Update on prenatal diagnosis and fetal surgery for myelomeningocele

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ABSTRACT

A seminal study titled Management of Myelomeningocele Study, from 2011, demonstrated that prenatal myelomeningocele defect repaired before 26 weeks of gestation improved neurological outcomes; based on this study, fetal surgery was introduced as a standard of care alternative. Thus, prenatal myelomeningocele diagnosis within the therapeutic window became a mandatory goal; therefore, research efforts on screening strategies were intensified, especially in the first trimester. In addition, different fetal surgery techniques were developed to improve neurological outcomes and reduce maternal risks. The objective of this review is to provide an update on the advances in prenatal screening and diagnosis during the first and second trimesters, and in open and fetoscopic fetal surgery for myelomeningocele.

Key words: myelomeningocele, fetal therapies, spina bifida, fetoscopy, antenatal care.

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INTRODUCTION

Until 2011, prenatal screening and diagnosis strategies regarding myelomeningocele were aimed at providing appropriate counseling to parents based on prognosis so that they were aware of management options, either adequate obstetric follow-up and delivery in a center with neonatal surgery availability or, depending on local laws, an abortion.^{1,2} A seminal study titled Management of Myelomeningocele Study (MOMS)³ demonstrated that prenatal myelomeningocele repair before 26 weeks of gestation improved neurological outcomes; based on this study, fetal surgery was introduced to standard of care alternatives for myelomeningocele management.^{2,4-7}

This powered research in two critical areas. On the one side, prenatal myelomeningocele diagnosis within the therapeutic window became a mandatory goal; therefore, research efforts on screening strategies were intensified, especially in the first trimester. On the other side, different fetal surgery techniques were assessed to improve neurological outcomes and reduce maternal risks. The objective of this review is to provide an update on the advances in prenatal screening and diagnosis and in fetal surgery for myelomeningocele.

EPIDEMIOLOGY

The prevalence of spina bifida varies markedly worldwide based on ethnic and geographic characteristics.^{8,9} In Argentina, since the implementation of the law for flour fortification with folic acid, spina bifida prevalence decreased approximately 60 %. Nowadays, it is approximately 1 in every 2000 live births.¹⁰ Its prevalence during pregnancy is higher and decreases towards the end due to intrauterine death caused by this disease, especially in syndromic cases.¹¹

Most myelomeningocele cases occur as a single defect. Some abnormalities are considered part of the disease spectrum and, therefore, it is still considered an isolated defect, such as ventriculomegaly, Arnold-Chiari II malformation, hypoplasia of the corpus callosum, and talipes equinovarus.^{2,10-12}

PRENATAL SCREENING AND DIAGNOSIS OF MYELOMENINGOCELE

Prenatal spina bifida detection has increased in recent decades, and it is now possible to do it in the first trimester. The European Surveillance of Congenital Anomalies (EUROCAT) reported, for the 2012-2017 period, a prenatal sensitivity close to 90 %, i.e., in approximately 10 % of cases, ultrasounds were wrongly classified as normal (false negative result).¹³ In turn, in regions with fewer resources, such as Latin America, prenatal detection is not as common and it is done at a more advanced gestational age.^{8,14}

In the 1970s, spina bifida was diagnosed by ultrasound in the prenatal period for the first time¹⁵ and maternal blood alpha-fetoprotein levels were added to second trimester screening tests.¹⁶ The biochemistry panel is practically not used anymore; screening and diagnosis are currently usually done in the second trimester and, more recently, also during the 11-14-week ultrasound.¹⁷⁻¹⁹

1. Second-trimester ultrasound

1.a. Direct spinal assessment: this is done as part of a routine, detailed ultrasound around week 18-24. The International Society of Ultrasound in Obstetrics & Gynecology (ISUOG) suggests re-assessing the spine using axial, sagittal, and coronal sections (*Figure 1*).^{20,21} The **direct** signs of spina bifida aperta include visualizing the bone defect and the sac protrusion (meningocele or myelomeningocele) (*Figure 2*).

It may be technically difficult to find them, such as when the fetus is back-to-back (with the spine away from the probe) or with the spine against the placenta or uterus. Therefore, it is critical to be aware of the **indirect** signs of spina bifida, which had been described in the 1980s and became the true pillars of myelomeningocele screening.²²

1.b. Assessment of intracranial signs of spina bifida: indirect cranial signs work for screening and help to diagnose spina bifida. They include, during the second trimester, a smaller biparietal diameter (BPD) and head circumference, flattened or concave frontal bones ("lemon sign"), ventriculomegaly, obliteration of the cisterna magna, and visualization of cerebellar abnormalities, including the absence of cerebellum in the posterior fossa, a small cerebellum or anterior concave shape ("banana sign") (*Figure 3*).²³ In fetus with myelomeningocele at less than 24 weeks of gestation, the "lemon sign" is almost invariably present (98 %), and the "banana sign" is observed in 70-80 % of cases; however, in fetuses with an older gestational age, the "lemon sign" is uncommon and, in the posterior fossa, the most common finding is an absent cerebellum due to the downward displacement through the foramen magnum.^{11,23,24} A smaller head size, with a BPD or head circumference below the 5th percentile, also

FIGURE 1. *a*) Sagittal section, *b*) axial section, *c*) coronal section, and *d*) 3D reconstruction of a normal spine at 20 weeks of gestation



tends to normalize towards the third trimester,¹¹ whereas ventriculomegaly (atrium > 10 mm) tends to progress throughout gestation, both in fetuses receiving routine treatment and those undergoing prenatal surgery.^{11,25}

2. First-trimester ultrasound

2.a. Direct spinal assessment: although it is possible to make a prenatal diagnosis based on direct visualization at 11-14 weeks, it is extremely

difficult.²⁶ Therefore, intracranial indirect signs have been described.

2.b. Assessment of intracranial signs: while measuring nuchal translucency (NT), it is possible to assess whether the posterior fossa is normal (*Figure 4*). Our group recently published a bibliographic review of spina bifida aperta detection in the first trimester, which provided details on the multiple intracranial indirect signs described, both in mid-sagittal and

FIGURE 2. Direct signs of spina bifida aperta. a) Sagittal section and b) axial section showing a spinal defect through which the meningeal sac protrudes (arrows). c) Coronal section showing the separation of lateral processes of lumbar vertebrae



FIGURE 3. a) Transverse section of the cephalic pole showing the posterior fossa of a normal fetus at 21 weeks of gestation: note the skull ovoid shape, the anterior complex made up of the anterior horns of the lateral ventricles and the cavum septum pellucidum (CSP) and, in the posterior fossa, the butterfly-shaped cerebellum and the presence of the cisterna magna. b) Twenty-week fetus with lumbosacral spina bifida aperta: ventriculomegaly (*) and concave frontal bone (thin arrows) shaping the skull in a particular manner (lemon sign). c) Image of posterior fossa of a 20-week fetus with myelomeningocele: obliteration of the cisterna magna caused by an abnormal cerebellum position and shape, showing posterior convexity (thick arrows), known as the banana sign.



axial sections.²⁶ The assessment of the posterior fossa may detect abnormalities such as reduced or absent intracranial translucency (or fetal fourth ventricle)^{17,27} or cisterna magna,^{17,27,28} or an abnormal relationship between the brainstem and the distance between the brainstem and the occipital bone (*Figure 5*). This space may be analyzed based on measurements or by simply looking at the 4 echogenic lines defining the 3 hypoechoic spaces.^{26-27,29-31} Abnormalities in axial sections include observation of the "lemon sign;"^{27,32} reduced BPD^{33,34} and its relationship with transverse abdominal diameter, if this is < 1, it detects approximately 70 % of fetal myelomeningocele cases with a 5 % false positive rate;³⁵ or the visualization of the ventricular system with a "dried up" appearance;^{19,36} or different measurements resulting from the posterior displacement

of brain structures.^{37,38}

These signs have a variable performance across studies and among observers.²⁶ However, using the same mid-sagittal section of the NT and while examining the posterior fossa "at first sight," it may be possible to detect most myelomeningocele cases.^{24,26}

PRENATAL DIAGNOSTIC EVALUATION OF MYELOMENINGOCELE

If myelomeningocele is suspected in the prenatal period, the diagnostic assessment should be completed in the first place; then, counseling and management alternatives should be provided, which include postnatal surgery, prenatal surgery in selected cases or, depending on local laws, abortion.^{1,2} As with other congenital anomalies, it is critical to establish if it is an isolated defect or in combination with other type

FIGURE 4. a) Mid-sagittal section of a normal fetus showing nuchal translucency (TN), diencephalon (D), and mesencephalon (M). b) Four echogenic lines (yellow) defining the 3 hypoechoic spaces: brainstem (TE), fourth ventricle or intracranial translucency (TI), and cisterna magna (CM)



FIGURE 5. *a*) Direct observation of spina bifida aperta (arrow) in a 12-week fetus and b) posterior fossa showing only 2 hypoechoic spaces, instead of 3, the brainstem (1) and the fourth ventricle/cisterna magna (2)



of defect or if it is part of a genetic syndrome, so detailed imaging tests and genetic assessments are required.

a. Genetic assessment: between 5 % and 20 % of myelomening ocele cases have chromosomal abnormalities. The most common one is trisomy $18.^{1,12,39,40}$

The inclusion criteria of all fetal surgery programs mention, at least, a normal standard karyotyping or quantitative fluorescence polymerase chain reaction (QF-PCR). Some centers also request a normal microarray analysis,^{2,41} a technique that is limited in our setting due to its high cost and low availability.

b. Imaging tests: these include a detailed morphology scan, a fetal echocardiogram, and, if available or if the patient is a candidate for fetal surgery, fetal magnetic resonance imaging (FMRI).

The detailed scan would allow to rule out associated malformations and kyphosis, and to determine the anatomical and functional levels of the lesion. The lower the defect, the better the prognosis (*Table 1*).⁴² The anatomical level is based on the highest level of the bone defect and is established via ultrasound (*Figure 6*) and/or FMRI. Motor function level is mainly defined by ultrasound based on the assessment of hip, knee, and ankle/foot mobility, similar to a postnatal neurological assessment (*Table 1*).⁴²

Another aspect that may be assessed with an ultrasound and FMRI is the presence and size of ventriculomegaly. If it is severe $(\geq 15 \text{ mm})$, it is a predictor of hydrocephalus and ventriculoperitoneal shunt (VPS) requirement, even in fetuses undergoing intrauterine surgery.²⁵

An FMRI allows to detect other associated intracranial abnormalities and also to assess and establish the size of cerebellar and brainstem herniation through the foramen magnum (Sutton grading) (*Figure 7*).⁴³ Finally, the cervix length should be measured as an indicator of risk for preterm birth (< 20 mm is an exclusion criterion for fetal surgery).

TABLE 1. Determination of the lesion's motor function level

Level	Function	Prognosis for ambulation and type of orthosis required Indoor ambulation with knee-ankle-foot orthoses and crutches Community ambulation with ankle-foot orthoses, with or without crutches			
L1-L2	Hip: flexion and adduction (adduction cannot be assessed prenatally)				
L3	Knee: extension				
L4 L5	Knee: flexion Ankle/foot: dorsal flexion	Community ambulation with ankle-foot orthoses, without crutches			
S1	Ankle/foot: plantar flexion	Community ambulation without orthoses			

(Adapted from E. Carreras et al.)42

FIGURE 6. Determination of the lesion's anatomical level in a 22-week fetus with spina bifida aperta. To establish the height of the lesion, you may start from the caudal region (a), knowing that, in the second trimester, the last ossified vertebra in the fetus is S4, or (b) from the last thoracic vertebra, which may be recognized by the presence of the last rib (arrow). In this example, the defect starts approximately in L4.



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FIGURE 7. Sagittal sections of fetal magnetic resonance imaging showing the grading system of Sutton et al. of brainstem and cerebellar herniation in relation to the foramen magnum (yellow line). A. Grade 0: normal. B. Grade 1: visible fourth ventricle and cisterna magna, without cerebellar displacement below the foramen magnum. The tentorium could be vertically oriented, and tectal beaking could be present. C. Grade 2: visible cisterna magna without displacement of the cerebellum below the foramen magnum. The fourth ventricle is not visible. D. Grade 3: displacement of the cerebellum below the foramen magnum and obliteration of cerebrospinal fluid spaces in the posterior fossa. The tip of the arrow points to the lower limit of the cerebellar tonsils.



FIGURE 8. Pros and cons of open fetal surgery for myelomeningocele compared to postnatal surgery (MOMS and MOMS2)



MOMS: Management of Myelomeningocele Study. MOMS2: Follow-up of the Management of Myelomeningocele Study. VPS: ventriculoperitoneal shunt.

(Data obtained from Adzick et al.,³ Joyeux et al.,⁶⁸ Brock et al.,⁴⁸ Mazzola et al.,⁶ and Houtrow et al.⁵⁰).

POSTNATAL SURGERY OR FETAL SURGERY

It has been demonstrated that intrauterine damage of the nervous system is progressive.⁴⁴ The "two-hit hypothesis" suggests that an initial lesion occurs, the anatomical defect itself, and then a second lesion due to the ongoing exposure of the nervous tissue to amniotic fluid.⁴⁵⁻⁴⁷ Therefore, based on the hypothesis that an early defect closure may be associated with improved postnatal outcomes by reducing exposure of the neural tissue to amniotic fluid for a prolonged time, the concept of prenatal repair was introduced.^{3,44,46}

In 2011, the MOMS trial was published, which compared the outcomes of open prenatal surgery and postnatal surgery.³ The study was ended early due to the clear benefits observed in the prenatal surgery group, which showed, at the 12-month follow-up, a reduction in VPS requirement (40 % in the prenatal versus 82 % in the postnatal surgery group; relative risk [RR] = 0.48; 97.7 % confidence interval [CI]: 0.36-0.64; *p* < 0.001) and, at the 30-month followup, an improved composite outcome of mental development and motor function.³ In addition, it doubled the ability to walk independently (42 % versus 21 %, p < 0.01) and increased the rate of complete reversal of Chiari II (36 % versus 4 %, p < 0.001). Therefore, based on different subsequent series with follow-up until school age,⁴⁸⁻⁵⁰ various societies agree that open fetal surgery for myelomeningocele should be offered as a management option (Figure 8).^{2,4-7}

Both the MOMS and subsequent series recorded significant maternal morbidity, including uterine dehiscence/thinning or rupture (35 % in the MOMS),⁴⁷ not only in the index pregnancy, but also in subsequent ones. An international prospective study showed that the risk for uterine rupture in pregnancies after an open surgery for myelomeningocele was 9.6 % (5/52), with a median gestational age of 28 weeks (26.0-31.5) and 2 fetal deaths included in the 5 uterine rupture cases.^{51,52} In order to reduce such maternal risks, different groups introduced changes in the original surgery, such as a smaller hysterotomy^{53,54} and fetoscopic surgery for myelomeningocele.⁵⁵

FETAL SURGERY FOR MYELOMENINGOCELE a. Inclusion and exclusion criteria

The typical inclusion and exclusion criteria are described in *Table 2*. They experienced some changes after the MOMS publication, such as an increase in the upper limit for gestational age (27-28 weeks) or body mass index (> 35 in the MOMS, then increased to 40), among others.^{41,56} Recent series described that 40-60 % of cases with a prenatal diagnosis of spina bifida would be candidates for fetal surgery.^{57,58}

b. Technical aspects of open fetal surgery

The surgical technique described in the MOMS is an open surgery consisting in laparotomy, uterine exteriorization, large hysterotomy (6-8 cm), exposing the fetus' back for defect closure,

TABLE 2. Inclusion and exclusion criteria of the Management of Myelomeningocele Study (Adzick et al.)³

Inclusion	Exclusion			
Singleton pregnancy	Fetal anomaly unrelated to myelomeningocele			
Maternal age ≥ 18 years	Kyphosis > 30 degrees			
Type of lesion: myelomeningocele or myeloschisis	Increased risk for spontaneous preterm birth (history of preterm birth, short cervix < 20 mm, cerclage) or iatrogenic preterm birth (e.g., uncontrolled HTN, insulin-dependent pregestational diabetes)			
19-25 ⁺⁶ weeks of gestation	Placental abnormalities (placenta previa, suspected adhesion disorder) or uterine abnormalities (e.g., bicornate uterus)			
Lesion location: T1-S1	Body mass index > 35			
Normal karyotype	Maternal alloimmunization			
Chiari II malformation present	Maternal HIV, hepatitis-B or hepatitis-C status positive			
Able to remain close to the treating center	Previous hysterotomy in the active uterine segment Psychosocial limitations			

HTN: arterial hypertension; HIV: human immunodeficiency virus.

and subsequent hysterorrhaphy (*Figure* 9).^{3,56} The defect closure technique is similar to that used in the postnatal period: identification and separation of the neural placode from the surrounding epithelium, dura mater closure, myofascial closure, and skin closure.⁵⁹

After the MOMS, different groups proposed changes in surgical approach. To reduce the complications of hysterotomy, some centers perform a 3-layer, instead of a 2-layer closure.⁶⁰ The concept of "mini-hysterotomy" was introduced, which measured approximately 3 cm or less,^{53,54} and alternative instruments were tested, such as using different types of retractors,⁵³ including a plastic retractor (Alexis).⁶¹ Another change was the use of atosiban as a tocolytic agent, which is not available in the USA, but which has been adopted by several centers because it demonstrated to be a better uterine relaxant than magnesium sulphate, with a better safety profile.⁶²⁻⁶⁴

c. Technical aspects of open fetoscopic surgery

The fetoscopic approach may be percutaneous⁶⁵⁻⁶⁷ or with a laparotomy with uterine exteriorization,^{5,47,55,68} with the use of 2,⁶⁹

3 (*Figure 10*) or 4 ports.⁶⁷ Given that fetoscopic techniques are heterogeneous, and in the absence of a randomized trial like the MOMS, fetoscopic repair is still under study. For the purpose of assessing the performance of different fetoscopic techniques, an international consortium was established, the International Fetoscopic Myelomeningocele Repair Consortium. The Argentine members are Hospital Universitario Austral and Hospital Italiano de Buenos Aires.

SOME FREQUENTLY ASKED QUESTIONS IN RELATION TO PERINATAL PROGNOSIS OF PRENATAL SURGERY FOR MYELOMENINGOCELE

a. Which one is better: open or fetoscopic fetal surgery?

The technique that has been supported by a randomized clinical trial is the open approach, whereas the fetoscopic strategy is still under study, so it is still not possible to answer this question.⁴⁷ There are approximately 50 centers around the world offering fetal surgery for myelomeningocele. Distribution, approach, and outcomes may be observed in an interactive map of the International Society for Prenatal

FIGURE 9. Open fetal surgery for myelomeningocele. a) Four monofilament traction sutures, 2 on each side, through the full thickness of the uterine wall. b-d) Hysterotomy performed to open the membranes, which are fixed with a continuous suture. e-f) Upon administering analgesia and prior fetal paralysis, the fetal defect is exposed and closed by the pediatric neurosurgeon. g) Finally, Ringer's lactate solution is restored with vancomycin to replace lost amniotic fluid and a 2-layer hysterorrhaphy is performed. h) Newborn infant in the reception room; from there, the baby and the mother were taken to the joint hospitalization room.



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Diagnosis (ISPD) (https://ispdhome.org/ISPD/ SIGs/Fetal_Therapy_Map.aspx) (*Figure 11*). In Argentina, 2 centers have been appointed: Hospital Universitario Austral and Hospital Italiano de Buenos Aires.^{64,70} In addition, outside this registry, the surgery is also performed in Centro de Educación Médica e Investigaciones Clínicas (CEMIC), where, in addition, the first ever fetal surgery for myelomeningocele in Argentina was performed in 2001, with the help of Doctor Michael Harrison from the University of San Francisco, California. A fetoscopic approach would appear to be more adequate from a maternal perspective if similar (or better) neuroprotection outcomes were demonstrated compared to the open surgery technique. The percutaneous fetoscopic approach is less invasive, but poses several technical challenges, including a very high rate (30-55 % at < 30 weeks) of premature rupture of membranes (PROM) and a high preterm birth rate, with a gestational age at birth of 32-33 weeks (*Table 3*).⁴⁷ However, the fetoscopic approach with uterine exteriorization shows a PROM rate

FIGURE 10. Fetoscopic surgery for myelomeningocele (posterior placenta). After uterine exteriorization, with the fetus in the desired position, 4 membrane fixation points are established, through which the first port is inserted under ultrasound guidance (a). Then, the amniotic fluid is removed and heated, humidified CO_2 is introduced. b) The second and third ports are inserted under fetoscopic guidance. c) Membranes are irrigated every 15 minutes. d) Neurosurgical time. e) Sutured fetal defect. f) Newborn in the reception room.



FIGURE 11. Map of centers offering prenatal surgery for myelomeningocele around the world (the interactive version can be found in https://ispdhome.org/ISPD/SIGs/Fetal_Therapy_Map.aspx)



similar to that of the open surgery approach (~ 10 % at < 30 weeks), apparently similar neurological outcomes, and an older gestational age at birth than the open approach.⁴⁷ An associated disadvantage is the greater need for neonatal treatment due to a higher rate of skin dehiscence or cerebrospinal fluid leakage through the wound,⁴⁷ although the 3-layer closure, versus single-layer, would reduce such complication (*Table 3*).

b. Is it possible to reduce the risk for premature rupture of membranes?

PROM is the Achilles heel of fetal surgery. In the surgery for myelomeningocele, it is possible to reduce the risk for PROM considering some factors:

• Gestational age at the time of surgery: the risk appears to decrease with a longer gestational age at the time of the procedure. Soni et al.⁷¹

TABLE 3. Characteristics and outcomes of different fetal surgery techniques for myelomeningocele. The numbers are estimations based on studies published by more experienced centers and in reports from conferences, courses or symposiums (adapted from Danzer et al.⁴⁷ and Joyeux et al.).⁷⁶

	Postnatal surgery	Open fetal surgery			Fetoscopic fetal surgery	
Parameter	MOMS Postnatal surgery group ³	MOMS Fetal surgery group ³	Standard hysterotomy ^{3,47,57,74,75,77-82}	Mini- hysterotomy ^{53,61}	Laparotomy- assisted ^{55,69,85}	Percutaneus ^{55,65-67,83,84}
Hysterotomy	-	6-8 cm		2,5-4 cm	2-3 ports	3-4 ports
Access to uterus	-	Scalpel incision			Seldinger technique, catheter 6 Fr-12 Fr	
Layers over placode	ayers over placode 2-3				1-3	1-2
Mode of delivery	Elective C-section				Vaginal delivery allowed	
Surgical outcomes						
Maternal deaths	0	0	0	0	0	0
Perinatal deaths	~ 2 % of neonatal deaths	≈ 0-2 % of intrauterine deaths			≈ 2 % of intrauterine deaths	≈ 2-5 % of intrauterine deaths
PROM < 30 weeks	Not reported	Not reported	≈ 10 %	≈ 2 %	≈ 10 %	30-55 %
GA at birth	37 weeks	34-35 weeks			38 weeks	32-33 weeks
< 37 weeks	15 %	70-80 %		50-80 %	30-90 %	90 %
< 30 weeks	0 %	12-13 %		0-5 %	2-25 %	10-20 %
Uterine thinning or dehiscence	0 %	30-40 %		5 %	0 %	0 %
Neuroprotection outo	comes					
Postnatal lesion treatment required	6 %	13 %	3-7 %	9 %	* 6-36 %	~ 25 %
Improved neonatal motor function	Not reported	Not reported	≈ 55 %	≈ 35 %	70-80 %	55-100 %
Complete reversal of Chiari II at 12 months	4 %	36 %	36 % ≈ 70 %		40-45 %	* 55-95 %
VPS at 12 months	82 %	44 %	≈ 40 %	≈ 40 %	≈ 40 %	30-60 %
^ Ambulation with or without assistance	57 %	71 %	≈ 70 %	Not reported	90 %	70 %

VPS: ventriculoperitoneal shunt; MOMS: Management of Myelomeningocele Study;

PROM: premature rupture of membranes; GA: gestational age.

Some groups perform hysterotomies of 1.5 cm (reported in a symposium and manuscript accepted for publication, Rogelio Cruz Martínez, 2020).

* The group with the most experience in laparotomy-assisted fetal surgery (Texas Children's Hospital) started with a single layer closure and then modified this technique to a 3-layer closure, which reduced the need for postnatal correction of the surgical site and increased the rate of Chiari reversal after 12 months (data reported in the course titled Simulation Training of Fetoscopic Repair of Meningomyelocele, December 14th-15th, 2019, Texas Children's Hospital, Texas, USA).

^ Ambulation at 24-30 months independently or with braces and / or crutches versus no ambulation.

observed a significantly higher PROM rate in open fetal surgery when performed at 20-21 weeks compared to those done after 25 weeks.

• Prevention of chorioamniotic separation: it is one of the main risk factors for preterm birth.^{72,73} Corroenne et al.⁷³ analyzed 91 fetal surgeries (52 fetoscopic and 39 open surgeries) and found a 34 % of chorioamniotic separation, with no differences between both approaches. Patients with chorioamniotic separation had a higher risk for PROM (48 % versus 12 %, p < 0.01) and preterm birth (68 % versus 38 %, p < 0.01), and a significant difference was observed between those that showed chorioamniotic separation before 30 weeks (90 % of preterm births) versus those that occurred after 30 weeks (36 %).⁷³ In fetoscopic surgeries, it is believed that certain aspects, such as membrane dehydration due to the effect of carbon dioxide (CO_2) , could play a role; for this reason, a common practice now is to use humidified CO₂ and hydrate the membranes every 15 minutes (Figure 10) or to separate the membranes during port insertion, so it was proposed to have 4 fixation points of the membranes to the myometrium for each port, instead of 2 (Figure 10).73

c. What are the prognostic factors for VPS requirement in fetuses subjected to prenatal surgery?

Several predictors of VPS requirement in the first year of life have been described.²⁵ The most significant ones are severe preoperative ventriculomegaly (> 15 mm), persistent Chiari II malformation in the FMRI 6 weeks after surgery, and a higher than expected increase in ventricle volume after surgery (*Figure 12*).²⁵

d. Is severe ventriculomegaly a contraindication to fetal surgery?

No. Although no reduction in VPS requirement has been observed in the fetuses with ventriculomegaly > 15 mm subjected to surgery, the benefits in relation to motor function may be maintained.^{25,47,74,75}

CONCLUSIONS

In recent years, the presence of indirect signs of myelomeningocele as a screening method has allowed to increase prenatal detection by making a diagnosis at an earlier gestational age. An optimal management of myelomeningocele patients includes a timely prenatal diagnosis, adequate pre- and postnatal follow-up, and, in selected cases, an optional fetal surgery.

FIGURE 12. MRI and volumetric ventricular 3D reconstruction with intrauterine myelomeningocele repair that did not require and did require VPS. Before surgery, case 1 had mild ventriculomegaly (12 mm), Chiari II malformation, grade 3 (a). b) Six weeks after surgery. Evidence of Chiari resolution and ventricular growth of 3 mL/week. In this case, no VPS was required. However, before surgery, case 2 had severe ventriculomegaly (17 mm), Chiari II malformation, grade 3 (a). Six weeks after surgery (b), evidence of persistent obliteration of CSF spaces of the posterior fossa and ventricular growth of 15 mL/week. In this case, a VPS was placed. VPS: ventriculoperitoneal shunt.



Although traditional open fetal surgery has shown benefits, it is associated with maternal risks that should be taken into consideration. Fetoscopic surgery has fewer maternal risks and is not a contraindication to vaginal delivery; however, fetoscopic techniques vary and outcomes are heterogeneous and still under study. Most likely, in the coming years, more adequate techniques that combine the greatest fetal benefits and the fewest maternal risks will be defined.

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