Fetal surgery nowadays - Fetal surgery in the current context

Cirurgia fetal no contexto atual

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ABSTRACT: Fetal surgery is now a reality in large centers that specialized in the field of fetal medicine. Fetal surgery emerged in the 1960s, primarily from the need to better identify and understand fetal pathologies, and its exponential development was driven by improvements in prenatal diagnostic techniques. Fetal surgery gradually became the main treatment for specific fetal pathologies, changing the course of these diseases. This study summarizes the history of the fetal surgeries that are most commonly performed worldwide, how they started and how they evolved over time, the main validation trials and the most widely used surgical technique in each case. The main surgeries include laser photocoagulation of placental anastomoses in twin-to-twin transfusion syndrome, in utero repair of fetal myelomeningocele and fetal endotracheal occlusion in cases of congenital diaphragmatic hernia. Other surgeries and procedures, whose benefits are less clear and whose results are still somewhat controversial, such as urinary interventions in cases of lower urinary tract obstruction, cardiac procedures in cases of critical aortic stenosis, thoracoamniotic shunts for the treatment of massive pleural effusions and intrauterine resection of sacrococcygeal teratomas and pulmonary masses, are also cited. The future of fetal surgery is also assessed.

Keywords: Fetus/surgery; Fetoscopy.

RESUMO: A cirurgia fetal é, hoje, uma realidade em grandes centros especializados na área da medicina fetal. Surgiu por volta da década de 1960, inicialmente atrelada à necessidade de melhor conhecer e entender as patologias fetais, e teve desenvolvimento exponencial impulsionado pelo aprimoramento das técnicas diagnósticas pré-natais. Foi aos poucos se consolidando e tornando-se o tratamento de escolha para algumas patologias específicas, mudando definitivamente o curso dessas doenças. Nesse estudo, encontra-se um breve histórico das cirurgias fetais mais comumente realizadas em todo o mundo, como elas surgiram e como foram evoluindo com o passar do tempo, os principais estudos que as validaram e a técnica cirúrgica mais amplamente utilizada em cada caso. Entre as principais cirurgias, são citadas a fotocoagulação a laser de anastomoses placentárias na síndrome de transfusão feto-fetal, a correção intrauterina a céu aberto da mielomeningocele fetal e a oclusão endotraqueal fetal por balão nos casos de hérnia diafragmática congênita. Também são abordadas cirurgias e procedimentos cujos benefícios são menos evidentes e os resultados ainda um tanto controversos, como as intervenções urinárias nos casos de obstrução ao trato urinário inferior, procedimentos cardíacos em casos de estenose aórtica crítica, derivações tóracoamnióticas para tratamento de derrames pleurais compressivos, além de ressecções intrauterinas de teratomas sacrococcígeos e de massas pulmonares. Também é feita uma avaliação a respeito do futuro da cirurgia fetal.

Descritores: Feto/cirurgia; Fetoscopia.

INTRODUCTION

Fetal medicine is part of modern obstetrics and may be defined as the science that studies the development of the fetus and its physiology, the pathophysiology of malformations and congenital disorders and the diagnosis and treatment of these abnormalities in the antenatal period, when possible[1]. Fetal medicine emerged in the 1960s and was initially focused more on diagnosing fetal changes and prenatal counseling than on treating the fetus itself.

Until approximately 40 years ago, developing fetuses were poorly accessible to obstetricians within the pregnant uterus. However, over the years, this paradigm shifted considerably thanks to breakthroughs in diagnostic technologies, particularly in imaging examinations, from the 1970s and 1980s, which furthered the knowledge and understanding of fetal pathologies[2].

A brief history of the emergence of fetal surgery

Fetal surgical procedures emerged from clinical need[3] because some congenital diseases were long known to possibly cause progressive and irreversible damage while the fetus was still in the intrauterine environment. Accordingly, the hypothesis that the antenatal repair of some lesions could prevent or reverse tissue damage, restore normal development and allow quality survival was proposed.

Michael Harrison is recognized as the father of fetal surgery. In the early 1980s, he created the Fetal Treatment Center at University of California, San Francisco (UCSF), where he pioneered open surgical treatments for fetal lower urinary tract obstruction, resection of congenital cystic adenomatoid malformation (CCAM) and repair of congenital diaphragmatic hernia (CDH). Together with his trainees, he established fetal treatment centers in many of the major pediatric hospitals in the United States of America (USA)[4]. He defined the criteria and indications for fetal surgeries in 1982, which were adapted and approved in 1991 by the International Fetal Medicine and Surgery Society (IFMSS)[5], as shown in Table 1.

Table 1 - Criteria for fetal surgery according to Harrison (Harrison, 1991)

1. Accurate diagnosis and staging possible, with the exclusion of associated anomalies;
2. Natural history of the disease is documented and prognosis established;
3. No effective postnatal therapy is available;
4. In utero surgery demonstrated as feasible in animal models, reversing deleterious effects of the condition;
5. Interventions performed in specialized fetal treatment centers within strict protocols and approval of the local ethics committee with the informed consent of the mother or both parents.

Another pioneer in the history of fetal surgeries is Julian De Lia. In the early 1980s, he developed an innovative technique for the treatment of twin-to-twin transfusion syndrome (TTTS): laser photocoagulation of placental anastomoses[4,6,7]. At that time, he also predicted that this would be the most performed procedure for treating sick fetuses[6]. This procedure was initially tested in animal models and then in humans through fetoscopy, accessing the uterine cavity by laparotomy and hysterotomy.

In the same period, in Europe, open surgeries for the treatment of fetal anomalies caused maternal morbidity at very high rates, which triggered the search for less invasive alternatives. A major milestone at the time was the modification of the technique used to treat fetuses diagnosed with TTTS. Ville and colleagues, together with the team of Dr. Kypros Nicolaides, in London, adopted the technique of De Lia, accessing the amniotic cavity percutaneously but without requiring laparotomy, thereby reducing the morbidity of the open procedure[4,6].

Thus, new fetal medicine centers emerged, boosted by the great advances made in Europe and in the USA. The collaboration between these centers enabled the development of multicenter clinical trials that validated some of the main invasive fetal therapies that are now routinely performed.

Main Fetal Surgical Procedures

I) Laser photocoagulation of placental anastomoses in twin-to-twin transfusion syndrome

TTTS is a complication in approximately 10-15% of all monochorionic twin pregnancies[8], and its general mortality rate reaches 73-100%[9]. TTTS results from uneven blood flow between twins due to the predominance of unidirectional arteriovenous (AV) anastomoses in the placenta, with an absent or decreased caliber of arterio-arterial (AA) or venovenous (VV) anastomoses[10]. Consequently, one of the twins has reduced amniotic fluid (donor), and the other has increased amniotic fluid (receptor). This condition may lead to a number of fetal changes and eventually to the death of one or both twins. The main and most accepted TTTS classification was proposed by Quintero et al in 1999[11], who divided the syndrome into 5 stages using ultrasound criteria.

Table 2 - Quintero classification of twin-to-twin transfusion syndrome (TTTS)

Stage I	Oligohydramnios in the donor twin (single deepest pocket ≤ 2 cm) and polyhydramnios in the receptor twin (single deepest pocket ≥ 8 cm), and the donor twin bladder remains visible in the ultrasound
Stage II	Donor twin bladder is not visible on the ultrasound
Stage III	Abnormal arterial or venous Doppler in one of the twins: absent or reversed diastolic umbilical artery flow, absent or reversed diastolic venous flow or pulsatile umbilical vein
Stage IV	Hydrops fetalis in at least one twin
Stage V	Death of at least one twin

The earliest mentions of the disease are very old and include a biblical reference, in the book of Genesis, in which the newly born twin brothers Esau and Jacob are described as "very red and very pale", respectively. Dating to the seventeenth century, the painting "The Swaddled Children", in which one of the twins is pale and the other is plethoric[12], is now considered a depiction of the disease.

However, TTTS was first described long before the current classification, in 1886, by the German obstetrician Fredrick Schatz[12], who, after placental ink injection experiments, observed a "third circulation in the monochorionic placenta". He also noted, by autopsy, that one of the twins was large and swollen and had a distended bladder, whereas the other was small and wrinkled and had an empty bladder.

The first treatment proposed for TTTS was amnioreduction, first recorded in the 1930s, but it was more widely applied starting in the late 1970s. Its purpose was to decrease the polyhydramnios and the risk of premature labor and to reduce the pressure on placental vessels, thereby improving blood flow[7]. Initially, small amounts of amniotic fluid were removed due to the theoretical risk of placental abruption and premature labor[13]. Starting in the 1980s, serial amniodrainages of higher volumes were performed[14-16], with improved survival rates and without increased rates of feared complications, and it became the first-line treatment for severe TTTS in the 1990s[7].

As technology advanced, a new treatment for the disease, proposed by the obstetrician Julian DeLia and the pathologist Kurt Benirschke, emerged in the late 1980s: laser ablation of placental vascular anastomoses[17]. Initially tested in animals, this approach was first performed in human fetuses in 1988 by fetoscopy through laparotomy and hysterotomy under general or regional anesthesia. In 1992, Ville and colleagues developed a less invasive technique, replacing laparotomy with percutaneous endoscopic laser photocoagulation under local anesthesia[18].

With apparently better results than those of amnioreduction, the new technique began to be used in various fetal medicine centers, but there was no satisfactory study comparing both forms of treatment. In 2004, Senat et al.[19] published a randomized, controlled, multicenter clinical trial with 142 women comparing the use of endoscopic surgery and amnioreduction to treat TTTS before 26 weeks. This clinical trial showed increased perinatal survival rates and improved neurological outcomes in the group treated by fetoscopy at Quintero stages I to IV; hence, this method became the treatment of choice.

The first published clinical trials described a non-selective vessel ablation technique in which all of the vessels crossing the amniotic membrane are coagulated[20]. This technique was gradually replaced by selective ablation, in which only vascular anastomoses are coagulated, defining an area known as the vascular equator (or shared placenta). Then, selective ablation started to be sequentially performed (first the AV, then the VV and lastly the AA)[21].

More recently, fetoscopic laser equatorial placental dichorionization, also known as the Solomon technique, was proposed. This technique aims to completely separate the territories of the monochorionic placenta[22]. The Solomon technique is performed by applying a laser to connect previously coagulated vessels, creating a virtual line that corresponds to the vascular equator. Its advantages include a reversal of hemodynamic changes and a reduction of TTTS recurrence and of complications such as Twin Anemia Polycythemia Sequence (TAPS), in addition to protecting the surviving twin if one of them dies by forming two completely independent vascular systems[20].

Currently, the main challenges for the treatment of TTTS include doubts about the benefit of photocoagulation of anastomoses in Quintero stage I[23] because the clinical condition may stabilize or spontaneously regress and the reduction of risks of premature labor and neurological sequelae in fetuses surviving the surgery.

II) Intrauterine myelomeningocele repair

Spina bifida is a congenital anomaly of the central nervous system, and its most common form is myelomeningocele (MMC), which is characterized by the extrusion of the spinal cord through open vertebral arches into a pouch containing cerebrospinal fluid. Individuals with the disease show various degrees of alterations in cognitive functions, urinary and intestinal dysfunctions and orthopedic disorders[24]. Major morbidity results from herniation of the brainstem into the medullary canal, Arnold-Chiari type II malformation and subsequent

hydrocephalus. Despite the great advance in prevention with folic acid supplementation, its incidence remains steady at approximately 1 in 3000 live births[25-27].

Neurological damage in fetal MMC is proposed based on the two-hit hypothesis: primary congenital abnormalities in anatomical development expose the relatively normal spinal cord to secondary damage due to contact with the amniotic fluid, direct trauma, hydrodynamic pressure or a combination of these factors[24]. This is the rationale for closing these lesions during the fetus' intrauterine life, with the goal of avoiding or mitigating such damages. In the 1980s, antenatal MMC repair was tested in animal models with different species, such as monkeys, rats, pigs and sheep, and it achieved good results, which made it possible to perform the surgery in humans[24].

The first case of intrauterine fetal MMC repair in humans was reported in 1997 and was an endoscopic procedure to cover the neural placode with skin grafts (28). However, due to poor results, the technique was abandoned. Then, cases of fetuses treated in open surgery with good results began to be reported (29, 30), and the procedure subsequently spread to other centers. By 2003, more than 90 cases of fetuses treated by open surgery had been reported[29,31,32], although the comparisons were with historical cohorts, not control groups, and the operated cases were highly selected[24].

Therefore, the United States National Institutes of Health (NIH) sponsored a multicenter, prospective, randomized clinical trial comparing the outcomes between prenatal and postnatal surgeries, which was known as MOMS[33]. The clinical trial started in 2003 and was interrupted in 2010, after the recruitment of 183 patients, due to the superior efficacy of prenatal surgery in the initial analysis. The results showed a reduced need for ventricular-peritoneal shunting at 1 year of life, improved motor and cognitive functions at 30 months of life and reversed brain stem herniation. Despite the positive results, the trial showed an increased risk of premature rupture of membranes (PROM), oligoamnios and premature labor.

This large clinical trial showed that intrauterine MMC repair had a higher efficacy than postnatal surgery did when using the same inclusion and exclusion criteria, which enabled new fetal medicine centers worldwide to start performing the procedure routinely, disseminating the technique.

Despite the clear evidence of the benefit of prenatal surgical correction, the search for a less invasive surgical technique with decreased maternal and fetal morbidity continues. Accordingly, Botelho et al improved the open surgical technique with a smaller uterine incision (mini-hysterotomy), which led to lower PROM rates, chorioamniotic separation and dehiscence of the uterine scar and lower extreme prematurity rates (after 34 weeks) [34]. Endoscopic studies have also been reported[35,36,37], but

their results are still worse than those of open surgery; thus, further studies are required to adequately and satisfactorily compare the open and endoscopic approaches and techniques.

III) Fetal endotracheal occlusion in congenital diaphragmatic hernia

Congenital diaphragmatic hernia (CDH) is a sporadic defect with a prevalence rate at birth of approximately 1 in 4000[38]. CDH occurs when the diaphragm fails to form correctly, allowing abdominal viscera to enter the thorax through the defect and leading to pulmonary hypoplasia and hypertension, which are the main causes of neonatal morbidity and mortality in this group of patients[39].

Some approaches were developed to assess the severity of CDH; the most commonly used methods are the lung to head ratio (LHR) assessment (measurement of the lung contralateral to the hernia/cephalic circumference) and the presence of liver in the chest, both easily performed in ultrasound examinations conducted by a trained operator. The detection of LHR < 1.0 and the presence of portions of intrathoracic liver are considered severe hernia.

The prenatal intervention approach to CDH was first proposed in 1963, when Areechon and Reid[40] suggested that a timely repair could promote pulmonary parenchyma growth. In the 1980s, after extensive experiments on sheep, Harrison and colleagues reported the first open surgery for CDH repair including hysterotomy and diaphragmatic defect repair[41]. Despite the success reported in some cases, these initial surgeries were not very encouraging due to high maternal and fetal morbidity.

Conversely, in the 1990s, Wilson and Di Fiore proposed performing tracheal occlusion toward stopping and reversing pulmonary hypoplasia based on the observation that in congenital high airway obstruction syndrome, the lungs are typically enlarged. They hypothesized that tracheal occlusion could prevent the release of fluid from the lungs, thereby causing its hyperinflation and promoting organ development through DNA synthesis and cell proliferation[42,43].

Thus, after numerous studies on tracheal occlusion in animal models, experiments in human fetuses began to be performed. Several tracheal occlusion techniques were tested, including surgical clips, cuffs, polymeric foam, magnetic valves, umbrellas and vascular occlusive balloons[44], with various degrees of success, and clinical trials were initiated in the USA and in Europe in the late 1990s.

Experimental studies conducted with animals and humans showed that, although fetal endotracheal occlusion increased lung mass and improved gas exchange, it also prevented the development and maturation of type II pneumocytes in the alveoli and the production of alveolar surfactant[45]. Thus, researchers proposed that fetal tracheal occlusion be reversed during the intrauterine period[46].

In 2004, Deprest et al.[38] published positive results of endotracheal occlusion in human fetuses. Twenty-one fetuses were subjected to the procedure performed from 25 to 29 weeks in fetuses with LHR < 1, endoscopically occluding the fetal trachea with a small vascular balloon 7 mm in diameter under direct visualization. Tracheal occlusion was reversed in the prenatal period, from 33 to 36 weeks, by either fetoscopy or ultrasound-guided vascular access, or during labor by ex utero intrapartum therapy (EXIT). The findings showed a large increase in 6-month survival and consolidated the developing technique but also raised key questions regarding the best time to perform tracheal occlusion and the duration of the intervention.

In 2009, Jani et al published a larger clinical trial, with 210 patients subjected to fetal endotracheal occlusion for severe isolated CDH, with LHR < 1[47]. The procedure was performed from 23 to 33 weeks, and the balloons were removed by fetoscopy, ultrasound-guided vascular access, EXIT or after delivery (tracheoscopy or percutaneous puncture). This trial showed a survival rate after surgery similar to the previous trial, although a randomized clinical trial was still required.

Thus, in 2012, Ruano et al.[48] published a randomized, controlled clinical trial of fetal endotracheal occlusion versus postnatal CDH treatment. In this trial, 38 patients were included, half allocated to each group, and the treatment consisted of fetal endotracheal occlusion by fetoscopy performed from 26 to 30 weeks in fetuses with LHR < 1 and at least one-third of the liver present in the thoracic cavity. All fetuses were subjected to EXIT at the gestational age of 38 weeks. The results showed an increased survival rate and a decreased frequency of severe pulmonary hypertension in the treatment group, albeit still with high prematurity and PROM incidence rates.

Because the risks of the procedure are high (including PROM, premature labor, antepartum hemorrhage, chorioamnionitis and neonatal death), it is performed only in severe cases, with a high likelihood of death with expectant management, that is, when the benefits of the surgery outweigh its risks, according to the findings of the aforementioned clinical trials. Tracheal occlusion, by stimulating lung growth, may also be beneficial in cases of intermediate prognosis. To investigate this hypothesis, a European, multicenter, randomized clinical trial termed the Tracheal Occlusion To Accelerate Lung growth (TOTAL) trial, whose objective is to compare expectant management with tracheal occlusion from 30 to 32 weeks in moderate cases, is currently underway[39].

IV) Intrauterine interventions in cases of lower urinary tract obstruction

Fetal lower urinary tract obstruction may lead to abnormal kidney development. The two most common congenital malformations that cause obstruction are the posterior urethral valve (PUV) and urethral atresia[49]. On ultrasound examination, the diseases are usually difficult to differentiate[50,51], showing megabladder, proximal urethral dilation and bilateral hydronephrosis, usually accompanied by oligoamnios/anhydramnios, and are related to a high prevalence of pulmonary hypoplasia due to the absence of amniotic fluid[49].

Postnatal treatments for urinary tract clearing are available, although irreparable renal damage has been frequently caused at birth; therefore, new approaches to treat diseases in the antenatal period, when renal changes have not yet occurred, or when they are mild and/or reversible, have long been researched[52].

The first published studies, conducted in animal models in the 1980s, consisted of open fetal surgeries with opening and marsupialization of the bladder mucosa, cutaneous ureterostomies and vesicoamniotic shunting[53]. They were soon performed in human fetuses, but the risks were very high in relation to the small survival benefit in fetuses with significantly damaged renal function[52]. Over the years, the open approach was gradually replaced by endoscopic or percutaneous techniques with a high potential to reduce the morbidity of traditional surgeries[54,55].

Vesicoamniotic shunts are placed percutaneously under ultrasound guidance. One end of the drain is located inside the bladder and the other end in the amniotic cavity, allowing the elimination of fetal urine. The endoscopic technique makes it possible to permanently treat the lower urinary tract obstructions; the fetoscope is inserted into the bladder, and under direct visualization, techniques of ablation of the valves are applied to restore the natural urine flow[56,57].

Despite advances in technology and, in theory, effective treatment options, fetal surgeries for lower urinary tract obstruction have not yet shown encouraging results. Some case series and systematic reviews have shown evidence of increased survival rates after bladder drainage, although no randomized clinical trial had been performed until the PLUTO trial, which started in 2006[49].

This study was a multicenter, randomized clinical trial aimed at assessing the effect of vesicoamniotic shunting on survival compared with that of expectant management. In this trial, 31 patients were randomized, 16 to the treatment group and 15 to the control group, but the study was interrupted due to recruitment difficulties. The primary outcome was 28-day survival, and the secondary outcomes were 1- and 2-year survival and 28-day and 1- and 2-year renal function. The main findings included increased survival in the group of fetuses treated with vesicoamniotic shunting, albeit non-significantly, although only two children reached the age of 2 years without impaired renal function in both groups[49].

The results from the PLUTO trial were discouraging and reinforced the idea that the natural history of this disease is very serious and that its morbidity and mortality are substantial, despite the treatment, suggesting that the

damage to the renal parenchyma is already irreversible at the time of diagnosis[49]. In other words, the gain in survival would not offset the postnatal morbidity caused by the disease. New studies and the development of new technologies remain necessary for a more satisfactory treatment approach to the disease.

V) Other procedures

A) Fetal cardiac interventions

Some congenital heart defects may manifest critically during the period of fetal development, with unfavorable progression and irreversible changes, which are often incompatible with extrauterine life[58]. Fetal cardiac interventions in the prenatal period have become possible, and positive results have been achieved in some centers[59], with improved ventricular growth and function and reduced intrauterine mortality[60].

Currently, candidate diseases for fetal cardiac intervention include critical aortic stenosis progressing to left heart hypoplasia syndrome (LHHS), pulmonary atresia with intact interventricular septum progressing to right heart hypoplasia syndrome (RHHS), LHHS with intact or highly restrictive atrial septum and fetal heart block[61]. The recommended therapeutic options include aortic valvuloplasty, pulmonary valvuloplasty, creation of atrial septal defect and pacemaker implantation in fetuses.

Of those interventions, the most commonly performed procedure is balloon aortic valvuloplasty in cases of aortic stenosis progressing to left heart hypoplasia syndrome. A group from the Boston Children's Hospital established well-defined criteria for the indication of the procedure toward finding patients with clear progression to left heart hypoplasia syndrome, albeit still at a reversible stage, obtaining the best risk-benefit ratio[62].

This procedure is performed transcutaneously and under ultrasound guidance, inserting a needle through the maternal abdomen and through the uterine wall until reaching the fetal heart. After entering the left ventricle, the needle is positioned in the aortic valve, inflating the balloon that dilates the valve. The balloon is then deflated, and the needle is removed[63].

By 2016, approximately 300 cases of aortic valvuloplasty had been published worldwide, with a success rate of approximately 80-90% of procedures performed in the institution with the largest sample and with fetal death rates of approximately 8-10%[63]. However, because the main objective of the procedure is to avoid heart disease progression to LHHS, the postnatal results are still rather inconsistent. Despite progress in the field of cardiac interventions, aortic valvuloplasty indications and results remain controversial, and case selection should be based on well-defined criteria for medium- and long-term follow-up.

B) Thoracoamniotic shunting

Pleural effusion is a rare pathological finding, with an incidence of 1 in every 10,000-15,000 pregnancies[64,65]. The condition consists of the accumulation of fluid in the fetal thorax and may be primary or secondary. Primary pleural effusion results from changes in the lymphatic system, whereas secondary pleural effusion may be caused by cardiac malformations, fetal anemia, congenital infections, aneuploidy or structural malformations that compress the lungs and mediastinum[66]. These conditions have variable clinical progression and may stabilize and spontaneously regress but may also rapidly progress to hydrops fetalis and perinatal death.

Some treatment options have been proposed over time, including thoracentesis, pleurodesis and thoracoamniotic shunting[66]; the last is now considered the most appropriate therapy because it prevents liquid build-up when the drain remains well positioned, thereby avoiding new procedures.

Currently, the shunt most used in thoracoamniotic shunting is the silicone double pigtail catheter[67], which is inserted through a percutaneous introducer under ultrasound guidance. The catheter is considered well positioned when its inner end is located in the pleural cavity, whereas its outer end must be located in the amniotic cavity.

Drainage placement is indicated when the hydrothorax shows signs of decompensation, such as mediastinal compression and diaphragmatic eversion, to avoid progression to hydrops fetalis, or when the fetus is already hydropic, to avoid the high mortality rate of hydrops fetalis.

C) Intrauterine resection of sacrococcygeal teratomas

Sacrococcygeal teratomas (SCT) are rare neoplasms, located in the posterior coccyx, containing tissues from the three germ cell layers. SCT usually manifest as heterogeneous caudal and/or intrapelvic masses and may be extremely vascularized[3]. The postnatal classification of the American Academy of Pediatrics divides SCT into 4 types according to their relative extent outside and inside the body. Type-I tumors are entirely outside, whereas type-IV tumors are entirely inside[68].

The main issues evaluated during prenatal ultrasound examinations include tumor size, growth rate and vascularization (due to the great potential for blood flow theft and high-output heart failure), potential for obstruction to vaginal delivery and progression to hydrops fetalis, with a risk of developing mirror syndrome[69,70].

The only indications for fetal surgery in a case of SCT are progression to high-output heart failure and hydrops fetalis with type-I lesion and before 27 weeks of gestation[3]. In these cases, hysterotomy and lesion resection are performed. In all other cases, the lesion is resected postnatally, and delivery is often brought forward to prevent fetal deterioration.

D) Intrauterine resection of congenital cystic lung lesions

Congenital cystic lung lesions are developmental lung abnormalities that result from the proliferation of terminal bronchioles and abnormal alveolar development and may be classified as microcystic or macrocystic[71]. Their natural history is variable because some lesions grow

rapidly and progress to hydrops fetalis and pulmonary hypoplasia, whereas others stabilize and may even completely regress.

The main predictor of the progression of lesions to hydrops fetalis, which is a worsened fetal prognosis, is the calculation of the congenital pulmonary airway malformation volume ratio (CVR), the volume of mass (length x height x depth x 0.52) divided by cephalic circumference in centimeters. When a CVR ≥ 1.6 is found, the risk of progression to hydrops fetalis is approximately 75%[3]. Other predictors of poor prognosis are the presence of dominant cysts and the presence of hydrops fetalis.

Previously, the main treatment option for large microcystic lesions with CVR ≥ 1.6 and/or with hydrops fetalis was open fetal surgery and lobectomy of the affected pulmonary segment[3]. In recent years, various studies have shown that most patients with this type of lesion respond well to maternal corticotherapy, without requiring invasive procedures[72].

Thus, invasive procedures in congenital lung lesions were reserved for cases of microcystic lesions with CVR ≥ 1.6 and/or with hydrops fetalis that failed to respond to corticotherapy, performing open lobectomy, and for cases of macrocystic lung lesions in which thoracoamniotic shunting is performed[3,73].

CONCLUSION

Despite the great progress made in the last 40 years and its fast pace, particularly after the 2000s, fetal surgery can be considered the first-line treatment only in selected cases of specific pathologies and is available in a small number of highly specialized centers.

The efficacy of fetal surgery has been validated in some diseases (particularly TTTS, MMC and CDH) by well-designed, randomized and controlled clinical trials, and new fetal surgery techniques and approaches are increasingly required to follow the practice of evidence-based medicine before their clinical application. However, because these events are rare, some procedures still require further studies for their validation and remain limited to attempts to avoid imminent death (lower urinary tract obstruction, solid lung lesions, massive pleural effusions, SCT).

Despite the aforementioned difficulties, the field of fetal surgery will likely follow technological advancements. Increasingly early diagnosis will allow improved surgical programming, and new technologies may allow less invasive access to the cavity for future treatment, possibly enabling a reduction in the high rates of prematurity, which is the main complication common to all fetal surgeries and invasive procedures.

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