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Medical Policy Manual

Topic: Fetal Surgery for Prenatally Diagnosed Malformations

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IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Fetal surgery is being investigated for specific congenital abnormalities that are associated with a poor postnatal prognosis. Prenatal surgery typically involves opening the gravid uterus (with a Cesarean surgical incision), surgically correcting the abnormality, and returning the fetus to the uterus and restoring uterine closure. Minimally invasive procedures through single or multiple fetoscopic port incisions are also being developed.

Most fetal anatomic malformations are best managed after birth. However, advances in methods of prenatal diagnosis, particularly prenatal ultrasound, have led to a new understanding of the natural history and physiologic outcomes of certain congenital anomalies. Fetal surgery is the logical extension of these diagnostic advances, related in part to technical advancement in anesthesia, tocolysis, and hysterotomy.

Fetal surgery is being investigated in fetuses at 32 weeks' gestation or less for specific congenital abnormalities that are associated with a poor post-natal prognosis. It is a specialized technique that requires a multidisciplinary approach, involving pediatric surgeons, perinatal obstetricians, sonographers, echocardiographers, neonatologists, intensive care specialists, geneticists, ethicists, and neonatal and obstetric nurses. Fetal surgery typically involves opening the gravid uterus (with either a

traditional Cesarean surgical incision or through single or multiple fetoscopic port incisions), surgically correcting a fetal abnormality, returning the fetus to the uterus, and restoring uterine closure. After 32 weeks' gestation, fetal lung maturity is adequate to permit Cesarean section and management of the condition postnatally.

This policy pertains to the following clinical conditions:

- Urinary tract obstruction

  Though few cases of prenatally diagnosed urinary tract obstruction require prenatal intervention, bilateral obstruction is often associated with serious disease such as pulmonary hypoplasia secondary to oligohydramnios. Therefore, fetuses with bilateral obstruction, oligohydramnios, adequate renal function reserve, and no other lethal or chromosomal abnormalities may be candidates for fetal surgery. The most common surgical approach is vesicoamniotic shunting by means of shunt or stent placement. The shunting procedure bypasses the obstructed urinary tract, permitting fetal urine to flow into the amniotic space. The goals of shunting are to protect the kidneys from increased pressure in the collecting system and to assure adequate amniotic fluid volume for lung development.

- Congenital diaphragmatic hernia (CDH)

  CDH is a defect of the diaphragm that permits abdominal viscera to enter the chest, frequently resulting in hypoplasia of the lungs. CDH can vary widely in severity, depending on the size of the hernia and the timing of herniation. For example, late herniation after 25 weeks of gestation may be adequately managed postnatally. In contrast, liver herniation into the chest prior to 25 weeks of gestation is associated with a poor prognosis; these fetuses have been considered candidates for fetal surgery. Temporary tracheal balloon occlusion prevents the normal efflux of fetal lung fluid, which in turn enhances positive pressure in the growing lungs, promoting lung growth and ultimately reducing abdominal viscera back into the abdominal cavity.

- Congenital cystic adenomatoid malformation (CCAM) or bronchopulmonary sequestration (BPS)

  CCAM and BPS are the two most common congenital cystic lung lesions and are characterized by a segment of lung being replaced by abnormally developing tissue. CCAMs can have connections to the pulmonary tree and contain air, while BPS does not connect to the airway and has blood flow from the aorta rather than the pulmonary circulation. In more severe cases, the malformations can compress adjacent normal lung tissue and distort thoracic structure. CCAM lesions typically increase in size in mid-trimester and then in the third trimester either involute or compress the fetal thorax, resulting in hydrops in the infant and sometimes mirror syndrome (a severe form of pre-eclampsia) in the mother. When associated with fetal hydrops (abnormal accumulation of fluid in two or more fetal compartments) before 32 weeks gestation, mortality is close to 100%. These patients may be candidates for prenatal surgical resection of a large mass or placement of a thoraco-amniotic shunt for a large unilocular cystic lesion.

- Sacrococcygeal teratoma

  Sacrococcygeal teratoma (SCT) is both a neoplasm with the power of autonomous growth and a malformation made up of multiple tissues foreign to the region of origin and lacking organ specificity. It is the most common tumor of the newborn. Postnatal SCT carries a good prognosis

with morbidity and mortality determined largely by extent of local disease and malignant potential. However, in utero fetal mortality has approached 100% when SCT is associated with fetal hydrops, which is related to high output heart failure secondary to arteriovenous shunting through the tumor.

- Myelomeningocele

  Myelomeningocele is a neural tube defect in which the spinal cord forms abnormally and is left open, exposing the meninges and neural tube to the intrauterine environment. Myelomeningocele is the most common cause of spina bifida, and depending on the location results in varying degrees of neurologic impairment affecting the legs and bowel and bladder function, brain malformation, i.e., hindbrain herniation, cognitive impairment, and disorders of cerebrospinal fluid circulation, i.e., hydrocephalus requiring placement of a ventriculoperitoneal shunt. Traditional treatment consists of surgical repair after term delivery, primarily to prevent infection and further neurologic dysfunction. Fetal surgical repair to cover the exposed spinal canal has been proposed as a means of preventing the deleterious exposure to the intrauterine environment with the hope of improving neurologic function and decreasing the incidence of other problems related to the condition.

- Cardiac malformations

  In utero interventions are being investigated for severe narrowing in one of the cardiac outflow tracts (aortic valve or pulmonary valve) that cause progressive damage to the heart in utero. In utero intervention has been proposed for the following lethal cardiac conditions: critical pulmonary stenosis, critical aortic stenosis, and hypoplastic left heart syndrome (HLHS). Critical pulmonary stenosis or atresia with intact ventricular septum is characterized by a very narrow pulmonary valve without a connection between the right and left ventricles. Critical aortic stenosis with impending HLHS is a very narrow aortic valve that develops early during gestation that may result in HLHS. In utero aortic balloon valvuloplasty has been suggested as a way to relieve aortic stenosis in an attempt to preserve left ventricular growth and halt the progression to HLHS. HLHS with intact atrial septum describes the absence of a connection between the left and right atrium. A subset of fetuses with HLHS will present with severe cyanosis and require immediate postnatal intervention in order to survive. In utero septostomy has been performed in an attempt to improve postnatal survival for this condition.

MEDICAL POLICY CRITERIA

Note: This policy does not address amnioreduction and fetoscopic laser surgery as treatment of twin-twin transfusion which is considered **medically necessary**.

I. Fetal surgery may be considered **medically necessary** for the following conditions:

   A. Vesico-amniotic shunting as a treatment of urinary tract obstruction when all of the following criteria are met:

      1. Evidence of hydronephrosis due to bilateral urinary tract obstruction, and

      2. Progressive oligohydramnios, and

      3. Adequate renal function, and

4. No other lethal abnormalities or chromosomal defects

B. Open in utero resection of malformed pulmonary tissue or placement of a thoraco-amniotic shunt as a treatment of either congenital cystic adenomatoid malformation (CCAM) or bronchopulmonary sequestration, when all of the following criteria are met:

1. Fetus is 32 weeks' gestation or less, and

2. There is evidence of fetal hydrops, placentomegaly, and/or the beginnings of severe pre-eclampsia (i.e., the maternal mirror syndrome.)

C. In utero removal of sacrococcygeal teratoma when all of the following criteria are met:

1. Fetus is 32 weeks' gestation or less, and

2. There is evidence of fetal hydrops, placentomegaly, and/or the beginnings of severe pre-eclampsia (i.e., the maternal mirror syndrome.)

D. In utero repair of myelomeningocele when all of the following criteria are met:

1. The fetus is at less than 26 weeks' gestation; AND

2. Myelomeningocele is present with an upper boundary located between T1 and S1 with evidence of hindbrain herniation.

3. Absence of all of the following:

a. Fetal anomaly unrelated to myelomeningocele

b. Severe kyphosis

c. Risk of preterm birth (e.g., short cervix or previous preterm birth)

d. Maternal body mass index of 35 or more

II. Other applications of fetal surgery are considered **investigational**, including but not limited to the following:

A. Temporary tracheal occlusion as a treatment of congenital diaphragmatic hernia

B. Aqueductal stenosis

C. Heart block

D. Pulmonary valve or aortic obstruction

E. Tracheal atresia or stenosis

F. Cleft lip and palate

G. Cardiac malformations

SCIENTIFIC EVIDENCE[1]

Literature Appraisal

Fetal Urinary Tract Obstruction

Technology Assessment

In 2011 the U.S. Agency for Healthcare Research and Quality (AHRQ) published a technology assessment for maternal-fetal surgical procedures.[2] The assessment identified 26 publications representing 25 unduplicated reports on fetal interventions for obstructive uropathy.[3] From the three prospective cohorts and eight retrospective cohorts identified, 24 fetuses had placements of shunts, 11 had other treatments for posterior urethral valves, 14 had no fetal intervention, and 13 pregnancies were terminated due to poor prognosis. Overall, 53% to 66% of infants who had shunt placement survived short-term. However, more than half of otherwise normal infants who have only isolated bladder outlet tract obstruction and do not have multiple anomalies or syndromes, do not recover normal renal function in childhood and the majority require dialysis and renal transplantation. In addition, a proportion of affected infants have clusters of syndromic features that are not readily diagnosed prenatally, increasing morbidity among survivors. For example, in a follow-up of 18 male children who had survived prenatal vesicoamniotic shunting (follow-up ranged from 1 – 14 years), parents and physicians reported the children to be neurodevelopmentally normal, with the majority having acceptable renal and bladder function and satisfactory self-reported quality of life.[4] One third of the children required dialysis or transplantation, and half exhibited respiratory, growth and development, or musculoskeletal abnormalities. There is a need to better identify appropriate surgical candidates and clarify health outcomes in children who do and do not receive fetal intervention in order to inform decision making. One publication describes the design of a multicenter randomized trial of percutaneous shunting for lower urinary tract obstruction (PLUTO) that will assess whether intrauterine vesicoamniotic shunting improves pre- and perinatal health outcomes in comparison with conservative, noninterventional care.[5]

Congenital Diaphragmatic Hernia (CDH)

Technology Assessment

The 2011 AHRQ technology assessment identified 25 publications with 21 unduplicated populations from ten U.S. sites, nine European, three multinational sites, and five other countries, with a total of 335 cases. The single randomized controlled trial was by Harrison and colleagues, with follow-up reported by Cortes and colleagues in 2005.[6] Growth failure occurred in 56% of controls and 86% of infants who had occlusion. No neurodevelopmental differences were observed between groups with follow-up at 1 or 2 years of age. This randomized study reinforces the importance of a concomitant control group, as the survival for CDH with post-natal repair also improved over time. Also noted were results of the Fetal Endoscopic Tracheal Occlusion (FETO) Task Group in Europe, which is using a control group of 86 fetuses with left-sided CDH and liver herniation, managed expectantly and live born after 30 weeks of gestation. In this control group, the survival rate increased from 0% for lung to head ratio (LHR) of 0.4 to 0.7 to about 15% for LHR of 0.8 to 0.9, 65% for LHR of 1.0 to 1.5, and 83% survival for LHR of 1.6 or more. This ongoing series currently has an 11% survival for LHR <1, which can be used as a reference value for Europe, but not for the United States. The AHRQ report concluded that studies of FETO reflects “movement toward improved outcomes for infants with CDH”, but notes that long-term outcomes “are not well reported and significant questions about fetal treatment for CDH remain.”

Randomized Controlled Trials

One well-designed RCT was published after the AHRQ technology assessment. Ruano et al.. randomly assigned 41 patients to either a treatment group (n=20) that underwent FETO or a control group (n=21) that received standard care.[7] Nineteen patients in each group completed the study. Inclusion criteria included women with singleton pregnancy between 22 and 26 wks gestation and no detectable fetal anomalies other than CDH, normal karyotype, fetal LHR < 1.0, and at least 1/3 of the fetal liver herniated into the thoracic cavity. FETO was performed between 26 and 30 weeks' gestation. Primary outcome was survival at 6 months. An intention-to-treat analysis showed survival at 6 months of age in 10 (50%) of the FETO group and 1 (4.8%) of the control group ($p<0.01$). The rate of severe pulmonary arterial hypertension (PAH) was significantly lower in the FETO group (50% vs. 85.7%, $p=0.02$). The rate of premature rupture of membranes, prematurity (deliver at <37 weeks), and extreme prematurity (delivery at <32 weeks) were not significantly different between the two groups.

Nonrandomized Trials

A number of papers from non-US centers examined tracheal changes including tracheomegaly and intermittent collapse of the posterior wall of the trachea observed after fetal balloon tracheal occlusion in severe CDH. For example, Fayoux and colleagues reported that tracheal widening and elongation and relaxation of the posterior tracheal wall intermittently obstructing the lumen during tidal breathing were seen in seven consecutive infants who underwent fetoscopic balloon tracheal occlusion.[8] In the five survivors, the changes were not symptomatic except for a barking cough during increased respiratory efforts. No new studies compared outcomes of fetal balloon tracheal occlusion with current management of diaphragmatic hernia.

In a nonrandomized comparative study, Ruano et al.[9] reported significantly higher fetal survival rates in a FETO group (n=35) than in a CDH group that did not undergo fetal surgery (54.3% vs. 5.4%, $p<0.01$). It is unknown whether some subjects in this study were also included in the Ruano et al. RCT summarized above. The FETO group also had significantly greater improvement in fetal lung size and pulmonary vascularity ($p<0.01$). The authors concluded that FETO improves survival rates by increasing lung size and pulmonary vascularity in CDH fetuses.

<u>Congenital Cystic Adenomatoid Malformation (CCAM) or Bronchopulmonary Sequestration (BPS)</u>

Technology Assessment

The 2011 AHRQ assessment identified 17 publications describing six distinct cohorts and four distinct case series from seven academic centers in the U.S., South America, Europe, and Asia.[3] Out of approximately 401 infants believed to have CCAMs, 54 had thoracoamniotic shunting and three had open procedures, with the goal of decompressing the lung lesion. An additional 13 fetuses with BPS were described. In the cohorts, 44% to 100% of infants who had thoracoamniotic shunts survived to birth or through neonatal hospitalization; there was an overall survival rate of 54% in the literature. For fetuses with hydrops, survival was a 20% to 30% following surgical treatment compared with 5.7% for untreated hydrops. Since some infants with large CCAMs respond to in utero medical treatment with steroids, failure to respond to steroids may be an entry criterion for future surgical interventions. The report concluded that current evidence on the outcomes of fetal surgery for these conditions is insufficient due to small sample sizes and between study heterogeneity which limits comparison.

<u>Sacrococcygeal Teratoma (SCT)</u>

Technology Assessment

The 2011 AHRQ assessment identified a total of seven retrospective cohorts and case series from three academic fetal surgery groups in the U.S. and United Kingdom.[3] The 17 fetuses reported to be treated with open surgery were compared with 94 cases with other interventions or no intervention; however, the expectant management cases were less severe. Other ablation methods included alcohol sclerosis (all three cases died), radiofrequency ablation (four of seven survived) and laser ablation (all four died). For open surgical procedures the survival rates were 33% to 75%. All fetal and neonatal deaths occurred among patients with hydrops or with prodromal cardiovascular changes concerning for developing hydrops. Challenges in this area are the early and reliable detection of development of hydrops and the timing of the fetal intervention.

Non-randomized trials

Paradies and others reviewed the most significant results from clinical, laboratory, radiological diagnostic results, pathologic findings, surgical procedures, and follow-up in 5 children (2 males and 3 females) suffering from sacrococcygeal teratomas.[10] Authors concluded that in order to improve the prognosis for patients, long-term clinical, laboratory and imaging surveillance is essential at shorter intervals during the first 5 years after the exeresis and annually thereafter. Further, in newborns or infants suffering from congenital malformations associated with teratomas, definitive surgical correction must be postponed to a proper time, especially in patients with multiple malformations or needing adjuvant chemotherapy, unless a complication arises or the repair cannot be delayed.

Myelomeningocele

The endoscopic approach has been abandoned due to high mortality, however, more than 200 fetuses with myelomeningocele have undergone open surgical repair in the U.S.[3]

Technology Assessment

The 2011 AHRQ technology assessment included the 2011 report of the results of the randomized National Institutes of Health (NIH)-sponsored trial, the Management of Myelomeningocele Study (MOMS), which compared prenatal repair with standard postnatal repair.[11] The trial began in 2003, and expected to enroll 200 women ages 18 years or older who are pregnant with fetuses with myelomeningocele. Women assigned to have prenatal surgery were scheduled for surgery within 1 to 3 days after they were randomized and stayed near the MOMS center until they delivered by C-section. Women in the postnatal group traveled back to their assigned MOMS center to deliver, also by C-section around the 37th week of their pregnancies. Follow-up on the children was performed at 1 year and 2 ½ years of age to evaluate motor function, developmental progress, and bladder, kidney, and brain development. At that time, there was a voluntary moratorium in the U.S. on conducting in utero repair of myelomeningocele outside of this trial.

The inclusion criteria included singleton pregnancy, myelomeningocele with the upper boundary located between T1 and S1, evidence of hindbrain herniation, gestational age of 19.0 to 25.9 weeks at randomization, normal karyotype, U.S. residency, and maternal age at least 18 years. Major exclusion criteria were fetal anomaly unrelated to myelomeningocele, severe kyphosis, risk of preterm birth, placental abruption, body-mass index of 35 or more, and contraindication to surgery, including previous hysterotomy in the active uterine segment. Surgeons had performed at least 15 cases before this

randomized study. Primary outcomes were a composite of fetal or neonatal death or the need for a cerebrospinal fluid shunt (shunt placement or meeting criteria for shunt) at 12 months and a composite score of the Mental Development Index of the Bayley Scales of Infant Development II and the child's motor function at 30 months adjusted by level of lesion. Secondary outcomes were surgical and pregnancy complications and neonatal morbidity and mortality. Women were randomized to treatment groups in a 1:1 ratio.

Recruitment for the trial, planned to include 200 subjects, was stopped at 183 subjects when a clear advantage of prenatal intervention was apparent. The report included 158 woman randomized before July 1, 2009. Outcomes up to 30 months are based on 138 women randomized before December 1, 2007. Groups were similar other than that there were more female fetuses and the lesion level was more severe in the prenatal surgery group. Two perinatal deaths occurred in each treatment group. Both deaths in the prenatal surgery group occurred on the 5th postoperative day, a still birth at 26 weeks and a neonatal death due to prematurity at 23 weeks gestation. Two neonates in the postnatal surgery group died with severe symptoms of the Chiari II malformation. Fetal or neonatal death or the need for shunt occurred in 68% of infants in the prenatal-surgery group and in 98% in the postnatal-surgery group (relative risk [RR], 0.70; 97.7% confidence interval [CI], 0.58 to 0.84; P<0.001). Shunts were placed in 40% of the prenatal-surgery and in 82% of postnatal-surgery groups (P<0.001). At 12 months, 4% of infants in the prenatal-surgery group had no evidence of hindbrain herniation versus 36% in the postnatal-surgery group. There was one death in each group between 12 and 30 months (coxsackie septicemia in a child who received prenatal surgery and complications of chemotherapy for choroid plexus carcinoma in a child who received postnatal surgery). The composite of score of Bayley Scales and motor function adjusted by lesion level at 30 months was significantly better in the prenatal surgery group: mean 148.6 +/- standard deviation (SD) 57.5 in the prenatal surgery group (n=64) versus mean 122.6 +/- SD 57.2 in the postnatal surgery group (n=70) (p=0.007).

Maternal morbidity and complications related to prenatal surgery included oligohydramnios, chorioamniotic separation, placental abruption, and spontaneous membrane rupture. At delivery, an area of dehiscence or a very thin prenatal uterine surgery scar was seen at delivery in one third of mothers who had prenatal fetal surgery (all subsequent pregnancies should be delivered by cesarean before the onset of labor). The average gestational age of babies in the prenatal surgery group was 34.1 weeks, and 13% were delivered before 30 weeks of gestation. One fifth of infants in the prenatal surgery group had evidence of the respiratory distress syndrome which was probably related to prematurity. The authors observe that "in the case of infants with low lumbar and sacral sessions, in whom less impairment in lower-limb function may be predicted, the normalization of hindbrain position and the minimization of the need for postnatal placement of cerebral spinal shunt may be the primary indication for surgery". They cautioned that the potential benefits of fetal surgery must be balanced against the risks of premature delivery and maternal morbidity and that continued assessment is required to learn if early benefits of prenatal surgery are sustained and the effects of fetal surgery on bowel and bladder continence, sexual function, and mental capacity. They warn that results of this trial should not be generalized to centers with less experience or to patients who do not meet eligibility criteria.

An additional 25 reports were included in the AHRQ technology assessment, all of which were based on four series of patients from four academic medical centers in the U.S.

- Two of the studies had concurrent comparisons.[12,13] One of these analyzed the first 29 cases of open myelomeningocele repair at Vanderbilt University Medical Center, finding significant reductions in the need for post-natal shunt placement (51% vs. 91%) and reduced hindbrain herniation (38% vs. 95%). However, both prospective studies found that in utero repair was associated with greater rates

of oligohydramnios (48% vs. 4%), lower gestational ages (33 vs. 37 weeks) and no difference in lower extremity function.

- In a study of 116 fetuses followed for a minimum of 12 months after intrauterine repair of spina bifida (myelomeningocele or myeloschisis), Bruner and colleagues reported 61 fetuses (54%) required ventriculoperitoneal shunt placement for hydrocephalus.[14] The authors' statistical analysis revealed fetuses were less likely to require ventriculoperitoneal shunt placement when surgery was performed at 25 weeks or earlier, when ventricular size was less than 14 mm at the time of surgery, and when the defects were located at L4 or below.
- Johnson and colleagues reported on the results of the largest case series of 50 fetuses who underwent open fetal closure of a myelomeningocele between 20 and 24 weeks' gestation.[15] Fetal selection criteria included the presence of hindbrain herniation and sonographic evidence of intact neurological function, i.e., movement of the lower extremities and absence of clubfoot deformities. Perinatal survival was 94%, and mean age at delivery was 34 weeks. All fetuses demonstrated reversal of hindbrain herniation and 43% required ventriculoperitoneal shunting compared to 68%–100% in historical controls, depending on the location of the myelomeningocele.
- Studies reporting leg function at longer follow-up showed no difference between patients treated with fetal surgery at 20 to 28 weeks versus traditional surgery.[12]In three papers, investigators at the University of Pennsylvania reported outcomes of myelomeningocele repair in 54 patients treated before the voluntary moratorium.[16-18]
    - At median follow-up of 66 months (range 36-54 months), 37/54 (69%) walked independently, 13/54 (24%) were assisted walkers, and 4/54 (7%) were wheelchair dependent. The strongest factors predicting a lower likelihood to walk independently were higher level lesion (>L4) and the development of clubfoot deformity after fetal intervention. The majority of independent ambulators, and all children who required assistive devices to walk, experienced significant deficits in lower extremity coordination.[17]
    - Thirty children returned at 5 years of age for neurocognitive examination. In this highly selected group, most children had average preschool neurodevelopmental scores and children who did not require shunt placement were more likely to have better scores.[18]
    - A survey of 48 families focused on hindbrain herniation (HH)-associated brainstem dysfunction, e.g., apnea, neurogenic dysphagia, gastro-esophageal reflux disease, neuro-ophthalmologic disturbances.[16] Half of the children required shunting. At a median age of 72 months, 15 non-shunted and 10 shunted children were free of HH symptoms. There were no HH-related deaths, and no children developed severe persistent cyanotic apnea. Most children had no or only mild brainstem dysfunction. The authors conclude that reversal of HH after fetal surgery may help reduce the incidence and severity of brainstem dysfunction.

Non-randomized Trials

Investigators at a German center performed a retrospective analysis of expectantly managed patients who received surgical intervention within 2 days of birth at their institution and compared them with reports of outcomes after fetal surgery from other centers including those noted above and to data from historical controls.[19] Patients were born between 1979 and 2009 and were 13.3 +/- 8.9 (mean +/- standard deviation [SD]) years old at the time of the analysis. Gestational age at birth in the expectantly managed group was 37.8 weeks, significantly higher than in the prenatal surgery patients. In the expectantly managed group, shunt placement was required in 69.8% at mean age of 16.0 +/- 10.7 days, which is less than for historical controls and comparable to data reported on patients who received fetal surgery. The authors suggested that inconsistency in clinical criteria for shunting used in studies might contribute to differences in this outcome. Among their expectantly managed patients, 56.4% were assisted walkers and 64.1% attended regular classes, both comparable to historical controls. Noting the

discrepancy in the rate of assisted walkers and wheelchair users between expectantly managed patients/historical controls and patients who received surgery, the authors observe that the mean age of the study population was 21.7 years for historical controls, 13.3 years for their population, and only 67.0 months after fetal surgery. They cited earlier papers reporting mobility decreases from early childhood to the early teens including one reporting that "the percentage of patients ambulating the majority of time decreased from 76% at 0-5 years to 46% at 20-25 years, with a flattening beyond 10 years".[20]

Aqueductal Stenosis

Stenosis of the aqueduct of Sylvius causes obstructive hydrocephalus — obstruction of the flow of cerebrospinal fluid produced by the choroid plexus dilates the cerebral ventricles — compresses the developing brain, damaging neurologic function. When this compression is identified in utero and it appears to be severe, it is theorized that decompressing the ventricles may ameliorate the adverse effects on the developing brain. However, analysis of fetal surgery registry data suggests that percutaneously placed ventriculoamniotic shunts have not improved the outcome. At this time, a moratorium on these procedures is being observed until there is better understanding of the natural history of fetal ventriculomegaly and until proper selection criteria can be developed.

Cardiac Malformations

The 2011 AHRQ technology assessment included the following evidence on fetal surgery for cardiac malformations:[3]

- Two case series (n=10) were identified on fetal surgery for pulmonary atresia and intact ventricular septum. The literature was described as scant, reflecting the early formative period of development of procedures for this rare condition.
- Eight prospective case series (n=90) were identified on balloon dilation for critical aortic stenosis. One center in the United Kingdom, two centers in Germany, two in Brazil, and one in the U.S. performed this procedure. The 2011 AHRQ technology assessment concluded that it is difficult to determine whether the procedure changes long-term outcomes, since it appears that it may also increase risk of fetal loss. However, it did appear that technical success improves over time within a dedicated team and center. For example, the North American center improved their success rate from 25% to 90% over a period of several years. Overall, the literature was considered to be very early in development.
- Three case series from one U.S. institution with a total of 24 patients were identified on creation in utero of an atrial septal defect for an intact atrial septum. The procedure appears to have technical success, however, mortality remains high and no controlled trials were available to compare outcomes in patients treated prenatally with those treated postnatally.

The AHRQ report concluded that overall, procedures for severe fetal cardiac anomalies are in an early stage. Preliminary work is being reported in a few highly specialized centers which are establishing the groundwork for feasibility and future directions for outcomes research in this area. The authors concluded that the most pressing challenge in this area is the ability to identify the "right" patient whose care would be compromised by waiting to do a postnatal repair.

Other Indications

The use of fetal surgery for other defects is expanding; recent case reports included prenatal correction of cleft lip and palate and decompression of the fetal trachea.[21,22] A review of 187 maternal-fetal

surgeries performed at the UCSF Fetal Treatment Center found significant short-term maternal morbidity but no maternal deaths.[23] Post-surgical complications included increased rates of cesarean birth, treatment in intensive care, prolonged hospitalization, and blood transfusion.

Clinical Practice Guidelines

- The 2013 American College of Obstetricians and Gynecologists (ACOG)'s Committee Opinion on maternal-fetal surgery for myelomeningocele recommends that maternal-fetal surgery should only be offered at facilities with the expertise, multidisciplinary teams, services, and facilities to provide the intensive care required for these patients.[24]

- The ACOG Committee on Ethics and the American Academy of Pediatrics Committee on Bioethics issued a committee opinion on maternal-fetal intervention and fetal care centers in 2011.[25] The committee opinion included the following recommendations:
  - Fetal intervention cannot be performed without the explicit informed consent of the pregnant woman.
  - Distinctions should be made to prospective parents between which protocols are standard or evidence-based therapies and which are innovative or experimental interventions.
  - The informed consent process should involve thorough discussion of the risks and benefits for both the fetus and the pregnant woman.
  - Safeguards should be in place to protect women considering fetal research.
  - Access to support services such as social services, palliative care and perinatal hospice services, genetic counseling, and ethics consultation should be provided, when appropriate.
  - The organization and governance of centers providing fetal interventions should involve a diverse group of professionals, including members without direct ties to the center involved.
  - Cooperation between fetal care centers should be encouraged to establish collaborative research networks and to support multicenter trials to accumulate more robust short- and long-term maternal and fetal outcome data on all categories of fetal intervention. In addition, the establishment of centers of excellence for those procedures that are particularly challenging and rare may help to optimize fetal and maternal outcomes.

- A consensus, endorsed by the International Fetal Medicine and Surgery Society proposed the following criteria for fetal surgery:[26]

  1. "Accurate diagnosis and staging possible, with exclusion of associated anomalies
  2. Natural history of the disease is documented, and prognosis established
  3. Currently no effective postnatal therapy
  4. In utero surgery proven feasible in animal models, reversing deleterious effects of the condition
  5. Interventions performed in specialized multidisciplinary fetal treatment centers within strict protocol and approval of the local Ethics Committee and with informed consent of the mother or parents"

Summary

Due to a number of factors, including the rarity of the conditions and the small number of centers specializing in fetal interventions, the evidence on fetal surgery remains limited. Fetal surgery for many congenital conditions such as congenital diaphragmatic hernia, and heart defects has not been shown to improve health outcomes in comparison with post-natal treatment. The available evidence is insufficient to demonstrate that fetal tracheal occlusion and aortic valvuloplasty provides improved health outcomes.

For these and other applications of fetal surgery that are currently considered investigational, additional studies are needed to identify appropriate candidates and to evaluate longer term outcomes compared with postnatal management.

For conditions leading to fetal hydrops (certain cases of congenital cystic adenomatoid malformation, bronchopulmonary sequestration, or sacrococcygeal teratoma), for which mortality approaches 100%, fetal surgery may be considered medically necessary. Vesico-amniotic shunting for bilateral urinary tract obstruction may also be considered medically necessary to minimize the effects of this condition on kidney and lung development. Additional studies for these surgeries are needed to better define the appropriate surgical candidates, the most effective timing of the interventions, and the long-term health outcomes in surviving children.

Data from the Management of Myelomeningocele Study (MOMS) showed that prenatal repair of myelomeningocele reduces the need for shunting in the first 12 months after delivery and improves a composite measure of mental and motor function, with adjustment for lesion level, at 30 months of age. Prenatal surgery also improves the degree of hindbrain herniation and the likelihood of being able to walk independently when compared with postnatal surgery. The long-term impact on function needs to be evaluated, and benefits must be balanced against risks to mother and child. Thus, fetal surgery may be considered medically necessary following informed decision making for cases of prenatal myelomeningocele that meet the criteria of the MOMS study.

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CROSS REFERENCES

None

CODES	NUMBER	DESCRIPTION
CPT	59076	Fetal shunt placement, including ultrasound guidance
	59897	Unlisted fetal invasive procedure, including ultrasound guidance
HCPCS	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