in Europe (Table 64.4A) and the United States (Table 64.4B).[80,82,87-89] More recently, the American Society of Regional Anesthesia and Pain Medicine (ASRA) in conjunction with the European Society of Anaesthesiology convened a Consensus Conference on Regional Anesthesia and Anticoagulation that updated the available data, representing the collective experience of recognized experts in the field of neuraxial anesthesia and anticoagulation.[89] These guidelines provide a comprehensive summary of evidence-based reviews, but emphasize that the decision to perform spinal or epidural anesthesia and the timing of catheter removal in a patient receiving antithrombotic therapy should be made on an individual basis, weighing the risks of spinal hematoma with the benefits of regional anesthesia for each individual.

PULMONARY, RENAL, HEMATOLOGIC, ENDOCRINE DISEASES, AND NUTRITIONAL STATUS

While cardiac diseases may be the most important considerations determining the overall outcome in high-risk orthopedic patients, other comorbidities such as pulmonary, renal, hematologic, endocrine, and nutritional diseases must also be examined during the preoperative evaluation of orthopedic patients. Although many studies examined postoperative pulmonary complications after noncardiothoracic surgery, they mainly focused on vascular, abdominal, or general surgical patients, and few studies focused on orthopedic surgery cases.[90] In one such orthopedic study, patients suffering from chronic obstructive pulmonary disease who underwent total hip replacement were found to have a longer hospital length of stay, were more likely to be discharged to an extended-care facility, and were at a significantly increased risk for any other complication such as mortality, myocardial infarction, pneumonia, and septic shock.[91] Another study in patients undergoing hip or knee replacements also reported a higher postoperative complication rate in patients with obstructive sleep apnea.[92] In addition, since spine surgery in the prone position is accompanied by a decreased respiratory compliance,[93,94] patients after major spine surgery are at increased risk of postoperative pulmonary complications. Therefore, a thorough pulmonary evaluation and physical examination, including a detailed history, and subsequent medical optimization are critical steps in the preoperative management of orthopedic patients.[95] In selected patients, additional investigations such as chest radiography, spirometry, and assessments of arterial blood gases, albumin levels (OR for pulmonary complications of 2.53 with an albumin level <3.5 g/dL), and BUN (OR 4.81 with a BUN level >7.5 mmol/L) should be considered.[96] In patients scheduled for major scoliosis operations, preoperative fluoroscopy or magnetic resonance imaging to evaluate diaphragm and chest wall movements and preoperative pulmonary function testing might be indicated.[97] The risk of postoperative pulmonary complications can also be estimated with easy-to-use risk scores.[98,99] A strong body of evidence suggests that lung expansion therapy, such as incentive spirometry or deep breathing exercises, can reduce postoperative pulmonary risk.

TABLE 64.4A Timing of Preoperative Interruption of Direct Oral Anticoagulants in Europe

	eGFR (mL/min)	Bleeding Risk Low to Moderate (h)	Bleeding Risk High (h)
Dabigatran	≥50	≥24	48
	30-50	48	72
	<30	≥72	≥120
Factor Xa-inhibitors (rivaroxaban, apixaban, edoxaban)	≥30	≥24	48
	<30	≥72	≥72

eGFR, estimated glomerular filtration rate.
From Yurttas T, Wanner PM, Filipovic M. Perioperative management of antithrombotic therapies. *Curr Opin Anaesthesiol*. 2017;30(4):466–473.

TABLE 64.4B Timing of Preoperative Interruption of Direct Thrombin Inhibitor (Dabigatran) and Factor Xa Inhibitors (Rivaroxaban, Apixaban) in the United States

	DIRECT THROMBIN INHIBITOR		FACTOR XA INHIBITORS	
Creatinine Clearance (mL/min)	Bleeding Risk Low	Bleeding Risk High	Bleeding Risk Low	Bleeding Risk High
>80	≥1 day	≥2-3 days	≥1 day	≥2 days
50-80	≥1-2 days	≥3-4 days		≥2-3 days
30-49		≥4 days		≥3-4 days
15-29	N/A	N/A	≥36 h	≥4 days

N/A, Not applicable.
From Arnold MJ, Beer J. Preoperative evaluation: a time-saving algorithm. *J Fam Pract*. 2016;65(10):702–710.

Today, with medical advancements leading to improved survival and function, an increasing number of patients with chronic kidney disease present for elective orthopedic surgery.[100] There is some discrepancy in the literature with respect to outcome of elective orthopedic surgery in patients with end-stage renal disease (ESRD). Two large retrospective studies failed to show an increased incidence of surgical site infections, thromboembolic events, and 90-day mortality in patients with ESRD undergoing hip replacement surgery.[101,102] Other investigators found higher rates of postoperative complications such as cardiovascular, pulmonary, infectious, and thromboembolic events as well as an increased readmission and mortality rate in patients with ESRD who underwent joint replacement surgery.[103,104] The main concerns for the anesthesiologist in these patients include timing of preoperative and postoperative dialysis to avoid hypervolemia, hyperkalemia, and acidosis; cardiovascular assessment and blood pressure control; electrolyte management, anemia, drug metabolism, and the balance between thromboembolic complications and higher bleeding risk, both of which can be increased in patients with ESRD. The pathophysiology of bone disease represents another important factor to consider preoperatively, since both low and high abnormal bone turnover contribute to the poor bone strength in these patients. Poor bone quality could lead to challenging surgical conditions requiring the use of locking plates or screws, cement fixation, and less rigorous postoperative ambulation, all of which potentially contribute to an increased rate of postoperative complications.[100]

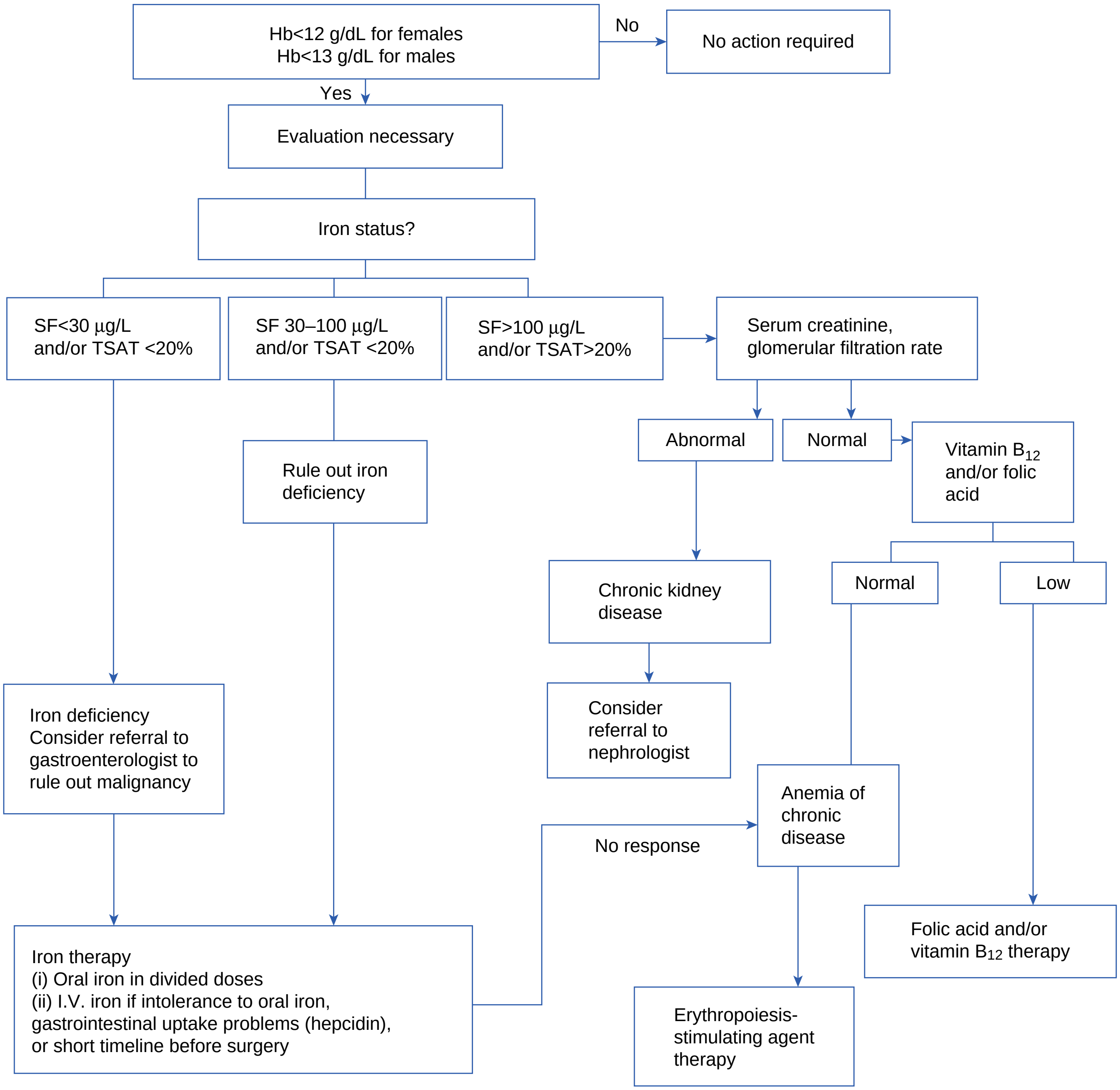

Fig. 64.4 Proposed algorithm for the detection, evaluation, and management of preoperative anemia. *SF*, Serum ferritin; *TSAT, transferrin saturation.* (With permission from Goodnough LT, Maniatis A, Earnshaw P, et al. Detection, evaluation, and management of preoperative anaemia in the elective orthopaedic surgical patient: NATA guidelines. *Br J Anaesth.* 2011;106(1):13–22.)

The overall incidence of anemia in the general population increases with age and is estimated to be 10% to 11% in the older adult aged 65 years or older. Until recently, anemia in older adults was often viewed simply as an abnormal laboratory test value with limited consequences. But today, substantial evidence in the literature reveals that previously undiagnosed anemia is common in elective orthopedic patients, and importantly is associated with increased likelihood of blood transfusion and increased perioperative morbidity and mortality.[105] The preoperative evaluation of anemia should, therefore, include considerations to optimize the endogenous red blood cell mass through targeted stimulation of erythropoiesis and treatment of modifiable underlying disorders.[106] Efforts should be made to diagnose and start appropriate treatment of preoperative anemia and minimize perioperative blood loss. This can be achieved through vigilant adherence to protocols including the measurement of hemoglobin, serum ferritin, transferrin saturation, transferrin receptor index, reticulocyte hemoglobin, vitamin B_{12}, folic acid, serum creatinine, and glomerular filtration rate starting as early as 28 days before surgery (Fig. 64.4).[105,106] Implementation of such anemia prevention and management in elective orthopedic patients can improve patient safety and outcomes. The preoperative administration of iron carboxymaltose in anemic patients undergoing major orthopedic surgery resulted in a significant decrease in postoperative infectious complications from 12.0% to 7.9%. Moreover, hospital length of stay was shortened by 1 day.[107]

In addition to the well-recognized risks of antiplatelet and anticoagulant therapy discussed earlier, some orthopedic patients present with impaired primary hemostasis. Since the management of impaired primary hemostasis is no different in orthopedic surgery than in other surgical fields with

TABLE 64.5 Questionnaire for the Detection of an Increased Risk of Bleeding

1. Have you ever experienced strong nose bleeding without prior reason?
2. Did you ever have—without trauma—"blue spots" (hematomas) or "small bleedings" (on the torso or other unusual regions of the body)?
3. Have your gums ever bled for no apparent reason?
4. How often do you have bleedings or "blue spots" (hematomas): 1 to 2 times a week or more often?
5. Do you have the impression that you have prolonged bleedings after minor wounds (e.g., razor cuts)?
6. Did you have prolonged or severe bleedings after or during operations (e.g., tonsillectomy, appendectomy, or during labor)?
7. Did you ever have prolonged or severe bleedings after a tooth extraction?
8. Did you ever receive blood transfusions or other blood products during an operation? If so, please define the operation(s):
9. Is there a history of bleeding disorders in your family?
10. Do you take analgesic drugs or drugs against rheumatic disease? If so, please specify:
11. Do you take other drugs? If so, please specify:
12. Do you have the impression that you have prolonged menstruation (>7 days) and/or a high frequency of tampon change?

From Koscielny J, Ziemer S, Radtke H, et al. A practical concept for preoperative identification of patients with impaired primary hemostasis. *Clin Appl Thromb Hemost*. 2004;10(3):195–204.

associated bleeding risks, such as neurosurgery, we will only briefly summarize here some relevant ideas. Based on robust evidence in the literature, it is recommended that patients with an increased risk of bleeding complications are identified using a standardized questionnaire and, only if indicated, the measurement of platelet count, prothrombin time, activated partial thromboplastin time, PFA-100 platelet function analyzer test, and von Willebrand factor (Table 64.5).[108,109]

Finally, endocrine and nutritional aspects also have an impact on outcome in orthopedic surgery. For severely obese patients, spine surgery is associated with decreased quality of preoperative and intraoperative imaging, surgical limitations due to inadequate operative exposure, increased anesthetic risk such as esophageal reflux and ventilation-perfusion mismatches, and an increased risk of perioperative complications such as wound infection, increased blood loss, venous thrombosis, pneumonia, and nerve injuries as a result of positioning difficulties.[110,111] Conversely, malnutrition is also associated with increased pulmonary risk, increased risk of surgical site infection, and poor surgical outcomes both in spinal and arthroplastic surgery.[90,112,113] Screening for malnutrition in orthopedic surgery includes the measurement of body mass index, anthropometric measurements such as calf or arm muscle circumference, and triceps skinfold, and the determination of serologic laboratory values such as total lymphocyte count (<1500 cells/mm^3), serum albumin (<3.5 g/dL), prealbumin (<16 mg/dL), transferrin (<200 mg/dL), and zinc levels (<66-95 μg/dL).[112] Various scoring systems have been used to detect malnutrition in orthopedic surgery. The Mini Nutritional Assessment is a simple and effective tool for identifying patients at severe nutritional risk.[113,114] While routine enteral or parenteral nutrition does not reduce perioperative risks, patients with severe malnutrition should undergo nutritional assessment by a dietician prior to surgery. The risks and benefits of delaying elective surgery until the nutritional status has improved should be discussed with the patient. Similarly, delaying elective orthopedic surgery in patients with diabetes mellitus with an increased level of hemoglobin A_{1C} (>7%) until after a better glycemic control has been obtained may reduce risk of surgical wound infection and improve outcome.

COMPLICATIONS AND OUTCOME

A very interesting study in more than 100,000 patients identified the determinants of 30-day postoperative mortality and long-term survival after major surgery exemplified by eight common operations, one being total hip replacement.[115] These authors found in a sample size of 12,184 patients undergoing total hip replacement a 30-day mortality rate of 1% and a mortality rate at any time during an average follow-up time of 8 years of 20%, compared with a 30-day mortality rate of 3% and 36% during the 8-year follow up in the whole study population. After a 10-year follow up, the survival rate in the hip replacement surgery patients was still almost 75%. The main complications in hip replacement surgery were urinary tract infection, deep vein thrombosis (DVT), pneumonia, superficial wound infection, deep wound infection, prosthesis failure, pulmonary embolism, myocardial infarction, and peripheral nerve injury. With the presence of any of these complications, the 30-day mortality rate increased from 1% to 6.4%. The occurrence of a postoperative pneumonia increased the 30-day mortality rate to 16.4% and the 5-year mortality rate to 62.7%, and the occurrence of a perioperative myocardial infarction increased the 30-day mortality rate to 29.2% and the 5-year mortality rate to 52.1%.[115] Given these high numbers of adverse outcomes after the occurrence of complications in total joint arthroplasty patients, every effort must be made during the preoperative evaluation to detect patients at risk, to treat potential underlying conditions, and to optimize the health status of patients. Preoperative medical assessment is an important part of the surgical plan. Identifying and treating modifiable risk factors in the preoperative setting can decrease the risk of surgical complications. A standard protocol that involves a multidisciplinary approach to patients in the preoperative, operative, and postoperative periods may ultimately lead to better outcomes and reduced costs.[116]

Special Considerations for Conditions Leading to Orthopedic Surgery

OSTEOARTHRITIS

OA is a degenerative joint disease characterized by articular cartilage loss and osteophyte formation, most often in the hands, knees, hips, feet, and spine. Symptoms include joint pain, which is typically worse with activity, and decreased range of motion. OA is one of the most common causes of chronic pain and disability among older individuals and is the most common reason that patients present for total knee and hip replacement surgery (USBJI). After age, the most important risk factors for OA include obesity and joint trauma or malalignment.

Although OA has no systemic manifestations, medical comorbidities such as cardiac disease and diabetes are common in these patients, and the combination of OA with one of these chronic conditions is associated with a greater degree of physical activity limitation.[117] Preoperative evaluation should take this into account. Patients with chronic pain related to OA, especially those with chronic opioid use, may benefit from a multimodal perioperative analgesic regimen. Patients who frequently take nonsteroidal antiinflammatory drugs (NSAIDs) should be questioned about symptoms of peptic ulcer disease and gastroesophageal reflux. Extra care should be taken when positioning these patients for surgery, being mindful of painful, stiff joints, and existing orthopedic hardware. Severe OA of the cervical spine may affect airway management, whereas severe disease of the thoracic or lumbar spine may make neuraxial techniques more challenging.

RHEUMATOID ARTHRITIS

Rheumatoid arthritis (RA) is an autoimmune inflammatory disease that affects the joints and often other organ systems. It affects approximately 1% of the population in developed nations, is twice as common in women as in men, and most often presents between 60 and 80 years of age.[118] Most patients have detectable autoantibodies such as rheumatoid factor and anticitrullinated protein antibody. Articular manifestations include synovial inflammation and hypertrophy and destruction of cartilage and bone. This presents clinically as painful joint swelling, stiffness, and progressive deformity. In contrast to OA, the pain and stiffness of RA are typically worse after periods of rest and improve with activity. RA most commonly affects the small joints of the hands and feet in a symmetric fashion but may progress to involve larger joints and atypical joints such as the temporomandibular and cricoarytenoid joints. Cervical spine involvement occurs in up to 80% of RA patients. Because RA is a systemic disease, anesthetic considerations can be complex (Table 64.6).

Similar to patients with OA, patients with RA require careful attention to positioning for surgery, especially if cervical spine disease is suspected. Cervical instability is common in RA, affecting up to 61% of RA patients undergoing elective total joint replacement in one study.[119] Instability may result from atlantoaxial or subaxial subluxation, and places the patient at risk for spinal cord compression if the neck is malpositioned (Fig. 64.5). No guidelines exist for preoperative cervical spine evaluation in RA patients. Certainly, patients should be questioned about neck range of motion and any symptoms of pain or radiculopathy. However, significant cervical disease may exist in the absence of symptoms. Radiography of the cervical spine may be considered, and if obtained should include lateral views in flexion and extension, frontal view of the entire cervical spine, and frontal open-mouth odontoid view. If the distance between the posterior border of the odontoid process and the anterior aspect of the posterior arch of C1 is less than 14 mm, a degree of spinal cord compression is likely present (Fig. 64.6).[120]

TABLE 64.6 Anesthetic Considerations for Patients With Rheumatoid Arthritis

Airway	Limited TMJ movement Narrow glottis opening
Cervical spine	Atlantoaxial instability
Cardiac	Pericarditis Pericardial fluid with tamponade physiology
Eyes	Sjögren syndrome
Gastrointestinal	Gastric ulcers secondary to ASA or steroids
Pulmonary	Diffuse interstitial fibrosis
Renal	Renal insufficiency secondary to NSAIDs

ASA, acetylsalicylic acid; *NSAIDs*, nonsteroidal antiinflammatory drugs; *TMJ*, temporomandibular joint

Fig. 64.5 Magnetic resonance image of a patient with advanced rheumatoid arthritis shows invagination of the odontoid process of C2 *(arrow)* through the foramen magnum, compressing the brainstem. Notice the degeneration of C4 and C5, a common problem in rheumatoid arthritis.

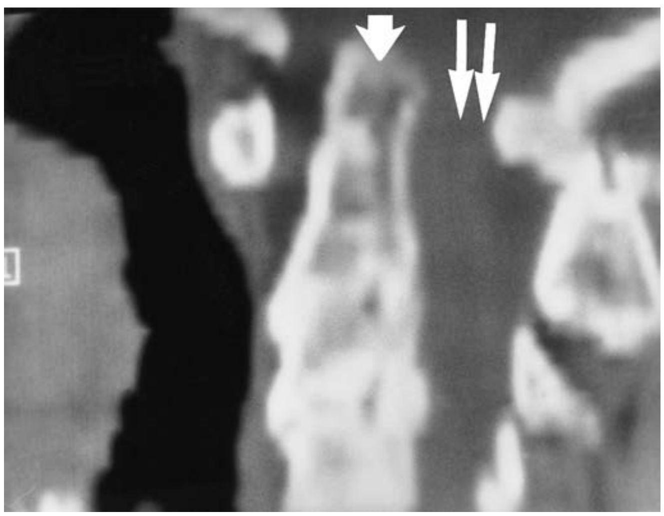

Fig. 64.6 Computed tomography scan of the neck shows moderate subluxation of C1 and C2. The odontoid *(single arrow)* tends to compress the spinal cord *(double arrow)* against the posterior arch of C1, especially during neck flexion.

If cervical instability is suspected, airway management should proceed cautiously with minimal manipulation of the neck. Even in the absence of cervical spine disease, patients with RA may present with challenging airways due to temporomandibular joint disease that limits mouth opening or cricoarytenoid joint stiffness that impedes passage of the endotracheal tube. Fiberoptic intubation or regional techniques with a natural airway may be attractive options for these patients.

Extraarticular manifestations of RA are common and are associated with increased morbidity and mortality, primarily related to cardiovascular disease.[121] The systemic inflammation caused by RA contributes to premature atherosclerosis. As a result, the risk of myocardial infarction, congestive heart failure, and stroke is twice as high in patients with RA compared to individuals without RA.[122] Pericarditis is the most common cardiac manifestation of RA but rarely results in clinically significant disease. Although RA has not been shown to be an independent risk factor for perioperative mortality or adverse cardiovascular events,[123] thorough preoperative cardiovascular risk assessment is warranted in these patients. Pulmonary involvement of RA is also relatively common in the form of pleural effusions and interstitial lung disease. Severity varies from subclinical to, rarely, severe. Preoperative chest radiography or pulmonary function tests may be informative when significant pulmonary disease is suspected. Other extraarticular manifestations of RA include subcutaneous rheumatoid nodules on bony prominences or extensor surfaces, small- to medium-vessel vasculitis, and hematologic abnormalities such as anemia and thrombocytosis.

Treatment for RA focuses on early initiation of disease-modifying antirheumatic drug (DMARD) therapy, with the goal of achieving clinical and radiographic disease remission. In addition to conventional DMARDs such as methotrexate, hydroxychloroquine, sulfasalazine, and leflunomide, many patients benefit from treatment with an ever-growing arsenal of biologic agents that use monoclonal antibodies or receptor proteins to inhibit inflammatory cytokines or cell lines. A notable risk with DMARDs is immunosuppression and possibly impaired wound healing. Current evidence supports continuation of methotrexate perioperatively but is inconclusive about the effect of other agents on perioperative infection and wound complication rates. A conservative approach is to hold biologic agents for at least one dosage cycle prior to surgery and resume once wound healing has progressed.[124] In each case, the benefit of improved immune function and wound healing must be balanced with the risk of disease flare, and it may be appropriate to continue DMARDs perioperatively for some patients. This plan should be developed with input from the patient's rheumatologist and surgeon. Patients taking corticosteroids for RA may require stress-dose steroids perioperatively. They should be questioned about symptoms of gastroesophageal reflux, as should patients who take NSAIDs chronically.

ANKYLOSING SPONDYLITIS

Ankylosing spondylitis is an autoimmune seronegative spondyloarthropathy that typically affects the spine and sacroiliac joints but may involve peripheral joints as well. It affects men disproportionately and most often presents between the ages of 20 to 30 years. Inflammation in affected joints leads to formation of fibrocartilage and ectopic bone, and ultimately fusion of the joint. The classic "bamboo spine" appearance seen radiographically in advanced disease is caused by ossification of the vertebral ligaments. This in combination with osteoporotic compression fractures can result in rigid kyphosis that may require surgical correction (Fig. 64.7).

Despite their rigidity, the spines of patients with advanced ankylosing spondylitis are also quite fragile. Vertebral fractures may occur spontaneously or with minimal trauma; the cervical spine is a common site.[125] Obviously, this has serious implications for intraoperative positioning and airway management. Neck range of motion and preexisting neurologic deficits should be thoroughly evaluated preoperatively, and adequate neck support must be provided at all times to avoid hyperextension. Cervical kyphosis may make direct laryngoscopy difficult or impossible, and temporomandibular joint disease may limit mouth opening. Awake fiberoptic intubation may be the safest option in patients with severe cervical disease, as it allows for spontaneous ventilation as well as neurologic monitoring throughout intubation. Video laryngoscopy has also been used successfully in ankylosing spondylitis patients.[126] The laryngeal mask airway (LMA) may be useful in cases where endotracheal intubation is not required, or as a bridge to intubation if an intubating LMA is used.[127]

The spinal pathology of ankylosing spondylitis may also result in difficulty with neuraxial techniques. Furthermore, the incidence of epidural hematoma after neuraxial anesthesia is higher in ankylosing spondylitis patients than in the general population. This may be related to an increased incidence of traumatic needle placement, the prevalence of NSAID use among ankylosing spondylitis patients, or narrowing of the

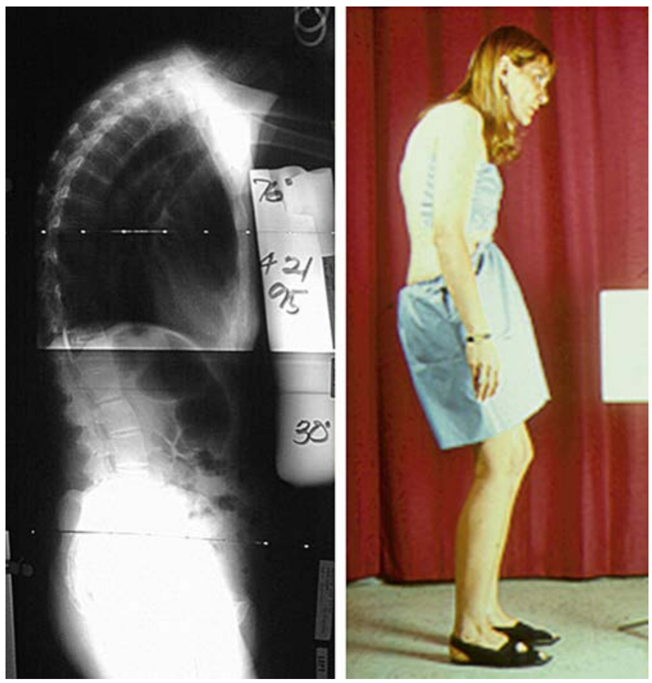

Fig. 64.7 Patient with ankylosing spondylitis, exhibiting significant kyphosis of the spine. Note significant kyphosis in the lateral radiograph.

epidural space that makes symptomatic spinal cord compression more likely when a hematoma occurs.[128] If neuraxial anesthesia is indicated, ultrasound or fluoroscopic guidance may facilitate placement. Subsequently, vigilance should be maintained for symptoms of epidural hematoma.

Extraarticular manifestations of ankylosing spondylitis occur more often in patients with severe disease. Inflammation and fibrosis of the ascending aorta and aortic root can lead to aortic insufficiency, and extension to the conduction system may result in heart block or supraventricular arrhythmias. The prevalence of aortic insufficiency and conduction abnormalities in ankylosing spondylitis patients increases with duration of disease, occurring in 3.5% and 2.7%, respectively, after 15 years and 10% and 8.5%, respectively, after 30 years.[129] As in RA, patients with ankylosing spondylitis also have an elevated risk of atherosclerosis.[130] Pulmonary manifestations of ankylosing spondylitis include restrictive lung disease due to kyphosis and chest wall rigidity. Pulmonary fibrosis may be seen in advanced disease. The duration and severity of disease should inform the extent of preoperative cardiopulmonary evaluation, which might include electrocardiography, echocardiography, and/or pulmonary function testing.

ACHONDROPLASIA

Achondroplasia is characterized by disproportionately short stature, lumbar lordosis, large head, midface hypoplasia, short hands, and normal cognitive development. Its incidence is estimated at 1 in 10,000 to 1 in 30,000. Although it is an autosomal-dominant condition, the majority of cases occur as a result of a de novo genetic mutation.[131] Patients with achondroplasia may present for orthopedic surgery as children or adults for correction of associated abnormalities such as tibial bowing and spinal stenosis.

The primary anesthetic challenge in patients with achondroplasia is airway management. Midface hypoplasia with a pharynx that is small in proportion to the tonsils, adenoids, and tongue makes these patients prone to upper airway obstruction and may hinder direct laryngoscopy. A flat nasal bridge and large mandible may make it difficult to obtain an adequate seal for mask ventilation. Hyperextension of the neck should be avoided due to the possibility of foramen magnum stenosis. Video laryngoscopy or fiberoptic intubation should be considered for these patients, and a range of endotracheal tube sizes should be on hand, as many patients require a size smaller than what would be expected based on age. Other anesthetic considerations in patients with achondroplasia include the possibility of difficult neuraxial anesthesia due to spinal deformity or stenosis, and cardiopulmonary sequelae such as restrictive lung disease, central and obstructive sleep apnea, and resultant pulmonary hypertension.[132] Preoperative echocardiogram to assess for pulmonary hypertension should be considered prior to major surgery.

Orthopedic Procedures in Children with Special Conditions

The anesthetic management of children undergoing orthopedic surgery is beyond the scope of this chapter. However, a number of musculoskeletal conditions will require multiple orthopedic surgeries during childhood and may pose special challenges to the anesthesiologist.

JUVENILE IDIOPATHIC ARTHRITIS

Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children. It is characterized by chronic arthritis with onset before the age of 16 and encompasses five distinct subtypes as described below. JIA may be seropositive or seronegative, is twice as common in girls as in boys, and may persist into adulthood.[133]

1. Oligoarticular JIA: Involves fewer than 5 joints. Accounts for at least 50% of JIA. Often has an indolent presentation.
2. Polyarticular JIA: Involves 5 or more joints. Accounts for 25% to 40% of JIA. Usually requires DMARD therapy.
3. Psoriatic JIA: Arthritis with psoriasis.
4. Enthesitis-related JIA: Affects the spine, sacroiliac joints, and points of tendon attachment to bone.
5. Systemic-onset JIA: Presents with daily fever and rash.

As in adult arthritis, special care should be paid to joint range of motion and intraoperative positioning for patients with JIA. The cervical spine and temporomandibular joints may be affected in JIA, especially in the polyarticular subtype, and appropriate precautions should be taken when planning for airway management. In children, awake fiberoptic intubation may not be a feasible option. In this case, fiberoptic intubation may be performed asleep with spontaneous ventilation maintained throughout induction. Common extraarticular manifestations of JIA include growth abnormalities and uveitis. Pericarditis and pleural effusions sometimes occur in systemic-onset JIA. Medical therapies for JIA are similar to those for RA, including conventional DMARDs and biologics, which raise similar considerations for perioperative risks and management.

OSTEOGENESIS IMPERFECTA

Osteogenesis imperfecta encompasses a group of heritable bone dysplasias caused by mutations in collagen-related genes. It occurs with an incidence of 1 in 10,000 and is characterized by bone fragility resulting in deformity and susceptibility to fracture. Secondary features include short stature, blue or gray sclerae, conductive hearing loss, abnormal dentin resulting in weak and discolored teeth, foramen magnum stenosis, cardiac valvular abnormalities, and bleeding diathesis. Although the most severe subtype of osteogenesis imperfecta results in perinatal death, the life expectancy for patients with other subtypes extends well into adulthood.[134]

Patients with osteogenesis imperfecta may require a number of orthopedic surgeries such as fracture fixation, intramedullary rodding for correction of long-bone deformities, spinal fusion for scoliosis, and joint replacement. Anesthetic management may be challenging (Table 64.7). Utmost care must be taken to avoid iatrogenic fracture when positioning these patients for surgery. The area under the blood pressure cuff should be padded or an arterial line placed to minimize the risk of humeral fracture. Tourniquets must be managed

TABLE 64.7 Anesthetic Considerations for Patients With Osteogenesis Imperfecta

Airway	Risk for fractures of the mandible, maxillary surface, and cervical spine
Bleeding	Platelet abnormalities
Cardiac	Congenital and valvular heart disease Cystic degeneration of proximal aorta
Eyes	Exophthalmos Risks associated with prone positioning
Hyperthermia	Malignant hyperthermia, hydration, possible cooling
Positioning	Risk for fractures
Pulmonary	Kyphoscoliosis, restrictive lung disease
Regional anesthesia	Fractures, intraosseous injections

with similar care. Succinylcholine should be avoided in patients with osteogenesis imperfecta because of the risk of fracture upon fasciculation. Airway management must be performed gently with minimal manipulation of the head and neck to avoid cervical, facial, and dental fractures. Fiberoptic intubation may facilitate this. Neuraxial techniques may be considered in patients with normal platelet function but may be challenging due to scoliosis. Care must be taken to avoid needle trauma to bone and intraosseous injection.

Several extraskeletal manifestations of osteogenesis imperfecta are relevant to the anesthesiologist. The same collagen abnormalities that affect bone may also affect the cardiac valves and aorta, resulting in regurgitant lesions, aortic root dilation, and even aortic dissection. Restrictive or obstructive lung disease may be present as a result of kyphoscoliosis or chest wall deformity. In fact, pulmonary complications are the leading cause of death in osteogenesis imperfecta. Preoperative echocardiography or pulmonary function testing should be considered if a murmur or symptoms of cardiopulmonary disease are noted. Patients with osteogenesis imperfecta are at risk for increased surgical bleeding due to platelet dysfunction and vessel fragility. Patients should be evaluated for coagulopathy preoperatively, and if necessary, treated with desmopressin (DDAVP) or platelet transfusion.

A link between osteogenesis imperfecta and malignant hyperthermia (MH) has been suggested in the literature, but the evidence for this association is weak. Intraoperative hyperthermia and metabolic acidosis have been observed in patients with osteogenesis imperfecta, but in most cases, this was not associated with other signs of hypermetabolism and resolved with cooling measures alone. There is a lack of consensus on the use of MH-triggering agents in patients with osteogenesis imperfecta. The most conservative approach is to administer a nontriggering anesthetic, but in cases where this presents a significant challenge (as in an uncooperative child with difficult intravenous access), use of volatile anesthetics may be considered. In all cases, patients should be carefully monitored for hyperthermia and acidosis, and appropriate treatment modalities should be readily available.[135]

CEREBRAL PALSY

Cerebral palsy is the most prevalent cause of persistent motor impairment in children, affecting 1 to 2 of every 1000 live births in developed countries. It is caused by antenatal or perinatal injury to the developing brain and is characterized by nonprogressive abnormalities of movement and posture such as spasticity, ataxia, and dyskinesias. The motor deficit may be mild or severe, isolated, or accompanied by other abnormalities including cognitive impairment, speech disorders, and seizures. Patients with cerebral palsy often require multiple orthopedic surgeries such as soft tissue release and tendon lengthening for contractures, osteotomies for hip deformities, and spinal fusion for scoliosis.

Anesthetic management of patients with cerebral palsy requires consideration of the psychosocial as well as medical aspects of their condition.[136] Communication may be challenging due to cognitive delay, behavioral problems, or speech difficulties, necessitating special accommodations and involvement of parents or caretakers in perioperative interactions. It is important to remember that speech impairment does not necessarily imply cognitive impairment. In patients with seizures, antiepileptic drugs should be continued perioperatively and inquiry made as to the frequency and semiology of seizures. Gastroesophageal reflux is common in cerebral palsy and may be an indication for rapid sequence intubation. Bulbar dysfunction can further contribute to chronic aspiration and feeding difficulties that sometimes requires gastrostomy tube placement. Chronic aspiration, recurrent respiratory infections, and restrictive deficits due to kyphoscoliosis result in significant pulmonary morbidity in these patients. Airway management may be challenging due to cervical kyphosis or dystonia, temporomandibular joint dysfunction, or poor dentition. Patients with cerebral palsy have a lower minimum alveolar concentration (MAC) than normal controls and may be prone to intraoperative hypothermia due to hypothalamic dysfunction. An association between cerebral palsy and latex allergy has been noted, likely related to the multiple surgical procedures many of these patients undergo.[137]

SPINA BIFIDA

Spina bifida is a term that is broadly applied to a diverse group of congenital malformations of the spine and spinal cord. Embryologically, these conditions result from a failure of fusion of the neural tube. Discussion of spina bifida is complicated by a lack of consistency in terminology and classification, but malformations can be broadly divided into open defects with exposed neural tissue such as myelomeningocele and myeloschisis, and closed defects with a skin covering such as meningocele, tethered cord, and split cord. Open defects are usually associated with a neurologic deficit and are almost always repaired perinatally, or with the advent of fetal surgery, prenatally. Closed defects may have an associated deficit or may be asymptomatic and undiagnosed until adulthood. Cutaneous abnormalities such as a sacral dimple, hemangioma, or tuft of hair may raise suspicion for a closed defect, but these are not always present.[138]

Neurologic abnormalities associated with spina bifida include motor and sensory deficits below the level of the defect, Chiari II malformation, hydrocephalus, and neurogenic bladder. Patients with spina bifida may present for orthopedic surgery for correction of congenital or acquired limb deformities such as clubfoot or hip dislocation, spinal fusion for scoliosis, or release of contractures. Patients with tethered cord syndrome may present for cord release as children or adults. As in cerebral palsy, repeated surgical exposures in spina bifida patients result in an increased incidence of latex allergy.

The most significant anesthetic implications of spina bifida are related to neuraxial anesthesia. Whether or not the patient has undergone corrective spinal surgery, anatomic abnormalities in the spine can lead to an increased risk of inadvertent dural puncture, failed block, and neurologic injury. For example, the ligamentum flavum may be malformed or absent, precluding identification of the epidural space with loss-of-resistance technique. The epidural space may be abnormal or nonexistent in patients who have undergone prior surgical repair. Cord tethering can result in low termination of the spinal cord and posterior placement of neural elements within the spinal canal, increasing the risk of neurologic injury with spinal anesthesia or inadvertent dural puncture. Neuraxial techniques should be approached with extreme caution in patients with tethered cord syndrome, if at all.

If neuraxial anesthesia is indicated in a patient with spina bifida, it should only be attempted if there is a thorough understanding of the patient's spinal anatomy. Magnetic resonance imaging (MRI) of the spine should be obtained to allow for examination of bony and ligamentous defects, the level of termination of the spinal cord, and the presence of masses such as lipoma or syrinx. Needle placement through surgical scars should be avoided, and epidurals should be placed above the level of the spinal defect. Smaller than usual epidural boluses are recommended, as abnormal anatomy might result in more extensive spread. Failed or incomplete block may result in the need for rescue analgesia or conversion to general anesthesia.[139]

DUCHENNE MUSCULAR DYSTROPHY

Duchenne muscular dystrophy (DMD) is an X-linked recessive neuromuscular disorder that occurs in 16 per 100,000 live male births in the United States. Mutations in the dystrophin gene result in muscular degeneration that is progressive and ultimately fatal. Weakness usually begins in early childhood with loss of ambulation by age 8 to 12 years, respiratory insufficiency and cardiomyopathy by the early 20s, and death before age 30 due to pulmonary complications or heart failure. However, with advancements in care, the life expectancy for DMD is improving, and some patients may survive into their 30s or 40s. Glucocorticoids are the mainstay of treatment for DMD. Patients with DMD may present for orthopedic surgery to correct lower extremity deformity, scoliosis, or contractures. These patients are also prone to osteoporosis with increased risk of fractures that may require operative fixation.

Patients with DMD have an elevated risk of perioperative cardiac and respiratory decompensation and should undergo a thorough cardiopulmonary evaluation prior to surgery. Depending on the stage of their disease, this may include an electrocardiogram, echocardiogram, and pulmonary function testing. Extubation to noninvasive positive pressure ventilation is recommended for patients with a forced vital capacity (FVC) less than 50% predicted, and essential for those with an FVC less than 30% predicted. Aggressive postoperative pulmonary hygiene should be strongly encouraged.[140]

Use of succinylcholine is strictly contraindicated in patients with DMD because of the risk of acute rhabdomyolysis. Inhaled anesthetics are also best avoided, as they have been implicated in cases of perioperative metabolic reactions ranging from intraoperative hyperthermia and tachycardia to rhabdomyolysis to hyperkalemic arrest. The mechanism of these reactions is thought to be distinct from that of MH.[141] Patients with DMD have both a delayed onset time and prolonged recovery time with nondepolarizing neuromuscular blockers, which places them at risk for residual neuromuscular blockade and recurarization. Quantitative monitoring of neuromuscular blockade is recommended to ensure full reversal. Cholinesterase inhibitors are safe and effective for reversal in these patients, and sugammadex has been used successfully as well.[142]

ARTHROGRYPOSIS MULTIPLEX CONGENITA

Arthrogryposis multiplex congenita is characterized by congenital nonprogressive contractures affecting at least two different areas of the body. It occurs with an incidence of about 1 in 4300 to 5100 live births. Arthrogryposis multiplex congenita is not a single disorder, as once thought, but actually encompasses hundreds of conditions with distinct etiologies, both genetic and environmental. A common theme in most of these is decreased fetal movement, which leads to abnormal joint development. Deformity may be limited to the limbs or associated with spine and craniofacial abnormalities. Neurologic dysfunction is present in some cases and portends a less favorable prognosis.[143]

Treatment of arthrogryposis multiplex congenita requires early orthopedic intervention with splinting and surgery to optimize a child's ability to ambulate and perform activities of daily living. The primary anesthetic challenge in arthrogryposis multiplex congenita is airway management, which may be complicated by craniofacial abnormalities such as small mouth opening, high arched palate, or micrognathia, as well as limited cervical range of motion. These patients are at risk of perioperative respiratory complications as a result of restrictive thoracic deformities and increased sensitivity to opioids and neuromuscular blockers. This makes regional and neuraxial anesthesia attractive options, but these techniques may be challenging due to limb contractures, scoliosis, or associated spina bifida.[144]

Two cases of suspected MH have been reported in patients with arthrogryposis multiplex congenita, as well as other cases of perioperative hyperthermia and hypermetabolism without skeletal muscle destruction. As such, succinylcholine should be avoided in these patients, and exposure to volatile anesthetics should be minimized.[135]

Perioperative Management of the Orthopedic Patient

SPECIAL CONSIDERATIONS

In addition to the perioperative cardiovascular, pulmonary, renal, and hepatic considerations described earlier, orthopedic procedures are associated with unique risks and complications related to bone injury, immobilization, and the use of implants and cement material. Bone hemostasis can be difficult, and without antifibrinolytic agents, even primary hip and knee arthroplasties can be associated with considerable bleeding requiring transfusion of blood products. Extensive review of these considerations is beyond the scope of this chapter, but given the rising interest in the literature and its clinical importance, perioperative use of antifibrinolytic agents is summarized below, along with the clinical presentation and management of fat embolism and bone cement implantation syndrome.

Antifibrinolytic Drugs

Blood transfusions are associated with an increased risk of adverse events including mortality, prolonged length of hospitalization, and higher overall costs associated with surgery. Antifibrinolytic agents, such as tranexamic acid (TXA) and epsilon-aminocaproic acid (EACA), bind reversibly to plasminogen by its lysin-binding site, inhibiting its association with fibrin. They also inhibit the proteolytic activity of plasmin. Both TXA and EACA are effective in reducing perioperative blood loss and the need for transfusion and reoperation for bleeding.

Among orthopedic surgeries, the strongest evidence for the use of TXA and EACA is found in multilevel spine surgeries and arthroplasties. Several comprehensive meta-analyses have examined the use of systemic TXA in these procedures. Two meta-analyses studying the use of intravenous TXA in spine surgeries demonstrated significant reductions in intraoperative and postoperative blood loss and allogenic blood transfusion compared with placebo. However, initiation doses (10-20 mg/kg, 100 mg/kg, or 1-2 g) and maintenance doses (1 mg/kg/h, 10 mg/kg/h, and 100 mg/kg/h) were highly variable.[145,146] Similar results with regard to efficacy and safety have been shown with the use of intravenous TXA in TKA and THA. TXA has been shown to reduce total blood loss, postoperative bleeding, and the transfusion rate when given intraoperatively with an intravenous infusion compared to a postoperative administration. A common approach is to administer 10 to 15 mg/kg before the incision, followed by a 1 mg/kg/h infusion during the surgery.[147,148] A recent meta-analysis also demonstrated that TXA resulted in significant reductions in total blood loss and transfusion requirements following total shoulder arthroplasty.[149] The rate of thromboembolic events was not significantly greater when the above dose of TXA was administered in selective patients without contraindications.

Topical administration of TXA, although not a US Food and Drug Administration (FDA)-approved route of administration, has a theoretical safety benefit over intravenous administration. Topical TXA has shown superior efficacy to placebo and similar efficacy (measured as reductions in total blood loss and transfusion rates) to intravenous TXA in TKA and THA. No difference in the rate of thromboembolic events has been demonstrated when comparing topical TXA to placebo or intravenous TXA. The doses of topical TXA used in studies are highly variable and usually range from 1 to 3 g. Thus, a standard topical dose has not yet been established.[150-152]

EACA has also been shown to decrease total blood loss and need for transfusion among patients undergoing spine surgeries.[153] Among TKA and THA patients, however, EACA did not reduce the need for blood transfusion.[154,155] An increased risk of DVT and pulmonary embolism has not been reported following the use of EACA in THA,[154] though sufficient data in TKA or spine surgeries are not yet available. Loading doses (100-150 mg/kg or 5 g) with a continuous infusion ranging from 10 to 15 mg/kg/h during spine surgeries have been used.[153] For THA and TKA, weight-based (12.5-100 mg/kg) and fixed doses (5-10 g) of EACA have been utilized.[154]

Although no increase in the incidence of venous thromboembolism was observed in the above randomized clinical trials, it is important to note that high-risk patients were excluded and none of the studies was adequately powered to detect smaller but clinically relevant differences between treatment groups. Therefore, because of concerns of venous thromboembolism, antifibrinolytic agents are commonly avoided in patients who have any of the following conditions: a history of arterial or venous thromboembolic disease; a recent placement of a cardiac stent; a history of severe ischemic heart disease (NYHA Class III or IV) or myocardial infarction; and history of cerebrovascular accident, renal impairment, or pregnancy. Currently, there is limited data to support the use of EACA in spine surgeries, THA, or TKA, whereas evidence for TXA is more robust. In select patients who are at high risk for transfusion, intravenous or topical TXA should be considered.

Fat Embolism Syndrome

The subclinical form of fat embolism occurs in nearly all patients following long bone or pelvic fractures, as well as after hip or knee replacement surgeries. A clinically significant fat embolism syndrome (FES) is present in up to 30% of these patients.[156,157] An increase in intramedullary pressure and a disruption of the venous sinusoids within the long bones following a fracture or a surgical manipulation such as reaming can result in fat and bone marrow debris entering the venous circulation. The debris lodges in the lung microvasculature, leading to a mechanical obstruction of pulmonary circulation. Free fatty acids released following hydrolysis of fat globules trigger systemic inflammatory response and induce injury to the pulmonary endothelium with an increased capillary leak and increased platelet adhesion with clot formation in the microvasculature. In the presence of intracardiac (patent foramen ovale) or pulmonary shunts, fat particles may also enter the systemic circulation leading to cerebral and cutaneous manifestations.

Symptoms of FES include hypoxemia, respiratory alkalosis, mental status changes, petechial rash (in the conjunctiva, oral mucosa, and skin folds of the neck and axilla), thrombocytopenia, and fat microglobulinemia. The presentation of FES can be gradual, developing between 12 and 72 hours after trauma or surgery. Intraoperatively, FES can also present as a cardiovascular collapse following reaming of long bones, intramedullary insertion of cemented prosthesis, or tourniquet release. Chest radiographs usually show bilateral diffuse infiltrates, particularly in the upper and middle lobes of the lung. MRI of the brain of the patients with significant mental status changes can reveal multiple hyperintensive lesions. Arterial blood gas assessment is useful to determine the degree of hypoxemia.[156] The best preventive management strategy of FES is an early surgical reduction and immobilization of the fracture site. Therapy of FES includes early supportive care with supplemental oxygen and, if necessary, mechanical ventilation to correct hypoxemia, and careful fluid management to prevent worsening of capillary leak. There is currently no evidence supporting the use of steroids, heparin, or dextran in the management of FES.[157] The overall mortality remains high (up to 20%).

Bone-Cement Implantation Syndrome

During arthroplasties, the prosthesis can be attached to the medullary canal of long bones using methyl methacrylate cement or through bone ingrowth. Cemented fixation of the prosthesis can be complicated by bone-cement implantation syndrome (BCIS) that manifests by marked intraoperative hypotension, bronchoconstriction, hypoxia, cardiac arrhythmias, increased pulmonary vascular resistance, right ventricle failure, or even cardiac arrest.[158] Several mechanisms of BCIS have been proposed, including embolization of bone marrow debris to the pulmonary circulation during pressurization of the medullary canal, toxic effects of circulating methyl methacrylate monomer, and release of cytokines and cyclooxygenase products during reaming of the medullary canal, which can induce pulmonary vasoconstriction and formation of microthrombi. Embolization is believed to occur as a result of high intramedullary pressures during cementing. In cemented arthroplasties, intramedullary pressure can peak at 680 mm Hg, compared to less than 100 mm Hg in arthroplasties without the use of cement. The presence of bone marrow debris has, indeed, been documented in the right heart with intraoperative transesophageal echocardiography (TEE) (Figs. 64.8 and 64.9).[159]

Risk factors for this complication include metastatic disease, a previously not instrumented femoral canal (it is thought that the inner surface of the femur becomes smooth and sclerotic once instrumented and cemented, and thus, offers a less permeable surface), a long-stem prosthesis, a THA for pathologic fractures, preexisting pulmonary hypertension and right ventricle failure, and a large quantity of cement used. The hemodynamic consequences of bone marrow embolization may be attenuated through a vigorous pulsatile lavage of the medullary canal and by drilling distal venting holes within the long bones before prosthesis insertion. However, the venting technique can result in significant cement extravasation. Use of noncemented prosthesis should thus be considered in high-risk patients.[160] These patients should be monitored with an arterial catheter and, possibly, also a central venous catheter. Management of BCIS is mainly supportive and includes adequate fluid resuscitation and ventilatory support. The hypotensive events following BCIS may require treatment with potent inotropic and vasopressor agents such as epinephrine.

ORTHOPEDIC TRAUMA

Pelvic Fractures

Pelvic fractures are among the most complicated orthopedic injuries and are associated with a high mortality rate (up to 32% in open fractures). They are typically a result of blunt force trauma, including motorcycle and motor vehicle accidents (60%-80%). The classification of pelvic trauma into minor, moderate, and severe is based on the pelvic ring injury's anatomic classification (Antero-Posterior Compression; Lateral Compression; Vertical Shear; Combined Mechanisms) and more importantly, the hemodynamic status.[161] Patients suffering from traumatic pelvic fractures often have other associated life-threatening injuries (to the head and neck, thoracoabdominal area, and extremities) that need to be taken into consideration during perioperative management.

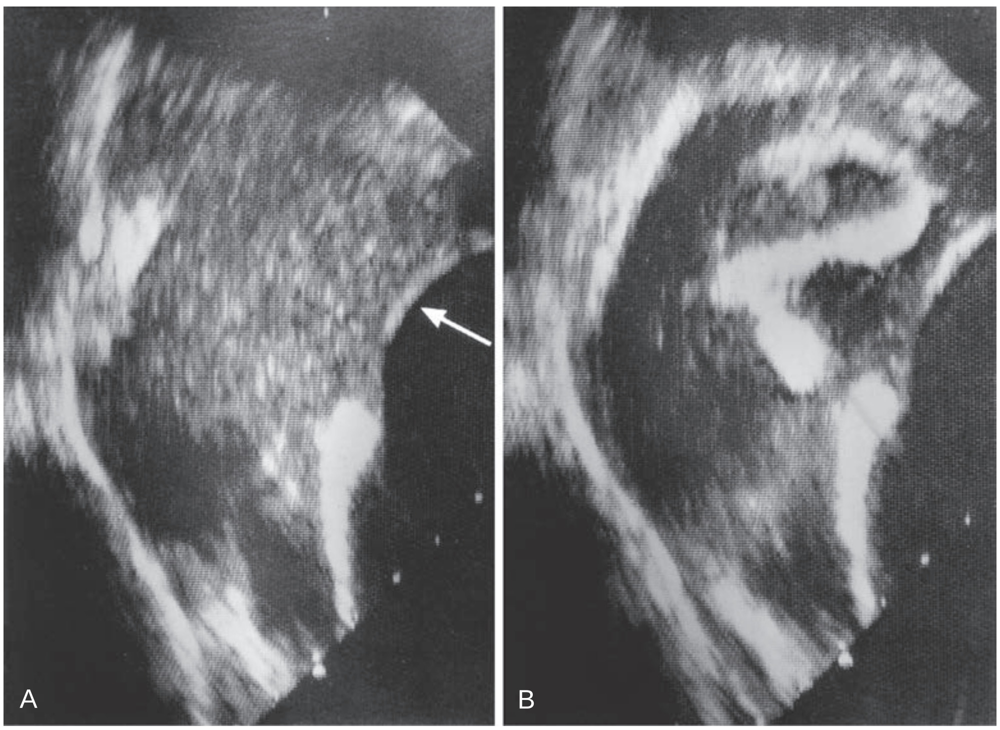

Fig. 64.8 Right atrium during echocardiography. (A) Multiple, small emboli *(arrow)* in the right atrium. (B) Large embolus (7 cm long), which is probably a cast of the femoral vein. (Modified from Christie J, Burnett R, Potts HR, et al. Echocardiography of transatrial embolism during cemented and uncemented hemiarthroplasty of the hip. *J Bone Joint Surg Br*. 1994;76:409–412.)

In addition, pelvic fractures can result in fatal retroperitoneal bleeding.[162] An accompanying blunt chest trauma can produce both cardiac contusion and aortic tear. Preoperative ECG and measurements of cardiac enzymes can help evaluate the extent of myocardial injury. Thorough preoperative neurologic assessment including mental status, motor, and sensory examination is indicated prior to inducing anesthesia. Injuries to the bladder and urethra are also common. Urologic evaluation may be needed before inserting an indwelling catheter. Insertion of chest tubes prior to surgery may also be needed if significant hemothorax or pneumothorax are present. These patients should be considered for a temporary inferior vena cava filter due to a high risk of DVT and pulmonary embolism.

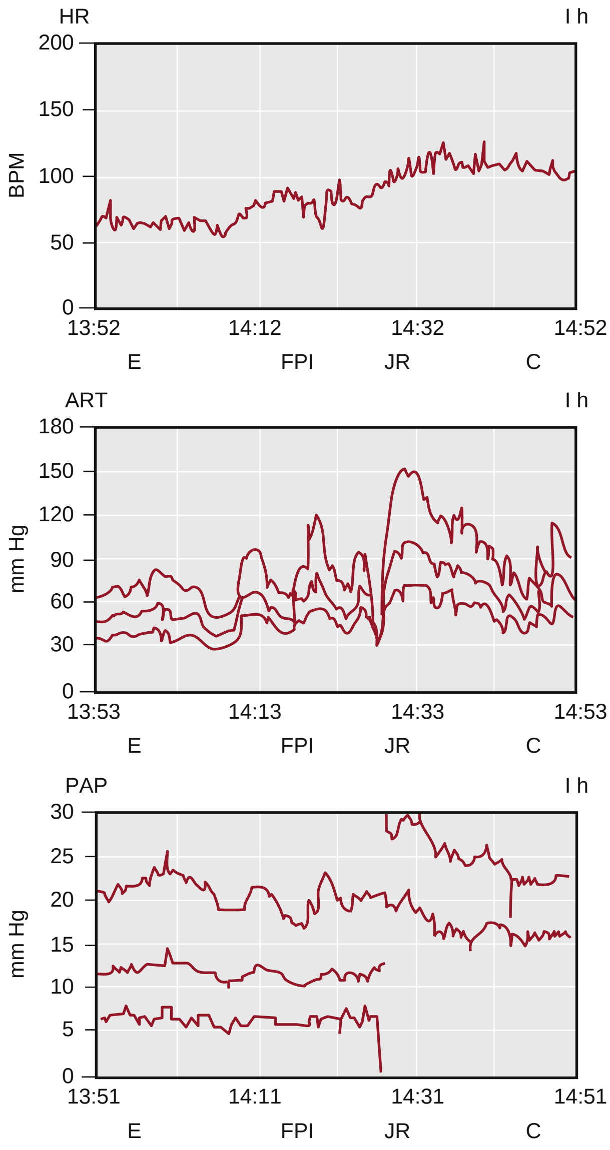

Fig. 64.9 Beats per minute *(BPM)*, intraoperative heart rate *(HR)*, systemic arterial blood pressure *(ART)*, and pulmonary arterial pressure *(PAP)* tracings of a patient undergoing revision total hip arthroplasty. *C,* wound closure; *E,* Induction of epidural anesthesia; *FPI,* insertion of a cemented femoral prosthesis; *JR,* reduction of prosthetic hip joint, producing hypotension with rebound from epinephrine injection. (From Urban MK, Sheppard R, Gordon MA, et al. Right ventricular function during revision total hip arthroplasty. *Anesth Analg*. 1996;82:1225–1229.)

A multidisciplinary approach that includes trauma and orthopedic surgeons, urologists, interventional radiologists, anesthesiologists, and intensive care unit (ICU) physicians is crucial during the immediate management of these patients and should focus on adequate volume resuscitation, achieving hemostasis, and mitigating tissue injuries.[161] As soon as possible after the primary evaluation and stabilization, a comprehensive radiologic workup should be performed. CT is the gold standard with a sensitivity and specificity for bone fractures close to 100%. Initial treatment of pelvic trauma generally involves damage-control resuscitation and application of noninvasive external pelvic compression to stabilize the pelvic ring and decrease the amount of pelvic hemorrhage. Patients with hemodynamic instability should be considered for pre-peritoneal pelvic packing, especially in hospitals with no angiography service. External pelvic fixation provides rigid temporary pelvic ring stability and serves as an adjunct to early bleeding control in hemodynamically unstable pelvic ring disruptions.[161,162] The optimal time for definitive surgical fixation of pelvic ring injuries is within the first week of trauma.

Anesthetic management of patients with pelvic trauma in the operating room can be very challenging. Because of the extent of the surgery, general endotracheal anesthesia with standard or rapid sequence induction based on clinical presentation is indicated. These patients often need an immediate and aggressive resuscitation and, frequently, angiography and embolization of the injured vasculature.[161,163] The primary goal of the rapid resuscitation is to restore blood volume and maintain perfusion to the vital organs, with continuous evaluation of the efficacy of the fluid replacement. Sensitive laboratory markers of tissue ischemia secondary to the acute traumatic hemorrhage include increased serum lactate and base deficit by arterial blood gas analysis.[161] It is important to restore hemoglobin to a level that provides adequate tissue oxygenation (usually considered more than 7-8 g/dL) prior to inducing anesthesia, and to have sufficient amount of blood products available because of the risk for significant intraoperative blood loss. Because of the large intraoperative blood loss and third-spacing of fluids, invasive hemodynamic monitoring, including an arterial line and central venous catheter, may be necessary. Intravenous access through several large-bore catheters is also critical. Intravenous fluids and blood products should be administered through a fluid warmer to prevent hypothermia. A rapid fluid infuser is commonly used. Cell-scavenging techniques are useful to reduce the requirement for donor packed red blood cells. Placement of an epidural catheter for postoperative pain control can be considered, provided that the patient is not coagulopathic and after the neurovascular integrity of the lower extremities has been confirmed. Patients may be admitted to the ICU postoperatively for monitoring, and are sometimes intubated, especially in the presence of evolving pulmonary injuries (fat embolism, aspiration, or lung contusion), or other complicating organ injuries.

Femur Fractures

Fractures of the proximal femur following mechanical falls are most common in elderly patients and are associated with high morbidity and mortality (1-year mortality of up to 30%).[164] In younger patients, femur fractures including fractures of the femoral shaft and distal femur are usually associated with trauma, such as following motorcycle and motor vehicle accidents. Perioperative complications are often related to preexisting cardiac and pulmonary conditions and include myocardial infarction and dysrhythmias, DVT, pulmonary embolism, and delirium. It has been shown that older patients admitted early into a dedicated orthogeriatric facility have a improved long-term mortality.[165]

Proximal femur fractures occur through the femoral neck, intertrochanteric, or subtrochanteric areas. Displaced femoral neck fractures are usually treated by prosthetic replacement, whereas intertrochanteric or subtrochanteric fractures can be treated with a sliding hip screw and side plate, cephalomedullary nail, or blade plate. Nondisplaced femoral neck fractures are usually managed by closed reduction and percutaneous pinning.[166] Surgical treatment of femoral shaft and distal femur fractures involves application of plates and screws along the femur for rigid internal fixation and intramedullary devices.

Pain and stress following hip fracture can often contribute to myocardial ischemia. Therefore, a thorough preoperative evaluation and preparation of these patients, as outlined earlier in this chapter, is crucial. Early surgery (<24 hours) has been associated with reduced pain and length of hospital stay but not improved function or mortality.[167] However, patients with significant medical comorbidities that delay surgery for more than 4 days have a nearly 2.5 times higher risk of death within 30 days after the surgery compared with patients who are initially considered fit for surgery.[164] Thus, early surgery for hip fractures combined with early mobilization and rehabilitation should be the goals for medically stable patients.

Given the existing evidence that regional anesthesia can be associated with lower morbidity (including reduced risk of DVT, pulmonary embolism and respiratory complications, and a decrease in intraoperative blood loss) and mortality,[168] it is reasonable to consider regional anesthesia in patients with hip fractures.[169] A carefully dosed spinal anesthetic with isobaric bupivacaine often provides stable anesthesia of sufficient duration for the surgical repair. Anesthesia from T12 to S2 is adequate. Use of anticoagulation for prevention of DVT and pulmonary embolism may limit the use of postoperative epidural analgesia. There is evidence that regional nerve blocks including fascia iliaca blocks can effectively reduce pain associated with hip fracture. There is also moderate evidence that nerve blocks may contribute to reduced rates of delirium, and potentially, reduced length of inpatient stay, morbidity, and mortality.[170]

Pulmonary embolization of bone marrow debris and bone cement leading to hypoxemia and right ventricle failure is a major determinant of mortality in these patients.[171] The presence of emboli detected by intraoperative TEE in the right heart and pulmonary artery appears to derive principally from the reaming of the femoral canal and the placement of the femoral stem, particularly during the placement of cemented prostheses (see earlier).[159] Although routine use of intraoperative TEE is not recommended, it may be considered in high-risk patients with femur fractures. Adequate intravenous access and cross-matched blood products should be available, because some of these procedures can involve a large blood loss. Placement of an arterial catheter allows timely and accurate blood pressure monitoring, and serial measurements of arterial blood gases and hemoglobin concentrations. The use of a central venous catheter may also be indicated in high-risk patients. Maintaining body temperature during surgery is particularly important in the older patient population. Medically unstable patients with significant comorbidities often require postoperative management in an ICU setting.

Tibia Fractures

Tibial plateau or proximal tibia fractures are most common in younger trauma patients, as well as elderly patients with degenerative arthritis of the knee. Open reduction internal fixation of tibial plateau fractures involves a reduction under direct visualization of the fracture fragments and application of plates and screws along the tibia for rigid internal fixation. An iliac crest bone graft may also be necessary. Compartment syndrome is one of the most frequent complications of this surgery (10%-20%). Tibial shaft fractures are commonly associated with trauma (95%) and are treated by intramedullary nailing of the tibia. Most nails are interlocked proximally and distally with screws. External fixation of tibia fractures involves placement of percutaneous pins that are clamped to an external frame. This procedure can be used for temporary stabilization of tibia fractures, especially in the setting of periarticular injuries. These fixators also may be useful for salvage of open and/or infected fractures that are unsuitable for internal fixation.[172] Tibia surgeries are frequently performed under general anesthesia, although spinal anesthesia could also be considered. Regional blocks can also be considered for postoperative pain control if compartment syndrome is not a major concern. In fact, evidence suggests that in most patients, regional techniques do not interfere with diagnosis of compartment syndrome.[173]

Upper Extremity Fractures

Trauma patients presenting for surgeries for upper extremity fractures are relatively young and often otherwise healthy. Most of these surgeries are performed on an elective basis with a standard preoperative evaluation. However, repairs of compound fractures and open fractures may necessitate emergency surgery. General or regional anesthesia or their combination can be used. A brachial plexus block via the supraclavicular, infraclavicular, or axillary approach is suitable for surgeries of the distal arm, whereas the interscalene approach is employed for more proximal humerus procedures. A peripheral nerve catheter may be considered for postoperative pain relief. Regional techniques can be safely applied when there is no concern for postoperative compartment syndrome.

Extremity Replantation

Functional recovery remains the overarching goal of extremity replantation. Traumatic amputation disproportionately affects males in a 4:1 ratio. Most upper extremity amputations occur at the level of the digits. Life-threatening injuries, if present, must be prioritized before consideration is given to replantation. The ultimate surgical plan is often deferred until after microscopic examination of the stump and amputated parts. Severe crush or burn injuries massive contamination, multiple injuries in the same digit, prolonged normothermic ischemia, and preservation of amputated parts in nonphysiologic solutions are relative contraindications to proceeding with replantation.

To minimize irreversible tissue injury, hypothermic preservation of the amputated part and measures to reduce the interval between amputation and replantation are routinely practiced. The goal for successful digit replantation is to be completed within 12 hours of warm or 24 hours of cold ischemia. The window is narrower for major upper extremity implantation (6 hours of warm and 12 hours of cold ischemia).[174] Extremity replantation is hence an emergent procedure and patients often present having full stomachs. Substance abuse is common in this population and acute intoxication may raise additional concerns, such as altered anesthetic requirement, diuresis, and hypovolemia or hypothermia. The patient may also present with acute blood loss anemia depending on the extent of the traumatic injury. Regional anesthesia is typically used either alone or in conjunction with general anesthesia to provide postoperative analgesia and most importantly, vasodilation to the vascular anastomosis. Indeed, brachial plexus nerve catheters have been shown to improve the blood flow to the implant through vasodilation.[174-176] As a surrogate marker of tissue perfusion, skin temperature is elevated in patients having brachial plexus blocks.[177] Furthermore, one study demonstrated a 0% reoperation rate for vascular insufficiency in patients having continuous supraclavicular blocks, versus 29% reoperation rate in patients managed with intravenous opioids alone.[178] The surgical team often performs the replantation in the following sequence: bone fixation, tendon repair, nerve repair, vascular anastomosis, and skin closure. Typical donor sites for skin grafts include stomach and thigh. Intravenous heparin and dextran are typically administered during the microvascular portion of the surgery to minimize the risk of thrombosis, which complicates 10% of cases. In theory, vasopressors should be avoided; however, there is little evidence to support this claim clinically. A tourniquet is routinely used to minimize blood loss, but a baseline complete blood count and a blood bank sample are prudent in the setting of any traumatic injury. Reperfusion intervals for tourniquet times of greater than 90 to 120 minutes should be considered. Lactic acidosis from a prolonged tourniquet time may be problematic in patients with underlying lung disease, and maintaining controlled ventilation is advisable in such patients in order to compensate the metabolic acidosis.

Surgical duration is variable. The clinician should meticulously position and monitor all pressure points, given probable length of procedure. Techniques to maintain perioperative normothermia, such as fluid warmers and heating blankets, are employed to prevent vasospasm. After the procedure, it can be helpful to admit the patient into a room with increased ambient temperature to promote vasodilation. In addition, anticoagulant therapy may need to be continued to prevent microthrombi. The peripheral catheters should be monitored regularly by a dedicated team and coagulation status should be checked prior to discontinuing the catheter. Patient controlled analgesia (PCA) is a useful alternative in the initial days following the procedure, but opioid utilization can be reduced by peripheral nerve block or catheter.

UPPER EXTREMITY SURGERIES

Hand Surgery

Hand surgeries are performed by several surgical specialties including general surgeons and orthopedic surgeons, as well as plastic and hand surgeons. These cases vary in complexity from a simple incision and drainage to complete neurovascular replantation of several digits and even the entire hand, as well as urgency from elective surgeries to emergent procedures such as replantation of ischemic digits. Hand procedures can vary widely in length from several minutes to several hours. Less complex procedures are performed at outpatient surgical centers, whereas complex procedures are reserved for tertiary care hospitals. Given the varying nature of hand surgeries, the anesthetic approaches to hand cases also vary from intravenous anesthesia or Bier block to regional anesthesia or general endotracheal anesthesia.

Intravenous regional anesthesia (or Bier block) is a simple technique that involves exsanguinating the arm by wrapping it with an elastic bandage (e.g., Esmarch bandage), inflating an upper arm tourniquet to between 50 and 100 mm Hg above the patient's systolic blood pressure (often to 250 mm Hg), and injecting a short-acting preservative-free local anesthetic (typically lidocaine) into a hand vein. A second tourniquet, distal to the first, may be inflated 15 minutes later with subsequent deflation of the first, to minimize tourniquet pain. The extremity veins distal to the tourniquet are filled with the anesthetic agent, which sets in after approximately 6 to 8 minutes. Complications occur when the tourniquet fails during initial anesthetic injection or if the tourniquet is deflated too early (<30 minutes), risking systemic local anesthesia toxicity. Adjuncts can be added to the local anesthetic injectate including ketorolac and clonidine to extend duration of analgesia, but their routine use is discouraged by most experts, because the potential benefits do not seem to outweigh the risk of increased complexity and side effects.

Regional anesthesia techniques for hand surgery include blocking the brachial plexus via an infraclavicular (ICB) or axillary approach. Two large series of infraclavicular blocks reported 90% to 94% success with only posterior cord stimulation using a nerve stimulator; other reports recommend a double stimulation technique for a better success rate. Ultrasound-guided ICB continues to gain popularity, as its first pass success is superior to the nerve stimulator technique. As with the nerve stimulator technique, injecting local anesthetic at the posterior cord increases the success rate.[179] Moreover, performing ICB with ultrasound guidance may shorten procedure time, avoid the need for multiple needle passes, and reduce complications of vascular puncture and pneumothorax.[180] For high-risk patients who are anticoagulated, an axillary block is a reasonable option, as the artery is easily compressible. With ultrasound guidance, selective nerve blockade can be achieved to minimize bleeding potential. For complex and emergent hand cases, general anesthesia is often chosen because of the prolonged duration of the procedure (see trauma section earlier).

Shoulder and Elbow Surgery

Over the past several decades, an increasing number of patients have undergone shoulder surgeries, as it has been shown that these procedures have a positive impact on the quality of life. Shoulder arthroplasty surgery can range from extensive open repairs, hours in duration, to simple shoulder arthroscopic procedures of short duration. Most of the surgeries are performed in the beach chair position, as this position offers superior surgical exposure and access, less distortion of muscle anatomy, and less tension on the brachial plexus than the lateral position. Therefore, anesthetic considerations are mostly tailored to counterbalance the physiologic derangements occurring in this position in anesthetized patients. Anesthetic techniques can range from general anesthesia to conscious sedation or monitored anesthesia care with regional block. For the most part, open procedures require muscle relaxation and therefore, general endotracheal anesthesia is often preferred. For arthroscopic procedures, muscle relaxation is not necessary, and these cases can be amenable for general anesthesia with a LMA or monitored anesthesia care with regional block. The anesthetic approach is largely influenced by the local practice culture. Surgeons may request controlled hypotension in arthroscopic cases, as visualization can be hindered by local bleeding. This can be problematic, especially in patients with chronic uncontrolled hypertension, as well as those with underlying cerebral vascular insufficiency. Cerebral perfusion pressure (CPP) is reported to decrease by 15% in sitting patients under general anesthesia. In patients with chronic hypertension, cerebral autoregulation is altered, and the curve is shifted to the right (Fig. 64.10). In patients with cerebrovascular disease, detrimental decrease in cerebral blood flow (CBF) can occur if the systemic pressure is kept below the minimal required CPP. Cerebral autoregulation is also influenced by ventilation via arterial PCO_2. Hypercapnia can result in cerebral vasodilation and increased CBF at a constant CPP. Conversely, hypocapnia causes a decrease in CBF due to cerebral vasoconstriction.[181] A randomized study suggested that cerebral oxygenation can indeed be improved with higher end tidal CO_2 during surgery in the beach chair position.[182] Therefore, permissive hypercapnia may be considered during shoulder surgery in the sitting position for patients with altered CBF. Additionally, the effects of vasopressors, such as phenylephrine, in the sitting position should be taken into account, as high doses of vasoconstrictors can affect CBF. In a study measuring cerebral oxygen saturation in the sitting position, desaturation occurred with the use of phenylephrine. The study concluded that cerebral oxygenation can be used to provide an endpoint for vasopressor therapy.[183] Another important anesthetic factor to consider when allowing hypotension in the beach chair is the distance discrepancy between the measurement of noninvasive blood pressure (NIBP) and the circle of Willis. In the supine position, the height of the NIBP at the arm and the circle of Willis are about the same. Therefore, the blood pressure reading closely approximates the CPP. However, in the sitting position, the blood pressure reading from the arm is different than the actual CPP at the circle of Willis. In general, for every 10 cm rise of an organ or tissue, there is 7.5 mm Hg drop in its mean arterial pressure. In the sitting position, the distance between the blood pressure cuff at the arm and Circle of Willis can approximate 20 cm. A technique to mitigate the distance is to decrease the angle of the sitting position. When inducing hypotension in the sitting position, all these factors have to be taken into account and discussed in a preoperative huddle with the surgeon. It is important to note that the role of the sitting position (beach chair) on postoperative neurological outcome remains controversial. According to the Anesthesia Patient Safety Foundation Beach Chair Study, there were no differences in postoperative cognition or brain injury biomarkers when compared to the supine position.[184]

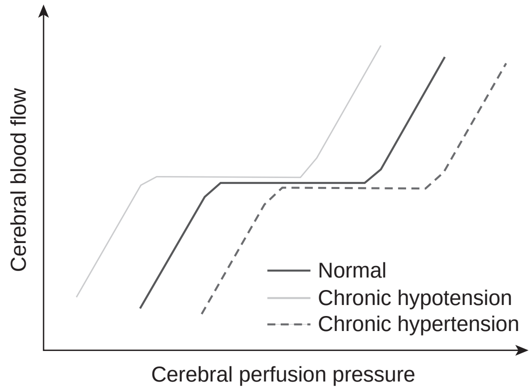

Fig. 64.10 Cerebral autoregulation curve.

Another serious complication that has been reported during shoulder surgery is excessive hypotensive and bradycardic events, some progressing to asystolic arrest, under monitored anesthesia care with regional anesthesia. There is some evidence that these events are the result of a cardiac inhibitory reflex, or the Bezold-Jarisch reflex, which occurs in response to diminished ventricular volume (venous pooling in the sitting position) in a hypercontractile ventricle. Prophylactic administration of β-blockers and intravenous fluids may reduce the incidence of these events.

Regional anesthesia, specifically interscalene block (ISB), continues to gain popularity for shoulder surgeries, as it can provide postoperative analgesia and decrease opioid consumption. For shoulder arthroscopies, single -shot ISB has been associated with less time spent in the postanesthesia care unit, better patient satisfaction, and fewer complications.[185] ISB can be utilized as the sole anesthetic for shoulder surgeries. However, this approach is not widely practiced.[186] One must be mindful of the impact ISB can have on pulmonary function secondary to ipsilateral phrenic nerve weakness. If prolonged analgesia is desired (>24 hours), placement of an interscalene catheter can be considered. Patients can be discharged with an infusion pump and can even self-discontinue the catheter at home.[187] Alternatives to ISB include selective suprascapular nerve (SSN) block, intraarticular analgesia, and oral analgesia. SSN block is performed with the patient sitting, and local anesthesia is injected at the suprascapular fossa, avoiding the vessels that travel with the nerve. This technique partially covers the shoulder but has no cutaneous coverage.[188] Ultrasound guidance can be used to block the nerve at the suprascapular fossa or at the suprascapular notch. An anterior ultrasound approach can be employed to trace the SSN from the interscalene groove at C5 down to below the omohyoid muscle. Injection at this site has been shown to result in less motor blockade than ISB and equivalent analgesia.[189] Intraarticular anesthesia is another alternative approach to postoperative pain control after shoulder surgery and involves injecting local anesthetic agents. This technique has been shown to significantly reduce post-surgical opioid consumption.[190] Recently, a long-acting formulation of bupivacaine, liposomal bupivacaine, was tested for perioperative peripheral nerve blockade. A small randomized prospective study compared locally infiltrated liposomal bupivacaine versus conventional ISB and found increased pain in the immediate postoperative period in patients receiving liposomal bupivacaine. However, opioid consumption was greater in the ISB group 13 to 16 hours after surgery. Beyond 24 hours, there was no difference in the two groups in terms of their pain scores, hospital length of stay, or number of complications. This study concluded that overall liposomal bupivacaine offered comparable analgesia to ISB, but could help reduce overall opioid consumption.[191] Larger studies are being conducted to further investigate the role of liposomal bupivacaine in shoulder surgery.

In contrast to shoulder surgery, elbow surgery does not require beach chair position, and the patient is usually in supine or lateral decubitus position. Common elbow surgeries include fixation of fractures as well as neurovascular repair. Most surgeries are performed under general anesthesia; however, monitored anesthesia care with regional block can be considered for selected patients and procedures and when there are no concerns for irreversible nerve injuries or compartment syndrome.

As with shoulder and hand surgeries, regional anesthesia can play a major role in postoperative analgesia after elbow surgery. The infraclavicular approach (ICB) to blocking the brachial plexus is common, but data suggest that a supraclavicular block may be just as effective.[192] Supraclavicular block spares the intercostobrachial nerve providing cutaneous innervation of the medial upper arm at the T2 dermatome. If a tourniquet is used, blocking the T2 can help decrease tourniquet pain.

LOWER EXTREMITY SURGERY

Knee and Hip Arthroscopy

Arthroscopic procedures for the knee, hip, and ankle are increasingly performed as ambulatory procedures. These cases can be challenging for the anesthesiologist who must decide on the appropriateness of the patient and procedure for outpatient surgery and an anesthetic that is adequate for the procedure, but also satisfy the patient's expectation of an uncomplicated postoperative recovery with minimal pain.

General anesthesia is safe and effective for arthroscopic surgery, but it has been associated with increased postoperative nausea and vomiting and pain. In a prospective study of 1088 patients for ambulatory surgery, Pavlin and coworkers reported that the most important factors in determining the time to discharge were pain, unresolved neuraxial blocks, nausea and vomiting, and urinary retention.[193] This study emphasizes the role of anesthesia in prolonging ambulatory surgical stay. A properly designed regional anesthetic approach may reduce the impact of some of these factors.

Arthroscopic knee surgery can be performed with a combination of extraarticular and intraarticular injections of local anesthetics. Short-duration local anesthetics may be combined with longer-acting local anesthetics (bupivacaine) and morphine to provide postoperative analgesia. Intraarticular morphine has not been shown to provide significant additional analgesia after arthroscopic knee surgery. For more involved arthroscopic procedures, such as an anterior cruciate ligament repair, surgical relaxation may be required. Spinal anesthesia provides excellent operating conditions for these procedures. Problems related to neuraxial anesthesia for ambulatory surgery include unpredictable onset and regression of the blockade, urinary retention, and transient neurologic symptoms (TNS). A dose of 45 mg of isobaric spinal mepivacaine has been reported to result in a mean motor block of 142 ± 37 minutes. Using 30 to 40 mg of spinal chloroprocaine, Yoos[194] reported 155 ± 34 minutes to ambulation in outpatient surgical patients. TNS include pain in the gluteal region that can radiate down both legs and appear within a few hours to 24 hours after an uneventful spinal anesthetic. The incidence of TNS is more frequent after outpatient surgery performed in the lithotomy position and in patients undergoing knee arthroscopy. The pain can vary from mild to severe and last 2 to 5 days. It is best treated with NSAIDs. TNS is more common after a spinal anesthetic with lidocaine (~14%) than with mepivacaine (6.5%) and bupivacaine (<1%). For ambulatory patients, the benefit of short-acting spinal anesthetic must be weighed against the risk for developing TNS. For postoperative analgesia after anterior cruciate ligament repairs, a femoral nerve block (FNB) with a long-acting local anesthetic is superior to intraarticular injections. Because the quadriceps muscle is blocked, however, it is important for the patient to be fitted with a knee brace before ambulation. Blocking the femoral nerve at the adductor canal (adductor canal block [ACB]) can also provide postoperative analgesia without interfering with early ambulation, as quadriceps strength is preserved when compared to FNB.[195] However, the analgesia does not cover the posterior aspect of the knee.

Hip arthroscopy has become a common outpatient procedure for the diagnosis and treatment of pathologic processes in the hip. The patient can be placed in either the supine or the lateral position (operative side up) with 50 to 75 lbs (22-34 kg) of traction applied to the operative limb to gain access to the joint with the arthroscope. In positioning the patient, the anesthesiologist must ensure that the perineal post is padded and not compressing the pudendal nerve and that excessive traction for prolonged periods is not applied. Because complete muscle relaxation is usually required for the procedure, the patient must have either a general anesthetic or a neuraxial block. A lumbar plexus block can be performed for postoperative analgesia.

Hip and Knee Arthroplasties

As was described earlier in this chapter, hip and knee joint replacement are among the most common surgeries in the United States. THA may be performed via an anterior or lateral approach. The anterior approach offers the advantage of exposure without violation of the muscles, but restricts full access to the femur, with the risk for lateral femoral cutaneous nerve injury. The lateral posterior approach provides excellent exposure to the femur and the acetabulum with minimal muscle damage but increases the risk for posterior dislocation. Most surgeons prefer the lateral posterior approach, which places the patient in the lateral decubitus position, surgical side up, for the operation. The anesthesiologist must be aware that this position may compromise oxygenation, particularly in obese and severely arthritic patients, as a result of ventilation-perfusion mismatch.

In addition, to prevent excessive pressure on the axillary artery and brachial plexus by the dependent shoulder, a soft roll or pad may be placed beneath the upper thorax.

The nerve supply to the hip joint includes the obturator, inferior gluteal, and superior gluteal nerves. Regional anesthesia for THA can be achieved with a spinal or epidural anesthetic. Although most studies suggest decreased postoperative respiratory complications, including venous thrombosis and pulmonary embolism with regional versus general anesthesia, some controversy still remains. It is, nevertheless, important to note that regional anesthesia has been associated with a reduction in deep surgical site infection rates and hospital length of stay.[196]

Blood loss during THA can be significant, particularly for revision surgeries. Controlled hypotensive anesthesia may reduce intraoperative blood loss. The administration of TXA has also been shown to reduce blood loss during joint arthroplasty (see earlier). The femoral vein can be obstructed during dislocation of the hip and reaming and insertion of the femoral prosthesis, which can result in blood stasis and clot formation. With relocation of the hip and unkinking of the femoral vein, the embolic material can be released into the circulation. An unfractionated heparin bolus before the femoral work has been suggested to reduce the strong thrombotic stimulus and should be considered in selected patients.

Similar to THA, anesthetic options for TKA include general or neuraxial anesthesia. A less common approach is the combination of a femoral and sciatic block, but in patients with valgus deformities, this approach may prevent the early detection of sciatic and peroneal nerve palsies. A 2016 systematic review of the literature found that neuraxial anesthesia is as effective as general anesthesia without increased morbidity, and that limited quantitative evidence supports the notion that perioperative outcomes are improved with neuraxial anesthesia.[197] Another benefit of regional anesthesia is decreased postprocedural opioid consumption.

Patients who have undergone TKA have severe postoperative pain, and several studies have reported a reduction in postoperative complications and improved outcomes when this pain is managed with regional anesthesia. Single-injection FNBs in combination with intravenous and epidural PCA have been employed to manage postoperative pain and improve functional recovery. Infusion of local anesthetics through continuous femoral nerve catheters may also be used in place of patient-controlled epidural analgesia. Both FNB and epidural anesthesia have been associated with delayed ambulation post TKA. There have been recent efforts to fast track recovery for arthroplasty patients and aim for early mobility via early physical therapy. This has been shown to improve long-term functional status. As a result, there has been a shift away from FNBs and epidural anesthesia in favor of ACBs. A large meta-analysis suggested that patients who received ACB combined with periarticular local anesthesia injection could ambulate sooner than those with periarticular injection alone. No differences in postoperative analgesia or opioid consumption were noted.[198] Intraarticular multimodal injection of ropivacaine, ketorolac, clonidine, and epinephrine in combination with oral acetaminophen, celecoxib, and oxycodone was, nevertheless, shown to decrease opioid-analgesic requirements and increase patient satisfaction after TKA.[199-201]

A pneumatic tourniquet is routinely inflated over the thigh during TKA to reduce intraoperative blood loss and provide a bloodless field for cement fixation of the femoral and tibial components. Bleeding begins with the deflation of the tourniquet and can continue for the next 24 hours. Tourniquets are usually inflated to a pressure 50 to 100 mm Hg above the patient's systolic blood pressure for a maximum of 3 hours. Nerve injury after tourniquet inflation has been attributed to the combined effects of ischemia and mechanical trauma. When prolonged tourniquet inflations are required, deflating the tourniquet for 30 minutes of reperfusion may reduce neural ischemia.

Pain related to tourniquet inflation also may occur after 60 minutes, despite the presence of a regional anesthetic that is adequate for the surgery. It has been postulated that tourniquet pain is caused by the unblocking of unmyelinated C fibers during recession of a neuraxial block. The addition of opioids to spinal or epidural anesthesia may ameliorate tourniquet pain. After tourniquet release, mean arterial blood pressure decreases significantly, partly owing to the release of metabolites from the ischemic limb into the circulation and the decrease in peripheral vascular resistance. In patients with known preexisting sciatic neurapraxias, neuropathic pain, and vascular disease in the operative leg, the operation can be performed without a tourniquet.

Many patients have symptomatic arthritis of both knees and require bilateral TKA to achieve functional improvement in pain and lifestyle. However, controversy still exists as to whether both knees should be replaced sequentially in a single operation (simultaneous bilateral total knee arthroplasty [SBTKA]) or through a two-stage procedure. The advantages of SBTKA include exposure to the risks of one anesthetic course one postoperative course of pain, reduced rehabilitation and hospitalization, and an earlier return to baseline function. However, SBTKA has been associated with a higher incidence of serious perioperative complications such as myocardial infarction, fat embolization, and thromboembolic events.

Foot and Ankle Surgery

Similar to most hand surgeries, foot and ankle surgeries are classified as low-risk procedures. However, the low-risk nature of the procedures can pose a challenge for clinicians when caring for high-risk patients. The risks and benefits must be carefully considered when crafting an anesthetic plan, which can include general endotracheal anesthesia, general anesthesia with a LMA, neuraxial anesthesia with spinal or epidural, and regional anesthesia. Muscle relaxation is often not required. In caring for patients undergoing these procedures, length of procedure, patient position, and institutional preferences are considered when deciding on anesthetic approach and patient monitoring. Unlike hand cases, patient positioning can vary from supine, to lateral decubitus, to prone positioning. Most elective cases are done as outpatient surgery. Trauma cases can be long in duration, especially with complex fractures of the distal tibia. Infected toe and foot surgeries can be performed quickly, but patients may present with sepsis due to gangrenous tissue. It is not unusual to find that the patient who requires foot and ankle surgery is immunocompromised, diabetic, or has vascular insufficiency. Bleeding can occur, but generally it is not a main concern. Thigh or leg tourniquets are often used to limit blood loss.

Surgery of the foot and ankle is associated with high postoperative pain. Regional anesthesia can be beneficial and is commonly used as the primary anesthetic or for postoperative analgesia. These cases are ideal for regional anesthesia also because many patients are instructed to avoid bearing weight after surgery, and hence motor weakness is not a concern. Regional anesthesia that combines sciatic and FNBs is sufficient for all surgical proceures below the knee that do not require a thigh tourniquet. The femoral nerve innervates the medial leg to the medial malleolus, and the remainder of the leg below the knee, including the foot, is innervated by sciatic nerve via the common peroneal nerve and tibial nerve. The sciatic nerve is usually blocked high in the popliteal fossa to ensure anesthesia to the tibial and peroneal nerves. The nerve can be identified via a nerve-stimulating needle with foot inversion as the motor response. Increasingly, however, the sciatic block is performed with ultrasound guidance. For procedures that also involve the medial aspect of the leg, the femoral nerve can be blocked, commonly at the adductor canal, at the level of the knee via the medial femoral condyle, below the knee with local infiltration distal to the medial condyle of the tibia, or above the medial malleolus of foot. Each of these approaches has various degrees of success, with the highest success being the ACB.[202] The popliteal sciatic nerve block has been shown to reduce postoperative pain and opioid requirements after foot and ankle surgery when performed as a single preoperative injection or as a continuous catheter infusion. Studies suggest that for ultrasound-guided sciatic blocks, optimal onset and analgesia is achieved when the local anesthetic is injected distal to the sciatic bifurcation.[203,204] For sciatic catheters, optimal analgesia is achieved when the catheter is placed 5 cm proximal to the sciatic bifurcation.[205] Liposomal bupivacaine is being investigated as an alternative to regional anesthesia for local infiltration.[206]

A discussion with the surgeon about the risk for compartment syndrome should occur before administering long-acting sciatic nerve blocks. However, there is increasing evidence that regional anesthesia may not mask ischemic pain from compartment syndrome, and this question remains controversial.[173,207] Ankle block can be used for surgical procedures on the foot that do not require the use of a thigh or calf tourniquet, although an ankle-level Esmarch tourniquet may be used. It is commonly used for toe amputations and is also a highly effective technique for bunion surgery.[208]

Five terminal nerves are usually blocked to provide complete anesthesia to the foot: (1) posterior tibial nerve, which provides sensation to the plantar surface; (2) saphenous nerve, which innervates the medial malleolus; (3) deep peroneal nerve, which supplies the interspace between the great and second toes; (4) superficial saphenous nerve, which supplies the dorsum of the foot and the second through the fifth toes; and (5) sural nerve, which supplies the lateral foot and lateral fifth toe (Fig. 64.11). Mineo and Sharrock reported that ankle block performed at the midtarsal level with 30 mL of 0.75% bupivacaine provided a mean duration of 17 hours of analgesia with safe blood levels of local anesthetic.[209]

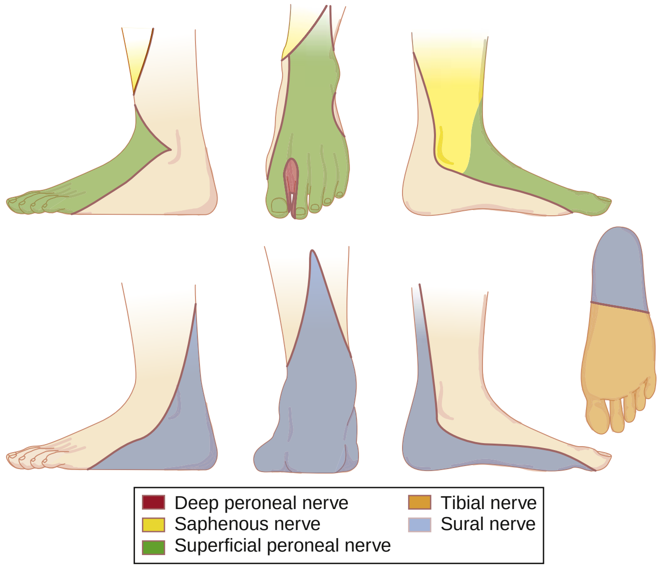

Fig. 64.11 Cutaneous distribution of anesthesia produced by an ankle block. (From Carron H, Korborn GA, Rowlingson JC. *Regional Anesthesia: Techniques and Clinical Applications*. New York: Grune & Stratton; 1984.)

Anesthesia for Spine Surgery

With the wide spectrum of spine disorders and an expanding array of treatment options, spinal surgeries have become increasingly prevalent over time. According to the Healthcare Cost and Utilization Project, spinal fusions and laminectomies were among the most common operations during inpatient stays in 2015, with an estimated rate of 147 and 136 per 100,000, respectively. In absolute numbers, it was estimated that an excess of 500,000 spinal fusions were performed in community hospitals alone in the United States.[210] Although only less than 10% of these surgeries are currently performed in an ambulatory setting, it is expected that with technical advances and enhanced perioperative care, an increasing number of these patients will qualify for outpatient surgery. Moreover, a growing number of patients with major comorbidities are being considered for complex spine surgeries such as scoliosis correction or spinal stabilization after trauma or neoplastic diseases. The underlying cardiovascular, respiratory, or neurologic disorders in combination with the physiologic stress from a large spinal procedure places the patient at a higher risk for perioperative complications. As described earlier in this chapter, preoperative optimization of the underlying diseases and careful perioperative care that involves the surgical, anesthesia, rehabilitation, and other medical teams can minimize the risk for these complications and improve the overall outcome.

PREOPERATIVE ASSESSMENT

The preoperative assessment for spinal surgeries should include a comprehensive evaluation of the neurologic function and possible symptoms or deficits associated with the underlying spinal disorder. The potential for difficulty in airway management should always be considered in patients with cervical and thoracic spine disease. Stability of the cervical spine and its range of motion should be assessed and documented, and the anatomic and functional relationship between the airway and the cervical column carefully considered. Video laryngoscopy or fiberoptic intubation may be needed and if awake intubation is considered, it is important to assess the patient's ability to cooperate. A multidisciplinary preoperative conference to review the suitability of each patient and discuss the medical, surgical, anesthesia, and rehabilitation implications of the procedure can improve the quality and safety in complex spine surgery.[211] In addition to a comprehensive review of the patient's preoperative cardiovascular, pulmonary, and neurologic comorbidities, basic hematologic, hepatic, and renal values, their preoperative optimization, perioperative pain control, and rehabilitation potentials also need to be considered.

SPINAL TRAUMA

Trauma victims with spinal cord injury (SCI) represent a group of patients with unique perioperative challenges. The incidence of nonfatal SCI is estimated to be 40 per 1 million population in the United States, or approximately 12,000 new cases each year.[212] Most injuries occur between the ages of 16 and 30. One retrospective analysis examined more than 500 patients with traumatic spinal fractures and found that 39% were caused by a high-energy fall and 26.5% by motor vehicle accidents.[213] The high-energy fall etiology resulted in injuries distributed throughout the spine, whereas motor vehicle accidents most frequently impacted the cervical and thoracic spine. Twenty-five percent of patients with spinal fracture had motor and/or sensory deficits, and the highest number of patients with complete motor and sensory neurologic deficits had sustained cervical fractures. Types of fractures were distributed as follows: compression fractures in 54.8% of patients, distraction fractures in 16.9%, and rotational fractures in 18.5%. Compression fractures occur when the vertebral body cannot handle a sudden force and fractures. This commonly occurs in the setting of osteoporosis and malignancy. A wedge fracture is a subtype, which often involves the anterior collapse of the vertebral body. Burst fractures occur as a result of severe trauma, such as a motor vehicle accident. Vertebrae are crushed by an extreme force and are impacted in multiple places. Flexion-distraction fractures typically involve the middle and posterior column of the spinal column. Flexion-dislocation fractures can include any of the aforementioned fracture types and occur when the vertebrae move significantly. Anterior, middle, and posterior columns are usually involved. This is an unstable fracture. With most SCIs caused by falls or motor vehicle collisions, it is not unusual that these patients also suffer injuries to the face and airway or present with traumatic brain injury, rib fractures and lung contusions, extremity or pelvic fractures, vascular injuries, or hepatic or splenic lacerations. The initial SCI may be caused by mechanical force from bony fragments from the vertebral body, facet or intervertebral joint dislocation, ligamentous tears or herniation of intervertebral discs, or arthropathies such as spondylosis or spondylolisthesis. Following the initial injury, systemic inflammation, ischemia or hypoxia, and excitotoxicity or lipid peroxidation and apoptosis of neurons can result in progression of the neurologic symptoms and worsening outcome. If facial or cervical spine injuries are present, airway management can be particularly challenging. Unstable cervical spine injury constitutes approximately 14% of SCI cases.[214] Techniques to minimize cervical movement should then be employed during management of the airway. Because of the urgent nature of airway interventions, many practitioners continue to use direct or indirect laryngoscopy with manual in-line stabilization (MILS), which applies opposite forces to the head and neck to limit the movement. The incidence of intubation-related neurologic impairment has been reported to be very low when MILS is applied during endotracheal intubation in patients with SCI.[215] However, MILS can worsen laryngeal visualization during direct laryngoscopy and increase the rate of tracheal intubation failure.[216] Rigid indirect video laryngoscopy is a reasonable alternative to conventional direct laryngoscopy and in skilled hands can minimize cervical motion during intubation, although studies have failed to confirm any clear advantages.[217] Obviously, fiberoptic intubation is often the safest approach in patients with cervical spine instability, but clinicians must also consider the patient's ability to cooperate during an awake fiberoptic intubation, as well as the risk of aspiration if deep sedation or general anesthesia is required. Neuromuscular blockade may be needed to facilitate intubation, but it is important to consider the risk of induced hyperkalemia associated with depolarizing neuromuscular blocking agents in these patients. Succinylcholine should be avoided after the initial 48 to 72 hours following an SCI.[218,219]

Another important challenge in patients with SCI is systemic hypotension, which can be caused by hemorrhage from associated injuries. In addition to hypovolemia, a common cause of hypotension in patients with high cervical SCI is neurogenic or spinal shock, which is characterized by bradycardia as well as vasodilation associated with the loss of central supraspinal sympathetic control.[220] If not appropriately managed, hypotension after SCI can compromise spinal cord perfusion and lead to secondary cord injury. The American Association of Neurological Surgeons (AANS) has, therefore, recommended that systemic arterial pressure be maintained at greater than 90 mm Hg for 5 to 7 days after SCI (class 3 evidence).[221] Although it remains controversial, data from a Cochrane review support a 48-hour course of high-dose steroids initiated within 8 hours of injury to those patients with incomplete neurologic deficits.[222]

COMMON SPINAL PROCEDURES

According to the Nationwide Inpatient Sample and the National Hospital Discharge Survey, discectomies, spinal decompression, instrumentation, and fusion are the most frequently performed spinal procedures in the United States. Anterior cervical discectomy is indicated in patients with spinal cord or nerve root compression from herniated disks or osteophytes. Patients often present with radiculopathy, myelopathy or, if they also suffer ligamentous laxity or disruption, cervical instability. A left-sided approach is usually preferred, as it minimizes the risk of recurrent laryngeal nerve injury. The disk is excised in a piecemeal fashion and bone graft placed in the intervertebral space with fusion performed to maintain stability, the disk height, and normal cervical lordosis. Posterior foraminotomy has the advantage that it does not require fusion and hence preserves the motion, but it is not effective for midline disk herniation and is more often associated with postoperative pain. Cervical canal stenosis or tumors may require decompressive laminectomy through a posterior approach. Obviously, the dura will need to be opened for resection of intradural masses, and it is then reasonable to avoid excessive reverse Trendelenburg, as it can increase the risk for pneumocephalus.[223] After the dura is closed, its integrity can be tested with a Valsalva maneuver.

Lumbar laminotomy and laminectomy are commonly employed for decompressing the neural elements of the lumbar spine. Posterior lumbar fusion is used for treatment of low-back pain associated with segmental or iatrogenic lumbar instability and spondylolisthesis and is commonly approached through a posterolateral fusion (PLF) or posterior lumbar interbody fusion (PLIF). PLF combines decompressive laminectomy and discectomy with PLF through decortication and bone grafting of the facet joints and transverse processes, whereas in PLIF the bone graft is packed into the disk space between the vertebral bodies after total discectomy and removal of the cartilaginous end plates. In both approaches, fusion is facilitated, and stability obtained through insertion of pedicle screws and a rod construct. Pedicle screw stabilization remains the preferred mode of instrumentation and provides rigid three-column fixation, but screw malposition can cause nerve-root injury. There are no major differences in clinical outcome or complication rates, but PLIF has been associated with better fusion rates and pain scores in the treatment of lumbar spondylolisthesis.[224] Minimally invasive surgery (MIS) techniques are increasingly employed and include direct or extreme lateral interbody fusion (DLIF or XLIF), where the spine is approached laterally through the retroperitoneal cavity, and transaxial lumbosacral fusion (Transl) through a 1 cm incision at the base of the sacrum. Blood loss is minimal with MIS, but occult injury to peritoneal contents have been reported.

Scoliosis can be classified as congenital, neuromuscular, or idiopathic. With an incidence of 4 per 1000, idiopathic scoliosis accounts for the majority (about 80%) of cases. A Cobb angle of 10 degrees is the minimum angulation to define scoliosis, while an angle of greater than 40 to 50 degrees is considered by most to be severe enough to require corrective surgery. Restrictive lung disease and increased alveolar-arterial oxygen difference may be present, as well as pulmonary hypertension as a result of compression of pulmonary vasculature and arterial hypoxia. Formal pulmonary function studies in these patients can guide decisions regarding the extent of surgery and requirement for postoperative ventilatory support. Transthoracic echocardiography can be helpful in assessing the severity of pulmonary hypertension and right ventricular hypertrophy. Correction of spinal deformities can be associated with large intraoperative blood loss, and measures to minimize blood transfusion should be considered. Deliberate controlled hypotension has been employed to limit blood loss but must be used with caution in the older adult, those with cardiovascular disease, or those at risk for ischemic complications[225] and postoperative vision loss. Antifibrinolytic agents are commonly administered to limit blood loss but may need to be avoided in some patients, such as those with a history of thromboembolic events, coronary stents, or renal impairment. TXA is more effective than aprotinin and EACA in reducing total blood loss, intraoperative blood loss, and blood transfusion.[226]

Scoliosis surgery has a variable but high rate of complications, with neurologic injury reported in 0.5% to 7.5% of cases.[227,228] Neurologic deficits can result from migration of bone graft into the spinal canal, penetration of instrumentation, and compression of the nerve roots. Intraoperative neurophysiologic monitoring (IONM) is a valuable technique that can be used in these patients for assessment of the integrity of neuronal structures. IONM is also of value during complex spine surgeries such as revision surgeries in patients with previous thoracolumbar fusion.

INTRAOPERATIVE NEUROPHYSIOLOGIC MONITORING

Somatosensory evoked potentials (SSEP) have been employed since the 1970s to assess the integrity of the larger fiber sensory system during scoliosis correction surgery. Nash and colleagues described a reversible loss of potentials with excessive elongation or derotation of the curve.[229] It was subsequently complemented with motor evoked potential (MEP) monitoring, as clinicians found that patients could become paraplegic despite unchanged intraoperative SSEPs, which monitor conduction of signals through the dorsal column but not the corticospinal tract.[230] MEPs are evoked through application of a train of high-voltage stimuli to electrodes on the surface of the head to activate motor pathways. Stimulation of the white matter produces an orthodromic nerve action potential that can be recorded as direct muscle responses (muscle MEPs) or at the spinal cord level using a flexible electrode once the laminectomy is completed and the dura opened. Direct stimulation of the corticospinal axons generates the D-waves, while stimulation of the axons of the cortico-cortical interneurons with excitatory projections to the corticospinal neurons produces indirect volleys that can be recorded as small deflections of higher threshold and longer latency (I waves).[231] Although D-wave monitoring is limited to the cervical and upper thoracic cord and requires an epidural recording electrode, it is helpful in addition to muscle MEP monitoring because it is resistant to anesthetic depression and neuromuscular blockade and has simple criteria for interpretation. A supplement to SSEP and MEP, triggered electromyography is an excellent technique for determining whether lumbar pedicle screws are properly placed. IONM has been increasingly employed for spine surgeries since its introduction in the 1970s, and is currently recommended for a number of procedures in addition to correction of spine deformities, including procedures with increased risk for SCI (e.g., resection of intramural tumors, unstable spine trauma, Chiari malformation, spinal cord vascular malformations) or risk for root damage (e.g., decompressive surgeries, tethered cord), as well as in patients with significant risk for compression neuropathies. These monitoring modalities are described in detail elsewhere (Chapter 39), but it is important to underscore the role of the anesthesiologist in providing optimal conditions for neuromonitoring, correct and timely detection of changes, and optimization of physiologic parameters to minimize risk for irreversible injuries.

In addition to the anesthetic agents, important physiologic factors such as hypotension, hypoxemia, hypothermia, and hypocarbia may lead to an attenuation of these potentials. In general, it is recommended to use total intravenous anesthesia during IONM, as volatile agents and nitrous oxide reduce the amplitude and increase the latency of the potentials in a dose-dependent manner. If volatile anesthetics are used, it is recommended to keep the concentration below half MAC and avoid any unnecessary or abrupt fluctuations. Opioids and benzodiazepines do not affect the potentials to the same extent, and ketamine or dexmedetomidine[232,233] have been suggested as reasonable complements to the anesthetic regimen. Assuming that the anesthetic effects on these modalities remain unchanged and the patient's physiologic parameters remain stable, an intraoperative loss of SSEPs or MEPs should warn the clinicians of impaired conduction through the dorsal columns or the corticospinal tracts; that is, structural damage has occurred. The damage from surgically-induced spinal cord compression, distraction, or derotation of the spinal column or spinal cord ischemia can be reversible if corrective actions are taken in a timely manner. Therefore, it is important that the surgical, neurophysiologic, and anesthesia teams work together to rapidly diagnose and correct these anatomic or physiologic disturbances. A predetermined checklist for response to IONM changes can guide the clinicians and facilitate rapid interventions aimed at diagnosing and correcting any surgical or physiologic insults. The anesthesiologist should immediately implement measures to optimize cord perfusion (optimize the hemodynamics and correct anemia, temperature and pH, and pCO_2 abnormalities) and be prepared for a possible wake-up test.[234] During a wake-up test, the plane of anesthesia is lightened, and the patient is instructed to make a specified motor response, usually in the lower limbs. If the patient is unable to move his or her legs, corrective measures will need to be instituted immediately. It is, nevertheless, also important to consider the limitations of the wake-up test, including the time needed to reverse any neuromuscular blockade and emerge from anesthesia, dependence on patient cooperation, and risk for complications such as inadvertent extubation, dislodgement of instrumentation, and air embolization during a deep inspiration.

PERIOPERATIVE VISUAL LOSS

An uncommon but devastating complication after spine surgery, perioperative visual loss can be caused by anterior or posterior ischemic optic neuropathy (ION, 89% of the cases), retinal ischemia, cortical blindness, or posterior reversible encephalopathy. In a case-control examination of 80 patients with ION compared with 315 matched control subjects, the ASA Task Force on Perioperative Visual Loss identified risk factors for ION after spinal fusion surgery to be male sex, obesity, Wilson frame use, longer procedural duration, greater estimated blood loss, and lower percent colloid administration.[235] The Task Force issued a detailed practice advisory to assist clinicians in the perioperative management of these patients and with the goal to reduce the frequency of perioperative visual loss.[236] Included are recommendations on perioperative blood pressure management, management of fluids, anemia, and vasopressors, as well as patient positioning and staging of surgical procedures. Of note, a lack of association between deliberate hypotension and perioperative visual loss is discussed by the Task Force, and clinicians are advised to approach this consideration on a case-by-case basis. Central venous pressure monitoring should be considered in high-risk patients and colloids should be used along with crystalloids to maintain intravascular volume in patients who have substantial blood loss. There is no documented lower limit of hemoglobin concentration, but hemoglobin or hematocrit values should be monitored periodically during surgery in high-risk patients with substantial blood loss. Similarly, the decision to use α-adrenergic agonists should be made on a case-by-case basis. Direct pressure on the eye should be avoided, and patients should be positioned so that the head is level with or higher than the heart when possible. Moreover, the high-risk patient's head should be maintained in a neutral forward position without significant neck flexion, extension, lateral flexion, or rotation when possible. Lastly, the use of staged spine surgery procedures reduces the risk of perioperative visual loss and should be considered in high-risk patients.

POSTOPERATIVE PAIN AFTER SPINAL SURGERY

Spinal procedures are associated with a high prevalence of moderate or severe postoperative pain (30%-64%).[237] Timely and effective pain control in this population is important for early ambulation and can facilitate improved functional outcome. The intensity of postoperative pain is directly proportional to the number of vertebrae involved in the surgery and originates from various nociceptors and mechanoreceptors that respond to mechanical irritation, compression, or postoperative inflammation in the vertebrae, intervertebral discs, ligaments, dura, nerve root sleeves, facet joint capsules, fascia, and muscles. It is hence essential that the perioperative team has a pain control plan in place in advance of the surgery, particularly for complex spine procedures involving multiple levels and extensive tissue dissection. The patient should be informed and instructed to set realistic expectations about the type and level of postoperative pain and how to respond when it occurs.

Intravenous opioid analgesics are the most common approach to the treatment of moderate to severe postoperative pain in this group of patients. Their widespread use is, nevertheless, limited by their many side effects, importantly respiratory depression and gastrointestinal side effects. Methadone is increasingly employed in this group of patients and is reported to improve postoperative pain control even when administered as a single bolus (0.2 mg/kg) before surgical incision.[238] A noncompetitive N-methyl-D-aspartate receptor antagonist, methadone is suggested to also reduce opioid tolerance in addition to providing analgesic effects. Ketamine can be used as an adjunct to perioperative opioids, and is demonstrated to reduce postoperative narcotic demand after spinal surgery.[239] NSAIDs have proven efficacy in ameliorating postoperative pain following spinal surgeries,[240] but their use has been limited because of concerns of their effects on bone metabolism and osteoblastic proliferation. Evidence suggests, nevertheless, that impaired bone healing may only be caused by higher doses and longer duration of NSAID administration, and smaller doses for the immediate postoperative period can be considered.[241] Corticosteroids are also occasionally administered, as they are shown to reduce opioid requirements after certain spine procedures, possibly through their antiinflammatory effects as well as the reduction in substance P release. Other options for treating the intensive postoperative pain after spinal surgery include the administration of intrathecal opioids, which has been shown to reduce the cumulative opioid demand. The use of intrathecal opioids is, nevertheless, limited by the associated risk of delayed respiratory depression, requiring close monitoring by skilled personnel. Intrathecal local anesthetic agents are usually not considered for these patients, as they affect the sensory and motor functions, masking any potential postoperative complications. In select patients, however, epidural administration of local anesthetics can provide effective analgesia without compromising the neurologic examination. The epidural catheter can be placed intraoperatively by surgeons under direct vision, and the infusion of local anesthetics can also be initiated after a reassuring neurologic exam has been obtained. Because of the inherent effects of neuraxial anesthesia on the neurologic examination, however, most clinicians choose alternative pain management strategies. More recently, α_2-adrenoreceptor antagonists including clonidine and dexmedetomidine have emerged as effective adjuncts to the aforementioned techniques, enhancing their analgesic properties. Dexmedetomidine is also reported to negate the opioid-induced hyperalgesia that may occur following intraoperative opioid treatment.[242]

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65 Geriatric Anesthesia

MILES BERGER, LEAH ACKER, and STACIE DEINER

KEY POINTS

- The proportion of adults over age 70 has increased throughout the world with a corresponding increase in older surgical patients.
- Normal aging is associated with changes in physiology and an increase in many pathologic conditions.
- The number and impact of normal and pathologic conditions varies significantly across elderly individuals.
- Preoperative screening recommendations and guidelines for older patients can provide a useful starting point to evaluate and optimize care.
- Some important geriatric specific areas that are amenable to screening include: cognition, frailty, depression, and polypharmacy.
- Best intraoperative practices follow from an understanding of geriatric physiology and awareness of medications which are contraindicated in the older population.
- Postoperative care tailored to the needs of high-risk adults may benefit the highest risk patients such as palliative care consultation and delirium prevention units.

America is growing old. The number of Americans over age 70 has increased from approximately 15 million in 1975 to over 30 million in 2015, with a corresponding increase in both the percentage of Americans over age 70 and the median American population age (Fig. 65.1A-C). Similarly, worldwide, the number of people over age 70 has increased from approximately 130 million in 1975 to over 400 million in 2015, accompanied by similar increases in the percentage of people over age 70 and the median population age (see Fig 65.1B,C).

The age-related population shifts have translated to similar changes in the population of patients undergoing anesthesia and surgery. In the United States alone, more than 16 million patients over age 60 underwent surgery in 2006. These profound shifts in the American population and the American surgical population have significant implications for anesthesiologists. First, most (though not all) diseases increase in frequency with age. Second, there are age-dependent physiologic changes in virtually every human organ system. These age-dependent physiologic changes typically result in a decrease in the physiologic and functional reserve capacity of each organ system. However, there is considerable variability in the extent of age-dependent changes across organ systems in individual patients, and considerable variability across older patients in the extent of these age-related changes. Indeed, a general principle of geriatric medicine is that as the population ages, the variance of virtually every physiologic measurement increases. Thus while older patients as a whole present additional challenges for perioperative management as a result of increases in comorbid disease and decreases in physiologic reserve, it is important to avoid overapplying these generalizations to individual older patients.

One potential reason that these generalizations apply to varying degrees among older patients is that aging itself involves a plethora of biological pathways (Fig. 65.2) which proceed at varying rates across patients. For example, two 80-year-old patients may show very different telomere lengths, genetic mutation accumulation, and cumulative oxidative stress. Differences in these types of biologic pathways involved in aging have led many to refer separately to chronological age (reflecting the number of years of life) versus biologic age (reflecting the actual accumulation of changes in biologic processes involved in aging).

In this chapter, we discuss common age-dependent physiologic and pathophysiologic changes, and their implications for the preoperative assessment, intraoperative management, and postoperative care of older adults. The significant increases in the age of the American population suggest that the perioperative management of older adults will likely become an increasingly large focus for anesthesiologists. Further, the significant increases in biomedical research expenditures focused on aging and older adults provide reason to hope that this research will lead to improved postoperative outcomes for older adults in the future.

Organ-Specific Age-Related Physiologic and Pathologic Changes

Except for those who exclusively treat pediatric or obstetric patients, most anesthesiologists are geriatric anesthesiologists at least some of the time. Therefore understanding the numerous physiologic changes of aging is critical for caring for the elderly population. Here we discuss these changes by organ system.

CARDIOVASCULAR SYSTEM

In the cardiovascular system, normal aging manifests as changes in vascular and sympathetic tone, the myocardium, the cardiac conduction system, the cardiac valves, and the baroreceptor system.

Vascular Changes With Age

With age, arterial stiffening results in increased afterload, which increases myocardial oxygen consumption and wall stress. Comorbid pathology such as atherosclerosis and decreased β-2 adrenergic vasodilation may compound this effect.

Partially because of age-related vascular changes, the incidence of venous thromboembolism (VTE) increases exponentially with age, affecting up to 600 people over the age of 80 years per 100,000 annually.[1] All three parts of Virchow's classic triad (venous stasis, hypercoagulability, and aberrant blood flow) affect older populations and contribute to this increased risk of VTE. For example, venous

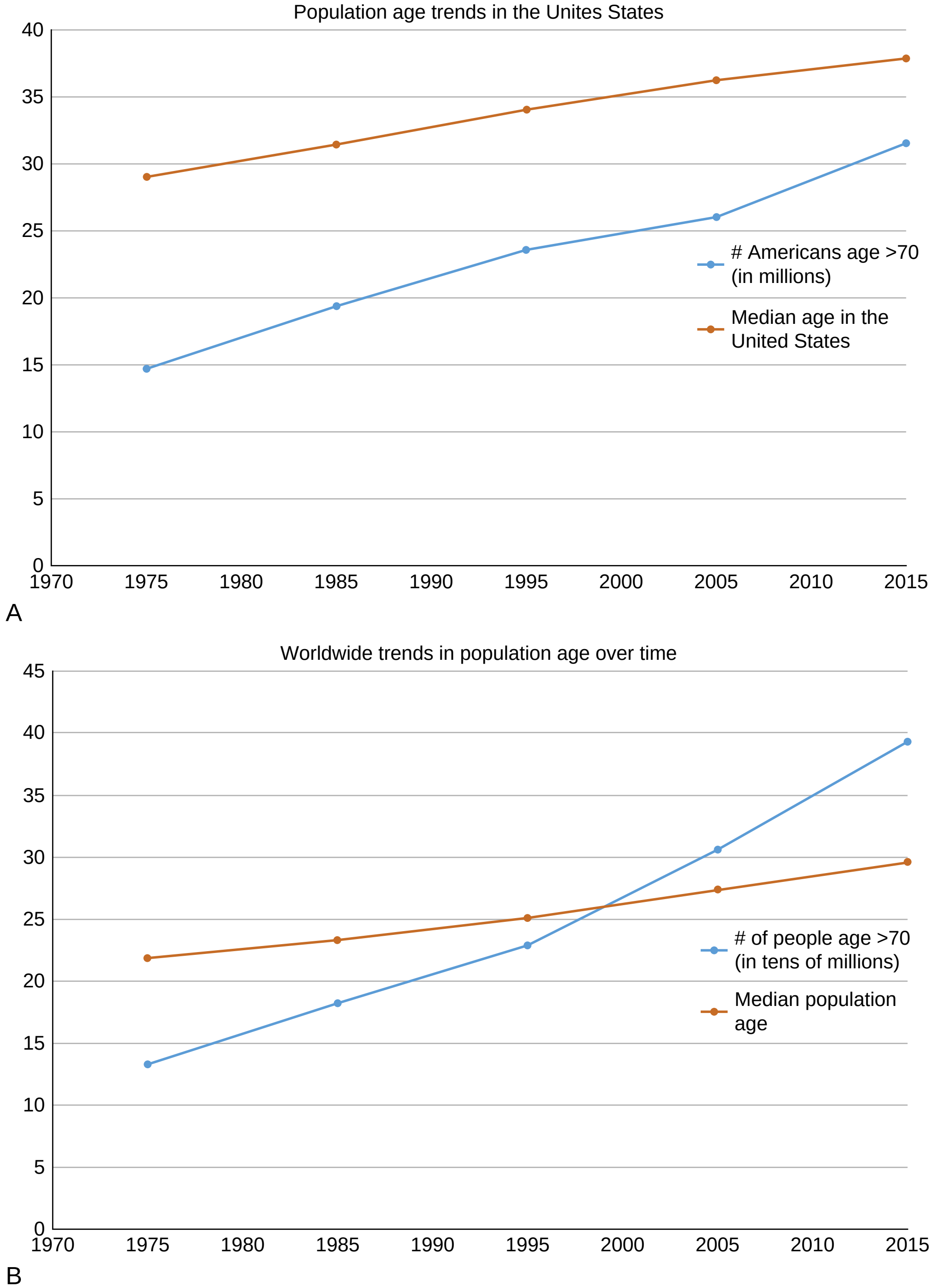

Fig. 65.1 (A) Population age trends in the United States. (B) Worldwide trends in population age over time. (C) Population percentage age >70 by decade.

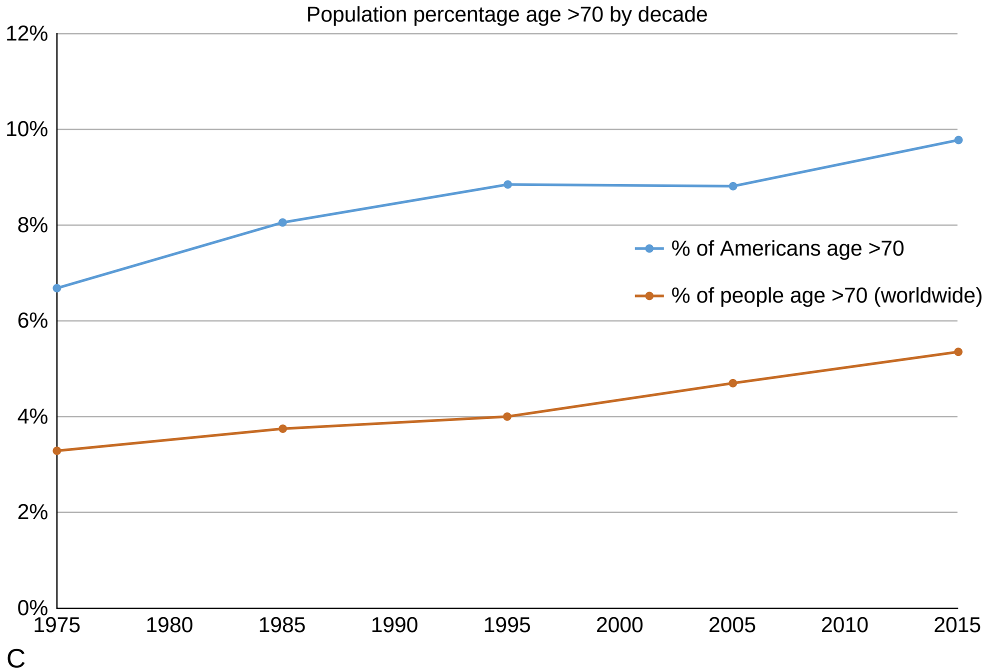

Fig. 65.1 cont'd

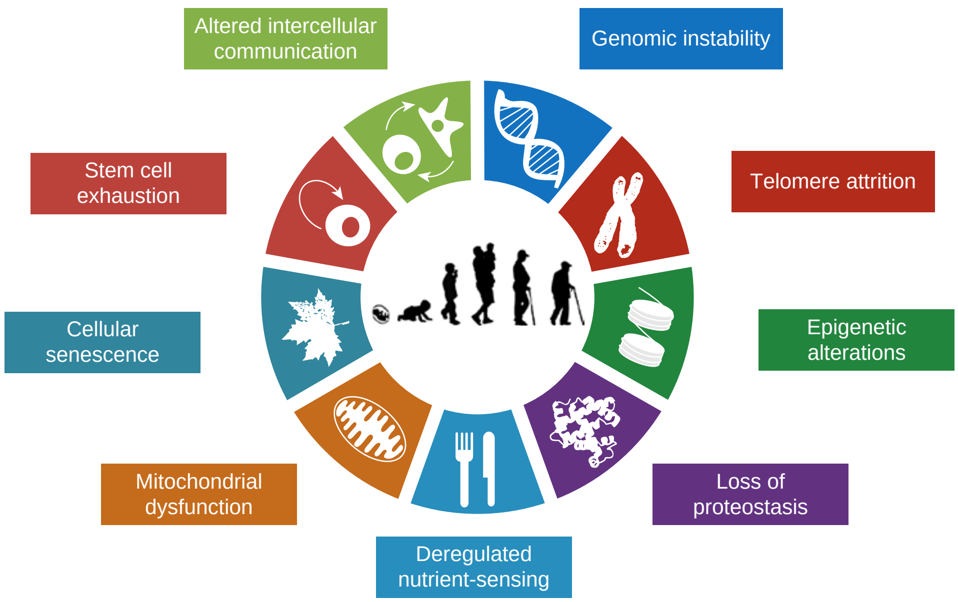

Fig. 65.2 Molecular, cellular, and organ-level mechanisms of aging. (Redrawn from López-Otín C, Blasco MA, Partridge L, et al. The hallmarks of aging. *Cell*. 2013;153[6]:1194–1217.)

stasis may result from decreased vascular compliance, a low-flow state such as congestive heart failure, immobility, varicose veins, postmenopausal estrogen replacement therapy, and smoking.[2]

Myocardium

In the absence of pathology, systolic function typically remains well preserved throughout life; however, diastolic dysfunction becomes more common. Age-related myocyte death and reciprocal increases in myocyte size lead to myocardial thickening and decreased elasticity.[3] Chronic hypertension can further exacerbate cardiac hypertrophy. Ventricular thickening and stiffening, in turn, impair early diastolic filling, which falls to 50% of its peak by the age of 80 years.[4] In order to maintain cardiac output, geriatric patients are increasingly dependent on preload and atrial kick. Conversely, small decreases in circulating blood volume can lead to inadequate cardiac filling, which can significantly decrease cardiac output.

Cardiac output is also limited by a lower maximal heart rate relative to younger adults[3]; maximal heart rate can be estimated as: HR (bpm) = 220 − age (years). In the absence of arrhythmia, aging of the cardiac conduction system and autonomic system leads to decreased heart rate variability and an increased incidence of ectopic beats.[4] Arrhythmia can dramatically decrease cardiac output in older adults. Atrial fibrillation is the most common arrhythmia, affecting 1 in 10 patients 80 years of age or older.[5] Atrial fibrillation eliminates the atrial kick that decreases left ventricular filling and results in decreased cardiac output.

Cardiac Valves

Normal aging results in a thickened and calcified aortic valve. In addition, the pathologic condition of aortic stenosis is more common with aging and is present in 12.4% of those aged 75 years or older.[5] Patients with aortic stenosis depend on good diastolic volume and normal sinus rhythm to maintain myocardial perfusion. Further, patients with aortic stenosis have increased left ventricular diastolic pressure, which means that they are susceptible to decreased coronary perfusion pressure. To avoid myocardial ischemia in patients with aortic stenosis, it is important to avoid hypotension and tachycardia (which reduces the length of diastole and further impairs coronary perfusion). Even minor left ventricular dilation or a relatively small decrease in left ventricular systolic function can increase the likelihood of intraoperative decompensation.[6]

Sympathetic and Autonomic System

The ability of the sympathetic and autonomic systems to respond to physiologic derangement decreases with age. Decreased β-adrenergic sensitivity leads to a lower maximal heart rate, decreased cardiac output, and limited responsiveness to beta agonists (e.g., dobutamine).[4] Baroreceptor impairment increases the incidence of orthostatic hypotension.[2] For this reason, older patients may be more sensitive to prolonged fasting times and may benefit from drinking clear liquids up to 2 hours before surgery.

RESPIRATORY SYSTEM

As the respiratory system ages, the lungs become less compliant and the muscles involved in respiration weaken. Central responses to hypercapnia and hypoxia are blunted, which puts patients at increased risk for pharmacologic-induced respiratory depression. The incidence of both restrictive and obstructive lung disease and sleep apnea increase with age.

With the aging process, the diaphragm weakens and the chest wall stiffens because of calcification of intercostal cartilage. There are also arthritic changes in the costovertebral joints, weakening and atrophy of the intercostal muscles, and height loss due to osteoporosis and/or kyphosis.[3] Lung compliance increases as elastic recoil decreases despite increased elastin production. Therefore while total lung capacity remains unchanged, functional residual volume increases 5% to 10% per decade, leading to an overall decrease in vital capacity.[7] Aging is also associated with alveolar airspace increases similar to those seen in emphysema, decreased gas exchange, and increased ventilation-perfusion (V-Q) mismatch.[3,7] Mechanical changes include decreased vital capacity, decreased pulmonary reserve, increased work of breathing, and increased residual volume, all of which predispose older adults to atelectasis.[7] Closing capacity, the point at which small airways close, increases with age. Functional residual capacity (FRC) is reduced relative to closing capacity, which may result in atelectasis, pulmonary shunting, and hypoxemia. Certain common intraoperative conditions, such as increased intraabdominal pressure due to carbon dioxide insufflation or Trendelenburg positioning, reduce the FRC and lung compliance. Strategies to minimize atelectasis in the postoperative period include early mobilization/ambulation after surgery, chest physiotherapy, and incentive spirometry.[2]

Compared to younger patients, older patients also have weaker pharyngeal muscles, decreased clearance of secretions, decreased mucociliary transport, less efficient coughing, decreased esophageal motility, and less effective protective upper airway reflexes.[7] Together, these factors place the older population at increased risk for aspiration and postoperative pneumonia. Anesthesiologists can implement four specific strategies to reduce the risk of aspiration and other pulmonary complications. First, using neuraxial or regional anesthesia with minimal sedation in lieu of general anesthesia (when possible) can reduce the risk of aspiration by reducing anesthetic-induced interference with the cough reflex. Second, avoiding intermediate and long-acting neuromuscular blocking agents, and ensuring adequate reversal of neuromuscular blockade, can also help reduce aspiration and postoperative pneumonia risk.[2] Residual neuromuscular blockade is a particular concern in older patients with reduced pulmonary function.[7] Third, respiratory depressants such as opioids can lead to hypoventilation and respiratory acidosis, which further potentiates the effects of neuromuscular blocking agents.[7] When appropriate, opioid-sparing analgesic strategies can be helpful in older patients.[8] Fourth, neutralization of stomach acid with nonparticulate antacids (such as sodium citrate) can be helpful in preventing chemical pneumonitis and pulmonary injury in case aspiration does occur.

In addition to mechanical changes, older adults have an approximate 50% decrease in the respiratory response to hypoxia and hypercarbia, which is even more pronounced during sleep.[9] Some geriatric patients may not awaken from rapid eye movement sleep until oxygen saturation decreases significantly (e.g., to 70% or lower).[7] The most common sleep-related respiratory derangements in older adults is sleep apnea, which may affect 50% to 75% of patients over age 65.[7,10] Older patients tend to have decreased hypopharyngeal and genioglossal muscle tone, which predisposes them to upper airway obstruction, particularly during sleep.[7] Patients can be screened preoperatively for obstructive sleep apnea (OSA) using one of several screening questionnaires such as the STOP-Bang, Berlin, or American Society of Anesthesiologists (ASA) questionnaires.[11] Patients with OSA should be recognized as having a potentially difficult mask airway and postoperatively may benefit from continuous positive airway pressure[11] and opioid-sparing management.[12]

RENAL SYSTEM

After 50 years of age, average kidney weight decreases from approximately 250 g to 180 g, mostly as a result of cortical atrophy from glomerulosclerosis. Along with this loss of renal cortex, the glomerular filtration rate (GFR) decreases by about 1 mL/min/m^2 per year starting at 40 years of age.[3] Chronic diseases frequently found in the older population (e.g., hypertension, diabetes mellitus, and atherosclerosis) can exacerbate this normal age-related decline in renal function. Although elderly patients typically have normal serum creatinine levels, they also tend to have decreased lean muscle mass and lower creatinine overall. Therefore a "normal" serum creatinine in an older patient may belie a reduced glomerular filtration reserve and obscure the resulting renal sensitivity to ischemic and nephrotoxic injuries. Specifically, in the setting of reduced GFR, medications that are excreted through the kidney may accumulate if the dose is not appropriately adjusted.

In addition to reduced GFR, blunted responses to aldosterone, vasopressin, and renin also reduce the older patient's ability to adjust volume status and may result in electrolyte and acid-base derangements. In particular, older adults are susceptible to dysnatremias; hyponatremia affects 11% of the geriatric ambulatory community and 5.3% of hospitalized geriatric patients. Hypernatremia affects 1% of hospitalized patients age 60 and older.[13] Further, because older adults often have inappropriate sodium excretion, they are particularly prone to hypotension and acute kidney injury in the setting of hypovolemia.[13]

The incidence of urologic disease (i.e., bladder and prostate) also increases with age. The incidence of postoperative urinary retention increases in older men and women.[14] This is an important point to recognize because discomfort due to urinary retention can be a common cause of postoperative agitation. Urinary tract infections (UTI) also increase in incidence in older men and women.[2] Elderly women may have skin breakdown in the genital area because of vaginal atrophy from decreased estrogen,[15] which increases the risk of UTI.[16] In addition, the incidence of pelvic prolapse in women increases with age and also increases the risk of UTI.

GASTROINTESTINAL AND HEPATIC SYSTEMS

The size and function of the liver decrease with age, which affects hepatic drug metabolism. After age 50, the liver decreases from 2.5% of total body mass to 1.5% in part due to fewer hepatocytes and decreased blood flow.[3] Despite having fewer hepatocytes, healthy older adults typically have normal liver synthetic function, though they have reduced reserve under stress.[3] Similarly, hepatic blood flow decreases with age such that the average 65 year old has 40% less hepatic blood flow than the average 25 year old.[17] Older populations may more slowly metabolize drugs that are cleared by phase-1 pathways (e.g., oxidation, reduction, and hydrolysis through the cytochrome P450 system) because of decreased hepatic blood flow,[18] but phase II metabolism (e.g., acetylation and conjugation) does not seem to be affected by age.[17] Anesthesiologists should be aware that older adults are slower at clearing high extraction drugs whose clearance depends directly on hepatic blood flow (e.g., ketamine, flumazenil, morphine, fentanyl, sufentanil, and lidocaine).[17]

The incidence of postoperative nausea and vomiting decreases with age, which is fortunate because many antiemetics act through anticholinergic and/or antihistaminergic mechanisms, which can cause altered mental status and delirium. The Beers criteria recommend against most of these medications as they increase the risk of delirium.[2] Specifically, the Beers criteria recommend avoiding prochlorperazine, promethazine, metoclopramide (except in the setting of gastroparesis), and corticosteroid prophylaxis.[2,19] The 5-HT3 receptor antagonists (e.g., ondansetron), are a better choice for older adults, although the 5-HT3 antagonists contribute to QTc interval prolongation.[2]

The incidence of some hepatic and gastrointestinal pathologies increases with age. For example, the incidence of nonalcoholic fatty liver disease (NAFLD) increases with age, affecting nearly half of geriatric patients; however, in contrast to younger populations, it is unclear whether NAFLD is associated with metabolic syndrome, cardiovascular disease, or cirrhosis when it is first diagnosed at an advanced age.[20] That said, as the obese diabetic patients with NAFLD age and become geriatric patients, they have an increased risk of complications, such as severe hepatic fibrosis, hepatocellular carcinoma, and cryptogenic cirrhosis.[20] Whereas hepatic pathology certainly impacts anesthetic management, other common gastrointestinal disorders of older adults, such as diverticulosis and cholelithiasis, typically do not.

MUSCULOSKELETAL SYSTEM

As with other organ systems, the aging musculoskeletal system undergoes changes relevant to anesthesiologists. Among the well-functioning older adult, lean muscle mass declines by roughly 1% annually while muscle strength declines by roughly 3% annually, meaning muscle function and quality decreases faster with age than muscle quantity does.[21] Maintaining strength in the perioperative period is critical in older people. Declining muscle strength is associated with increased mortality risk,[22] and older adults lose muscle mass much faster than their younger counterparts. For example, healthy older adults who were placed on bedrest for 10 days experienced greater loss of muscle mass than healthy younger adults who were placed on bed rest for 28 days.[23]

Decreased lean muscle mass can prove misleading among older patients, whose weight may remain stable, while their total body fat increases and their subcutaneous (insulating) fat reserves decrease. A 10-year longitudinal study of older adults showed a 23% per decade decline in subcutaneous fat with a concurrent average 11% per decade increase in total body fat.[24] Diminished subcutaneous fat thickness and age-related dysregulation of cutaneous circulation help to explain why older patients are much more prone to temperature dysregulation intraoperatively even though the basal core temperature of the elderly (aged 65-95) is only about 0.4°C (0.7°F) lower than that of other adults (aged 25-64).[25] Age-related dysregulation of the cutaneous microcirculation also contributes to impaired wound healing. Anesthesiologists can optimize surgical healing in this population by maintaining adequate hydration, normothermia, and good tissue oxygenation.[26]

Along with age-related changes in the muscles and skin, aging affects the skeletal system as well. Osteoarthritis affects about half of those aged 75 and older and can lead to limited joint mobility in older patients. Anesthesiologists should be aware of this and inquire about this with older patients to avoid exacerbating preexisting joint issues while positioning the patient in the operating room.[27]

CENTRAL NERVOUS SYSTEM

Changes in the aging central nervous system can give rise to a host of age-related concerns, such as cognitive decline, memory loss, sleep derangements, dementia, movement disorders, depression, and an increased risk of delirium. Although the number of neurons in the brain does not decrease in normal aging, older brains have fewer dendrites and synapses, which contributes to decreased brain volume and to decreased neuronal connectivity, particularly in the hippocampus, frontal/prefrontal cortex, and the temporal lobe.[28] Specifically, magnetic resonance imaging studies have shown that cortical gray matter thins at a rate of 0.5% to 1% per year in the geriatric brain.[29] Further, age-related dysregulation of neuronal transmission, baseline neuronal firing, calcium metabolism, and gene expression diminishes both connectivity and plasticity.[30] Functionally, these physiologic changes contribute to normal, age-related cognitive decline in many domains such as executive function, cognitive processing speed, working and spatial memory, and maintenance of circadian rhythm. Of particular relevance to anesthesiologists, these age-dependent decreases in cognitive reserve may manifest as increased sensitivity to anesthetic medications, an increased risk of postoperative cognitive dysfunction and delirium, and a decrease in function.

Specifically, in dementia, the decline in memory and cognition becomes severe enough to interfere with daily activities whereas in mild cognitive impairment, cognitive decline is measurable and noticeable, but does not interfere with one's ability to perform daily activities. Frank neuron loss typically occurs in dementia, regardless of the dementia subtype. In Alzheimer disease, a complex interplay between abnormal tau and beta-amyloid proteins seems to precipitate global neuronal cell death while in vascular dementia, neuronal cells die because of hemodynamic compromise, leading to a step-wise decline in cognitive function. Finally, in Lewy body dementia abnormal α-synuclein deposits give rise to neuronal death. Overall, dementia increases dramatically in prevalence with advancing age in a step-wise manner (Fig. 65.3), affecting nearly two-thirds of patients over the age of 90 years.[31]

Dementia presents challenges for anesthesiologists, particularly regarding pain management. For example, patient-controlled analgesia may not be an option. Opioid administration is often difficult to titrate in these patients, and patients may not be able to cooperate with regional anesthesia. Further, patients with dementia may also develop concurrent delirium, which can be difficult to disambiguate from underlying dementia. Similarly, Parkinson disease presents a particular challenge for the anesthesiologist. Patients with Parkinson disease are more prone to developing immobility and thus deep venous thrombosis; dysphagia and respiratory dysfunction and thus aspiration and pneumonia; urinary retention and thus UTI; and psychiatric complications and thus delirium.[32] Drug interactions can be a particular concern in patients with Parkinson disease. For example, many antiemetic drugs such as metoclopramide and promethazine antagonize dopamine and may worsen extrapyramidal symptoms. Inhibitors of the enzyme monoamine oxidase (MAO)-B, which are frequently used in Parkinson disease, can predispose patients to serotonin syndrome, particularly if used in conjunction with certain opiates such as tramadol.[33] Propofol can induce dyskinesia in this population,[34] which can be managed with dexmedetomidine.[33]

Mood disorders, particularly depression, are often underrecognized in older adults. Minor depression affects approximately 7.7% of geriatric primary care patients, approximately 14.4% of geriatric patients in hospital settings, and nearly 20% of those with minor cognitive impairment.[35] Depression predisposes patients to postoperative cognitive dysfunction (POCD), in-hospital delirium, major adverse cardiac events, increased postoperative analgesic use, and suboptimal postoperative outcomes.[36-38] Discussion of mood symptoms prior to anesthesia can help to inform perioperative management and the use of antidepressant medications. Typically, antidepressants are continued during the perioperative period because of the risks of "discontinuation syndrome" and because of their benefits for pain management[39]; however, MAO inhibitors can lead to severe hypotension in the setting of sympathetic stimulation or in conjunction with sympathomimetic drugs. Even selective serotonin reuptake inhibitors, the most commonly

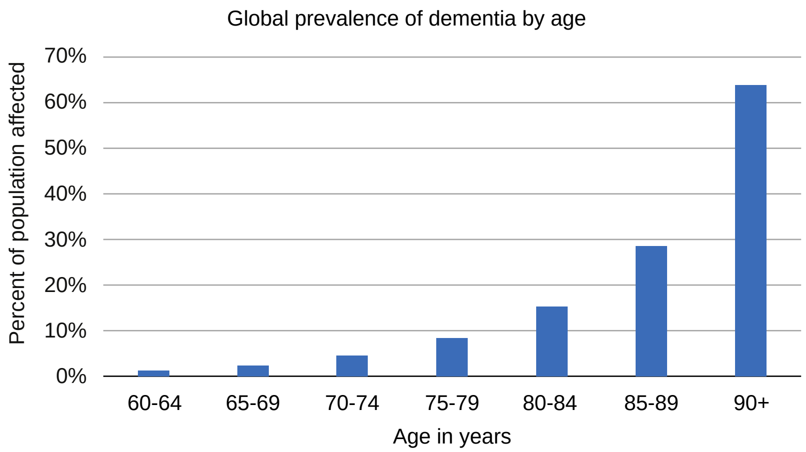

Fig. 65.3 Global prevalence of dementia by age. (Redrawn from Prince M, Bryce R, Albanese E, et al. The global prevalence of dementia: a systematic review and metaanalysis. *Alzheimers Dement*. 2013;9:63–75.)

used and "safest" antidepressants, have been associated with a higher risk of in-hospital mortality, bleeding, and readmission.[40]

Finally, delirium and POCD are two common postoperative complications in older patients. Each of these topics have dedicated chapters in this text, so they are only briefly reviewed here. Delirium, which affects about 10% of older postoperative patients overall and 60% to 80% of intensive care unit (ICU) patients, manifests as acute, fluctuating confusion with altered attention and awareness that cannot be better explained by preexisting or developing dementia. Common delirium screening tools include the Confusion Assessment Method (CAM) and the CAM-ICU for ventilated ICU patients. Few treatments for delirium have proven efficacious; however, management of underlying medical conditions (e.g., electrolyte imbalances, infections), modifying risk factors (e.g., reducing sleep deprivation, increasing mobility, giving patients their glasses and hearing aids, ensuring good hydration), and avoiding or limiting medications known to trigger delirium (e.g., benzodiazepines, dihydropyridines, antihistamines, opioids) may prove beneficial. In contrast to delirium, POCD is a syndrome defined by worsening performance on neuropsychologic tests postoperatively compared to a perioperative baseline.[41] Overall, this decline in cognitive performance across multiple domains presents days to weeks after surgery and is associated more strongly with age than any other risk factor.[42] By and large, POCD resolves within months of both cardiac and noncardiac surgery; however, individual patients may follow different trajectories with declines remaining up to 5 years or longer.[41]

Preoperative Assessment

Preoperative assessment of the geriatric surgical patient follows the general principles of good medical care while adding special attention to issues that may have greater incidence or impact in older adults. In 2014, the American College of Surgeons (ACS) convened an expert panel and published a consensus statement with evidence-based recommendations.[43] Good medical care–type recommendations include the use of the American College of Cardiology and American Heart Association algorithm for patients undergoing noncardiac surgery,[44] ordering appropriate laboratory tests based on comorbidity, and determination of the risk for postoperative pulmonary complications. Geriatric-specific evaluation includes assessment of the patient's cognitive ability, identifying the risk for postoperative delirium (covered in detail in Chapter 82), documentation of functional/frailty/fall-risk status, monitoring for polypharmacy, screening for depression and alcohol use, understanding patient's expectations, and advanced directives.

COGNITIVE ASSESSMENT AND DELIRIUM RISK

In the immediate perioperative period, occult preoperative cognitive impairment in older adults is common; the incidence is more than 20% of patients over 65 years of age presenting for presurgical testing with the highest prevalence in the oldest patients.[45] However, talking with patients and families about cognitive health before and after surgery is a new challenge for anesthesiologists. In 2016, the ASA launched the Brain Health Initiative, which is a "low barrier access program to minimize the impact of preexisting cognitive deficits, and optimize the cognitive recovery and perioperative experience for adults 65 and over…." The basic principles of the program include screening for preoperative cognitive impairment and that anesthesiologists lead discussions regarding the potential for postoperative delirium and cognitive dysfunction.

The cognitive assessment of patients prior to surgery can be challenging. In-depth neuropsychiatric testing is not practical for most pretesting centers since it often involves an hour or more of tests administered by a trained individual. More practical for the presurgical arena is the use of brief screening tools that are meant to identify patients who are likely to have cognitive impairment (Table 65.1). A recent large study suggests that cognitive screening in a pretesting clinic is practical and well accepted by patients and staff members.[45] An obvious but difficult question for anesthesiologists is how to proceed when a patient is identified as likely to have cognitive impairment. Informing patients and offering

TABLE 65.1 Brief Cognitive Screening Tools

Tool/Test	Advantage	Disadvantage	Sensitivity (%)*	Specificity (%)*	Time to Administer
Minicog[45,49,75-77]	Brief, minimal language, education, race bias	Use of different word lists may affect scoring	76-100 (54-100)	54-85.2 (43-88.4)	2-4 min
Montreal Cognitive Assessment (MoCA)[78-81]	Can identify mild cognitive impairment, available in multiple languages	Education bias, limited published data	n/a	n/a	10-15 min
Mini-Mental State Examination (MMSE)[77,82,83]	Widely used and studied	Subject to age and cultural bias, ceiling effects	88.3 (81.3-92.9)	86.2 (81.8-89.7)	7-10 min
Clock-drawing Test[77,84]	Very brief	No standards for administration and scoring	67-97.9 (39-100)	69-94.2(54-97.1)	<2 min
Verbal Fluency Test[77,85]	Brief	Cut point not obvious	37-89.5 (19-100)	62-97 (48-99)	2-4 min
Cognitive Disorder Examination (CODEX)[86-88]	Brief	Less well-studied	81-93	81-85	≤3 min

*Sensitivity and specificity values are for the detection of cognitive impairment or dementia—see references for more detail.

them postsurgical follow-up with an expert in cognition is important. The same study showed that patients believe that screening before surgery is important and that they want to know their results. Baseline cognition is also important for delirium-risk stratification; patients with cognitive impairment are at higher risk and therefore may benefit the most from delirium prevention programs. Additionally patients, caregivers, and the perioperative team should have this information since these patients are more likely to require a higher level of care after surgery such as a skilled nursing facility.[46] The ACS guidelines strongly recommend performing cognitive assessment early in the patient evaluation because impairment suggests that medication information and functional status reporting may be unreliable, although in the latter there is some evidence to the contrary.[47]

Although preoperative cognitive impairment is a risk factor for the occurrence and severity of postoperative delirium, it is not the only risk factor.[48] There are several delirium-risk prediction indices and examples of two delirium prediction tools are listed in Table 65.2. Whereas each index is a bit different, most include age, cognitive status before surgery, then some index of medical illness, and the invasive nature of the surgery.[49-51]

FUNCTIONAL/FRAILTY SCREENING

Frailty is a common and morbid condition found with a higher prevalence in older adults before surgery (25%-56%)[52,53] than in community-dwelling elders (10%).[54] Frailty has been conceptualized in two major ways: one includes decreased reserve to physiologic stress and is characterized by decline across organ systems; and the other is an accumulation of deficits, that is, the accumulation of comorbid states that can result in overall physiologic vulnerability. Frailty has been shown to correlate with poor postoperative outcomes (death, complications) in a wide range of major surgeries.

Although frailty is a geriatric syndrome it does not need to be measured by a geriatrician. The classic frailty phenotype measured by Linda Fried[55] did require expertise; however, there are now several validated frailty screening tools.[56] It is not clear which of the screening tools best measures frailty and the answer may vary for different populations and settings.[53,57] For instance, a frailty screen that includes grip strength may not be best suited for a cervical spine population that often has cervical myelopathy. The preoperative testing facility may dictate the type of assessment possible; some preoperative clinic areas are not suitable for a 5-meter gait speed test. Table 65.3 has examples of frailty assessment tools.[58]

Frail and/or prefrailty has been shown to correlate strongly with complications and mortality in a wide range of surgeries. Ideally frailty can inform procedure selection, patient-doctor conversations, and discharge planning. Prehabilitation including nutritional support and exercise may be considered, although exact protocols have not been well vetted. Certainly, malnutrition is more common in preoperative older surgical patients and is associated with postoperative complications and increased length of stay.[59] Frailty is also a risk factor for delirium and frail patients may benefit from multidisciplinary interventions to support orientation, early mobilization, and maintenance of sleep-wake cycles. Preoperative identification of frailty for the surgical team has been shown to increase utilization of palliative care consults and improve patient outcomes.[60,61]

PALLIATIVE CARE

Palliative care focuses on relief of suffering and improvement of quality of life in patients with serious but not necessarily terminal illness. The use of palliative care expert consultants to support patients undergoing surgical intervention is relatively new.[62] Palliative care was recognized as a medical specialty in 2006 and certified its first physicians in 2008. In 2012 there were fewer than 100 surgeons and anesthesiologists certified in palliative care, and although the fellowship spots are increasing, there is a relative shortage.[62] This implies that most palliative care for surgical patients is provided by nonsurgical subspecialty providers. Research regarding the use of surgery

TABLE 65.2 Validated Risk Models for Prediction of Postoperative Delirium in Cardiac and Noncardiac Surgery Patients

Authors	Patients and Surgery	Risk Factors	Results
Rudolph and colleagues[96]	Cardiac surgery (n = 122 for derivation cohort, n = 109 for validation cohort)	▪ Previous stroke (1 point) ▪ Geriatric Depression Scale >4 (1 point) ▪ Abnormal albumin (1 point) ▪ MMSE 24-27 (1 point) or MMSE <24 (2 points)	In the validation cohort, the cumulative incidence of delirium for each point level was as follows: 0 points, 18%; 1 point, 43%; 2 points, 60%; and ≥3 points, 87%
Marcantonio and colleagues[50]	General, orthopedic, and gynecologic surgery (n = 876 for derivation cohort, n = 465 for validation cohort)	▪ Age >70 years ▪ Alcohol abuse ▪ Poor cognitive status* ▪ Poor functional status† ▪ Markedly abnormal sodium, potassium, or glucose‡ ▪ Noncardiac thoracic surgery ▪ Aortic aneurysm surgery	In the validation cohort, the cumulative incidence of delirium for each point level was as follows: 0 points, <1%; 1 point, 8%; 2 points, 19%; and ≥3 points, 45%

*Defined as telephone interview for cognitive status <30.
†Specific Activity Scale = IV.
‡Defined as sodium <130 or >150 mmol/L, potassium <3.0 or >6.0 mmol/L, and glucose <60 or >300 mg/dL.
MMSE, Mini-Mental State Examination.
(From Brown C IV, Deiner S. Perioperative cognitive protection. *Br J Anaesth.* 2016;117(S3):iii52–iii63.)

TABLE 65.3 Frailty Assessment Tools and Scoring Systems in Current Literature

Frailty Measure	Description	Clinical Outcome	Source
Frailty phenotype	Weight loss, grip strength, exhaustion, low physical activity, and 15 feet walking speed	30 days postoperative complications, institutionalization, and length of stay	Makary et al.[52] Revenig et al.[97]
Frailty index/deficit accumulation	30-70 measures of comorbidity, ADL, physical and neurological exam	Mortality and institutionalization	Mitnitski et al.[98] Rockwood et al.[99]
Modified frailty index	History of diabetes, COPD or pneumonia; congestive heart failure; myocardial infarction; angina/PCI; hypertension requiring medication; peripheral vascular disease; dementia; TIA or CVA; CVA with neurological deficit; ADL	30-day, 1-year, and 2-year mortality, 30-day major postoperative complications	Adams et al.[100] Farhat et al.[101] Karam et al.[102] Obeid et al.[103] Patel et al.[104] Tsiouris et al.[105] Velanovich et al.[106]
Gait speed	5-m gait ≥6 s	Mortality, major postoperative complications, institutionalization, and length of stay	Afilalo et al.[107]
Timed up and go	TUG ≤10 s; 11-14 s; ≥15 s	1-year mortality	Robinson et al.[108]
Falls	6-month hx of falls	30-day major postoperative complications, institutionalization, and 30-day readmission	Jones et al.[109]
Robinson	Katz Score, Mini cognition, Charlson Index, anemia <35%, albumin <3.4, hx of falls	30-day major postoperative complications, length of stay, 30-day readmission, 6-month postoperative mortality	Robinson et al.[110,111]

ADL, Activities of daily living; *Cog*, cognition; *COPD*, chronic obstructive pulmonary disease; *CVA*, cerebrovascular accident; *PCI*, percutaneous coronary intervention; *TIA*, transient ischemic attack; *TUG*, Timed Up and Go.
(From Amrock LG, Deiner S. The implication of frailty on preoperative risk assessment. *Curr Opin Anaesthesiol*. 2014;27[3]:330–335.)

and palliative care is relatively new; however one study found that frailty screening in an elderly veterans' hospital surgical cohort increased preoperative palliative care consultation and was associated with a 33% reduction in 180-day mortality.[61]

POLYPHARMACY

Preoperative assessment of medications is very important; studies suggest that the incidence of discrepancies between surgical and anesthesiology assessments are greater than 70%.[63] The advent of computerized medical records can be helpful or harmful as medications which are not deleted from the record may continue to appear as current. Therefore medical reconciliation at admission and discharge is required to assure up-to-date information. Best practice may include working with pharmacists to review patient medications for polypharmacy and potential drug interactions and contraindicated medications for older adults. These include the American Geriatric Society's Beers Criteria for Potentially Inappropriate Medication Use in Older Adults.[64] The list includes several medications commonly seen in anesthesia order sets: meperidine, scopolamine, benzodiazepines (Table 65.4).

DEPRESSION AND ALCOHOL SCREENING

Depression and alcohol abuse each have approximately a 10% incidence in older adults, and each are associated with a more difficult postoperative course. The former is associated with greater pain perception and increased need for postoperative analgesics, and the latter postoperative complications such as pneumonia and sepsis.[65] Depression can be assessed using tools such as the Patient Health Questionnaire -2[66] which asks:

"In the past 12 months have you ever had a time when you felt sad, blue, depressed or down for most of the time for at least 2 weeks?"

"In the past 12 months have you ever had a time lasting at least 2 weeks when you didn't care about the things you usually cared about or when you didn't enjoy the things that you usually enjoyed?"

"Yes" to either constitutes a positive screen which needs further evaluation.

The classic screening tool for alcohol use is the modified CAGE questionnaire which has been validated for use in older adults.[67,68] The questionnaire consists of four questions:

- Have you ever felt you needed to cut down on your drinking?
- Have people annoyed you by criticizing your drinking?
- Have you ever felt guilty about drinking?
- Have you ever felt you needed a drink first thing in the morning (Eye Opener) to steady your nerves or get rid of a hangover?

"Yes" to any question triggers consideration for perioperative prophylaxis for withdrawal syndromes, supplementation of folic acid and thiamine, and consideration of the need for a detoxification protocol supervised by an addiction specialist.[43]

CAPACITY/ADVANCED DIRECTIVES/ EXPECTATIONS/SUPPORT

Capacity

In working with older adults, it is important to understand whether they retain the capacity for medical decision making. Cognition may overlap with capacity but is not the same thing. Many patients with mild cognitive

TABLE 65.4 Common Medications in the Perioperative Period With Potential Neurological Side Effects That Are Also on the 2012 Beers Criteria List for Potentially Inappropriate Medication Use in Older Adults

Drug	Rationale
Diphenhydramine	Highly anticholinergic; may increase confusion
Hydroxyzine	Highly anticholinergic; may increase confusion
Scopolamine	Highly anticholinergic
Amitriptyline	Highly anticholinergic; sedating
Antipsychotics	Increased risk of stroke and mortality in persons with dementia
Benzodiazepines	Older adults have increased sensitivity and decreased metabolism; risk of cognitive impairment, delirium, and falls
Metoclopramide	Extrapyramidal side-effects; risk may be increased in older adults
Pethidine	Not effective analgesic; may cause neurotoxicity
Pentazocine	May cause central nervous system adverse events, including confusion and hallucinations
Neuromuscular blocking drugs	Poorly tolerated by older adults, with anticholinergic adverse effects

From Brown C IV, Deiner S. Perioperative cognitive protection. *Br J Anaesth*. 2016;117(S3):iii52–iii-63.

impairment may retain capacity. The legal definition of capacity includes[69]:

- Ability to communicate treatment choice.
- Comprehension of the information given by the physicians.
- Able to voice understanding of their medical condition, options for therapy, and outcomes.
- The ability to conduct a rational discussion regarding their treatment options.

Patients may retain capacity for some decisions and not others, or not have capacity for medical decision making entirely. In the case where an older patient does not have capacity for medical decision making it is important to understand whether there is someone who has power of attorney. Working with the power of attorney and with respect to the patient's wishes, the older adult can be included in the discussion as appropriate.

Shared Decision Making/Expectations

Advanced directives are documents that provide information on patient wishes for healthcare decisions in the event that they cannot participate in decision making (Fig. 65.4). Discussion of advanced directives is an important part of understanding and respecting patient's goals of care. The ASA guidelines state that Do-Not-Resuscitate orders should not be automatically suspended in the perioperative period. According to the patient's wishes they may choose to accept limited attempts at resuscitation in the case of certain procedures or in certain contexts (e.g., quickly and easily reversible adverse events such as a drop in blood pressure or need for transfusion). As administration of anesthesia may involve procedures that overlap with resuscitation, the nuances of which procedures are acceptable to the patient and/or surrogate should be reviewed before the procedure. The anesthesiologist should discuss and document any modification of the directive, such as the patient's wishes in the event of complications and plans for postoperative care. These should be communicated to the surgeon before the procedure; the case of conflict between providers may require institutional clarification.

Intraoperative Management Considerations for Older Adults

Once preoperative assessment and preprocedure consent have been completed, the anesthesiologist's task is to design an intraoperative anesthetic plan for each individual older patient that provides adequate intraoperative and postoperative analgesia, effective sedation or amnesia, hemodynamic stability, and optimal operating conditions (i.e., surgical site immobility) for the surgical team. It is difficult to make general intraoperative recommendations for older adults, partly because of the wide heterogeneity in organ system reserve and overall functional status across older patients. The anesthetic plan for each individual older patient should be based on each patient's comorbid illnesses, organ system reserve, and overall functional status.

Nonetheless, a large body of research has examined specific anesthetic techniques in older adults, and several general recommendations can be made (Box 65.1). Likely due to decreased physiologic reserve, many older adults require more careful intraoperative management than younger, healthier patients with greater physiologic reserve. Thus drug administration, "anesthetic depth," and hemodynamic status should be titrated even more carefully in older adults than in other patient groups. Increased monitoring, such as electroencephalogram-based anesthetic titration, may be helpful in this regard. Overall, no specific anesthetic drug or technique (e.g., regional versus general anesthesia) has been consistently associated with an increased (or decreased) incidence of postoperative neurocognitive disorders, such as delirium or postoperative cognitive dysfunction in older patients.

Postoperative Concerns

Best practice guidelines from the ACS for the postoperative period include adequate pain control and a geriatric-focused prevention checklist that includes: delirium, pulmonary complications, falls, postoperative UTIs or urinary retention, pressure ulcer prevention, and care transitions. There are no specific recommendations for care of the older adult in the recovery room. However, the physiology of aging and common diseases suggests that these patients are at higher risk for desaturation (because of decreased closing capacity and a tendency toward atelectasis) and aspiration (for example, due to a less vigorous ability to cough). Maximizing the patient's ability to take deep breaths by elevating the

NOTICE OF
ADVANCE DIRECTIVE ACTIVATION
(a licensed physician or mental health professional must complete this form)

Patient Name: ____________________________________ Medical Record #:_______________
Date: ____

Following appropriate evaluation and/or discussion with the above-named patient, the following has been determined: *(initial only one)*

________ This patient is *now* unable to adequately comprehend his/her medical condition and/or is unable to provide informed consent for necessary treatment(s).

________ This patient is *intermittently* unable to comprehend his/her medical condition and/or to provide informed consent for necessary treatment(s). An advance directive agent/proxy is needed on an emergent/stand-by basis.

________ This patient *has* decisional capacity, but due to the burdens of illness and/or informed consent criteria, he/she *elects to defer* decision-making to his/her agent/proxy as named in a valid advance directive document on file at this medical facility.

Reliance on an advance directive agent is expected to be:
(initial only one)

________ Temporary. The patient will be continuously reevaluated, and the agent/proxy will be notified if the patient regains decision-making capacity and/or desires to resume a decision-making role.

________ Permanent. The patient's loss of decision-making capacity is expected to be enduring. Reevaluation of decision-making capacity will take place only if the patient's cognitive condition substantially and unexpectedly changes.

An agent/proxy named in this patient's advance directive has been notified of the above on this date at the following time: _________. He/she has been advised of the patient's overall medical condition, and agrees to remain reasonably available for ongoing consultation and decision-making participation. In the event he/she will not be available, he/she agrees to notify the facility staff and any alternate agent/proxy in advance.

Signed: ____
(Attending physician or other health care provider)
Printed Name: ______________________________________ Date: ____________________
Address ____ Phone ___________________

Fig. 65.4 Example of a Notice of Advance Directive Activation Form. (Modified from http://www.lifecaredirectives.com/assets/Brochures/AD%20ACTIVATION%2009.pdf.)

head of the bed and providing adequate but not excessive pain management may combat these issues.

The issue of pain perception and tolerance has been a controversial area of study. A recent meta-analysis suggests that aging has no strong effect on pain tolerance although there may be some decreased sensitivity for low-intensity pain, most specifically to heat.[70] Therefore it is important to aggressively monitor and treat older adults for pain and regularly reassess their condition to avoid oversedation. In the case of patients with dementia, and/or nonverbal patients, it may be important to employ tools that can help identify pain behaviors, such as the Pain Assessment in Impaired Cognition tool. Measures for adequate pain control include the judicious use of multimodal therapy and regional anesthesia. Care must be taken to avoid use of Beers list medications, which include gabapentin and long-acting opioids.

Delirium prevention is covered in Chapters 23, 52, and 80. Some general strategies are listed in Table 65.5. In brief, multidisciplinary nonpharmacologic programs have been the most successful efforts to reduce delirium. The

BOX 65.1 Delirium Prevention Strategies

- Education targeted to healthcare professionals about delirium
- Multicomponent, multidisciplinary nonpharmacologic interventions that may include:
  - Daily physical activity
  - Cognitive reorientation
  - Bedside presence of a family member whenever possible
  - Sleep enhancement (e.g., nonpharmacologic sleep protocol and sleep hygiene)
  - Early mobility and/or physical rehabilitation
  - Adaptations for visual and hearing impairment
  - Nutrition and fluid repletion
  - Pain management
  - Appropriate medication usage
  - Adequate oxygenation
  - Prevention of constipation
  - Minimization of patient tethers whenever possible (e.g., Foley catheters, periodic removal of sequential compression devices, electrocardiogram cords)

program most commonly used is the Hospital Elder Life Program (HELP), which includes reorientation, mobilization, and promotion of regular sleep-wake cycles. HELP has been shown to reduce delirium, cognitive and functional decline, and to be cost effective.[71,72] Antipsychotic medication should only be used to treat agitated delirium in the patient who may be a danger to self or staff and never used as prophylaxis.[64] Benzodiazepines are contraindicated for this situation and may worsen a delirium episode.

Outcomes

As previous editions noted, the goal of surgery for the older adult includes preserving independence and function while treating the presenting condition. Large administrative datasets are just beginning to collect enough in-depth information to help practitioners understand outcomes in greater depth than 30-day mortality. The National Surgical Quality Improvement Database launched a

TABLE 65.5 Recommended Intraoperative Practices for Older Adults (By Systems)

	Practice Suggestion	Rationale
GENERAL PHARMACOLOGIC POINTS		
	Careful drug titration	Age-related changes in the volume of distribution for many drugs, albumin concentration, and other changes cause changes in the pharmacokinetics and pharmacodynamics of many anesthetic drugs[95]
NERVOUS SYSTEM		
	Consider using EEG-based anesthetic dosage titration	Reduces postoperative delirium rates[89-93]; may reduce postoperative cognitive dysfunction rates[89,91]
	Consider titrating intraoperative hemodynamics and transfusion management in response to cerebral oximetry	May reduce postoperative delirium rates[91,92]
	Reduce MAC fraction	MAC and MAC-awake decline by 6% per decade after age 30; increased MAC fraction is associated with increased rates of PONV, POCD, delirium[92,94]
	Reduce opioid administration	Opioid sensitivity increases with age; reducing opioid dosage may reduce postoperative respiratory depression
	Minimize dosage of neuromuscular blocking agents, and/or ensure that they are fully reversed (i.e., Train-of-four ratio >90%) prior to extubation	Reduces postoperative pulmonary complications
	Avoid use of drugs on Beers list (see Table 65.4)	Reduces rates of postoperative delirium, altered mental status
CARDIOVASCULAR		
	Avoid hypotension	Helps reduce rates of acute kidney injury; helps ensure adequate coronary perfusion
	Avoid hypertension	Helps reduce myocardial ischemia by avoiding excessive afterload and resultant increases in myocardial oxygen consumption (i.e., myocardial workload)
SKIN		
	Pad skin carefully	Helps avoid pressure ulcers
MUSCULOSKELETAL		
	Pad joints and exposed nerves (e.g., ulnar nerve)	Helps minimize the increased risk of intraoperative nerve injury, which is increased in elderly due to loss of soft tissue/padding

POCD, Postoperative cognitive decline; *PONV*, postoperative nausea and vomiting.

geriatric-specific data collection in January 2014. This enhanced collection included risk factors and outcomes in areas such as cognition, decision making, function, and mobility. An early report demonstrated that among general vascular and orthopedic surgery, functional decline occurred in 42.9% percent of patients.[73] Factors associated with an increased risk of functional decline included cognitive impairment, need for surrogate consent, use of mobility aids, and a history of falls.[74] While some of these factors are currently part of a preoperative evaluation, others (cognitive screening) are not often evaluated. More work is needed to employ geriatric screening and to understand how preexisting states impact postoperative outcomes. While many conditions may not be amenable to change, it is clear that understanding risk is an important part of informed consent, impacts surgical decision making, and postoperative support.

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66 Anesthesia for Trauma

SAMUEL MICHAEL GALVAGNO JR., MARC P. STEURER, and
THOMAS E. GRISSOM

KEY POINTS

- Perioperative anesthesia care for patients who have undergone acute trauma depends on an understanding of trauma system design and surgical priorities.
- Successful emergency airway management is based on having a clear plan, such as the American Society of Anesthesiologists algorithm for difficult airways adapted for trauma. In general, rapid sequence induction of anesthesia and in-line cervical stabilization, followed by direct laryngoscopy or video laryngoscopy, is the safest and most effective approach. The use of cricoid pressure is controversial and is no longer a class I recommendation.
- Recognition of hemorrhagic shock is at the center of advanced trauma life support. Hemorrhagic shock indicates the need for rapid operative treatment, with the possibility of a damage control approach. Although establishing an adequate airway remains the initial priority, obvious hemorrhage should be concurrently addressed through immediate application of tourniquets or direct pressure.
- Resuscitation during acute hemorrhagic shock has undergone a significant change in emphasis. Current recommendations are to allow permissive hypotension during active bleeding by limitation of crystalloid infusion. Recognizing the impact of early coagulopathy in trauma, a "hemostatic" resuscitation should be employed, with an emphasis on maintenance of blood composition by early transfusion of red blood cells, plasma, and platelets, and viscoelastic monitoring when available.
- Management of patients with severe traumatic brain injury requires monitoring and maintenance of cerebral perfusion and oxygenation for successful operative and intensive care management.
- Operative timing for the surgical management of traumatic injuries, including orthopedic trauma, must be balanced between early definitive repairs and the potential for worsening overall physiologic stress.
- Trauma anesthesiology includes a substantial component of critical care practice (see also Chapter 83).

Introduction

EPIDEMIOLOGY

Death and disability caused by injuries remain a public health threat worldwide. For both children and adults younger than age 45, traumatic injuries remain the leading cause of death in the United States.[1,2] Moreover, injury-associated deaths have substantial economic consequences; the total estimated lifetime medical and work-lost costs associated with fatal injuries has been reported to be over $240 billion and is projected to increase.[1,3] Unintentional injuries (i.e., injuries due to motor vehicle accidents, falls) remain the top cause of death in adults younger than age 45, followed by suicide, and homicide.[2]

As with other endemic diseases, successful treatment of trauma extends well beyond the boundaries of an individual hospital. Community-based prevention has included efforts to incorporate airbags in motor vehicles, mandate the use of helmets on motorcycles, encourage citizens to wear seat belts, punish intoxicated drivers, and promote responsible handgun ownership. All these measures have had an impact on the demographics of injury in much the same manner that smoking cessation, dietary modification, and routine mammography have affected the incidence of heart disease and cancer. When prevention fails, outcomes after injury are heavily influenced by the community's commitment to an organized system of trauma care.

MODERN TRAUMA SYSTEMS AND REGIONALIZATION

Following the landmark National Academy of Sciences report "Accidental Death and Disability: The Neglected Disease of Modern Society" in 1966,[4] a framework for trauma systems was developed by the American College of Surgeons (ACS) Committee on Trauma.[5,6] Comprised of governmentally designated or internally validated trauma centers, trauma systems represent a coordinated, organized, and patient-centric approach to the care of the injured patient.[7] A distinction between trauma center designation and verification is made to identify the types of resources available and the number of patients treated annually. Trauma center designation is a process outlined and developed at a state or local level. Trauma center verification is an evaluation process done by the ACS to evaluate and improve trauma care; the verification process is voluntary and identifies the presence of resources considered essential for the optimal care of the injured patient.[8] Trauma center levels range from Level I (a comprehensive regional resource providing 24-hour in-house coverage, referral resource for communities in nearby regions, leadership in prevention, research, and more) to Level V (basic emergency department [ED] facilities to implement advanced trauma life support [ATLS], after-hours activation protocols, limited surgery and critical care). Level I and Level II centers represent tertiary care centers; the standards for the provision of clinical care to injured patients for Level I and Level II trauma centers are identical. A trauma system is an example of tiered regionalization because the most seriously injured patients in a geographical catchment area are cared for at designated tertiary care trauma centers.[7] Over the past three decades, many studies have demonstrated significantly improved mortality,[9-15] morbidity,[16,17] and cost savings[17,18] after establishment of regionalized trauma systems.

THE ROLE OF THE ANESTHESIOLOGIST

At all levels of trauma care, anesthesiologists are uniquely juxtaposed with the multidisciplinary trauma team, serving both an administrative role in preparing the operating room (OR) and allocating resources for resuscitation, while providing direct patient care through definitive airway management and advanced resuscitation where appropriate.[19] Anesthesiologists also play a significant role as intensivists and pain management experts. Trauma patients represent a significant proportion of all OR cases handled during night and weekend shifts.[20] Regrettably, very few anesthesiologists in the United States consider trauma their primary specialty. This is distinct from European practice, where anesthesiologists frequently are found working in the prehospital environment, as an ED director, or as leader of a trauma team. The United States model, in which all anesthesiologists treat trauma patients—but few do so exclusively—has led to a relative dearth of research, publication, and education in this field.[20,21] This situation is unfortunate because trauma is a rapidly evolving field of study that presents unique challenges to the clinician and one in which improvements in care can have a dramatic impact on society as a whole.

Anesthesia for trauma patients is different from routine OR practice. Most urgent cases occur during off-hours, when the most experienced OR and anesthesia personnel may not be available. In small hospitals and military and humanitarian practice, austere conditions may influence the resources available. Patient information may be limited, and allergies, genetic abnormalities, and previous surgeries may create sudden crises. Patients are frequently intoxicated, with full stomachs and the potential for cervical spine instability. Simple operations may become complicated, and specialty surgical and anesthesia equipment may be required on short notice. Patients often have multiple injuries requiring complex positioning, multiple procedures, and the need to consider priorities in management. Occult injuries, such as tension pneumothorax, can manifest at unexpected times. Fortunately, there does not appear to be a higher risk for medical liability associated with the provision of anesthesia for trauma versus nontrauma surgical anesthesia cases.[22] Successful perioperative care of these patients requires a good understanding of the basics, supplemented by preparation, flexibility, and the ability to react quickly to changing circumstances.

This chapter provides an overview of important areas of trauma care for the anesthesiologist beginning with a description of the initial approach to an injured patient, followed by discussions of emergency airway management, resuscitation, and care of patients with central nervous system (CNS) injuries. The needs of orthopedic and reconstructive surgery patients are outlined and the chapter concludes with a discussion of postoperative issues for the anesthesiologist managing the trauma patient.

Prioritizing Trauma Care

PREHOSPITAL TRIAGE

Prehospital triage of the seriously injured trauma patient begins in the field, and is fraught with difficulty. Estimations of blood loss are imprecise and classically taught shock classifications are commonly confounded by extremes of age and variations in physiological reserve.[23] In 2011, the Centers for Disease Control and Prevention along with the National Highway Traffic Safety Administration collaborated with the ACS Committee on Trauma to revise previous field triage decision schemes in order to reduce over triage of patients with non–life-threatening injuries, and to help direct patients in most need of lifesaving interventions to appropriate trauma centers.[24] Current guidelines recommend a four-step assessment to assist prehospital providers with making decisions about which patients are most in need of transport to a trauma center (Box 66.1).

BOX 66.1 Four Steps for Assessing Need for Trauma Center Referral

Physiological Considerations

Systolic blood pressure <90 mm Hg
Glasgow Coma Scale ≤13
Respiratory rate <10 or >29 (or need for ventilatory support)

Anatomical Considerations

Any penetrating injury to the head, neck, torso, and extremities (proximal to the elbow or knee)
Chest wall instability/deformity
Amputation proximal to the wrist or ankle
Pelvic fracture
Open/depressed skull fracture
Paralysis

Mechanisms of Injury

Death of occupant in same vehicle
Fall from >20 feet
Extrication time >20 min

Special Patient or System Considerations

Age >55 years
Children
Patients on anticoagulants or with bleeding disorders
Burns (to be triaged to designated burn centers)
Pregnancy >20 weeks

Traditionally, mechanism of injury has been referred to as blunt versus penetrating trauma, with no further delineation as to how much energy was imparted, or information regarding anatomical and physiological insults. Some studies have suggested that mechanism of injury alone is a poor predictor for trauma center referral.[25,26] Others have demonstrated that distinct mechanisms, such as ejection from a vehicle or prolonged extrication time, clearly warrant trauma team activation.[27,28] In a study by Lerner and associates, the ACS Field Triage Decision scheme was examined, and interviews conducted with emergency medical technicians who transported patients to trauma centers based on mechanism alone.[29] Only three mechanisms of injury reliably predicted the need for referral to a trauma center when patients did not meet anatomical or physiological injury criteria: death of an occupant in the vehicle, fall greater than 20 feet, and extrication time greater than 20 minutes. Additional studies have justified mechanism of injury as a parameter that helps reduce inappropriate transport of patients with major trauma to nontrauma centers.[30,31] For more information on this subject see Chapter 67.

BLUNT VERSUS PENETRATING TRAUMA

Blunt and penetrating injuries are regularly disparate in presentation but may share similarities in terms of extent of injury.[19] Penetrating injuries are identified as ballistic and nonballistic. The point of injury in the patient with penetrating trauma may be utterly discernible—even to the inexpert provider—but the extent of tissue damage and depth of shock may be less detectible compared to the patient suffering from a blunt traumatic injury. Conversely, the patient with penetrating trauma will lose blood volume externally together with loss into body cavities, whereas the patient with blunt trauma may present in hemorrhagic shock with no obvious signs of hemorrhage. Multiple blunt traumatic insults, bleeding into compartments (e.g., unstable long-bone fractures), retroperitoneal hemorrhage (e.g., pelvic fractures, major vascular injury, solid organ damage), and bleeding into other body cavities may present as indolent hemorrhagic shock.[32]

ADVANCED TRAUMA LIFE SUPPORT

The performance of a thorough patient assessment, application of rapid diagnostic tests, and early activation of resources is vital for ensuring optimal outcomes in patients with severe traumatic injuries.[19] The ATLS course of the ACS is the most widely recognized training program for trauma physicians of all disciplines.[33] Although not comprehensive in subspecialty areas, the ATLS curriculum provides a framework and a common language for the care of injured patients. ATLS is based on a "primary survey" that includes simultaneous efforts to identify and treat life- and limb-threatening injuries, beginning with the most immediate. This focus on urgent problems first is captured by the "golden hour" catchphrase and is the most important lesson of ATLS. Resolution of urgent needs is followed by a meticulous secondary survey and further diagnostic studies designed to reduce the incidence of missed injuries. Knowing the basics of ATLS is essential for *any* physician who interacts with trauma patients. Fig. 66.1 is a simplified representation of the ATLS protocol.

ATLS emphasizes the "ABCDE" mnemonic: airway, breathing, circulation, disability, and exposure. Verification of an open airway and acceptable respiratory mechanics is of primary importance because hypoxia is the most immediate threat to life. Inability to oxygenate the patient will lead to permanent brain injury and death within 5 to 10 minutes. Trauma patients are at risk for airway obstruction and inadequate respiration for the reasons listed in Box 66.2. Endotracheal intubation, whether performed in the prehospital environment or in the ED,

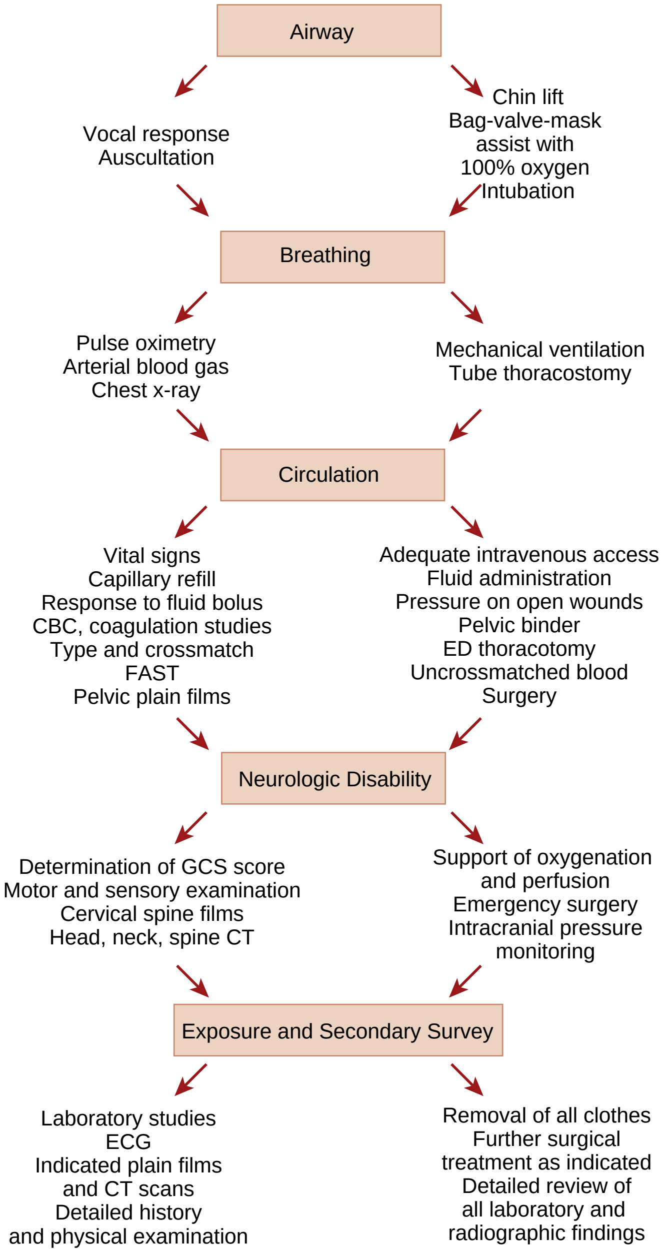

Fig. 66.1 Simplified assessment and management of the trauma patient. *CBC,* Complete blood count; *CT,* computed tomography; *ECG,* electrocardiogram; *ED,* emergency department; *FAST,* focused assessment by sonography for trauma; *GCS,* Glasgow Coma Scale. (Modified from the Advanced Trauma Life Support curriculum of the American College of Surgeons.)