Chapter 26: Anesthesia for Fetal Surgery

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INTRODUCTION

FOCUS POINTS

1. What are the indications for fetal surgery?
2. What are the maternal and fetal physiological considerations?
3. What are the surgical considerations and how can the anesthetic plan best facilitate surgical conditions?

Fetal surgery is a rapidly evolving field in which the developing fetus receives therapy with the goal of decreasing mortality and/or morbidity. It provides unique challenges and requires the integration of both obstetric and pediatric anesthesia practice. Fetal therapies range from minimally invasive techniques to open mid-gestation procedures to near-term procedures performed with the fetus partially delivered while on placental circulation. In this chapter, we describe the indications for fetal surgery, review the principles for providing anesthesia for these cases, and outline the anesthetic approach to minimally invasive, open mid-gestation, and ex utero intrapartum treatment (EXIT) procedures.

A BRIEF HISTORY OF FETAL SURGERY

The first successful fetal therapy in humans began in the 1960s when hydrops fetalis caused by Rh sensitization was treated with in utero transfusion. However, successful exposure of the fetus would have to wait until the 1980s when better prenatal imaging techniques such as sonography and MRI, surgical techniques, and safer anesthetic agents were available. Select milestones in fetal surgery include the first congenital cystic adenomatous malformation (CCAM) resection in 1984, congenital diaphragmatic hernia (CDH) repair in 1989, aortic valvuloplasty in 1991, sacrococcygeal tumor (SCT) resection in 1992, laser ablation of placental vessels in 1995, EXIT procedure in 1995, fetoscopic surgery in 1996, myelomeningocele (MMC) open repair in 1997, hypoplastic left heart balloon septoplasty and valve dilation in 2004, and hypoplastic left heart laser atrial septotomy in 2005.[1] Many of these therapies have since become standard of care and the field of fetal surgery continues to evolve rapidly.

INDICATIONS FOR FETAL SURGERY

While many fetal anomalies can be detected prenatally with sonography and MRI, only select cases have compelling physiological rational for intrauterine therapy. Untreated, the risk of death or severe disability to the fetus must be high. The risk of surgery to the mother should be relatively low. In twin-twin transfusion syndrome, blood passes unequally between twins that share a placenta. The smaller donor twin pumps blood to the larger recipient twin. Twin reversed arterial perfusion (TRAP) sequence is a severe form of twin-twin transfusion syndrome in which one twin is developmentally normal and the other has a serious condition such as a missing heart or missing head that prevents it from surviving on its own. The goal of therapy in twin syndromes is to interrupt the blood flow between the twins. This can be accomplished under visualization with a fetoscope and laser coagulation of the shared vessels. In the case of TRAP syndrome, radiofrequency ablation or ligation of the cord of the abnormal twin can be used to stop the blood flow to the abnormal twin (Figure 26-1). These surgeries are usually performed at 18 to 25 weeks' gestation.[2]

Figure 26-1

Minimally invasive radiofrequency ablation (RFA) for twin reversed arterial perfusion (TRAP) sequence. Procedure is performed under ultrasound

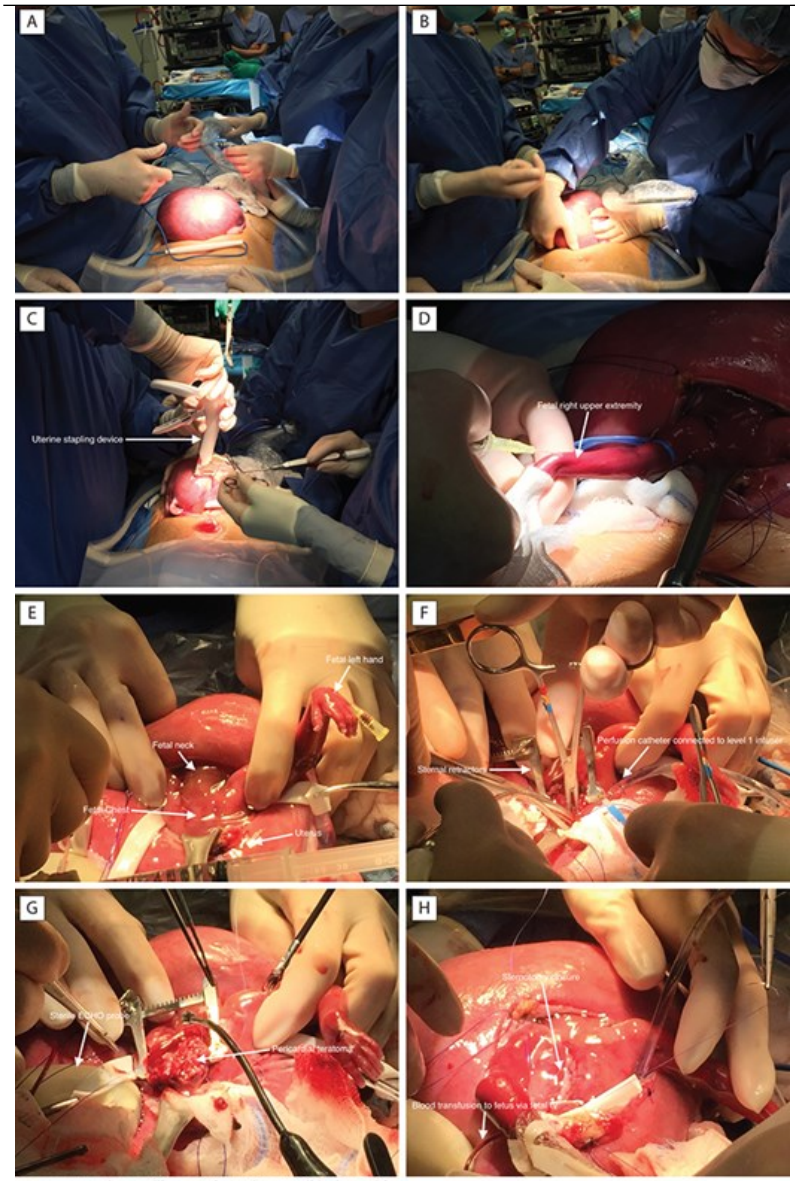
guidance. (Used with permission, from Dr. Lin and Dr. Tran. The Children's Hospital of Philadelphia.)

Thoracic diseases such as CCAM, pulmonary sequestration, and other intrathoracic masses can cause severe pulmonary hypoplasia and heart failure. Depending on the size, location, and composition of the lesion, treatments can range from minimally invasive ultrasound-guided cyst drainage to full laparotomy, hysterotomy, and surgical resection of the lesion. Minimally invasive cyst drainage is generally performed at 18 to 25 weeks' gestation.[3] Open mid-gestation resection is an option if the pulmonary lesion is preventing sufficient lung development to be incompatible with ex-uterine life or such severe heart failure that the fetus is not expected to survive. The goal of open mid-gestation resection or debulking is to remove enough of the mass to allow the lungs and heart to remodel and develop during the rest of gestation. After surgery, the fetus is returned to the uterus and pregnancy continued to as close to term as possible.[4] EXIT procedure is an option that allows for the controlled resection of large fetal lung lesions at delivery. Performing the surgery while on placental bypass avoids acute respiratory decompensation related to mediastinal shift, air trapping, and compression of the normal lung during surgery.[5]

Congenital cardiac malformations can be treated with minimally invasive techniques. Severe aortic stenosis is treated with fetal aortic valvuloplasty[6] and hypoplastic left heart syndrome (HLHS) with an intact atrial septum is treated with atrial septostomy.[7] Pericardial teratomas that are large enough to cause hydrops can be resected or debulked with an open mid-gestation procedure (Figure 26-2A–H).[8]

Figure 26-2

A. With an anterior placenta, the uterus is externalized to expose the posterior aspect for incision. **B.** Fetus undergoes version with ultrasound guidance to place it in correct position for surgical exposure. **C.** Uterine stapler is used to incise uterus while maintaining hemostasis. **D**. Peripheral IV catheter is placed in right upper extremity of fetus. **E**. Bilateral upper extremities and fetal chest are exposed through hysterotomy site. **F**. Fetal sternotomy is performed. Perfusion catheter infuses body temperature lactated ringers into uterine cavity to replace lost amniotic fluid. **G**. Fetal pericardial teratoma is exposed for resection. Continuous echocardiography is used to monitor fetal heart rate, heart function, valvular dysfunction, and volume status. **H**. Fetal chest after sternal closure prior to return of fetus to uterus. (Used with permission, from Dr. Lin and Dr. Tran. The Children's Hospital of Philadelphia.)

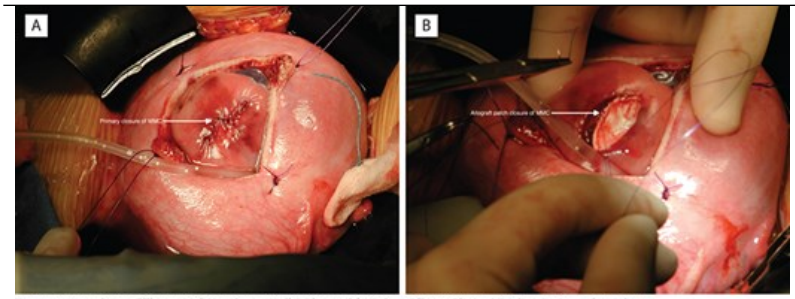


Source: Herodotos Ellinas, Kai Matthes, Walid Alrayashi, Aykut Bilge: *Clinical Pediatric Anesthesiology*

Myelomeningocele repair is performed at 22 to 26 weeks gestation. The mother undergoes laparotomy and hysterotomy and the defect is exposed. It is then closed primarily or with a patch (Figure 26-3A–B) and the fetus is returned to the uterus with the goal of continuing pregnancy until 37 weeks' gestation, at which time the fetus is delivered via C-section. Maternal complications after open fetal myelomeningocele repair include membrane separation, preterm premature rupture of membranes, preterm labor, and need for blood transfusion.[9] Sacrococcygeal teratomas are resected in utero generally around 20 to 25 weeks' gestation if the highly vascular tumors are causing life-threatening high-output cardiac failure and fetal hydrops.[10]

Figure 26-3

A. Fetal myelomeningocele with primary closure. **B**. Fetal myelomeningocele with allograft patch closure. (Used with permission, from Dr. Lin and Dr. Tran. The Children's Hospital of Philadelphia.)



Fetal neck masses such as cervical teratomas and lymphangiomas are masses that can grow so large as to block the fetal airway and esophagus. These airway malformations usually do not present a problem for the fetus while they are on placental circulation. However, these lesions are not compatible with ex utero life as the airway obstruction prevents the neonate from breathing normally. These lesions are managed by EXIT procedure, in which the airway is secured while the fetus is still on placental circulation, and the placenta is acting as the organ of respiration. This involves maternal laparotomy and hysterectomy. The securing of the airway is accomplished by intubation, tracheostomy, and/or partial or full mass resection (Figure 26-4). After the airway is secured, the umbilical cord is cut and the fetus is delivered immediately after the procedure. These procedures are usually performed as close to term as possible to minimize the problems associated with prematurity.[11] Congenital high airway obstruction syndrome (CHAOS) is a syndrome in which there is blockage of the upper airway of the fetus from laryngeal cysts, webs, or atresia. CHAOS can prevent the fluid, which is normally produced by the lungs, from draining into the amniotic space; the lungs may become massively distended, causing cardiac compression, heart failure, and fetal demise. If the CHAOS is causing life-threatening hydrops, the fetus may be treated with a mid-gestation percutaneous laser decompression to relieve the tracheal obstruction. The fetus may then subsequently be delivered via EXIT procedure or cesarean section depending on the anticipated residual obstruction (Table 26-1).[12]

Figure 26-4

Fetus with cervical lymphangioma delivered via EXIT procedure for bronchoscopy and intubation. (Used with permission, from Dr. Lin and Dr. Tran. The Children's Hospital of Philadelphia.)

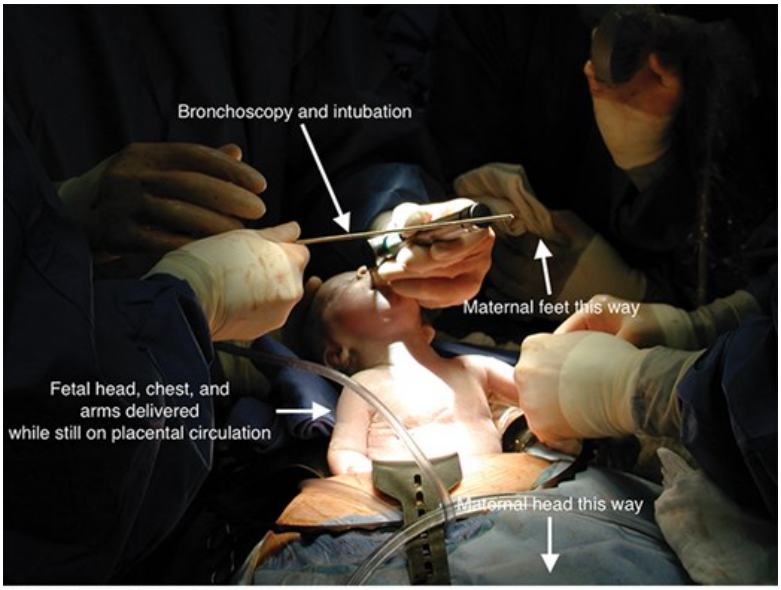


Table 26-1

Fetal Surgery Treatment Options

Fetal Anomaly	Surgical Management
Twin syndromes ○ TTTS ○ TRAP	• Amnioreduction • Fetoscopic laser photocoagulation • Fetoscopic radiofrequency ablation
Lung lesions ○ CCAM ○ BPS	• Minimally invasive thoracoamniotic shunt placement • Mid-gestation surgical resection • EXIT procedure surgical resection
Heart lesions ○ Aortic stenosis ○ HLHS with intact atrial septum ○ Pericardial teratoma	• Percutaneous balloon aortic valvuloplasty • Percutaneous balloon atrial septostomy • Mid-gestation surgical resection
Neurological lesions ○ MMC	• Primary closure or patch closure of MMC
Airway lesions ○ Large cervical mass ○ CHAOS	• EXIT procedure intubation, tracheostomy, partial or complete resection of lesion • Mid-gestation laser decompression
Abdominal lesions ○ CDH	• Fetoscopic temporary tracheal occlusion

Fetal surgery for other conditions such as repair of posterior urethral valves causing bladder outlet obstruction,[13] aqueductal stenosis of the fourth ventricle causing hydrocephalus, and diaphragmatic hernia with liver in the chest causing severe pulmonary hypoplasia have been attempted in the past but with poor results. However, new techniques are under development for these conditions.

CONTRAINDICATIONS

Contraindications to fetal surgery include maternal medical disease such as morbid obesity, cardiac disease, maternal hypertension that would increase the risk of preeclampsia or preterm delivery, or psychosocial factors that would put the mother at high risk for morbidity or mortality, and other concomitant fatal or severely disabling abnormalities in the fetus.

PRINCIPLES IN PROVIDING ANESTHESIA FOR FETAL SURGERY

Maternal Factors

Maternal Physiology

The mother undergoes significant physiological changes during pregnancy. She is at increased risk of aspiration due to the following factors:

enlargement of the uterus pushing up on the gastroesophageal junction and causing sphincter incompetence, slower gastric emptying rate, and increased gastrin production increasing acidic content of stomach. Therefore, as of mid to late second trimester, the pregnant patient should be treated as a full stomach with measures to minimize risk of aspiration.

Maternal respiration also undergoes significant changes during pregnancy. Functional residual capacity decreases due to the gravid uterus. Minute ventilation increases by 50% and increases oxygen consumption, increasing the risk for hypoxia. The airway may also become edematous and along with increased breast size may make intubation more challenging.[14]

Compression of the inferior vena cava and aorta by the gravid uterus can cause decrease in systemic venous return and uterine perfusion, hypotension, and hypoxia. The mother should be put in left uterine displacement to minimize the compression. The pregnant patient requires less anesthetic as compared to the same patient in the nonpregnant state. Minimal alveolar concentration (MAC) is thought to be reduced by 30%[15,16] due to increased progesterone and endorphins. Epidural anesthetics also have increased effect due to decreased protein levels, pH changes in the cerebrospinal fluid, increased nerve sensitivity, and hormonal changes.[17]

Uteroplacental Physiology

Adequate uterine blood flow is necessary for placental and fetal perfusion. Uterine blood flow depends on the pressure gradient between the uterine artery and uterine vein and is inversely proportional to uterine vascular resistance [(uterine arterial – uterine venous pressure)/uterine vascular resistance]. Many factors, including medications, surgical manipulation of the uterus, maternal hemodynamics, and maternal respiration, can affect uterine blood flow. Hypotension, caval compression, uterine contraction, valsalva, and hypocapnia decrease uterine blood flow. However, some anesthetic interventions such as use of vasopressors, regional anesthesia, volatile anesthetic agents, vasodilators, and magnesium can have variable effect on uterine blood flow.

The location of the placenta (anterior vs. posterior) will affect the surgical approach so that incision is not made through the placenta. Uterine relaxation in mid-gestation procedures during and after the procedure to prevent preterm labor is vital. Volatile anesthetics are powerful tocolytics and are currently used to provide uterine relaxation during surgery. Intravenous nitroglycerin is a powerful tocolytic with fast onset of action and limited duration. However, the tocolytic effects of these drugs must be balanced with the maternal hypotension, decrease in uteroplacental perfusion, and decrease in fetal cardiovascular function also caused by use of high doses of volatile anesthetics.[18] To maintain placental blood flow, maternal blood pressure must be maintained, often with the assistance of vasopressors. There is also the danger of placental abruption if uterine tone is too high or amniotic fluid is lost too rapidly after hysterotomy. Compression or kinking of the umbilical cord must also be avoided. Some medications cross the placenta from mother to fetus.[19] Drugs that are lipid soluble, not ionized, and of low molecular weight cross the placenta more easily.

Fetal Factors

Fetal physiology is unique from that of children or adults. The fetal circulation is a parallel system. The combined cardiac output (sum of left and right ventricular output) is 425 to 550 mL/kg/min, with the right ventricle contributing 60% to 70% of the combined cardiac output. The fetal myocardium is stiffer than that of adults and therefore cardiac output is more heart-rate dependent than preload dependent.[20] The fetal blood volume is approximately 120 to 162 cc/kg estimated fetal weight at 16 to 22 weeks, and 93 cc/kg estimated fetal weight by 31 weeks. However, two-thirds of the blood volume is on the placental side. Fetuses are hypocoagulable as compared to infants, with coagulation factors increasing with gestational age. The anesthetic requirements of fetuses are lower than that of their pregnant mothers.[21] While there is substantial evidence of fetal autonomic and endocrine response to noxious stimuli,[22,23] it is unclear as to whether fetuses have conscious perception of pain. Pharmacological interventions can be delivered to the fetus via placental blood transmission from the mother, or via umbilical artery, fetal intravenous, and fetal intramuscular administration. One should consider providing pharmacological intervention to blunt the fetal stress response to surgical stimuli via one or more of these routes.

Preoperative Evaluation and Preparation

Fetal anomalies are usually first diagnosed by ultrasound. After initial suspicion of anomaly, further imaging via detailed fetal ultrasound, MRI, echocardiography, and chromosomal analysis may be warranted to better understand the anomaly and any other associated disorders. A comprehensive prenatal team of maternal fetal medicine specialists, surgeons, neonatologists, geneticists, psychologists, and social workers must

work together to diagnose and counsel patients with their treatment options. Prior to any fetal intervention, the mother must also have a complete workup, including a thorough history and physical, electrocardiogram, blood work, and other diagnostic tests that may be warranted in order to devise a safe anesthetic plan.

Anesthesia for Minimally Invasive Fetal Surgery

Minimally invasive surgery involves using a percutaneous approach with a fiberscope and/or visualization by transabdominal ultrasound. The anesthetic approach to these cases can be quite variable, depending on the procedure and surgical and maternal factors. Surgical factors to consider include position of the placenta, umbilical cord, location of the lesion, duration of the procedure, and experience of the surgeons. Maternal factors to consider include any comorbidities and preoperative level of maternal discomfort and anxiety. Local anesthesia, sedation, general anesthesia, and regional anesthesia are all potential approaches to these cases. Local anesthesia or sedation may be appropriate for the procedure that is not anticipated to have a long duration with a mother that is able to cooperate. General anesthesia or regional anesthesia may be more appropriate for longer procedures or where maternal anxiety or discomfort makes cooperation more difficult. In general, the risk of blood loss is low in these cases and one peripheral IV catheter should suffice. Postoperative pain is usually minimal due to the small incision size. Postoperative tocolysis is usually achieved with oral nifedipine, with the addition of intravenous magnesium if needed.[24] There is the potential for fetal distress during minimally invasive surgery. Depending on the gestational age at the time of procedure, the fetus may or may not be viable outside the womb. In the event that the fetus is viable, staff should be prepared to perform emergency cesarean section and fetal resuscitation, if required.

Anesthesia for Open Mid-Gestation Fetal Surgery

Open fetal surgery requires that both the mother and fetus be anesthetized and the uterus be relaxed during the procedure to prevent uteroplacental compromise. This is generally achieved with general endotracheal tube anesthesia with high doses of volatile anesthetic (>2 MAC volatile agent). However, some centers prefer to use moderate doses of volatile anesthetic supplemented with intravenous anesthesia with the thought that this may decrease fetal cardiac dysfunction.[25] Prior to induction of anesthesia, a type and cross should be completed for the mother with type-specific red blood cells available for the mother in case of hemorrhage. O-negative red blood cells should be prepared for the fetus and cross-checked against the mother's sample, with the addition of AB-negative fresh frozen plasma and platelets if needed. Resuscitation medications for the fetus (atropine and epinephrine) as well as analgesia (fentanyl) and muscle relaxant (vecuronium) should be prepared in unit dosing based on the estimated fetal weight from the most recent ultrasound.

On the day of surgery, the mother should be appropriately NPO. An intravenous line is placed in the preoperative area. A preoperative low thoracic/high lumbar epidural is placed in the preoperative area for postoperative pain control. A good postoperative analgesia for the mother is associated with less uterine irritability.[26] An epidural test dose is administered to ensure it is not intravascular, but a bolus dose is not recommended as this may exacerbate the anticipated hypotension from high doses of volatile anesthetic. On arrival to the operating suite, the mother is placed in left uterine displacement. After preoxygenation, the mother is then induced with a rapid sequence induction and an endotracheal tube is placed. A second intravenous line is placed as well as an arterial line for careful monitoring of hemodynamics. A Foley catheter is placed. Volatile anesthetic is increased to >2 MAC and uterine tone is assessed by the surgeon prior to hysterotomy. Uterine relaxation may be augmented with the use of intravenous nitroglycerin. The maternal blood pressure will almost certainly require support with vasopressors, generally achieved with a phenylephrine infusion and ephedrine boluses as needed. Maternal fluid administration is limited to decrease the incidence of pulmonary edema.[27,28] At the authors' institution, fetal cardiac function is monitored with intraoperative fetal echocardiography. If the fetal cardiac function appears to be depressed, the volatile anesthetic is decreased and the umbilical cord is checked to make sure that there is no compression or kinks. If cardiac dysfunction persists, fetal resuscitation medications can be given through the umbilical vein, intramuscular, or through a fetal intravenous line if one is placed. Fetal intravenous lines are generally placed in open mid-gestation procedures such as resection of lung lesions or sacrococcygeal tumors where at least one fetal limb is externalized from the uterus. In cases of severe cardiac dysfunction, intraoperative fetal chest compressions may be necessary.

Toward the end of the procedure, intravenous magnesium sulfate is initiated for tocolysis. The epidural is dosed for postoperative pain control. Serious postoperative complications include preterm labor, pulmonary edema, amniotic fluid leak, chorioamniotic membrane separation, and fetal demise.[15]

Anesthesia for EXIT Procedure

The preoperative preparation, anesthetic induction, and preincision preparation for an EXIT procedure are similar to that of an open mid-gestation procedure. For an obstructive airway lesion, the EXIT procedure may involve intubation of the fetus, tracheostomy, bronchoscopy, and/or partial or complete resection of the obstructive airway lesion prior to clamping the cord. In the case of large CCAM, the lesion is resected while on placental circulation. In either situation, it is important that no ventilation of the fetal lungs take place until the cord is ready to be clamped. Otherwise, the fetus will transition from fetal to neonatal physiology prematurely, with loss of placental support. The difference in the EXIT procedure compared to the open mid-gestation procedure is that the fetus is delivered immediately after the procedure. Therefore, magnesium sulfate is not needed for tocolysis, and oxytocin is administered after the cord is clamped to prevent uterine atony and hemorrhage. Given the fact that high levels of volatile agent were used to promote uterine relaxation during the procedure, additional medications such as methylergonovine and prostaglandin F2 alpha are occasionally required. Crystalloid administration may be more liberal during these cases as there is less risk of pulmonary edema. In the event that the surgical procedure cannot be completed on placental circulation (due to events such as premature placental separation, maternal complications, fetal intolerance) and the fetus must emergently be separated from the mother, a second operating room should already be setup and a second operating room team should be immediately available to resuscitate and manage the neonate (Table 26-2).[24,29]

Table 26-2

Anesthetic Techniques for Fetal Surgery

	Minimally Invasive Surgery	Open Fetal Surgery	EXIT Procedure
Maternal anesthesia	• Generally well tolerated with IV sedation • Regional anesthesia or general anesthesia can also be used, especially if there is a concern that fetus may have to be delivered by emergent c-section	• General anesthesia with epidural for postoperative pain control • Regional anesthesia with nitroglycerin for uterine relaxation	• General anesthesia with or without epidural for postoperative pain control
Fetal anesthesia	• Transplacental drug delivery from mother	• Transplacental drug delivery from mother • IM or IV narcotics, muscle relaxant, or resuscitation medications • Umbilical vein resuscitation medications	• Transplacental drug delivery from mother • IM or IV narcotics, muscle relaxant, or resuscitation medications • Umbilical vein resuscitation medications
Intraoperative tocolysis	• No—tocolysis contraindicated	• Yes—with high dose volatile agent, IV nitroglycerin, IV magnesium sulfate	• Yes—with high dose volatile agent, IV nitroglycerin
Risk of preterm labor	• Minimally increased	• Significantly increased	• Not applicable—fetus delivered at end of procedure

Intraoperative Fetal Monitoring and Resuscitation

Fetal monitoring during fetal procedures depends on the procedure being performed, risk of fetal compromise, and availability of certain monitoring

techniques at the local institution. Fetal monitoring may range from preoperative and postoperative monitoring of fetal heart rate to continuous fetal echocardiography. In the case of open procedures, fetal heart rate and oxygen saturation may be monitored with pulse oximeter attached to an externalized fetal limb. Depending on the gestational age, normal fetal heart rate is expected to be 120 to 160 beats per minute. Normal fetal oxygen saturation is expected to be 40% to 60%.[30] Blood samples drawn from the umbilical artery may also be sent for laboratory analysis. When available, continuous intraoperative fetal echocardiography may be helpful in monitoring fetal well-being during the procedure and helping to guide anesthetic management and fetal resuscitation if needed.[31]

In instances of fetal distress, resuscitation medications may be administered to the fetus through the umbilical vein, an intramuscular injection, or an intravenous line if available. Maternal factors such as hypotension, impaired venous return, and insufficient amniotic fluid should be considered and treated if relevant. Uteroplacental factors such as a compressed or kinked umbilical cord or uterine contractility should be evaluated and ameliorated.

Future Directions

Fetal surgery is a field that continues to grow. New techniques, such as minimally invasive endoscopic myelomeningocele repair,[32,33] continue to be developed. Providing anesthesia for these procedures requires detailed understanding of both maternal and fetal physiology and the anesthetic plan must balance the physiology of two patients at the same time. Further research is needed to refine anesthetic technique as the field continues to evolve.

Practical High-Yield Concepts and Tips for the Practitioner

- First do no harm; maternal safety is paramount.
- The anesthetic plan must incorporate maternal and fetal physiology as well as an understanding of the surgical needs of the case.
- Preoperative, intraoperative, and postoperative communication and coordination of care among multiple teams (surgery, maternal fetal medicine, neonatology, anesthesia, and nursing) are imperative.
- Anesthesia for minimally invasive cases can range from light sedation to general anesthesia.
- Anesthesia for open mid-gestation cases must facilitate intraoperative uterine relaxation and postoperative tocolysis.
- Anesthesia for EXIT procedures must facilitate intraoperative uterine relaxation but normal postpartum uterine contractility. Post-EXIT care of a potentially critical neonate requires the coordination of a neonatology team and secondary operating room team for the neonate.

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