

INTRAUTERINE FETAL SURGERY

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Community Plan Policy
• Intrauterine Fetal Surgery

INSTRUCTIONS FOR USE

This Medical Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the member specific benefit plan document must be referenced. The terms of the member specific benefit plan document [e.g., Certificate of Coverage (COC), Schedule of Benefits (SOB), and/or Summary Plan Description (SPD)] may differ greatly from the standard benefit plan upon which this Medical Policy is based. In the event of a conflict, the member specific benefit plan document supersedes this Medical Policy. All reviewers must first identify member eligibility, any federal or state regulatory requirements, and the member specific benefit plan coverage prior to use of this Medical Policy. Other Policies and Coverage Determination Guidelines may apply. UnitedHealthcare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.

BENEFIT CONSIDERATIONS

Before using this policy, please check the member specific benefit plan document and any federal or state mandates, if applicable.

When deciding coverage for intrauterine fetal surgery, refer to the member specific benefit plan document language for further information on benefit coverage for treatment of life-threatening conditions. In some benefit documents, coverage exists for unproven services for persons with life-threatening conditions, under certain circumstances.

Essential Health Benefits for Individual and Small Group

For plan years beginning on or after January 1, 2014, the Affordable Care Act of 2010 (ACA) requires fully insured non-grandfathered individual and small group plans (inside and outside of Exchanges) to provide coverage for ten categories of Essential Health Benefits (“EHBs”). Large group plans (both self-funded and fully insured), and small group ASO plans, are not subject to the requirement to offer coverage for EHBs. However, if such plans choose to provide coverage for benefits which are deemed EHBs, the ACA requires all dollar limits on those benefits to be removed on all Grandfathered and Non-Grandfathered plans. The determination of which benefits constitute EHBs is made on a state by state basis. As such, when using this policy, it is important to refer to the member specific benefit plan document to determine benefit coverage.

COVERAGE RATIONALE

Intrauterine fetal surgery (IUFS) is proven and medically necessary for treating the following conditions:

- Congenital cystic adenomatoid malformation (CCAM) and extralobar pulmonary sequestration (EPS): Fetal lobectomy or thoracoamniotic shunt placement for CCAM and thoracoamniotic shunt placement for EPS

- Sacrococcygeal teratoma (SCT): SCT resection
- Urinary tract obstruction (UTO): Urinary decompression via vesicoamniotic shunt placement
- Twin-twin transfusion syndrome (TTTS): Fetoscopic laser surgery
- Twin reversed arterial perfusion (TRAP): Ablation or occlusion of anastomotic vessels (e.g., laser coagulation or radiofrequency ablation)
- Myelomeningocele (MMC) repair

IUFS is unproven and not medically necessary for treating the following conditions due to insufficient evidence of efficacy:

- Congenital diaphragmatic hernia (CDH)
- Congenital heart disease (CHD)

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

CPT Code	Description
59070	Transabdominal amnioinfusion, including ultrasound guidance
59072	Fetal umbilical cord occlusion, including ultrasound guidance
59074	Fetal fluid drainage (e.g., vesicocentesis, thoracocentesis, paracentesis), including ultrasound guidance
59076	Fetal shunt placement, including ultrasound guidance
59897	Unlisted fetal invasive procedure, including ultrasound guidance

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HCPCS Code	Description
S2400	Repair, congenital diaphragmatic hernia in the fetus using temporary tracheal occlusion, procedure performed in utero
S2401	Repair, urinary tract obstruction in the fetus, procedure performed in utero
S2402	Repair, congenital cystic adenomatoid malformation in the fetus, procedure performed in utero
S2403	Repair, extralobar pulmonary sequestration in the fetus, procedure performed in utero
S2404	Repair, myelomeningocele in the fetus, procedure performed in utero
S2405	Repair of sacrococcygeal teratoma in the fetus, procedure performed in utero
S2409	Repair, congenital malformation of fetus, procedure performed in utero, not otherwise classified
S2411	Fetoscopic laser therapy for treatment of twin-to-twin transfusion syndrome

DESCRIPTION OF SERVICES

This policy addresses the use of intrauterine fetal surgery (IUFS), an open surgical treatment of fetuses with specific life-threatening conditions that involve a fetal malformation. During IUFS, a hysterotomy is performed, and the fetus is partially removed to correct a fetal malformation.

IUFS uses minimally invasive techniques (i.e., small incisions) and instruments to correct the fetal malformation. The primary medical conditions indicated for IUFS include the following:

- Congenital cystic adenomatoid malformation
- Extralobar pulmonary sequestration
- Sacrococcygeal teratoma
- Urinary tract obstruction
- Twin-twin transfusion syndrome
- Twin reversed arterial perfusion syndrome
- Myelomeningocele repair

- Congenital diaphragmatic hernia
- Congenital heart disease

Thoracic Lesions

Congenital cystic adenomatoid malformation (CCAM) and bronchopulmonary sequestration (BPS) are congenital anomalies of the lung. Appropriate candidates for in utero treatment include a small subset of patients with congenital pulmonary airway malformations. In this subset, the fetal mediastinum is compressed, leading to impaired venous return with resulting fetal hydrops, secondary to cardiac failure (Walsh et al., 2011).

Sacroccygeal Teratoma (SCT)

Fetuses with large, vascular SCTs have a high incidence of prenatal mortality from high-output cardiac failure or spontaneous hemorrhage of the growing tumor. Fetal surgical procedures for SCT have focused on the small subgroup of fetuses with SCT and hydrops because untreated cases are expected to die in utero or at birth. In severe cases, SCT with hydrops is associated with a maternal risk of developing mirror syndrome, a severe form of preeclampsia (Walsh et al., 2011).

Urinary Tract Obstruction (UTO)

Fetal UTO interferes with normal development of the kidneys and lungs, particularly when involving the lower urinary tract. Goals of fetal surgery have emphasized decompression procedures, such as percutaneous shunting, rather than repair of the specific lesion. The goal of decompression of the distended portion of the urinary tract is to protect function of the remaining kidney and to promote lung development (Walsh et al., 2011).

Twin-Twin Transfusion Syndrome (TTTS)

In TTTS, twins share a single chorionic membrane and a single placenta but have separate amniotic sacs. Women with severe TTTS, who have not undergone treatment before 26 weeks, will usually experience loss of both fetuses. However, if both twins survive, they often experience severe neurologic compromise and organ failure. Treatment options include amnioreduction to relieve pressure and uterine size, termination of the sicker twin, or fetoscopic laser ablation of the communicating vessels. In nonselective ablation, all vessels crossing the dividing membrane are ablated, whereas selective ablation is limited to certain vessels connecting the two fetuses (Walsh et al., 2011).

Twin Reversed Arterial Perfusion (TRAP)

TRAP sequence is a condition in which an acardiac/acephalic twin receives all of its blood supply from a normal twin, the so-called "pump" twin. Blood enters the acardiac twin through a retrograde flow via the umbilical artery and exits via the umbilical vein. The extra work places an increased demand on the heart of the pump twin, resulting in cardiac failure. Twin death occurs more frequently when the size of the acardiac twin is greater than half that of the pump twin. The goal of fetal surgery is to interrupt blood supply to the non-viable twin.

Myelomeningocele (MMC)

MMC (also known as spinal bifida) is a neural tube defect in which the spinal cord forms but remains open. Although MMC is rarely fatal, individuals affected with it have a range of disabilities, including paraplegia, hydrocephalus, skeletal deformities, bowel and bladder incontinence and cognitive impairment. Standard therapy is postnatal surgical closure of the MMC followed by shunting for hydrocephalus if needed (Walsh et al., 2011).

Congenital Diaphragmatic Hernia (CDH)

CDH results from abnormal development of the diaphragm, which allows abdominal organs like the bowel, stomach, and liver to protrude into the chest cavity. Fetuses diagnosed in utero as a result of maternal symptoms have a high mortality risk. Less invasive fetal procedures are being developed that focus on methods to accomplish tracheal occlusion (Walsh et al., 2011).

Congenital Heart Disease

In utero procedures are performed for cardiac conditions such as pulmonary atresia with intact ventricular septum, critical aortic stenosis with impending hypoplastic left heart syndrome, and hypoplastic left heart syndrome with intact atrial septum. All of these conditions, if untreated either in utero or soon after birth, are fatal (Walsh et al., 2011).

CLINICAL EVIDENCE

In a Technical Brief, the Agency for Healthcare Research and Quality (AHRQ) presented an overview of the current state of practice and research regarding in utero fetal surgical procedures for the following conditions: CDH, cardiac malformations, MMC, obstructive uropathy, SCT, TTTS and thoracic lesions (Walsh et al., 2011).

Congenital Cystic Adenomatoid Malformation (CCAM) and Extralobar Pulmonary Sequestration (EPS)

A prospective study evaluating 58 fetuses with CCAM found that 29% were at risk for hydrops and required fetal intervention. The overall survival rate was 71% after fetal surgery; however, the survival rate for hysterotomy and open fetal lobectomy was 29% compared with 100% for fetoscopic shunting or cyst aspiration. The perinatal mortality rate was 29% in those fetuses who were considered unlikely to survive (Crombleholme et al., 2002).

Sacroccygeal Teratoma (SCT)

Fetal surgery is not considered appropriate in the presence of the maternal mirror syndrome or in cases of advanced high-output cardiac failure (Hedrick et al., 2004).

Urinary Tract Obstruction (UTO)

In utero fetal surgery for UTO improves perinatal survival in selected fetuses and children who are at high risk for mortality due to renal failure and pulmonary complications. Perinatal survival rates ranged from approximately 57% to 80%. The prognosis appears to be worse for fetuses with elevated urinary electrolytes or prolonged anhydramnios at the time of surgery. Despite initial surgical success and improved survival, more than 25% of children have residual renal disease that requires subsequent transplantation, urinary tract surgery, or other medical interventions. Most children also demonstrate growth retardation, and many void spontaneously. Pulmonary dysfunction is apparent, despite fetal surgery, and has been reported to result in death in 18% to 25% of children followed for a period up to 114 months. A meta-analysis evaluated the efficacy and safety of prenatal bladder drainage. Results showed significantly improved perinatal survival among 195 fetuses in controlled trials that received the intervention compared with those who did not (Clark et al., 2003; Freedman et al., 1999; McLorie et al., 2001; Welsh et al., 2003).

Twin-Twin Transfusion Syndrome (TTTS)

A total of 120 infants with TTTS were enrolled in a randomized clinical trial (RCT) of laser photocoagulation versus amnioreduction. Investigators assessed long-term neurological and developmental outcomes. The primary outcome was a composite of death and major neurological impairment. The authors found that, at 6 years of age, 82% of the children in the laser group and 70% of the children in the amnioreduction group had a normal neurological evaluation; the differences between the groups was not significant. Laser therapy was associated with a 40% reduction in the risk of fetal death or long-term neurologic impairment when compared with amnioreduction (Salomon et al., 2010).

Roberts et al. (2008) assessed which treatments for TTTS improved fetal, childhood and maternal outcomes. The authors compared outcomes from 3 randomized and quasi-randomized studies of amnioreduction, laser coagulation, and septostomy (253 women). Laser coagulation resulted in reduced overall mortality and neonatal mortality when compared with amnioreduction. There was no difference in perinatal outcome between amnioreduction and septostomy. The results suggest that endoscopic laser coagulation of anastomotic vessels should be considered for treatment of all stages of TTTS to improve perinatal and neonatal outcome. In a later publication, Roberts et al. (2014) concluded that endoscopic laser coagulation of anastomotic vessels should be considered in the treatment of all stages of TTTS to improve neurodevelopmental outcomes. Further research to assess the effect of treatment on milder and more severe forms of TTTS and long-term survival outcomes are still required.

Senat et al. (2007) conducted a RCT and evaluated pregnant women with severe TTTS before 26 weeks of gestation, who were randomly assigned to laser therapy (n=72) or amnioreduction (n=70). The study concluded early because an interim analysis demonstrated a significant survival benefit in the laser group. Compared to the amnioreduction group, the laser group had a higher likelihood of survival (of at least 1 twin) to 28 days of age (76% in laser group and 56% in amnioreduction group). The laser group also had a lower incidence of cystic periventricular leukomalacia, and were more likely to have no neurological complications at 6 months of age (52% in laser group and 31% in amnioreduction group).

Graef et al. evaluated 167 children (median age 3 years, 2 months) to investigate long-term neurodevelopment after intrauterine laser coagulation for TTTS. A total of 145 children (86.8%) demonstrated normal development, 12 children (7.2%) showed minor neurological abnormalities, and 10 children (6%) demonstrated major neurological abnormalities. The investigators concluded that intrauterine laser coagulation was the relatively best treatment option for severe TTTS (2006).

Professional Societies

Society for Maternal-Fetal Medicine (SMFM)

A SMFM clinical guideline states that over 75% of stage I TTTS cases remain stable or regress without invasive intervention, with perinatal survival of about 86%. Therefore, many patients with stage I TTTS can often be managed expectantly. For stages II-IV, fetoscopic laser photocoagulation of placental anastomoses is considered by most experts to be the best available approach in continuing pregnancies at < 26 weeks. However, expectant management and amnioreduction remain 2 options for TTTS > stage I at < 26 weeks when the patient does not have the ability to travel to a center that performs fetoscopic laser photocoagulation. Published meta-analysis data have demonstrated

no significant survival benefit, and long-term neurologic outcomes in the Eurofetus trial were not different between the laser and non-laser groups. Laser-treated TTTS has been shown to be associated with a perinatal mortality rate of 30-50%, and a 5-20% chance of long-term neurologic handicap. For stage \geq III TTTS and for those undergoing invasive interventions, steroids for fetal maturation should be considered at 24 0/7 to 33 6/7 weeks (2013).

Twin Reversed Arterial Perfusion (TRAP)

Lee et al. (2013) reported the North American Fetal Therapy Network (NAFTNet) Registry data on the outcomes of using radiofrequency ablation (RFA) to treat TRAP. This was a retrospective review of all patients who underwent percutaneous RFA of an acardiac twin after referral to a NAFTNet institution. The primary outcome was neonatal survival to 30 days of age. Of the 98 patients identified, there were no maternal deaths. Mean gestational age at delivery was 33.4 weeks overall and 36.0 weeks for survivors. Median gestational age at delivery was 37 weeks. Survival of the pump twin to 30 days was 80% in the overall cohort. The authors concluded that this data suggests that RFA of the acardiac twin is an effective treatment for TRAP sequence.

Pagani et al. (2013) conducted a retrospective cohort study and meta-analysis of intrafetal laser treatment for TRAP sequence. A total of 23 cases of TRAP were identified during the study period. Of these, 6 were managed conservatively and 17 were treated with laser therapy. All cases managed conservatively were complicated by intrauterine death (IUD) at a median gestational age of 14 weeks. Among the treated cases, 14 (82%) delivered a healthy twin at a median gestational age of 37 weeks. The overall neonatal survival was 80%. Adverse pregnancy outcome was significantly lower when the treatment was performed before 16 weeks' gestation.

Cabassa et al. (2013) evaluated the treatment of monochorionic twin pregnancies complicated by TRAP using RFA. Between July 2007 and October 2010, 11 monochorionic twin pregnancies complicated by TRAP were identified. A total of 7 patients underwent intrafetal ablation of the acardiac twin with RFA. Median gestational age at the intervention was 17 weeks. A total of 5 fetuses (71%) were delivered at a median gestational age of 33 weeks; all were alive and had a normal examination at 6 months of age. The overall neonatal survival was 85%. The authors noted that further research is needed to define the best timing of the procedure.

Lee et al. (2007) evaluated the treatment of 29 patients with TRAP sequence using RFA to stop perfusion to the acardiac twin and protect the pump twin. The investigators concluded that RFA of the acardiac twin effectively protects the pump twin from high-output cardiac failure and death. Greater than 90% survival can be achieved in monochorionic-diamniotic pregnancies complicated by TRAP sequence with a mean gestation age at time of delivery close to term.

Myelomeningocele (MMC)

A Hayes report concluded that there is moderate quality evidence that IUFS for MMC is associated with improved motor function, excretory function and neuroanatomical outcomes, as well as reduced need for shunt placement. However, IUFS did not influence cognitive outcomes and did result in lower gestational age at birth (premature birth) relative to postnatal controls. One RCT and 10 nonrandomized controlled studies compared IUFS with standard postnatal surgery. Most of the studies were retrospective and did not follow up on the developmental outcomes of IUFS past 3 years of age. As a consequence, the relationship between many of the findings and longer-term clinical outcomes is not clear at this time (Hayes, 2012a; updated August 29, 2016).

The Management of Myelomeningocele Study (MOMS) compared outcomes of prenatal versus postnatal repair of MMC. Patients (n=183) were randomized to undergo either prenatal surgery before 26 weeks of gestation or standard postnatal repair. Primary outcomes were fetal or neonatal death, the need for a cerebrospinal shunt by the age of 12 months and mental development and motor function at 30 months. The children of 158 patients were available for evaluation at 12 months. The children of 134 patients were available for evaluation at 30 months. The trial was stopped after recruiting 183 of the planned 200 patients due to demonstrated efficacy of prenatal versus postnatal repair. Despite having more severe lesions and an increased risk of preterm delivery, the study found that the prenatal surgery group had significantly better outcomes than the postnatal surgery group. Prenatal surgery for MMC decreased the risk of death or need for shunting by the age of 12 months. Prenatal surgery also improved scores on a composite measure of mental and motor function at 30 months. However, prenatal surgery was associated with an increased risk of preterm delivery and uterine dehiscence at delivery. The authors noted that the potential benefits of prenatal surgery must be balanced against the risks of prematurity and maternal morbidity (Adzick, 2011).

Danzer et al. (2009) evaluated lower extremity neuromotor function (LENF) and short-term ambulatory potential following fetal myelomeningocele (fMMC) closure in a retrospective chart review of 54 children. Neonatal LENF was compared to predicted function based on spinal lesion level assigned by prenatal ultrasound. A total of 31 out of 54 of fMMC children (57.4%) had better than predicted, 13/54 (24.1%) same as predicted and 10/54 (18.5%) worse than predicted LENF at birth. At a median follow-up age of 66 months, 37/54 (69%) walk independently, 13/54 (24%) are assisted walkers, and 4/54 (7%) are wheelchair dependent. Despite the observed improved ambulatory status, structured evaluation of coordinative skills revealed that the majority of independent walkers and all children that

require assistive devices to walk experience significant deficits in lower extremity coordination. The investigators concluded that fMMC surgery results in better than predicted LENF at birth and short-term ambulatory status. However, fMMC children continue to demonstrate deficits in movement coordination that are characteristic for children with spina bifida.

Danzer et al. (2008) evaluated the incidence and clinical implications of the development of cutaneously derived intradural inclusion cysts (ICs) following fMMC closure in retrospective databases and responses to a parental questionnaire. The investigators found that cutaneously derived intradural ICs can develop following fMMC surgery. Deterioration of bladder function, risk of recurrence, and loss of lower-extremity function appear to be the most important long-term complications of IC in children with fMMCs.

Koh et al. (2006) compared urodynamic findings in patients who underwent prenatal closure of MMC (n=5) with those of patients who underwent postnatal closure (n=88). All 5 prenatally treated patients had lower lumbosacral lesions on neurological examination. In comparison, 34 of the 88 patients in the postnatal cohort (39%) lacked sphincter activity at newborn examination, with similar findings noted at 1-year evaluation. In terms of bladder function, all 5 patients in the prenatal cohort showed detrusor overactivity, compared to 33 of the 88 patients (38%) in the postnatal cohort at the newborn examination, with similar findings at 1-year evaluation. The investigators concluded that fetal closure of MMC is associated with a higher incidence of complete denervation of the external urethral sphincter and detrusor overactivity compared to postnatal closure.

Professional Societies

American College of Obstetricians and Gynecologists (ACOG)

ACOG's Maternal-Fetal Management Task Force published a position statement (Cohen et al., 2014) regarding fMMC repair with the goal of developing "optimal practice criteria for medical and surgical leadership." Members of the task force reported the following:

- "fMMC repairs should be performed in established fetal therapy centers using a multidisciplinary team approach.
- The fetal surgery team must have experience working together and individual members have a level of expertise in their field.
- The level of fetal surgical technical expertise demanded requires an adequate annual volume of open fetal and EXIT procedures to maintain competency.
- The level of technical expertise in fMMC repair requires an initial experience of at least 5 cases and an ongoing adequate annual volume of cases evaluated for fetal surgery to maintain competency.
- Centers developing new programs must receive guidance and training from established programs and experienced individuals.
- The MOMS protocol should be followed for preoperative, intraoperative, and immediate postoperative care. This applies to inclusion and exclusion criteria for in utero MMC repair.
- Modification of the long-term postoperative and delivery care is acceptable in certain circumstances.
- Modifications to the perioperative protocol are only permissible after the results of fMMC repair performed by an expanded number of centers have been shown to be consistent with the results obtained in the MOMS trial. Such modifications would, ideally, be developed by means of a series of cooperative trials.
- Ongoing neonatal and pediatric care should be performed in multidisciplinary spina bifida clinics. This can be done at outside centers but must be standardized.
- Counseling should be full disclosure and nondirective in nature. It should also include reproductive implications for future pregnancies.
- A reflective period of at least 24 hours is recommended.
- Short-term and long-term outcomes data from all centers should be kept in a national registry with periodic review.
- Centers performing open MMC repair must maintain a collaborative approach to outcomes reporting and future research, including participating in the long-term outcomes data collection and evaluation. Close links between fetal centers throughout the country and community providers are essential."

An ACOG practice bulletin states that despite the maternal and obstetric risks, in utero repair is an option for women who meet appropriate criteria. Counseling should be nondirective and include all options, with full disclosure of all potential benefits and risks for the fetus and woman, including the implications for future pregnancies (2017).

An ACOG committee opinion states open maternal-fetal surgery for MMC repair is a major procedure for the woman and her affected fetus. Although there is demonstrated potential for fetal and pediatric benefit, there are significant maternal implications and complications that may occur acutely, postoperatively, for the duration of the pregnancy, and in subsequent pregnancies. It is a highly technical procedure with potential for significant morbidity and possibly mortality, even with the best and most experienced surgeons. Maternal-fetal surgery for MMC repair should only be offered to carefully selected patients at facilities with an appropriate level of personnel and resources (2017).

Congenital Diaphragmatic Hernia (CDH)

For the use of IUFS as a treatment for CDH, there is some low quality evidence that survival rates may be increased; however, findings were not consistent across studies. Several studies included randomization, however most had small sample sizes and limited follow-up periods. There were 7 studies representing 3 separate data sets; of these, two studies provided descriptive findings only and lacked statistical analyses. Only 1 study examined longer-term outcomes (1 and 2 years) and found no differences between treatment and control patients across a range of outcomes (pulmonary, neurodevelopmental, growth, and sensory) (Hayes, 2012b; updated August 29, 2016).

A systematic review and meta-analysis by Grivell et al. (2015) compared the effects of prenatal versus postnatal interventions for CDH on perinatal mortality and morbidity, longer-term infant outcomes and maternal morbidity. The review also looked to compare the effects of different prenatal interventions with each other. Three studies were included involving 97 women. Two trials examined in utero fetal tracheal occlusion with standard (postnatal) care in fetuses with severe diaphragmatic hernia. One trial examined the effect of antenatal corticosteroids versus placebo. The authors concluded that there is currently insufficient evidence to recommend in utero intervention for fetuses with CDH as a part of routine clinical practice. Only 1 of the studies adequately reported on perinatal mortality, but there were no data suitable for inclusion in the analysis. More studies are needed to further examine the effect of both in utero fetal tracheal occlusion and the use of antenatal corticosteroids on important neonatal outcomes and long-term infant survival and health.

Ruano et al. (2012) conducted a RCT to determine whether fetal endoscopic tracheal occlusion (FETO) improved survival in cases of CDH. Patients whose fetuses had severe isolated CDH (lung-to-head ratio < 1.0, liver herniation into the thoracic cavity and no other detectable anomalies) were randomly assigned to FETO (n=20) or to standard postnatal management (n=21). Tracheal balloon placement was achieved with ultrasound guidance and fetoscopy between 26 and 30 weeks of gestation. Postnatal therapy was the same for both treated fetuses and controls. The primary outcome was survival to 6 months of age. Delivery occurred at 35.6 ± 2.4 weeks in the FETO group and at 37.4 ± 1.9 weeks in the control group. In the intention-to-treat analysis, 10/20 (50.0%) infants in the FETO group survived, while 1/21 (4.8%) controls survived. In the received-treatment analysis, 10/19 (52.6%) infants in the FETO group and 1/19 (5.3%) controls survived. The authors concluded that FETO improved infant survival in isolated severe CDH; however, the risk of prematurity and preterm premature rupture of membranes was high.

Runao et al. (2011) treated 16 fetuses with severe CDH with FETO and compared their outcome to 18 similar cases treated with standard neonatal therapy. The primary outcome was neonatal survival (up to 28 days after birth). Survival in the FETO group was 53% compared to 6% in the standard therapy group. This study is limited by small sample size and lack of randomization.

A case series reported the results of 24 fetuses with severe CDH who underwent percutaneous FETO with a balloon. Premature prelabor rupture of the membrane occurred in 16.7% and 33.3% at 28 and 32 weeks respectively. Seven-day, 28-day, and survival at discharge were 75%, 58.3%, and 50%, respectively. The investigators concluded that FETO may improve survival in highly selected CDH cases (Deprest et al., 2006).

Hirose et al. (2004) conducted a retrospective review of 52 patients who underwent an ex utero intrapartum treatment (EXIT) procedure. Fifty-one of 52 patients were born alive. At the time of the study, 27 of 52 patients (52%) were alive. All deaths have been in patients with CDH. The investigators concluded that the EXIT procedures can be performed with minimal maternal morbidity and with good outcomes.

Kunisaki et al. (2007) evaluated whether the EXIT procedure with extracorporeal membrane oxygenation (EXIT to ECMO) is a reasonable approach for managing patients antenatally diagnosed with severe CDH. Fourteen patients underwent EXIT with a trial of ventilation. Fetuses with poor preductal oxygen saturations despite mechanical ventilation received ECMO before their delivery. Three neonates passed the ventilation trial and survived, but 2 of them required ECMO within 48 hours. The remaining 11 fetuses received ECMO before their delivery. Overall survival after EXIT-to-ECMO was 64%. At 1-year follow-up, all survivors had weaned off supplemental oxygen, but 57% required diuretics and/or bronchodilators. The investigators concluded that the EXIT-to-ECMO procedure is associated with favorable survival rates and acceptable pulmonary morbidity in fetuses expected to have a poor prognosis under conventional management.

Congenital Heart Disease (CHD)

Pedra et al. (2014) reported results of a small case series of fetal cardiac procedures for various cardiac conditions (21 fetuses; 22 procedures). The procedures included atrial septostomy, fetal aortic valvuloplasty (FAV), pulmonary valvuloplasty, or a combination of aortic septostomy and FAV. The fetal clinical conditions consisted of critical aortic stenosis (AS) (n=13), hypoplastic left heart syndrome (HLHS) and intact interatrial septum or small patent foramen ovale (n=4), pulmonary atresia with intact ventricular septum (n=1), and critical pulmonary stenosis (n=3). A total of 91% of procedures (20 of 22) were considered successful. Two procedures, FAV and pulmonary valvuloplasty, failed.

One fetus died and no maternal complications were reported. Long-term morbidity was frequent, and 12 fetal deaths eventually occurred.

A retrospective review was conducted of 100 patients who underwent FAV for severe mid-gestation AS with evolving HLHS from March 2000 to January 2013. The median gestational age at intervention was 23.8 weeks. Patients were categorized based on postnatal management as biventricular (BV) or HLHS. Eighty-eight fetuses were live-born, and 38 had a BV circulation (31 from birth, 7 converted after initial univentricular palliation). Left-sided structures, namely aortic and mitral valve sizes and LV volume, were significantly larger in the BV group at the time of birth. After a median follow-up of 5.4 years, freedom from cardiac death among all BV patients was $96 \pm 4\%$ at 5 years and $84 \pm 12\%$ at 10 years, which was better than HLHS patients. There was no cardiac mortality in patients with a BV circulation from birth. All but 1 of the BV patients required postnatal intervention; 42% underwent aortic and/or mitral valve replacement. On most recent echocardiogram, the median LV end-diastolic volume z-score was +1.7 (range: -1.3, +8.2), and 80% had normal ejection fraction. The authors concluded that short- and intermediate-term survival among patients who underwent FAV and achieved a BV circulation postnatally is encouraging. However, morbidity still exists, and on-going assessment is warranted (Freud et al., 2014).

A total of 70 fetuses underwent attempted FAV for critical AS with evolving HLHS. The procedure was technically successful (increased flow across the valve) in 52 fetuses (74%). Forty-five of these resulted in a viable live birth. Relative to 21 untreated comparison fetuses, subsequent prenatal growth of the aortic and mitral valves, but not the left ventricle, was improved after intervention. Nine pregnancies (13%) did not reach a viable term or preterm birth. Seventeen patients had BV circulation postnatally, 15 from birth. Larger left heart structures and higher left ventricular pressure at the time of intervention were associated with BV outcome. Technically successful FAV alters left heart valvar growth in fetuses with AS and evolving HLHS and, in a subset of cases, appeared to contribute to a BV outcome after birth. The authors note that FAV carries a risk of fetal demise. Further studies from well-designed clinical trials are needed to confirm these results (McElhinney et al., 2009).

Vida et al. (2007) retrospectively identified 32 neonates with a diagnosis of HLHS and intact or highly restrictive atrial septum (I/HRAS) who underwent left atrial decompression in utero or postnatally before surgery. Fourteen patients (44%) underwent fetal intervention, either atrial septoplasty (n=9) or FAV (n=5). The investigators concluded that prenatal decompression of the left atrium may be associated with greater hospital survival. Proposed effects of fetal intervention on lung pathology and longer-term survival require further study.

There are multiple ongoing clinical trials evaluating several types of IUFS. Additional information is available at www.clinicaltrials.gov.

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

The fetal interventions described in this policy are surgical procedures and are not subject to FDA approval.

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not have a National Coverage Determination (NCD) for intrauterine fetal surgery. Local Coverage Determinations (LCDs) do not exist at this time. (Accessed February 14, 2018)

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POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
12/01/2018	<ul style="list-style-type: none">Simplified coverage rationale (no change to guidelines)Archived previous policy version 2018T0035R