OBSTETRICS

# Experience of 300 cases of prenatal fetoscopic open spina bifida repair: report of the International Fetoscopic Neural Tube Defect Repair Consortium



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**BACKGROUND:** The multicenter randomized controlled trial Management of Myelomeningocele Study demonstrated that prenatal repair of open spina bifida by hysterotomy, compared with postnatal repair, decreases the need for ventriculoperitoneal shunting and increases the chances of independent ambulation. However, the hysterotomy approach is associated with risks that are inherent to the uterine incision. Fetal surgeons from around the world embarked on fetoscopic open spina bifida repair aiming to reduce maternal and fetal/neonatal risks while preserving the neurologic benefits of in utero surgery to the child.

**OBJECTIVE:** This study aimed to report the main obstetrical, perinatal, and neurosurgical outcomes in the first 12 months of life of children undergoing prenatal fetoscopic repair of open spina bifida included in an international registry and to compare these with the results reported in the Management of Myelomeningocele Study and in a subsequent large cohort of patients who received an open fetal surgery repair.

**STUDY DESIGN:** All known centers performing fetoscopic spina bifida repair were contacted and invited to participate in a Fetoscopic Myelomeningocele Repair Consortium and enroll their patients in a registry. Patient data entered into this fetoscopic registry were analyzed for this report. Fisher exact test was performed for comparison of categorical variables in the registry with both the Management of Myelomeningocele Study and a post—Management of Myelomeningocele Study cohort. Binary logistic regression analyses were used to assess the registry data for predictors of preterm birth at <30 weeks' gestation, preterm premature rupture of membranes, and need for postnatal cerebrospinal fluid diversion in the fetoscopic registry.

**RESULTS:** There were 300 patients in the fetoscopic registry, 78 in the Management of Myelomeningocele Study, and 100 in the post—Management of Myelomeningocele Study cohort. The 3 data sets showed similar anatomic levels of the spinal lesion, mean gestational age at delivery, distribution of motor function compared with upper anatomic level of the lesion in the neonates, and perinatal death. In the Management of Myelomeningocele Study (26.16±1.6 weeks) and post—Management of Myelomeningocele Study cohort (23.3 [20.2—25.6] weeks), compared with the fetoscopic registry group (23.6±1.4 weeks), the gestational age at surgery was lower (comparing fetoscopic repair group with the Management of Myelomeningocele Study; $P<.01$). After open fetal surgery, all patients were delivered by cesarean delivery, whereas in the fetoscopic registry approximately one-third were delivered vaginally ($P<.01$). At cesarean delivery, areas of dehiscence or thinning in the scar were observed in 34% of cases in the Management of Myelomeningocele Study, in 49% in the post—Management of Myelomeningocele Study cohort, and in 0% in the fetoscopic registry ($P<.01$ for both comparisons). At 12 months of age, there was no significant difference in the number of patients requiring treatment for hydrocephalus between those in the fetoscopic registry and the Management of Myelomeningocele Study.

**CONCLUSION:** Prenatal and postnatal outcomes up to 12 months of age after prenatal fetoscopic and open fetal surgery repair of open spina bifida are similar. Fetoscopic repair allows for having a vaginal delivery and eliminates the risk of uterine scar dehiscence, therefore protecting subsequent pregnancies of unnecessary maternal and fetal risks.

**Key words:** fetal intervention, fetal surgery, fetoscopic repair, hydrocephalus, MOMS, myelomeningocele, myeloschisis, neural tube defect, open spina bifida, registry

## Introduction

The multicenter randomized controlled trial Management of Myelomeningocele Study (MOMS) demonstrated that prenatal repair of open spina bifida (OSB) by hysterotomy, compared with postnatal repair, decreases the need for ventriculoperitoneal shunting and increases the chances of independent ambulation.[1] A subsequent large study[2] from the main center that participated in MOMS showed that open hysterotomy repair of fetal OSB is a reproducible technique and proved that many of the advantages reported by MOMS were also observed in nonexperimental settings. However, the hysterotomy approach is associated with risks that are inherent to the uterine incision, including an increased risk of uterine dehiscence and rupture for the index and all future pregnancies.[1–5] A study by Goodnight et al[3] reported a 10% risk of uterine rupture in the subsequent pregnancy, which occurred between 26 and 32 weeks' gestation and resulted in fetal

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## AJOG at a Glance

### Why was this study conducted?

This study aimed to report short-term outcomes of prenatal fetoscopic open spina bifida (OSB) repair and compare these with data from open fetal surgery repair.

### Key findings

The data sets of the fetoscopic registry, Management of Myelomeningocele Study (MOMS), and a post-MOMS cohorts were similar in terms of the distribution of the anatomic level of the spinal lesion, mean gestational age at delivery, distribution of neonatal motor function compared with upper anatomic level of the lesion, perinatal death, and the rate of treatment of hydrocephalus by 12 months of age. In the open fetal surgery OSB repair, all patients were delivered by cesarean delivery, whereas in the fetoscopic registry approximately one-third delivered vaginally and areas of dehiscence or thinning of the uterine scar were observed in 34% to 49% vs 0% of cases, respectively.

### What does this add to what is known?

Prenatal and postnatal outcomes up to 12 months of age after prenatal fetoscopic and the MOMS open fetal surgery spina bifida repair are similar.

demise in 2 of 5 cases. For this reason, fetal surgeons worldwide have started approaching fetal OSB repair using minimally invasive techniques. The development of fetoscopic spina bifida repair in humans was preceded by extensive animal model experimentation to prove its feasibility, safety, and neurologic benefits.[6–14] The objective has been to reduce maternal and fetal/neonatal risks while at the same time preserving the neurologic benefits to the child.[15–20] Nevertheless, some of the complications reported in the MOMS, such as preterm premature rupture of membranes (PPROM) and preterm birth, are also observed with fetoscopic OSB repair.[15–21]

In an attempt to move the field forward and understand which component of each technique is more beneficial in improving outcomes, the International Fetoscopic Myelomeningocele Repair Consortium was created in 2018.[21] Participants agreed in writing to transparently and collaboratively work together to provide accurate and complete data to a common registry.

This study of registry data aimed, first, to examine the main obstetrical, perinatal, and neurosurgical outcomes up to 12 months of age and, second, to compare these outcomes with those seen after open fetal surgery repair as reported in the MOMS[1] and in a large post-MOMS cohort.[2]

## Methods

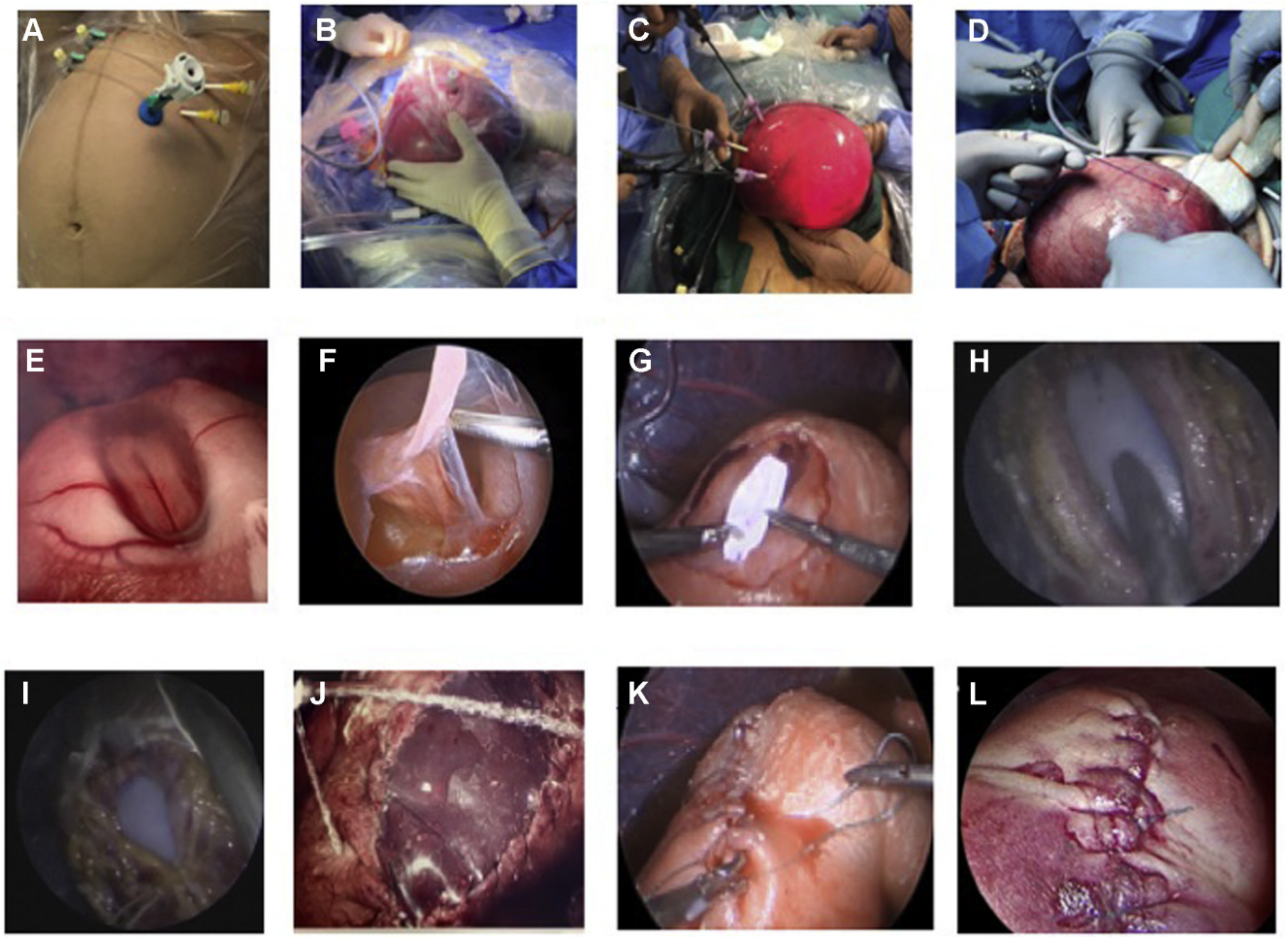
A prospective observational registry was created by the International Fetoscopic Neural Tube Defect Repair Consortium to track maternal, neonatal, perinatal, and neurosurgical outcomes after fetoscopic OSB repairs.[21]

At the time of the inception of this Consortium, all known centers performing fetoscopic spina bifida repair were contacted and invited to participate. All of the partaking centers enrolling patients in this registry needed to fulfill all of the inclusion and none of the exclusion criteria established by the group.[21] All centers required confirmed normal genetic testing, no associated major structural anomalies, singleton pregnancies, no maternal chronic medical conditions, and no history of preterm birth attributable to preterm labor as part of the eligibility criteria for prenatal repair. The inclusion criteria were OSB defects with the upper level of the anatomic lesion at T1 to S1. There is one case included in this cohort with an anatomic level of the lesion at S2 that presented with ventriculomegaly and Chiari II malformation. Patient data introduced in the fetoscopic registry from those centers that had completed the necessary steps to be part of the Consortium by December 2019 were collected and analyzed for this report. All patients that were taken to the operating room to undergo fetoscopic repair were included in the registry. Proceedings of the first annual meeting of the Consortium have been previously published.[21]

The registry received an institutional review board (IRB) approval from Baylor College of Medicine as the coordinating center, and individual centers obtained IRB approval for their respective boards for prospective observation of consenting patients. Retrospective data were obtained from prenatal and delivery records of the mother and the neonatal records of the infant. Data were collected from each center and were entered into a combined deidentified data set using REDCap. Centers participating in the fetoscopic registry obtained executed data user agreements. Data were analyzed using REDCap electronic data capture tools hosted by the Texas Children's Hospital, Houston, Texas. The investigators analyzing the deidentified data were blinded to the clinical sites, and data were analyzed collectively at all times. The data used for this analysis include patients who began evaluation for prenatal neural tube defect repair in May of 2013 and were last accessed on December 31, 2019; however, if there were any ongoing pregnancies from this group of patients, pregnancy outcomes were requested during the composition of this manuscript until May 2020. Similarly, if there were any infants who were already enrolled in the fetoscopic registry and turned 12 months of age during that same period, information on their outcomes was requested from the principal investigators.

The following data in the fetoscopic registry were used for this publication: first, maternal demographic characteristics, including age, body mass index, racial origin and parity; second, findings of ultrasound and magnetic resonance imaging (MRI) before surgery, including anatomic level of the lesion, defined as the level of the upper bony spinal defect as seen by ultrasound, diameter of the

FIGURE 1
**Fully percutaneous approach for the fetoscopic repair of OSB**




**A,** Four trocars placed in a case of an anterior placenta. **B,** Exteriorized uterus with 2 trocars placed in a laparotomy-assisted repair. **C,** Three trocars placed in the uterus in a laparotomy-assisted fetoscopic OSB repair. **D,** Stitches are placed in the uterus to plicate the membranes before trocar placement at a laparotomy-assisted fetoscopic OSB repair. **E,** Visualization of the fetal spinal defect (myeloschisis) in utero. **F,** Dissection of the placode in a case of a myelomeningocele. **G,** Introduction of a bovine collagen patch inside of the uterus to be placed on top of the dura. **H,** Appearance of the patch once it is placed on top of the dura. Myofascial flaps are seen on both sides of the dissected defect. **I,** Myofascial flaps are sutured with interrupted stitches. **J,** Large defect that is closed with a skin substitute. **K,** Running stitches are used to close skin. **L,** Appearance of sutured skin once the defect repair is completed.

*OSB*, open spina bifida.

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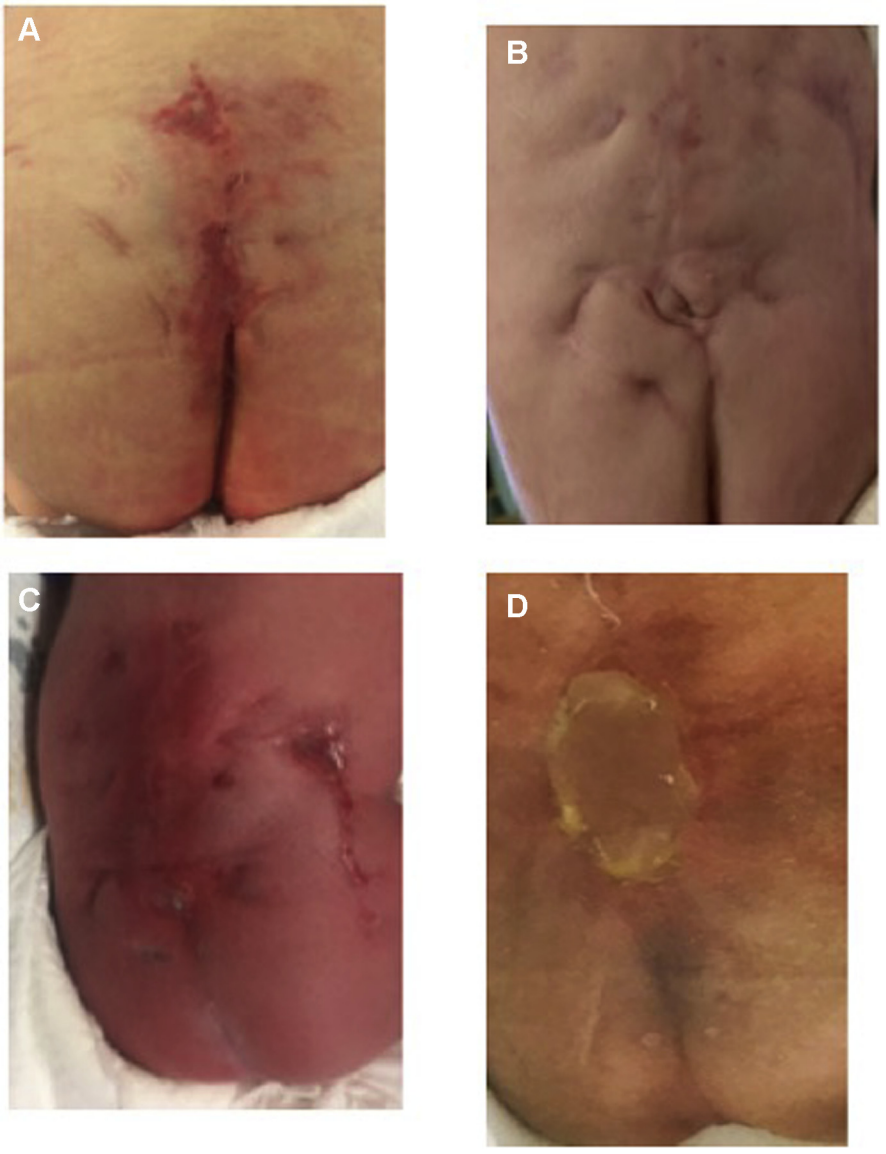
lateral cerebral ventricles to determine whether there was ventriculomegaly as defined by the largest ventricle of ≥10 mm or severe ventriculomegaly as defined by the largest ventricle of >15 mm, presence or absence of clubbed feet, placental location, and cervical length; third, surgical details, including gestational age at surgery, surgical approach (percutaneous or laparotomy-assisted) (Figure 1), duration of surgery (skin to skin), and intraoperative fetal bradycardia requiring resuscitation; fourth, postoperative outcomes, including maternal pulmonary edema, maternal blood transfusion, placental abruption, chorioamniotic membrane separation (defined as floating membranes inside the uterine cavity in any of the follow-up scans up until the time of delivery), oligohydramnios (defined as an amniotic fluid index of <5 cm from the time of surgery to delivery), PPROM, and failure of postoperative hindbrain herniation reversal; fifth, delivery and findings at cesarean delivery, including gestational age at birth, method of delivery, birthweight, gender, and status of the port-insertion site scars visualized at the time of the cesarean delivery (described as intact or well healed, thinned, or dehiscent); sixth, neonatal findings after birth, including dehiscence at the spinal

FIGURE 2
**Appearance of the repaired spinal defect at the time of birth**




**A** and **B,** Skin repair after using interrupted stitches. **C,** Skin repair using interrupted stitches and a relaxing incision. **D,** Skin repair performed by using bilaminar artificial skin (Nevelia), this approach is used in some centers when direct skin approximation is not possible.

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repair site (Figure 2), and the difference between upper anatomic level of the lesion and motor function (expressed as the highest myotome from both lower extremities with motor function) observed at birth classified as ≥2 levels better, 1 level better, same, 1 level worse, or ≥2 levels worse; seventh, neonatal complications, including perinatal death (defined as fetal demise or death during the first 30 days of life), periventricular leukomalacia, respiratory distress syndrome, sepsis, necrotizing enterocolitis, patent ductus arteriosus that required intervention, and retinopathy; and eighth, neonatal and infant outcomes up to and including 12 months of age, including death before hydrocephalus treatment (either ventriculoperitoneal shunt or endoscopic third ventriculostomy [ETV] with or without choroid plexus cauterization) and the need for hydrocephalus treatment by 12 months of age.

### Statistical methods

Results from quantitative variables were expressed as mean (standard deviation) if they had a normal distribution, as assessed by Kolmogorov-Smirnov test, and as median (range) if they had a nonnormal distribution. Fisher exact test was performed for comparisons of categorical variables in the fetoscopic registry with the MOMS[1] and a post-MOMS cohort.[2] Continuous data could not be compared because we did not have access to the individual values from the MOMS and post-MOMS cohort of 100 patients treated with open fetal surgery fetal OSB repair[2] except when expressed as mean±standard deviation.

Data analysis was performed using the Statistical Package for Social Sciences, version 21.0 (IBM Corporation, Armonk, NY).

## Results

### Outcome of the cases in the fetoscopic registry

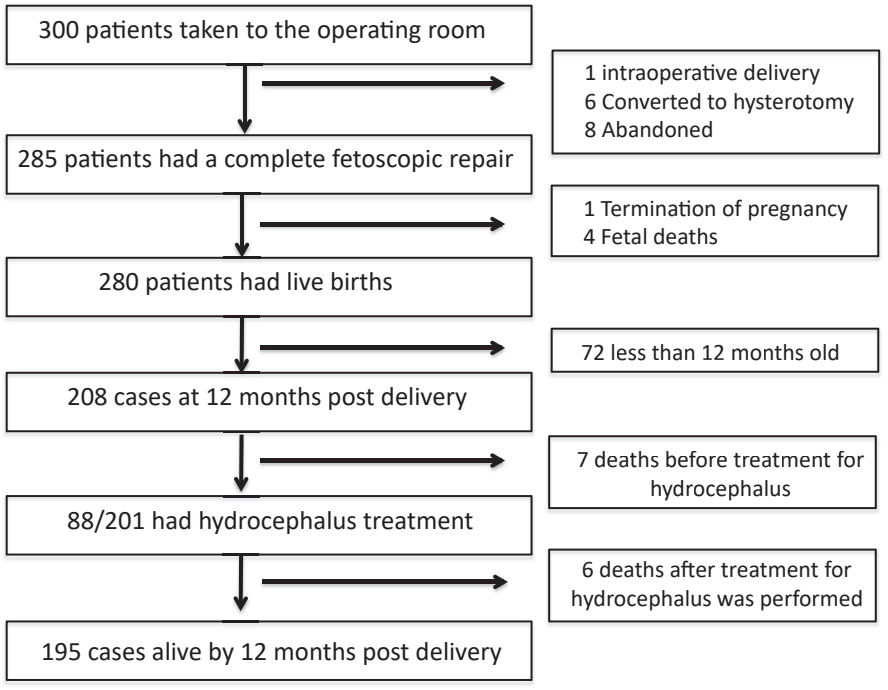
At the time of analysis, there were a total of 300 eligible patients who underwent an attempted fetoscopic repair. These cases were provided by 14 centers from the United States, Brazil, Spain, Mexico, Israel, Poland, Italy, Argentina, Chile, South Africa, and England. Most surgeries (65%) were performed at 2 hospitals (Hospital Israelita Albert Einstein, São Paulo, Brazil [n=118], and Texas Children's Hospital, Houston, TX [n=78]) with the remaining 104 operations occurring at 12 centers that each performed between 1 and 22 operations. No patients taken to the operating room for a possible fetoscopic repair were excluded from the analysis.

Of the 300 patients intended for fetoscopic spina bifida repair (Figure 3), 285 patients (95.0%) had successful completion of surgery; 1 case was delivered intraoperatively for fetal bradycardia unresponsive to in utero resuscitation, 6 were converted to a hysterotomy repair because the lesion was considered to be too large for fetoscopic closure, and in 8 cases surgery was abandoned: in 2 cases, because of the

detection of closed neural tube defects at the time of visual inspection through the fetoscope (n=2). In 6 cases, there was fetal intolerance to the procedure (n=6): 2 had bradycardia before trocar placement at the time of fetal positioning—one required cesarean delivery at that time and another was found to be demised within 24 hours with suspected placental abruption (n=2). In 2 cases (n=2), port displacement occurred right after their insertion, fetal bradycardia was observed and the cases were abandoned, and one resulted in demise 5 days later. In 2 cases, fetal bradycardia presented after trocar insertion (n=2), and one of these patients had a suspected maternal gas embolism with a cesarean delivery at that time.

In the 285 patients who had a completed fetoscopic repair, there were 4 fetal deaths and 1 termination of pregnancy at the request of the parents, leaving a total of 280 live births. At the time of data analysis, 72 of the 280 live births were younger than 12 months of age. Thus, results of the 1-year outcomes were based on 208 cases (71.8%). In 7 of the 208 (3.4%) with 1-year follow-up, there was death before any hydrocephalus treatment was performed; in the remaining 201 cases, 88 cases (43.8%) required either ventriculoperitoneal shunt insertion or an ETV. Notably, 6 children died after hydrocephalus treatment during the first year of life. In 12 of the 13 cases of postnatal death, the cause was sepsis, related to meningoencephalitis or shunt infection, and in 1 case, it was pneumonia. There were no maternal deaths.

FIGURE 3
**Flowchart**




Flowchart of the patients enrolled included in the registry.

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## Comparison of data in the fetoscopic registry with those in the Management of Myelomeningocele Study and post–Management of Myelomeningocele Study cohort

The data from the registry and those from the MOMS post-MOMS cohort are summarized in Tables 1 and 2.[1,2] The 3 data sets were similar in maternal age and body mass index. In the MOMS, 94% of patients were of White racial origin, compared with 64% in the fetoscopic group ($P<.01$). The 3 data sets were similar in imaging findings before surgery, including the distribution of the anatomic level of the lesion and incidence of clubfeet. Cervical length was significantly longer in the MOMS group (38.9±7.3 mm) than in the fetoscopic Consortium registry (37.0±6.0 mm; $P=.036$). Fetal surgery was undertaken at an earlier gestational age in the MOMS and post-MOMS cohort (23.6±1.4 weeks and 23.3 [20.2–25.6] weeks, respectively) than in the fetoscopic registry (mean, 26.2±1.4 weeks; median, 25.9 [22.7–31.6] weeks; $P<.01$ compared with MOMS). In the MOMS and post-MOMS cohort, all fetal repairs were performed through a hysterotomy, whereas in the fetoscopic registry the repair was entirely percutaneous in 55% of cases and laparotomy-assisted in 45%. The incidence of intraoperative fetal bradycardia requiring resuscitation was 6-fold higher in the MOMS than in the fetoscopic registry ($P<.01$). However, differing intraoperative fetal monitoring regimens makes comparison difficult, because the open technique allows for more continuous fetal heart rate monitoring, whereas continuous ultrasound monitoring is not always possible during the fetoscopic spina bifida repair, especially if there is gas in the maternal abdomen. The duration of fetoscopic surgery was on average 2.6 times longer than in the post-MOMS cohort; in the MOMS, the duration of surgery was not reported.

Postoperatively, the incidence rates of pulmonary edema, placental abruption, chorioamniotic membrane separation, oligohydramnios, and PPROM were not significantly different between the fetoscopic registry and the MOMS. However, the need for maternal blood transfusion after delivery was 3.5-fold higher in the MOMS group. In the post-MOMS cohort, the incidence rates of placental abruption ($P=.02$), chorioamniotic membrane separation ($P=.01$), oligohydramnios ($P<.01$), and PPROM ($P<.01$) were lower than in the fetoscopic registry. A total of 180 of the fetoscopic cases underwent a fetal MRI

**TABLE 1**
**Maternal demographics, characteristics of the lesion, and surgical and postsurgical variables—comparison between data from this study and those from the MOMS[1] and a post-MOMS cohort[2]**

| Variable | This study (N=300) | MOMS (N=78) | *P* value[a] | Post-MOMS (N=100) | *P* value[a] |
|---|---|---|---|---|---|
| Maternal demographics | | | | | |
| Age, y | 30.4 (16–45)<br>30.4±5.54 | 29.3±5.3 | .11 | 29.7 (18–41) | — |
| Body mass index, kg/m$^2$ | 26.1 (18–42)<br>26.86±4.47 | 26.2±3.7 | .18 | 26.3 (18.7–35) | — |
| Racial origin: | | | | | |
| White | 109 (36.3) | 73 (93.6) | <.001 | 88 (88) | <.001 |
| Asian | 4 (1.3) | — | | 1 (1.0) | |
| Black | 5 (1.7) | 1 (1.3) | | 4 (4.0) | |
| Mixed | 103 (34.3) | — | | — | |
| Hispanic | 79 (26.3) | 2 (2.6) | | 6 (6.0) | |
| Other | — | 2 (2.6) | | 1(1.0) | |
| Parity: nulliparous | 131 (43.7) | 33 (42.3) | .898 | 35 (35.0) | .160 |
| Findings of presurgical imaging | | | | | |
| Type of spinal lesion: myeloschisis | 94 (31.3) | — | — | 33 (33.0) | .804 |
| Anatomic level of the lesion: | | | | | |
| L3 or lower | 233 (77.7) | 53 (67.9) | .078 | 73 (73.0) | .343 |
| Thoracic | 15 (5) | 4 (5.1) | 1.000 | 6 (6.0) | .802 |
| L1–L2 | 52 (17.3) | 21 (26.9) | .075 | 21 (21.0) | .455 |
| L3–L4 | 133 (44.3) | 30 (38.5) | .372 | 66 (66.0) | .0002 |
| L5–S1[b] | 100 (33.3) | 23 (29.5) | .588 | 7 (7.0) | <.0001 |
| Mean ventricular width of largest ventricle, mm | 12 (5.6–31.5)<br>12.8±4.36 | — | — | 10.0 (4–18) | — |
| Club feet | 50 (16.7) | 20 (25.6) | .074 | 15 (15.0) | .756 |
| Placental location: anterior | 138 (46.0) | 36 (46.2) | 1.000 | 46 (46.0) | 1.000 |
| Cervical length before surgery, mm | 37.0±6.0 | 38.9±7.3 | .036 | — | — |
| Surgical details | | | | | |
| Gestational age at surgery, wk | 25.9 (22.7–31.6)<br>26.16±1.6 (N=300) | 23.6±1.4 | <.01 | 23.3 (20.2–25.6) | — |
| Type of technique | | | | | |
| Hysterotomy | — | 78 (100) | <.0001 | 100 (100) | <.0001 |
| Percutaneous | 165 (55.0) | — | <.0001 | — | <.0001 |
| Laparotomy assisted | 135 (45.0) | — | <.0001 | — | <.0001 |
| Duration of surgery (skin to skin), min | 204 (72–458)<br>217.5±84.17 | — | — | 78.5 (54–106) | — |
| Intraoperative fetal bradycardia requiring resuscitation | 5 (1.7) | 8 (10.3) | .001 | 5 (5.0) | .130 |
| Postoperative complications | | | | | |
| Maternal hospital length of stay, d | 4.0 (2–54)<br>5.75±6.38 | — | — | 4.2 (3–8) | — |
| Maternal pulmonary edema | 15/300 (5.0) | 5 (6.4) | .577 | 2 (2.0) | .260 |
| Maternal blood transfusion | 9/300 (3) | — | — | 1/100 (1) | .46 |

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*(continued)*

**TABLE 1**
**Maternal demographics, characteristics of the lesion, and surgical and postsurgical variables—comparison between data from this study and those from the MOMS[1] and a post-MOMS cohort[2]** *(continued)*

| Variable | This study (N=300) | MOMS (N=78) | *P* value[a] | Post-MOMS (N=100) | *P* value[a] |
|---|---|---|---|---|---|
| Placental abruption | 25/280 (8.9) | 5 (6.4) | .645 | 2/96 (2.1) | .022 |
| Chorioamniotic membrane separation | 72/190 (37.9) | 20 (25.6) | .066 | 22/96 (22.9) | .012 |
| Oligohydramnios | 53/267 (19.9) | 16 (20.5) | .874 | 6/96 (6.3) | .001 |
| Preterm premature rupture of membranes[c] | 153/280 (54.6) | 36 (46.2) | .201 | 31/96 (32.3) | .0002 |

Values are expressed as mean±standard deviation, if data were normally distributed, and as median (range), if nonnormally distributed, or as ratio (percentage), as appropriate.

*MOMS*, Management of Myelomeningocele Study.

[a] Comparisons of categorical variables were performed by the Fisher exact test; [b] One case had an S2 anatomic level of the lesion; [c] Preterm premature rupture of membranes was defined as any vaginal leakage of fluid occurring at <37 weeks with positive Nitrazine test.

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scan after the fetoscopic repair, and hindbrain herniation reversal (including partial and complete) was seen in 153 of the cases (85%).

The mean gestational age at delivery was 34 weeks in all 3 data sets, and there were no significant differences between the groups in the incidence of delivery at ≥37 or <30 weeks' gestation. In the MOMS and the post-MOMS cohort, all patients were delivered by cesarean delivery, whereas in the fetoscopic registry approximately one-third of the patients delivered vaginally ($P<.01$ for both comparisons). At the time of cesarean delivery, areas of dehiscence, or thinning of the hysterotomy scar, were observed in 34.2% of cases included in the MOMS and in 49.4% of the post-MOMS cohort. None of the cases who had a cesarean delivery and the appearance of the trocar site scars was included in the operative report (N=162) in the fetoscopic registry showed any areas of thinning or dehiscence ($P<.01$ for both comparisons). One of the patients in the registry had a hysterectomy 10 days after her fifth cesarean delivery, performed at 32 weeks (7 weeks after fetoscopic repair) owing to nonresponsive uterine bleeding.

At birth, there were no significant differences between the 3 groups in the distribution of motor function compared with upper anatomic level of the lesion. The incidence of dehiscence at the spinal repair site was significantly lower in the post-MOMS cohort (3.6%) than in the fetoscopic registry (20.1%; $P<.01$). There were no significant differences among the 3 groups in the rates of perinatal death and necrotizing enterocolitis (Table 2). The incidence of respiratory distress syndrome was significantly lower in the fetoscopic registry (25.2%) than in the post-MOMS (51.8%; $P<.01$). There were no significant differences in the rates of periventricular leukomalacia, sepsis, necrotizing enterocolitis, and patent ductus arteriosus that required intervention between the fetoscopic registry and MOMS. The incidence of retinopathy was significantly higher in the fetoscopic surgery group (6.4%) than in the MOMS (0%, $P=.016$).

Outcomes observed by 12 months of age showed that there were no significant differences between the fetoscopic registry cohort and the MOMS cohort in terms of the rates of death before treatment for hydrocephalus and treatment of hydrocephalus; the post-MOMS cohort did not report these rates because that study is limited to the neonatal period.

## Comment

### Principal findings

The data sets of the fetoscopic registry, MOMS,[1] and post-MOMS cohort[2] were similar in terms of the distribution of the anatomic level of the spinal lesion, mean gestational age at delivery, distribution of motor function compared with upper anatomic level of the lesion in the neonates, and perinatal death. The fetoscopic registry and MOMS were also similar for most postoperative complications and most adverse neonatal outcomes. However, the incidence of many of these complications was lower in the post-MOMS cohort indicating an improvement in outcome in cumulative experience. It should be emphasized that many of the cases included in the fetoscopic cohort represent the initial and early experience of the various centers, whereas the MOMS and particularly the post-MOMS cohort represent cases from experienced centers well beyond their initial learning curve.

### Results and clinical implications

In the MOMS[1] and post-MOMS cohort,[2] compared with the fetoscopic registry, the gestational age at surgery was lower (23 vs 26 weeks). Although the incidence of intraoperative fetal bradycardia requiring resuscitation was 6-fold higher in the MOMS than in the fetoscopic registry, this difference was insignificant compared with the post-MOMS cohort. After fetal surgery through a hysterotomy, all patients were delivered by cesarean delivery, whereas in the fetoscopic registry approximately one-third delivered vaginally. At the time of cesarean delivery, areas of dehiscence or thinning in the scar were observed in 34% of cases in the MOMS, in 49% in the post-MOMS cohort, and in 0% in the fetoscopic registry. At 12

**TABLE 2**
**Delivery, perinatal outcomes, motor function at birth, and neurosurgical outcomes during the first year of life—comparison between data from this study and those from the MOMS[1] and a post-MOMS cohort[2]**

| Variable | This study (N=300) | MOMS (N=78) | *P* value[a] | Post-MOMS (N=100) | *P* value[a] |
|---|---|---|---|---|---|
| Delivery and findings at cesarean delivery | | | | | |
| Gestational age at delivery, wk | 34.3±3.6 | 34.1±3.1 | .63 | 34.3 (22.2–37.4) | — |
| Delivery at ≥37 wk | 79/280 (28.2) | 16 (20.5) | .194 | 26/96 (27.1) | .896 |
| Delivery at <30 wk | 38/280 (13.6) | 10 (12.8) | 1.000 | 9/96 (9.4) | .371 |
| Birthweight, g | 2270 (810–4435) 2289.93±771.74 | 2383±688 | .3 | 2416 (501–3636) | — |
| Cesarean delivery | 192:280 (68.6) | 78 (100) | <.0001 | 96:96 (100) | <.0001 |
| Status of hysterotomy scar (open) and port site scar | | | | | |
| (fetoscopic) at cesarean delivery: | | | | | |
| Intact, well healed | 162/162[b] (100) | 49/76 (64.5) | .0008 | 44/87 (50.6) | <.0001 |
| Thinning | 0/162 (0.0) | 19/76 (25.0) | <.0001 | 36/87 (41.4) | <.0001 |
| Area of dehiscence | 0/162 (0.0) | 7/76 (9.2) | .0001 | 7/87 (8.0) | .0002 |
| Findings at birth | | | | | |
| Dehiscence at spinal repair site | 56/279 (20.1) | 10/77 (13.0) | .186 | 3/83 (3.6) | .0001 |
| Motor function compared with upper anatomic level of the lesion: | | | | | |
| ≥2 levels better | 98/257 (38.1) | 20/62 (32.3) | .464 | 24/80 (30.0) | .231 |
| 1 level better | 63/257 (24.5) | 7/62 (11.3) | .007 | 20/80 (25.0) | 1.000 |
| Same | 49/257 (19.1) | 14/62 (22.6) | .594 | 26/80 (32.5) | .014 |
| 1 level worse | 35/257 (13.6) | 13/62 (21.0) | .166 | 9/80 (11.3) | .705 |
| ≥2 levels worse | 12/257 (4.7) | 8/62 (12.9) | .035 | 1/80 (1.3) | .315 |
| Neonatal complications | | | | | |
| Length of stay in neonatal intensive care unit, d | 17.0 (0–253) | — | — | 24.5 (3–133) | — |
| Perinatal death[c] | 9/280 (3.2) | 2 (2.6) | 1.000 | 6/98 (6.1) | .231 |
| Periventricular leukomalacia | 8/258 (3.1) | 4/77 (5.2) | .482 | — | — |
| Respiratory distress syndrome | 40/159 (25.2) | 16/77 (20.8) | .516 | 43/83 (51.8) | <.0001 |
| Sepsis | 25/276 (9.1) | 4/77 (5.2) | .352 | — | — |
| Necrotizing enterocolitis | 8/273 (2.9) | 1/77 (1.3) | .690 | 1/83 (1.2) | .691 |
| Patent ductus arteriosus | 14/276 (5.1) | 3/77 (3.9) | 1.000 | — | — |
| Retinopathy | 16/250 (6.4) | 0 (0.0) | .016 | — | — |
| Outcomes at 12 mo | | | | | |
| Death before shunt placement or ETV | 7/208 (3.4) | 2/78 (2.6) | 1.000 | — | — |
| Hydrocephalus treated by shunt or ETV | 88/201 (43.8) | 31/76 (40.8) | .591 | — | — |

Values are expressed as mean±standard deviation, if data were normally distributed, and as median (range), if nonnormally distributed, or as ratio (percentage), as appropriate.

*ETV*, endoscopic third ventriculostomy; *MOMS*, Management of Myelomeningocele Study.

[a] Comparisons of categorical variables were performed by the Fisher exact test; [b] Only 162 of 192 cases who had a cesarean delivery had in their surgical report information about the status of the uterine port site scars; [c] Perinatal death includes 5 neonatal deaths (5/277 [1.8%]) and 4 fetal demises (4/284 [1.4%]).

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months of age, there were no significant differences in the rates of treatment of hydrocephalus between the fetoscopic registry and MOMS[1]; this outcome was not reported in the post-MOMS cohort[2]

There are 2 reasons why the mean gestational age at surgery in the fetoscopy group is higher than that in MOMS[1] and post-MOMS cohort.[2] First, some centers deliberately performed the surgery at a later gestational age to

improve viability in the event of delivery soon after surgery. A second reason was that, in some countries, late diagnosis of OSB is common because routine fetal anomaly screening programs are not well established. Despite such delayed surgery, there was no apparent adverse effect on neurologic outcome, reflected in motor function in the neonates and the need for treatment of hydrocephalus at 12 months of age. In the evaluation of motor function preservation, it may be more accurate to compare fetal motor function before surgery with physical evaluation at birth rather than motor function at birth to the upper anatomic level of the lesion[22,23]; however, in this study, we used the latter because our goal was to compare with the MOMS where the prenatal evaluation of motor level was not performed.

The duration of surgery was 2.6 times longer for fetoscopic than open fetal surgery repairs. This is likely attributable to the time required for port placement and the increased technical demands of a minimally invasive spinal repair (performed using a multilayer approach in most of the cases) compared with open hysterotomy. In addition, because all cases performed in each of the participating centers were included in this registry, the learning curves are captured in the data. In MOMS and particularly in the post-MOMS reports, the centers were already proficient at performing the open hysterotomy OSB repairs, thus limiting the comparability of the data. Nevertheless, we acknowledge that even once the teams become experienced in performing fetoscopic repairs, these surgeries will undoubtedly be longer given the preparation time and minimally invasive nature of the surgeries.

The lack of areas of dehiscence or thinning of the uterine scar in patients who had fetoscopic surgery compared with the open fetal surgery approach is an important advantage of fetoscopic surgery. It is well established that once an open hysterotomy is performed, a cesarean delivery at no later than 37 weeks is indicated in the index pregnancy and in all subsequent pregnancies to reduce the risk of uterine rupture.[24] Recent evidence shows that 10% of subsequent pregnancies develop uterine rupture and even fetal death after a hysterotomy based repair.[3] By avoiding the spectrum of complications that can occur from the initial hysterotomy, both the index and subsequent pregnancies incur lower obstetrical risks, which is a major benefit particularly for women in lower resource settings. Patients who underwent a fetoscopic repair should be able to carry subsequent pregnancies without complications, given the small sized trocars used and the lack of any area of dehiscence seen in the index pregnancy.

## Research implications

Clearly, the ideal approach to compare fetoscopic and open fetal surgery fetal OSB repair for risks and benefits is with a randomized controlled trial. However, such a trial is unlikely to take place for a number of practical reasons. First, many new centers do not offer the open fetal surgery method, and some of those that currently do have the option report that the patients almost always choose the fetoscopic approach. Second, the costs of such a trial would be prohibitive. Finally, the current diverse methodologies used in both open fetal surgery and fetoscopic approaches would need to be standardized, and the difficulties with achieving and monitoring such standardized methods across multiple systems and countries would be prodigious. Thus, we are left with a comparison of the results from a fetoscopic registry with those of the MOMS (the most robust and accepted study regarding prenatal OSB repair), which, while being completely different in methodology and level of evidence, may be our most practical approach. The data presented from this registry suggest a lack of equipoise that one approach is superior in terms of fetal outcome. However, the fetoscopic approach is superior in terms of maternal complications.

## Strengths and limitations

The main strengths of the study are as follows: (1) the comparison of outcome data from a large number of patients reported in the fetoscopic registry with those of open fetal surgery and such large study population can increase the power to detect potentially important low frequency outcomes; (2) standardized operational definitions; (3) standardized outcome metrics; and (4) different neurosurgical repair fetoscopic techniques which will provide insights on the pros and cons of each specific type of fetal repair.

There are several limitations of the study. First, in contrast to the MOMS and post-MOMS cohorts, which employed standardized surgical technique and prospective collection of data, there is the risk of significant selection bias. This bias is inherent and cannot be adjusted for because the retrospective design and data reporting from multiple centers with heterogeneous infrastructure, academic affiliation, and stage in their learning curve (varying from >100 to <5 procedures). Second, in the fetoscopic centers, there were significant differences in uterine access (percutaneous vs laparotomy-assisted), choice of instruments, number of access ports, use of membrane plication, use of humidified or warmed $CO_2$, and different neurosurgical approaches for repair of the spinal lesion, including the use and type of dural substitute patch, myofascial flap closure, and type of skin closure. For example, in 189 of the fetoscopic cases (63%), a $CO_2$ heater and humidifier device were used during uterine insufflation. We did not attempt to determine which of the fetoscopic methods is superior because patient numbers within some of the different methods were too small for valid conclusions to be drawn. Despite this limitation, the finding that the combined data for most outcome measures were not significantly different from those in the MOMS is encouraging. Third, some of the variables collected in the fetoscopic registry, such as the rate of oligohydramnios and chorioamniotic separation, are susceptible to underreporting bias because their diagnosis depends on the number of ultrasound scans performed after surgery, which varied among centers. Similarly, the information collected on the integrity of the

uterine scar at delivery was only obtained from those cases delivered by cesarean delivery, and the reporting method was based on a subjective impression at the time of delivery. Fourth, in the MOMS, there was follow-up to 12 months in all cases except 2, in which there was perinatal death, whereas, in the fetoscopic registry, one-third of the subjects were <12 months of age at the time of study analysis.

## Conclusions

Prenatal and postnatal outcomes after fetoscopic and open fetal surgery repair of OSB are similar up to 12 months of age. Fetoscopic repair seems to offer significant obstetrical advantages to the pregnant patient because it allows vaginal delivery and is not associated with dehiscence in the uterine scar. Further study is required to determine whether the neurologic outcomes such as childhood ambulation and bladder function are sustained in the long term (Video 1). ■


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