IN UTERO FETAL SURGERY

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Table of Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>BENEFIT CONSIDERATIONS</td>
<td>1</td>
</tr>
<tr>
<td>COVERAGE RATIONALE</td>
<td>2</td>
</tr>
<tr>
<td>APPLICABLE CODES</td>
<td>2</td>
</tr>
<tr>
<td>DESCRIPTION OF SERVICES</td>
<td>3</td>
</tr>
<tr>
<td>CLINICAL EVIDENCE</td>
<td>4</td>
</tr>
<tr>
<td>U.S. FOOD AND DRUG ADMINISTRATION</td>
<td>12</td>
</tr>
<tr>
<td>CENTERS FOR MEDICARE AND MEDICAID</td>
<td>12</td>
</tr>
<tr>
<td>REFERENCES</td>
<td>12</td>
</tr>
<tr>
<td>POLICY HISTORY/REVISION INFORMATION</td>
<td>15</td>
</tr>
</tbody>
</table>

INSTRUCTIONS FOR USE

This Medical Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the enrollee specific document must be referenced. The terms of an enrollee’s document (e.g., Certificate of Coverage (COC) or Summary Plan Description (SPD) and Medicaid State Contracts) may differ greatly from the standard benefit plans upon which this Medical Policy is based. In the event of a conflict, the enrollee’s specific benefit document supersedes this Medical Policy. All reviewers must first identify enrollee eligibility, any federal or state regulatory requirements and the enrollee specific plan benefit 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

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 (such as maternity benefits), 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 guideline, it is important to refer to the enrollee’s specific plan document to determine benefit coverage.

When deciding coverage for in utero fetal surgery, refer to the enrollee-specific benefit 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.

**COVERAGE RATIONALE**

Intrauterine fetal surgery is proven and medically necessary for the following diagnoses and procedures:

1. Congenital cystic adenomatoid malformation (CCAM) and extralobar pulmonary sequestration (EPS): fetal lobectomy or thoracoamniotic shunt placement for CCAM and thoracoamniotic shunt placement for EPS
2. Sacrococcygeal teratoma (SCT): SCT resection
3. Urinary tract obstruction (UTO): urinary decompression via vesicoamniotic shunt placement
5. Twin reversed arterial perfusion (TRAP): ablation or occlusion of anastomotic vessels (e.g., laser coagulation or radiofrequency ablation)
6. Myelomeningocele (MMC) repair

Intrauterine fetal surgery is unproven and not medically necessary for the following:

1. Congenital diaphragmatic hernia (CDH)
   There is insufficient evidence that in utero correction of CDH improves health outcomes for fetuses with CDH compared with standard postnatal surgery. Consistent improvements in survival following in utero fetal surgery have not been observed.
2. Congenital heart disease (CHD)
   There is insufficient evidence that in utero fetal surgery for complex heart disease improves health outcomes or survival.

**APPLICABLE CODES**

The Current Procedural Terminology (CPT®) codes and Healthcare Common Procedure Coding System (HCPCS) codes listed in this policy are for reference purposes only. Listing of a service code in this policy does not imply that the service described by this code is a covered or non-covered health service. Coverage is determined by the enrollee specific benefit 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 claims payment. Other policies and coverage determination guidelines may apply. This list of codes may not be all inclusive.

<table>
<thead>
<tr>
<th>Proven CPT® Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>59070</td>
<td>Transabdominal amnioinfusion, including ultrasound guidance</td>
</tr>
<tr>
<td>59072</td>
<td>Fetal umbilical cord occlusion, including ultrasound guidance</td>
</tr>
<tr>
<td>59074</td>
<td>Fetal fluid drainage (e.g., vesicocentesis, thoracocentesis, paracentesis), including ultrasound guidance</td>
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<tr>
<td>59076</td>
<td>Fetal shunt placement, including ultrasound guidance</td>
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<th>Unproven CPT® Code</th>
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<tr>
<td>59897</td>
<td>Unlisted fetal invasive procedure, including ultrasound guidance</td>
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*CPT® is a registered trademark of the American Medical Association.*
In utero fetal surgery is surgical treatment of a fetus with certain life-threatening conditions. During open fetal surgery, a hysterotomy is performed and the fetus is partially removed to correct the malformation. Fetoscopic surgery uses minimally invasive techniques and instruments to correct the malformation through small incisions. The primary conditions that have been researched are 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 and congenital heart disease.

**Thoracic Lesions**
Congenital cystic adenomatoid malformation (CCAM) and bronchopulmonary sequestration (BPS) are congenital anomalies of the lung that share the characteristic of a segment of lung being replaced by abnormally developing tissue. Only a small subset of patients with congenital pulmonary airway malformations are candidates for in utero treatment. In this subset, the mass is large enough and in such an anatomically critical position that the fetal mediastinum is compressed, leading to impaired venous return with resulting fetal hydrops secondary to cardiac failure (Walsh et al., 2011).

**Sacrococcygeal Teratoma**
Fetuses with large, vascular sacrococcygeal teratomas (SCT) have a high incidence of prenatal mortality from high-output cardiac failure or spontaneous hemorrhage into or rupture 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 maternal risk of developing mirror syndrome, a severe form of preeclampsia (Walsh et al., 2011).

**Urinary Tract Obstruction**
Fetal urinary tract obstruction (UTO) interferes with normal development of the kidneys and lungs, particularly when involving the lower urinary tract. Goals of fetal surgery have emphasized decompression rather than repair of the specific lesion. The goal of decompression of the distended portion of the urinary tract is to protect remaining renal function and to promote lung

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<tr>
<td>S2401</td>
<td>Repair, urinary tract obstruction in the fetus, procedure performed in utero</td>
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<tr>
<td>S2402</td>
<td>Repair, congenital cystic adenomatoid malformation in the fetus, procedure performed in utero</td>
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<tr>
<td>S2403</td>
<td>Repair, extralobar pulmonary sequestration in the fetus, procedure performed in utero</td>
</tr>
<tr>
<td>S2404</td>
<td>Repair, myelomeningocele in the fetus, procedure performed in utero</td>
</tr>
<tr>
<td>S2405</td>
<td>Repair of sacrococcygeal teratoma in the fetus, procedure performed in utero</td>
</tr>
<tr>
<td>S2411</td>
<td>Fetoscopic laser therapy for treatment of twin-to-twin transfusion syndrome</td>
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</tbody>
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<thead>
<tr>
<th>Unproven HCPCS Code</th>
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<tr>
<td>S2400</td>
<td>Repair, congenital diaphragmatic hernia in the fetus using temporary tracheal occlusion, procedure performed in utero</td>
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<tr>
<td>S2409</td>
<td>Repair, congenital malformation of fetus, procedure performed in utero, not otherwise classified</td>
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development. The trend in decompression is towards percutaneous shunting procedures (Walsh et al., 2011).

**Twin-twin Transfusion Syndrome**
In twin-twin transfusion syndrome (TTTS), twins share a single chorionic membrane and therefore a single placenta, but have separate amniotic sacs. Most pregnancies presenting with severe TTTS prior to 26 weeks and not undergoing some sort of therapy will end with dual fetal demise. When both twins do survive, there is often severe neurologic compromise in survivors as well as other organ failure, including cardiac impairment. 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 vessels shown to be communicating between the two fetuses (Walsh et al., 2011).

**Twin Reversed Arterial Perfusion**
Twin reversed arterial perfusion (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**
Myelomeningocele (MMC) or 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**
Congenital diaphragmatic hernia (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 lethal (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 of in utero fetal surgical procedures for the following conditions: congenital diaphragmatic hernia, cardiac malformations, myelomeningocele, obstructive uropathy, sacrococcygeal teratoma, twin-twin transfusion syndrome and thoracic lesions (Walsh et al., 2011).

**Congenital Cystic Adenomatoid Malformation (CCAM) and Extralobar Pulmonary Sequestration (EPS)**
A prospective study found that 29% of a population of 58 fetuses with CCAM were determined to be at risk for hydrops and to require fetal intervention. The overall survival rate was 71% after fetal surgery although the survival rate for hysterotomy and open fetal lobectomy was only 29%
compared with 100% for fetoscopic shunting or cyst aspiration. The perinatal mortality rate was 29% in the patients whose likelihood of survival was otherwise very poor (Crombleholme, 2002).

**Sacrococcygeal Teratoma (SCT)**
In a small retrospective series evaluating the efficacy of surgery via hysterotomy for 4 fetuses with SCT, 3 (75%) survived and were alive with no evidence of disease at 20 months to 6 years of age. The remaining infant died shortly after birth. Fetal surgery is not deemed appropriate in the presence of the maternal mirror syndrome or in cases of advanced high-output cardiac failure (Hedrick, 2004).

**Urinary Tract Obstruction (UTO)**
In utero fetal surgery for UTO improves perinatal survival in selected fetuses and children 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 poorer for fetuses with elevated urinary electrolytes or prolonged anhydramnios at the time of surgery. Despite initial surgical success and improved survival, a number of children (greater than 25%) have residual renal disease ultimately requiring transplantation, urinary tract surgery, or other medical interventions during mean follow-up times of 3 to 4 years. Most children demonstrate growth retardation. Many are able to void spontaneously. Pulmonary dysfunction remains problematic despite fetal surgery and resulted in death in from 18% to 25% of children who were followed for up to 114 months. The results of a meta-analysis evaluating the efficacy and safety of prenatal bladder drainage demonstrated significantly improved perinatal survival among 195 fetuses in controlled trials that received the intervention compared with those that did not. Significant improvement was observed in a subgroup identified as having a poor prognosis. Improved perinatal survival was also suggested for the subgroup of fetuses that had a good prognosis although the improvement was not statistically significant (Clark, 2003; Freedman, 1999; McLorie, 2001; Welsh, 2003).

Biard et al. (2005) reported on long-term outcomes in 20 male children treated by prenatal vesicoamniotic shunting for urinary tract obstruction. Overall 1-year survival was 91%; 2 deaths occurred from pulmonary hypoplasia. Eight of the survivors had acceptable renal function, 4 had mild insufficiency, and 6 required dialysis and renal transplant.

**Twin-Twin Transfusion Syndrome (TTTS)**
One hundred twenty infants with twin-to-twin transfusion syndrome (TTTS) were enrolled in a randomized clinical trial of laser photocoagulation versus amnioreduction. The children were followed up to 6 years of age to assess long-term neurological and developmental outcomes. The children were evaluated by standardized neurological examination and by Ages and Stages Questionnaires (ASQ). 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 (p = 0.12). Laser therapy was associated with a 40% reduction in the risk of fetal death or long-term neurologic impairment when compared to amnioreduction (Salomon, 2010).

Roberts et al. (2008) assessed which treatments for twin-twin transfusion syndrome (TTTS) improved fetal, childhood and maternal outcomes. The authors compared outcomes from three (253 women) randomized and quasi-randomized studies of amnioreduction, laser coagulation and septostomy. Laser coagulation resulted in less overall death and neonatal death 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 in the treatment of all stages of TTTS to improve perinatal and neonatal outcome. A 2014 update concluded that endoscopic laser coagulation of anastomotic vessels should continue to be considered in the treatment of all stages of twin-twin transfusion syndrome to improve neurodevelopmental outcomes. Further research targeted towards assessing the effect of treatment on milder (Quintero stage 1 and 2) and more severe (Quintero stage 4) forms of twin-twin transfusion syndrome is required. Studies should aim to assess long-term outcomes of survivors (Roberts, et al.).
There is some evidence that fetoscopic laser surgery to ablate placental vascular anastomoses is relatively efficacious for treating clinically and ultrasonographically confirmed, severe TTTS less than 26 weeks gestation in monozygotic, monochorionic twin pregnancies. The surgery improves fetal and neonatal survival rates and perinatal outcomes compared with conservative management and serial amnioreduction; however, serial amnioreduction or delivery is more appropriate for TTTS diagnosed at 26 weeks gestation or more. Serial amnioreduction, which reduces polyhydramnios and prevents premature rupture of the membranes (PROM) and preterm delivery (PTD), may be more appropriate for TTTS diagnosed at 26 weeks or more since it is less likely to result in intrauterine fetal death than laser surgery and therefore is more beneficial for pregnancies that are closer to viability and delivery (Berghella, 2001; van Gemert, 2001).

In a randomized trial, pregnant women with severe TTTS before 26 weeks of gestation were randomly assigned to laser therapy (n=72) or amnioreduction (n=70). The study was concluded early because an interim analysis demonstrated a significant 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), 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) (Senat, 2004).

A total of 167 children (median age 3 years and 2 months) were evaluated to investigate long-term neurodevelopment after intrauterine laser coagulation for TTTS. One-hundred forty-five 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 seems to be the best treatment option for severe TTTS (Graef, 2006).

There are significant risks associated with fetoscopic laser surgery, including fetal loss (De Lia, 1999).

Professional Societies

Society for Maternal-Fetal Medicine (SMFM)
A SMFM clinical guideline reviewed the natural history, pathophysiology, diagnosis and treatment options for twin-twin transfusion syndrome (TTTS). The guideline recommends that extensive counseling be provided to patients with pregnancies complicated by TTTS including natural history of the disease, as well as management options and their risks and benefits. More than three-fourths 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 may often be managed expectantly. Fetoscopic laser photocoagulation of placental anastomoses is considered by most experts to be the best available approach for stages II, III and IV TTTS in continuing pregnancies at <26 weeks, but the metaanalysis data show no significant survival benefit, and the long-term neurologic outcomes in the Eurofetus trial were not different than in nonlaser-treated controls. Even laser-treated TTTS is associated with a perinatal mortality rate of 30-50%, and a 5-20% chance of long-term neurologic handicap. Steroids for fetal maturation should be considered at 24 0/7 to 33 6/7 weeks, particularly in pregnancies complicated by stage ≥III TTTS, and those undergoing invasive interventions (SMFM, 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 to treat twin reversed arterial perfusion (TRAP). This was a retrospective review of all patients who underwent percutaneous radiofrequency ablation 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 37.0 weeks. Survival of the pump twin to 30 days was 80% in the...
Pagani et al. (2013) conducted a retrospective cohort study and meta-analysis of intrafetal laser treatment for twin reversed arterial perfusion (TRAP) sequence. Twenty-three cases of TRAP were identified during the study period. Six 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 twin reversed arterial perfusion sequence (TRAP) using radiofrequency ablation (RFA). Between July 2007 and October 2010, 11 monochorionic twin pregnancies complicated by TRAP were identified. Seven patients underwent intrafetal ablation of the acardiac twin with RFA. Median gestational age at the intervention was 17 weeks. Five fetuses were delivered at a median gestational age of 33 weeks. All five infants (71%) 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.

The results of some studies demonstrate improved outcomes for umbilical cord laser photocoagulation. A prospective multicenter study evaluated the outcome of laser coagulation of placental anastomoses (n=18) or the umbilical cord of the acardiac twin (n=42). The overall survival rate of the pump twin was 80% (Hecher, 2006).

Another approach is to use radiofrequency ablation to obliterate blood supply to an acardiac twin. Tsao et al. (2002) evaluated 13 monochorionic twin gestations with twin reversed arterial perfusion sequence who underwent selective reduction of the abnormal twin with the use of radiofrequency ablation. All 13 pump fetuses were delivered. At the time of the study, 12 of 13 infants were alive and well. The first patient in this series was delivered at 24.4 weeks and the infant subsequently died from complications of prematurity. Average gestational age at intervention was 20.7 weeks, and the average gestational age at delivery was 36.2 weeks. The investigators concluded that radiofrequency ablation is a minimally invasive, percutaneous technique that can effectively obliterate blood supply to an acardiac twin to preserve and protect the pump twin.

Tan et al. (2003) identified 32 reports involving 74 cases of acardiac twin treated by minimally invasive techniques. Seventy-one cases were included for analysis including 40 treated by cord occlusion and 31 by intrafetal ablation. Cord occlusion was first attempted by embolization (n = 5), cord ligation (n = 15), laser coagulation (n = 10), bipolar diathermy (n = 7) and monopolar diathermy (n = 3). Intrafetal ablation was performed by alcohol (n = 5), monopolar diathermy (n = 9), interstitial laser (n = 4) and radiofrequency (n = 13). The overall pump twin survival rate was 76% (n = 54). Intrafetal ablation was associated with later median gestational age at delivery (37 vs. 32 weeks) and higher median treatment-delivery interval (16 vs. 9.5 weeks) compared with cord occlusion techniques. It was also associated with a lower technical failure rate (13% vs. 35%), lower rate of premature delivery or rupture of membranes before 32 weeks (23% vs. 58%) and higher rate of clinical success (77% vs. 50%) than cord occlusion techniques. This review suggests that intrafetal ablation is the treatment of choice for acardiac twins because it is simpler, safer and more effective when compared with the cord occlusion techniques.

Lee et al. (2007) evaluated the treatment of 29 patients with twin reversed arterial perfusion (TRAP) sequence using radiofrequency ablation to stop perfusion to the acardiac twin and protect the pump twin. The investigators concluded that radiofrequency ablation of the acardiac twin effectively protects the pump twin from high-output cardiac failure and death. Greater than 90%
In utero fetal surgery: medical policy (Effective 05/01/2014)

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 in utero fetal surgery (IUFS) for myelomeningocele (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 randomized controlled trial and ten nonrandomized controlled studies compared in utero fetal surgery (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 2013).

The Management of Myelomeningocele Study (MOMS) compared outcomes of prenatal versus postnatal repair of myelomeningocele. 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 myelomeningocele 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 fetal myelomeningocele (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 myelomeningocele with those of patients who underwent postnatal closure. Urodynamic studies of 5 patients who underwent prenatal closure of myelomeningocele were compared to those of 88 patients with similar level lesions who underwent postnatal repair. 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 myelomeningocele is associated with a higher incidence of complete denervation of the external urethral sphincter and detrusor overactivity compared to postnatal closure.

In a comparative study, pre- and postnatal head biometry and cerebrospinal fluid (CSF) space data were obtained from in utero repaired MMC fetuses (n=22) and were compared to measurement of MMC patients that underwent standard MMC repair after birth (n=16) and a cohort of age-matched control patients. No differences in postnatal CSF spaces were found between controls and prenatally repaired MMC patients. In patients with postnatal repair, CSF spaces remained significantly reduced. In utero repair fetuses showed a significant reversal of hindbrain herniation and normalization of the CSF spaces compared to postnatally repaired patients (Danzer 2007). Another study followed 51 patients who underwent MMC closure. Forty-eight patients survived and passed their second birthday. Neuro-developmental testing indicated that 67% of the patients had cognitive language and social skills in the normal range, 20% with mild delays, and 13% with significant delays. The investigators concluded that children who have undergone fetal MMC surgery have characteristic neuro-developmental deficits that may not be worsened by fetal surgery (Johnson, 2006).

Adelberg et al. (2005) examined the impact of intrauterine repair on the progression of ventriculomegaly in utero. A retrospective cohort design was used to evaluate the impact of intrauterine repair on ventricular progression. Fourteen fetuses with intrauterine repair and 39 fetuses with postnatal repair were identified. The natural history of progression of ventricular diameter increased in a linear fashion throughout gestation (0.57 mm/week). After adjusting for confounding variables, no transient or sustained difference was observed in the rate progression of ventriculomegaly between intrauterine and postnatal repair. The investigators concluded that intrauterine MMC repair does not impact the progression of ventriculomegaly.

Professional Societies

American College of Obstetricians and Gynecologists (ACOG)

An ACOG practice bulletin addresses the role of fetal surgery in treating neural tube defects but makes no specific recommendations (ACOG, 2003; reaffirmed 2013).

An ACOG committee opinion states that maternal-fetal surgery is a major procedure for the woman and her fetus, and it has significant implications and complications that occur acutely, postoperatively, for the duration of the pregnancy and in subsequent pregnancies. Therefore, it should only be offered at facilities with the expertise, multidisciplinary teams, services and facilities to provide the intensive care required for these patients (ACOG, 2013).

Congenital Diaphragmatic Hernia (CDH)

A Hayes report concluded that there is some evidence that survival rates may be increased by in utero fetal surgery (IUFS) as a treatment for congenital diaphragmatic hernia; however, findings were not consistent across studies. The quality of the evidence was low. Several studies included randomization; however, there were only seven studies representing three separate data sets. Most studies had small sample sizes and limited follow-up. In addition, outcome measures varied across studies, and two of the studies provided descriptive findings only and did not include statistical analyses (Hayes, 2012b; updated 2013).

Ruano et al. (2012) conducted a randomized controlled trial to determine whether fetal endoscopic tracheal occlusion (FETO) improved survival in cases of congenital diaphragmatic hernia (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 congenital diaphragmatic hernia (CDH) with fetal endoscopic tracheal occlusion (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.

Two uncontrolled studies showed that in carefully selected fetuses, in utero tracheal occlusion can promote lung growth and improve the likelihood of neonatal survival compared with standard postnatal surgery (Flake 2000; Harrison 2003a). However, questions about treatment efficacy have been raised by a recent RCT that found no significant improvement in survival rates or health outcomes among fetuses treated with in utero tracheal occlusion compared with standard postnatal surgery (Harrison, 2003b).

Fetendo appears to promote fetal lung growth as shown by fetal and postnatal US. Despite observations of enhanced lung growth, in utero tracheal occlusion has limitations, including the occurrence of pulmonary complications, the need for postnatal interventions, prematurity, and a lack of correlation of lung maturation with improved postnatal outcomes, including survival. Preterm labor was common and virtually all infants were born prematurely (i.e., at less than 37 weeks). In utero tracheal occlusion was associated with numerous complications. Postnatal complications included the need for extracorporeal membrane oxygenation (ECMO) (a form of long-term heart-lung bypass) and mechanical ventilation as well as barotrauma, chylothorax, and renal failure. Tracheal injury is common and some patients require permanent tracheostomies. Survivors displayed significant morbidity including gastroesophageal reflux (some required surgery), respiratory problems, problems with the operative site, and neurological disabilities. However, one study found no significant neurologic abnormalities among the survivors (Harrison 2003b). Perinatal mortality rates ranged from 36% to 67%. Causes of death included prematurity (at less than 37 weeks), lung immaturity at birth, multiorgan failure, and sepsis. Mortality is higher when the procedure is performed via maternal hysterotomy than by fetoscopy. No maternal deaths were reported; however, maternal complications included preterm labor, pulmonary edema, vaginal bleeding, premature rupture of the membrane (PROM), and chorioamniotic membrane separation (Flake, 2000; Harrison, 2003a; Harrison, 2003b; Sydorak, 2003)).

A case series reported the results of 24 fetuses with severe CDH who underwent percutaneous fetal endoluminal tracheal occlusion (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, 2006).

Hirose et al. (2004) conducted a retrospective review of 52 patients who underwent an 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 congenital diaphragmatic hernia. The investigators concluded that the EXIT procedures can be performed with minimal maternal morbidity and with good outcomes.

Saura et al. (2007) reported their experience in the postnatal management of congenital diaphragmatic hernia (CDH) in 19 fetuses after fetal endoluminal balloon tracheal occlusion (FETO). The investigators found that CDH patients with a poor prognosis undergoing FETO had
postnatal outcomes similar to non-prenatally studied cases and good prognosis cases.

Kunisaki et al. (2007) evaluated whether ex utero intrapartum treatment with extracorporeal membrane oxygenation (EXIT to ECMO) is a reasonable approach for managing patients antenatally diagnosed with severe congenital diaphragmatic hernia. Fourteen patients underwent EXIT with a trial of ventilation. Fetuses with poor preductal oxygen saturations despite mechanical ventilation received ECMO before their delivery. Three babies 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.

There are several ongoing trials exploring tracheal occlusion for fetal surgery, including the Tracheal Occlusion to Accelerate Lung Growth (TOTAL) Trial for Severe Pulmonary Hypoplasia (NCT01240057). The TOTAL trial is designed to investigate whether prenatal intervention improves survival rate of fetuses with isolated congenital diaphragmatic hernia and severe pulmonary hypoplasia, as compared to expectant management during pregnancy. Accessed February 11, 2014.

**Congenital Heart Disease (CHD)**

Seventy fetuses underwent attempted aortic valvuloplasty for critical aortic stenosis with evolving hypoplastic left heart syndrome. 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 biventricular circulation postnatally, 15 from birth. Larger left heart structures and higher left ventricular pressure at the time of intervention were associated with biventricular outcome. Technically successful aortic valvuloplasty alters left heart valvar growth in fetuses with aortic stenosis and evolving hypoplastic left heart syndrome and, in a subset of cases, appeared to contribute to a biventricular outcome after birth. The authors note that fetal aortic valvuloplasty carries a risk of fetal demise. Further studies from well-designed clinical trials are needed to confirm these results (McElhinney, 2009).

One international retrospective study evaluated the efficacy and safety of percutaneous US-guided balloon valvuloplasty for treatment of severe aortic valve obstruction in 12 fetuses. Technically successful valvuloplasties were achieved in 7 (58%) fetuses, none of which had atresias. There was 1 (8%) long-term survivor following fetal surgery who remained alive with near-normal recovery of cardiac contractility and ejection fraction at 4 years of age. A second survivor failed fetal valvuloplasty but survived postnatal surgery. Twenty-five percent of the mothers required emergency cesarean section deliveries for sustained fetal bradycardia or chorioamnionitis (Kohl 2000). Tulzer and colleagues (2002) described 2 cases of fetal pulmonary valvuloplasty for critical pulmonary stenosis or atresia with intact septum associated with imminent hydrops. Both children survived to delivery and had repeat valvuloplasty after birth. At last follow-up, one child was alive at 12 months of age and another at 18 months of age. In utero balloon dilation of severe aortic stenosis was attempted in 20 fetuses with technical success in 14 of the fetuses. Of the 14 fetuses with technically successful interventions, 3 had two-ventricle circulation at 1 month of age and 2 infants underwent surgical repair and maintained two-ventricle circulation. Of the remaining 9 fetuses, two died after the technically successful intervention and the remaining 7 fetuses developed hypoplastic left heart syndrome (Tworetzky, 2004).

Selamet et al. (2007) evaluated the effects of mid-gestation fetal balloon aortic valvuloplasty in 30 fetuses with aortic stenosis. In 26 fetuses, aortic valvuloplasty was technically successful and improved left ventricular systolic function and left heart Doppler characteristics.
Vida et al. (2007) retrospectively identified 32 neonates with a diagnosis of hypoplastic left heart syndrome (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 aortic valvuloplasty (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.

Marshall et al. (2008) reviewed the medical records and imaging of 21 fetuses undergoing intervention for atrial septal defect creation for hypoplastic left heart syndrome and intact atrial septum. Of the 21 procedures attempted between 24 and 34 weeks' gestation, 19 were technically successful. Fetal demise occurred in two cases.

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 January 31, 2014)

REFERENCES


Crombleholme T, Coleman B, Hedrick H, et al. Cystic adenomatoid malformation volume ratio


POLICY HISTORY/REVISION INFORMATION

<table>
<thead>
<tr>
<th>Date</th>
<th>Action/Description</th>
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| 05/01/2014 | • Reorganized policy content  
|            | • Updated benefit considerations; added language for Essential Health Benefits for Individual and Small Group plans to indicate:  
<p>|            | o 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 |</p>
<table>
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<th>of Essential Health Benefits (“EHBs”)</th>
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<td>o 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 (such as maternity benefits), the ACA requires all dollar limits on those benefits to be removed on all Grandfathered and Non-Grandfathered plans</td>
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<tr>
<td>o The determination of which benefits constitute EHBs is made on a state by state basis; as such, when using this guideline, it is important to refer to the enrollee’s specific plan document to determine benefit coverage</td>
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<td>• Updated coverage rationale; added language to indicate if service is “medically necessary” or “not medically necessary” to applicable proven/unproven statement</td>
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<td>• Updated supporting information to reflect the most current description of services, clinical evidence, CMS information, and references</td>
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<td>• Archived previous policy version 2013T0035L</td>
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