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Fetoscopic two-layer closure for open neural tube defects: prospective study of obstetric, surgical and perinatal outcomes in the first 50 cases

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KEYWORDS: fetal therapy; fetoscopy; myelomeningocele; neural tube defect; prenatal repair; spina bifida

ABSTRACT

Objective *Fetoscopic repair for open neural tube defects (ONTDs) has gained acceptance among leading groups, although it remains controversial owing to the lack of a standardized neurosurgical technique. In 2018, our group described a new fetoscopic two-layer procedure with an exteriorized uterus for ONTD reconstruction. This study aimed to report obstetric, surgical and perinatal outcomes for the first 50 cases since the implementation of this technique and to provide comparative data with open fetal surgery studies.*

Methods *This was a single-center, observational, prospective study conducted between February 2017 and September 2024. Patients scheduled for fetoscopic repair of ONTD using the two-layer technique with uterine exteriorization were included, and variables such as maternal characteristics, prenatal diagnosis, surgical technique, obstetric outcome, perinatal outcome and complications were evaluated. We compared these with the outcomes of the Management of Myelomeningocele Study (MOMS) cohort and a post-MOMS cohort.*

Results *Fetoscopic repair of ONTD was performed successfully in all 50 (100%) cases, with no conversions to hysterotomy repair. Of these, 48 cases resulted in a live birth, one in stillbirth and one pregnancy was terminated. Presurgical ultrasound identified myelomeningocele in 29 (58.0%) and ventriculomegaly in 27 (54.0%) cases. The mean ± SD gestational age at surgery was 25.0 ± 1.1 weeks, and the mean procedure duration was 178 ± 37.6 min. In 42 (84.0%) cases, the repair was performed using a two-layer technique. Complications included preterm prelabor rupture of membranes in 24/49 (49.0%) cases and chorioamniotic membrane separation in 11/49 (22.4%). Among the live births, delivery occurred at a median gestational age of 36.0 (interquartile range (IQR), 33.9–37.2) weeks, with 14/48 (29.2%) delivering at term. Median birth weight was 2510 (IQR, 2178–2816) g, and no cases of neonatal death were reported. Postnatal motor function was equal or better than the presurgery motor level in 26/34 (76.5%) cases. No case of cerebrospinal fluid leakage at the spinal repair site was reported. Comparison with the MOMS and post-MOMS studies showed a higher gestational age at delivery, improved motor outcome and less respiratory distress syndrome than in the post-MOMS cohort. Vaginal delivery occurred in 47.9% of cases in our cohort, in contrast to the MOMS and post-MOMS cohorts, in which all deliveries were by Cesarean section.*

Conclusion *The hybrid two-layer closure of ONTDs is a safe procedure, yielding obstetric and perinatal outcomes comparable with those of open surgery. However, it may not be suitable for all types of defect. Long-term data are required to allow for comprehensive comparisons and to determine whether this technique should be*

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recommended over other current surgical options. © 2025 The Author(s). Ultrasound in Obstetrics & Gynecology published by John Wiley & Sons Ltd on behalf of International Society of Ultrasound in Obstetrics and Gynecology.

INTRODUCTION

Fetoscopy for open neural tube defects (ONTDs), although initially controversial, has gained acceptance among leading groups managing these malformations. A major challenge that remains is the lack of a standardized neurosurgical technique, with reported methods ranging from patch use to full three-layer closures complicating outcome analysis. Additionally, the choice between fully percutaneous or exteriorized uterus approaches introduces bias in comparisons, as both are often grouped under the same 'fetoscopic' label, as reported by the International Fetoscopic Neural Tube Defect Repair Consortium[1].

Our group began fetoscopic treatment of ONTDs in 2012, initially using patches (Tutopatch®; Evergen, Alachua, FL, USA) and glue (Coseal®; Baxter, Deerfield, IL, USA) in 12 cases, but the results were unsatisfactory for adequate defect coverage. We then transitioned to a three-port single-layer closure technique, as described by Belfort *et al.*[2], in 10 additional patients. Although this approach achieved better results, it was less favorable from a neurosurgical perspective. In 2017 we introduced a new procedure, the two-layer approach with an exteriorized uterus for ONTD reconstruction, publishing the outcomes for the first five cases in 2018[3]. This study aimed to report obstetric, surgical and perinatal outcomes following prenatal ONTD repair using this technique in the first 50 cases at our center, and to compare these outcomes with those of the open approach.

METHODS

Study design and participants

This observational prospective cohort study was conducted at Hospital Universitari Vall d'Hebron, Barcelona, Spain, from February 2017 to September 2024. The local ethics committee (CEIm-Vall d'Hebron Institut de Recerca) approved the study (PR(AMI)152/2015), and written informed consent was obtained from all participants.

The study included all pregnant women with a fetus that underwent prenatal repair of open spina bifida at our center following the implementation of the hybrid two-layer technique in February 2017.

Clinical management

Pregnant women with a fetus diagnosed with ONTD were referred to the fetal medicine unit at our center. Detailed ultrasound scans assessed fetal anatomy, growth, placental location and cervical length. Neural tube defects were classified as open or closed. Open defects were further categorized as myelomeningocele (with a cystic lesion) or myeloschisis (with a flat lesion). Intermediate forms, such as limited dorsal myeloschisis (LDM) and myelic limited dorsal malformation, were also included[4–6]. Anatomical lesion level, determined on ultrasound examination, was defined as the highest open posterior vertebral arch. Prenatal motor level was determined by the most distal muscle with active function on neurological examination[7]. Lateral ventricle posterior horn width and posterior fossa for Chiari-II malformation were assessed. The presence of talipes (unilateral or bilateral) was noted. Presurgical ultrasound was typically performed between 20 and 24 weeks' gestation.

The presurgery assessment also included amniocentesis. When amniocentesis was performed at our center, a chromosomal microarray analysis was also conducted. If performed elsewhere, quantitative fluorescence polymerase chain reaction results or karyotype were accepted; however, an additional amniotic fluid sample was collected during surgery for subsequent chromosomal microarray analysis.

Following counseling, parents were offered the option of termination or continuation of the pregnancy. For those electing to continue, prenatal or postnatal repair options were presented.

Surgery was typically performed between 24 and 26 weeks' gestation. The inclusion criteria included maternal age $\geq$ 18 years, singleton pregnancy, gestational age 18.0 to 26.9 weeks, isolated neural tube defect (T1–S1) and Chiari-II malformation. Exclusion criteria were: other fetal malformations, genetic/chromosomal abnormalities with poor prognosis, kyphosis $> 30°$ and maternal contraindications for surgery.

Since 2017, the intended surgical approach for the repair of ONTDs at our center has been a three-port, two-layer technique with an exteriorized uterus, as previously reported in 2018[3]. The technique involves uterine exteriorization following a Pfannenstiel approach, insertion of three 10-Fr cannulas after securing the membranes with two lateral anchoring sutures at the port entry sites, dissection of the neural placode from the surrounding cystic tissue, which was resected, and defect closure in two layers: the myofascial layer and the skin, following dissection of the subcutaneous plane from the myofascial layer. Several modifications to the original technique have been introduced consecutively since then: the initial 7-cm cannulas were shortened to 2.5 cm with the head secured in contact with the myometrium to prevent displacement during instrument introduction and extraction and to provide more room inside the uterine cavity for better maneuverability; warmed and humified carbon dioxide (CO_2) insufflation (PneumoClear CO_2 Conditioning Insufflator (an integrated heating, humidification and smoke evacuation platform); Stryker, Kalamazoo, MI, USA) from Case 8 onwards to keep the membranes moist and warm; membrane plication evolved from two lateral stitches to a four-suture square fixation from Case 44 onwards with two additional myometrial non-transmural sutures inside the square to fix the cannulas in place; dural patch use from Case 6 onwards to prevent adhesion of neural tissue

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to the myofascial suture, transitioning from Gore-Tex to a biological dural substitute patch (Lyoplant®; Aesculap AG, Tuttlingen, Germany) in the last seven cases; and reintroduction of amniotic fluid at the end of fetoscopy was replaced by the introduction of warmed Ringer's lactate solution with 2 g/L of cefazolin from Case 4 onwards.

Additional techniques were employed when the two-layer procedure was not feasible or indicated: three-layer reconstruction (dural, myofascial and skin) in cases with favorable anatomy; one-layer reconstruction, which involves a single suture of all layers without undermining them, in cases of very low sacral diastasis without a muscular layer; myofascial patch and skin closure when myofascial suturing risked neural compression or when diastasis was excessive; and both myofascial and skin patches were employed for wide diastasis of both layers.

Fetal heart rate was monitored and recorded every 10–20 min during the procedure[8]. All patients received combined epidural and general anesthesia, as described previously[9].

After surgery, bupivacaine 0.1% was administered via an epidural catheter for 48 to 72 h. Intravenous paracetamol (2 g every 8 h) was also given, with additional intravenous morphine administered as needed. Special attention was given to detecting and managing early signs of pulmonary edema. A continuous infusion of atosiban was maintained in the early days after surgery, and oral nifedipine (20 mg every 8 h) was added if required. To prevent deep vein thrombosis, subcutaneous low-molecular-weight heparin was administered[9].

Maternal discharge typically occurred 5 to 7 days after surgery. Women from other regions or abroad were followed up in their place of origin, with an appointment scheduled in our center for an ultrasound scan and magnetic resonance imaging 6 weeks postsurgery. Women from our region were monitored weekly, with visits spaced further apart if their recovery progressed well.

Variables

We recorded demographic maternal characteristics, including maternal age, weight, racial origin, method of conception, parity and previous Cesarean section; ultrasound findings before surgery, including type of defect, anatomical level, motor level, measurement of the ventricular posterior horn, ventriculomegaly ≥ 10 mm, presence or absence of kyphosis, presence or absence of talipes, placental location and cervical length; surgical details, including gestational age at surgery, surgical approach, surgical repair technique, lateral incisions, duration of surgery (skin-to-skin), duration of fetoscopic procedure (trocar-to-trocar) and intraoperative fetal bradycardia (< 110 bpm) requiring resuscitation; postoperative outcomes, including number of days admitted to hospital, days of epidural catheter, days of atosiban, maternal blood transfusion, pulmonary edema, placental abruption, preterm prelabor rupture of membranes (PPROM) before 37 weeks, chorioamniotic membrane separation (floating membranes in the amniotic cavity on any scan) and oligohydramnios (deepest pool < 2 cm); delivery outcomes, including perinatal result (live birth, stillbirth, termination of pregnancy), gestational age at birth, mode of delivery and status of the port insertion site scars; neonatal outcomes, including birth weight, sex, 5-min Apgar score and dehiscence of the spinal scar; and neonatal complications, which included extended perinatal mortality (stillbirth from 22 weeks onwards and neonatal demise during the first 28 days after birth), periventricular leukomalacia, respiratory distress syndrome, sepsis, necrotizing enterocolitis, patent ductus arteriosus that required intervention, and retinopathy. All neonates were assessed by a rehabilitation specialist from the spina bifida unit, who determined their motor level through physical examination within the first few days after birth, before neonatal discharge.

Statistical analysis

Quantitative variables are presented as mean ± SD or as median and interquartile range (IQR), depending on whether they followed a normal distribution. Categorical variables are reported as *n* (%). For comparisons with the Management of Myelomeningocele Study (MOMS) and the post-MOMS study, categorical variables were analyzed using the chi-square or Fisher's exact test, as appropriate. Continuous variables could not be compared because the data were aggregated. Statistical analysis was performed using R software (R Foundation for Statistical Computing, Vienna, Austria), with a significance level set at $P < 0.05$.

RESULTS

During the study period, 50 patients underwent fetoscopic repair of an ONTD. Of these, 48 pregnancies resulted in a live birth, one in a stillbirth and there was one termination of pregnancy.

Maternal demographic and presurgical ultrasound characteristics

The mean maternal age was 31.3 ± 6.0 years, and the median body mass index was 25.2 (IQR, 23.0–28.6) kg/m^2. Thirty-eight (76.0%) women were white, two (4.0%) were black, and ten (20.0%) were Latin-American. Additionally, twenty-one (42.0%) women were nulliparous (Table 1).

On presurgical ultrasound examination, 29 (58.0%) cases were diagnosed with myelomeningocele, 19 (38.0%) with myeloschisis and two (4.0%) with LDM. The distributions of the anatomical and prenatal motor levels are shown in Figure 1. The mean width of the largest lateral ventricle was 10.4 ± 2.3 mm, and 27 (54.0%) fetuses had ventriculomegaly measuring more than 10 mm (Table 1). Five (10.0%) fetuses had bilateral talipes, three (6.0%) had unilateral talipes and 42 (84.0%) did not present with talipes. Placental location was anterior in 25 (50.0%) cases, posterior in 23 (46.0%) and fundal in two (4.0%). The mean cervical length

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was 38.6 ± 4.5 mm. Three (6.0%) fetuses presented with kyphosis.

Surgical procedure and postsurgical complications

The mean gestational age at the time of surgery was 25.0 ± 1.1 weeks (Table 1). All 50 patients successfully completed surgery, with no conversions to hysterotomy repair. In 42 (84.0%) cases, a two-layer technique was used, while a single-layer technique was employed in three (6.0%). A myofascial patch and skin closure was performed in three (6.0%) cases, a myofascial and skin patch in one (2.0%) case and a three-layer closure (dura mater, myofascial and skin) in one (2.0%) case.

The mean duration of surgery (skin-to-skin) was 178 ± 37.6 min, and the mean duration of fetoscopic repair (trocar-to-trocar) was 123 ± 38.4 min. Lateral incisions were performed in 11 (22.0%) cases, with five unilateral and six bilateral, all of which involved cases of myeloschisis. No complications were recorded in relation to the lateral incisions during surgery or after birth. Fetal bradycardia was observed in two cases: in one case, the heart rate dropped to 103 bpm but recovered spontaneously, and in the other case it resolved after the

Table 1 Comparison of maternal, presurgical imaging and surgical characteristics of the first 50 cases scheduled for fetoscopic two-layer closure with uterine exteriorization for open neural tube defects at our center with Management Of Myelomeningocele Study (MOMS)[22] and post-MOMS[23] cohorts

Characteristic	*Current study (n = 50)*	*MOMS trial (n = 78)*	P*	*Post-MOMS trial (n = 100)*	P*
Maternal					
Age (years)	31.3 ± 6.0	29.3 ± 5.3	—	29.7 (18–41)	—
Body mass index (kg/m^2)	25.2 (23.0–28.6)	26.2 ± 3.7	—	26.3 (18.7–35)	—
Racial origin			< 0.001		0.063
White	38 (76.0)	73 (93.6)		88 (88.0)	
Asian	—	—		1 (1.0)	
Black	2 (4.0)	1 (1.3)		4 (4.0)	
Latin-American	10 (20.0)	2 (2.6)		6 (6.0)	
Other	—	2 (2.6)		1 (1.0)	
Nulliparous	21 (42.0)	33 (42.3)	0.973	35 (35.0)	0.403
Presurgical imaging					
Type of spinal lesion			—		0.112
Myeloschisis	19 (38.0)	—		33 (33.0)	
Myelomeningocele	29 (58.0)	—		67 (67.0)	
Limited dorsal myeloschisis	2 (4.0)	—		—	
Anatomical level of lesion†			0.318		0.014
Thoracic	6 (12.0)	4 (5.1)		6 (6.0)	
L1–L2	15 (30.0)	21 (26.9)		21 (21.0)	
L3–L4	20 (40.0)	30 (38.5)		66 (66.0)	
L5–S1	9 (18.0)	23 (29.5)		7 (7.0)	
Anatomical level of lesion†: L3 or lower	29 (58.0)	53 (67.9)	0.339	73 (73.0)	0.095
Mean ventricular width of largest lateral ventricle (mm)	10.4 ± 2.3	—	—	10.0 (4–18)	—
Ventriculomegaly > 10 mm	27 (54.0)	—	—	—	—
Talipes	8 (16.0)	20 (25.6)	0.198	15 (15.0)	0.873
Anterior placenta	25 (50.0)	36 (46.2)	0.671	46 (46.0)	0.644
Cervical length before surgery (mm)	38.6 ± 4.5	38.9 ± 7.3	—	—	—
Surgical					
Gestational age at surgery (weeks)	25.0 ± 1.1	23.6 ± 1.4	—	23.3 (20.2–25.6)	—
Technique used					
Hysterotomy	—	78 (100)	—	100 (100)	—
Laparotomy-assisted	50 (100)	—	—	—	—
Duration of surgery (skin-to-skin) (min)	178 ± 37.6	—	—	78.5 (54–106)	—
Intraoperative fetal bradycardia requiring resuscitation	1 (2.0)	8 (10.3)	0.089	5 (5.0)	0.664
Postoperative complication					
Maternal hospital length of stay (days)	6.8 ± 1.4	—	—	4.2 (3–8)	—
Maternal pulmonary edema	2 (4.0)	5 (6.4)	0.704	2 (2.0)	0.601
Maternal blood transfusion	1 (2.0)	—	—	1 (1.0)	1.0
Placental abruption	2/49 (4.1)	5 (6.4)	0.706	2/96 (2.1)	0.604
Chorioamniotic membrane separation	11/49 (22.4)	20 (25.6)	0.684	22/96 (22.9)	0.949
Oligohydramnios	3/49 (6.1)	16 (20.5)	0.027	6/96 (6.3)	1.0
Preterm prelabor rupture of membranes	24/49 (49.0)	36 (46.2)	0.756	31/96 (32.3)	0.050
Chorioamnionitis	6/49 (12.2)	2 (2.6)	0.054	4/96 (4.2)	0.088

Data are given as mean ± SD, median (interquartile range), *n* (%) or *n*/*N* (%). Continuous variables could not be compared because data were aggregated. *Chi-square or Fisher's test, as appropriate. †Grouped according to MOMS and post-MOMS studies.

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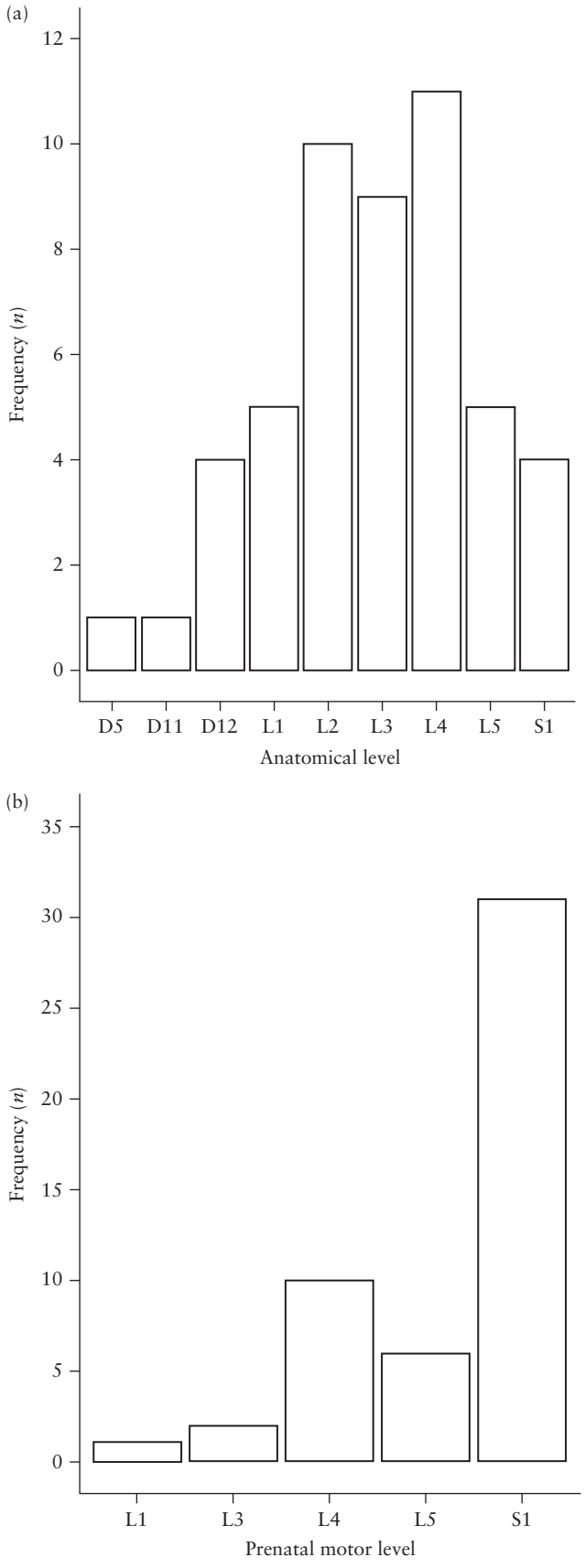

Figure 1 Graphs showing distribution of anatomical levels (a) and prenatal motor levels (b) on presurgical ultrasound examination in 50 cases scheduled for fetoscopic two-layer closure with uterine exteriorization for open neural tube defects.

administration of a single dose of intramuscular atropine. No other complications were reported during surgery.

The mean hospital length of stay was 6.8 ± 1.4 days (Table 1). During hospitalization, two (4.0%) women developed acute pulmonary edema; one was treated with furosemide, while the other was managed with bilevel positive airway pressure and oxygen, and required admission to the intensive care unit for 3 days. One (2.0%) woman required a transfusion of one unit of red blood cells the day after surgery. The median duration of atosiban administration was 5 (IQR, 4.0–6.0) days, and 21 (42.0%) women required additional tocolysis. The epidural catheter was removed after a median of 2 (IQR, 2–2) days.

Pregnancy complications and perinatal outcomes

Of the 50 cases, one (2.0%) resulted in termination of pregnancy at 27.9 weeks. In this case, the fetus developed severe ventriculomegaly (length, 23 mm; preoperative measurement was 11 mm) 1 week after surgery, and the mother opted for termination of pregnancy. Among the remaining 49 cases, two (4.1%) experienced placental abruption at 28.3 and 33.3 weeks, and 11 (22.4%) had chorioamniotic separation, with one (2.0%) case subsequently resulting in stillbirth at 29.9 weeks. There were 24 (49.0%) women who experienced PPROM, at a mean gestational age of 32.0 ± 2.9 weeks, three (6.1%) developed oligohydramnios and six (12.2%) had chorioamnionitis at a mean gestational age of 30.6 ± 3.0 weeks (Table 1). All cases of chorioamnionitis were preceded by PPROM or chorioamniotic separation. No case of chorioamnionitis was reported in the last 24 patients.

The remaining 48 cases resulted in a live birth at a median gestational age of 36.0 (IQR, 33.9–37.2) weeks (Table 2). Fourteen (29.2%) women delivered at term (≥ 37 weeks), 12 (25.0%) delivered before 34 weeks, and four (8.3%) before 30 weeks. Twenty-five (52.1%) women underwent a Cesarean section, while 23 (47.9%) had a vaginal delivery. No case of uterine dehiscence was reported. The mean interval from surgery to delivery was 70.9 ± 23.2 days.

There was no significant correlation between gestational age at surgery and gestational age at delivery ($P = 0.527$), or between gestational age at surgery and the surgery-to-delivery interval ($P = 0.126$).

The median birth weight was 2510 (IQR, 2178–2816) g, the median neonatal length was 45 (IQR, 43–47) cm and the median head circumference was 33.9 (IQR, 32.8–34.0) cm. Postnatal motor level data were available for 34 cases (Figure 2). Compared with the presurgery motor level, the motor level at birth was at least two levels poorer (higher level) in three (8.8%) cases, one level poorer in five (14.7%), one level better (lower level) in nine (26.5%) and two levels better in one (2.9%) case, while there was no difference between the prenatal and postnatal motor level in 16 (47.1%) cases. No postnatal complications associated with the lateral incisions were observed.

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Table 2 Comparison of delivery characteristics, perinatal outcomes and neurosurgical outcomes of 48 liveborn cases, which underwent fetoscopic repair of open neural tube defects, with Management Of Myelomeningocele Study (MOMS)[22] and post-MOMS[23] cohorts

Variable	*Current study (n = 48)*	*MOMS trial (n = 78)*	P*	*Post-MOMS trial (n = 96)*	P*
Delivery and findings at Cesarean section					
Gestational age at delivery (weeks)	35.2 ± 3.3; 36.0 (33.9–37.2)	34.1 ± 3.1	—	34.3 (22.2–37.4)	—
Delivery ≥ 37 weeks	14 (29.2)	16 (20.5)	0.268	26 (27.1)	0.793
Delivery < 30 weeks	4 (8.3)	10 (12.8)	0.436	9 (9.4)	1.0
Birth weight (g)	2510 (2178–2816)	2383 ± 688	—	2416 (501–3636)	—
Cesarean section delivery	25 (52.1)	78 (100)	< 0.001	96 (100)	< 0.001
Hysterotomy scar (open) or port-site scar (fetoscopic) at Cesarean delivery:					
Intact, well healed	—	49/76 (64.5)	—	44/87 (50.6)	—
Thinning	—	19/76 (25.0)	—	36/87 (41.4)	—
Area of dehiscence	—	7/76 (9.2)	—	7/87 (8.0)	—
Complete dehiscence	—	1/76 (1.3)	—	0/87 (0)	—
Findings at birth					
Dehiscence at spinal repair site	2 (4.2)	10/77 (13.0)	0.130	3/83 (3.6)	1.0
Motor function compared with upper anatomical level of lesion:			0.035		0.020
≥ 2 levels better	20/34 (58.8)	20/62 (32.3)		24/80 (30.0)	
One level better	5/34 (14.7)	7/62 (11.3)		20/80 (25.0)	
Same	4/34 (11.8)	14/62 (22.6)		26/80 (32.5)	
One level worse	5/34 (14.7)	13/62 (21.0)		9/80 (11.3)	
≥ 2 levels worse	0/34 (0)	8/62 (12.9)		1/80 (1.3)	
Neonatal complications†					
Length of stay in neonatal intensive care unit (days)	—	—	—	24.5 (3–133)	—
Perinatal death	1/49 (2.0)‡	2 (2.6)	1.0	6/98 (6.1)§	0.425
Periventricular leukomalacia	0/31 (0)	4/77 (5.2)	0.323	—	—
Respiratory distress syndrome	7/31 (22.6)	16/77 (20.8)	1.0	43/83 (51.8)	0.010
Sepsis	3/31 (9.7)	4/77 (5.2)	1.0	—	—
Necrotizing enterocolitis	0/31 (0)	1/77 (1.3)	1.0	1/83 (1.2)	1.0
Patent ductus arteriosus	1/31 (3.2)	3/77 (3.9)	1.0	—	—
Retinopathy	0/31 (0)	0 (0)	1.0	—	—
Outcomes at 12 months of age					
Death before shunt placement or ETV	0/41 (0)	2 (2.6)	1.000	—	—
Hydrocephalus treated by shunt and/or ETV	18/33 (54.5)	31/76 (40.8)	0.185	—	—

Data are given as mean ± SD, median (interquartile range), *n* (%) or *n*/*N* (%). Continuous variables could not be compared because data were aggregated. *Chi-square or Fisher's test, as appropriate. †Neonates delivered in our hospital (*n* = 24) and neonatal reports provided or were referred to our center after birth (*n* = 7). ‡Only termination of pregnancy (*n* = 1) was excluded from this particular analysis; one case stillborn at 29 + 6 weeks' gestation was included. §Two cases of intrauterine fetal death were included in this particular analysis. ETV, endoscopic third ventriculostomy.

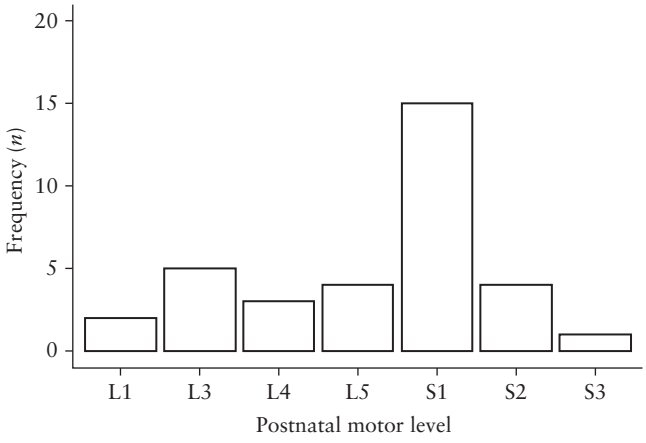

Figure 2 Graph showing distribution of postnatal motor levels available for 34 of 50 cases scheduled for fetoscopic two-layer closure with uterine exteriorization for open neural tube defects.

No case experienced a cerebrospinal fluid (CSF) leak at the spinal repair site; therefore, no secondary surgery was required for CSF leakage. However, of the 48 liveborn cases, four (8.3%) required surgical site repair: three (6.3%) within the first week after birth and one (2.1%) at 31 months of age. In two (4.2%) cases, a skin defect was present, while the other two (4.2%), including the case operated on at 31 months, had skin fistulas that did not extend to the medullary canal.

Complete neonatal follow-up data were available for 31 neonates, 24 delivered at our center and seven for which neonatal reports were provided by other centers or were referred to our center after birth. No neonatal death occurred. Of the 24 deliveries at our center, six (25.0%) developed respiratory distress syndrome, two (8.3%) had sepsis and one (4.2%) had a patent ductus arteriosus. There were no reported cases of necrotizing

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enterocolitis, periventricular leukomalacia or retinopathy of prematurity.

Comparison with MOMS and post-MOMS cohorts

Tables 1 and 2 show a comparison of our results with those from the MOMS and post-MOMS cohorts. Regarding maternal demographic characteristics, we observed differences in racial origin, with a higher proportion of Latin-American participants in the present study. Additionally, there were significant differences in the distribution of the anatomical level of the lesion compared with that in the post-MOMS cohort, with a greater proportion of thoracic and high lumbar levels in our cohort. However, we found no significant difference in intraoperative or postoperative complications compared with the post-MOMS cohort, although there was a significantly smaller proportion of oligohydramnios cases in our series compared with the MOMS study.

Regarding delivery outcomes, our study, compared with the MOMS or post-MOMS cohorts, had a significantly lower proportion of Cesarean section deliveries ($P < 0.001$ for both comparisons) and we observed no significant difference in the proportion of deliveries before 37 or 30 weeks. Gestational age at birth was later in this study compared with the MOMS and post-MOMS cohorts, although we were unable to make a statistical comparison.

In terms of motor function at birth, a higher proportion of cases in our study demonstrated motor function that was two or more levels better than the anatomical level (58.8% in this study *vs* 32.3% in the MOMS and 30.0% in the post-MOMS cohorts). Conversely, the proportion of cases with motor function worse than the anatomical level was 14.7% in this study, compared with 33.9% in MOMS and 12.5% in the post-MOMS cohort. Compared with the MOMS cohort, no significant differences were observed in outcomes at 12 months of age.

DISCUSSION

Main findings

This study confirms the feasibility, safety and effectiveness of the two-layer fetoscopic repair technique with uterine exteriorization for ONTD, achieving high procedural success with favorable maternal, obstetric and neonatal outcomes. Among 50 cases, no conversion to open hysterotomy was needed, and intraoperative complications were minimal. Maternal recovery was uneventful in most cases, with low rates of severe complications and an average hospital stay of 6.8 ± 1.4 days. The median gestational age at delivery was 36.0 (IQR, 33.9–37.2) weeks, with 29.2% of cases reaching term, suggesting that this approach may extend gestation when compared with previous studies.

Neonatal outcomes were promising, with 76.5% (26/34) of cases demonstrating the same or an improved motor function level compared with presurgery. These data are consistent with our previous report, despite overlapping patients[10]. Moreover, 73.5% (25/34) had postnatal motor function levels better than the anatomical level. Additionally, the absence of neonatal death and low rates of severe complications support the safety of this procedure. Innovative modifications to the surgical technique, such as using humidified CO_2 and improved membrane fixation, probably contributed to these outcomes.

Compared with the MOMS and post-MOMS studies, this technique demonstrated several advantages, including higher motor improvement rates, a lower rate of oligohydramnios and comparable or better neonatal outcomes, even with a higher proportion of high-risk cases. However, we observed a higher rate of chorioamnionitis in our series compared with the open approaches, although the difference did not reach statistical significance. This may be related to increased membrane manipulation and longer operative times. Notably, no case of chorioamnionitis occurred in the last 24 procedures performed, suggesting that improvements in the learning curve and membrane-fixation techniques may have contributed to reducing this complication.

Fetoscopic two-layer closure was feasible in most cases (84.0%), but not in specific situations. In two cases, a myofascial patch was used owing to a narrow intracanal space that risked neural tissue compression. In two others, excessive muscular diastasis necessitated a patch. While creating muscular flaps, as described by other groups[11], may address this, we prioritize preserving untouched lumbar musculature, which may be critical for the future of these patients. In three of these four cases, the skin was successfully closed at the midline over the patch; in one, a dermal substitute was required owing to the size of the defect.

Three patients had low defects with minimal neural tissue exposure, making a single-layer closure a suitable option owing to the absence of a myofascial layer over the sacrum. Conversely, one patient with LDM presented an ideal anatomy for a three-layer reconstruction. These findings underscore the need for tailored approaches to ensure the optimal surgical outcome for each child.

Comparison with the literature

Two critical aspects of the technique merit attention: the surgical approach and the neurosurgical procedure. The approach (i.e. whether open fetal surgery with varying hysterotomy sizes, fully percutaneous fetoscopy or a hybrid technique with an exteriorized uterus) primarily influences obstetric outcomes. Previous comparisons of open and fetoscopic approaches have grouped percutaneous and hybrid techniques under the same term 'fetoscopy'[1].

When comparing MOMS and post-MOMS open approaches with the data of the International Fetoscopic Neural Tube Defect Repair Consortium (that includes all fetoscopic techniques), fetoscopy shows fewer cases of uterine dehiscence and enables vaginal delivery, with comparable complication rates. In contrast, comparing MOMS and post-MOMS open approaches with our data suggests a trend favoring the hybrid fetoscopic approach for greater gestational age at birth. However,

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as MOMS trial surgery occurred 1 week earlier (at a mean gestational age of 23.6 ± 1.4 *vs* 25.0 ± 1.1 weeks), the 'time-to-delivery' was similar. Notably, comparing these outcomes with the hybrid approach of Belfort *et al.*[12], a significant difference in gestational age at birth is revealed. A recent publication by Sanz-Cortes *et al.*[13] reported lower rates of complications, including chorioamnionitis (1.0%) and PPROM (29.0%), which may be key contributors to the favorable gestational age at birth achieved in their series.

In this study, we did not find a significant association between gestational age at the time of surgery and gestational age at delivery, in contrast to the findings reported by Peralta *et al.*[14] using the mini-hysterotomy technique.

The fully percutaneous approach, as currently practiced, may shorten the 'time-to-delivery' owing to its later timing in gestation and earlier deliveries[15]. Factors such as membrane fixation, the number and size of ports used, uterine manipulation and the duration of the procedure likely influence these outcomes. In terms of long-term outcomes, data from the Skin-over-biocellulose for Antenatal Fetoscopic Repair (SAFER) technique have reported low rates of tethered-cord syndrome and favorable functional outcomes at 30 months of age, including independent ambulation and social function in many patients[16]. These results suggest potential advantages, particularly with techniques that promote neoduramater formation and avoid dura-mater sutures. Ongoing comparison of long-term outcomes across different fetoscopic methods is warranted to guide optimal clinical decision-making.

The second key consideration is the neurosurgical technique, which lacks standardization and varies widely, even within the same group. Minimally invasive reconstruction presents significant challenges, with many attempts to simplify the process using patches. Neurulation of the placode and dural suturing, while particularly difficult via fetoscopy, are not impossible. Three-layer reconstruction remains a major surgical challenge, requiring advanced minimally invasive skills and specialized instrumentation owing to tissue fragility and variability in spinal anatomy. It is considered the next step forward in fetoscopic repair and will demand continued refinement during the surgeon's learning curve, as noted by several authors[17–19]. However, standardizing this learning curve will be difficult, given the wide variability in surgical proficiency and neurosurgical expertise among practitioners. Moreover, these techniques substantially increase operative time and membrane manipulation, which may negatively impact other outcomes, such as gestational age at birth and membrane-related complications.

This variability complicates outcome comparisons, not only for watertight closure, hindbrain herniation reversal or shunting requirements, but also for long-term factors such as inclusion cyst formation, motor function preservation, neural tissue adhesion to myofascial closure, reoperation rates and standardized assessments of urologic and bowel function.

In addition to the variability of techniques, many are continuously evolving. Recent advances include muscle flaps, novel synthetic and biological patches[20] and mini-laparotomy for fetoscopic reconstruction with membrane fixation[21]. Therefore, a focus on long-term neurosurgical outcomes and obstetric results in large patient cohorts remains crucial.

Strengths and limitations

This study shows that the fetoscopic two-layer closure technique with an exteriorized uterus is a reliable option for ONTD reconstruction in many patients, offering obstetric and perinatal outcomes comparable with those of other open and fetoscopic methods. Continuous refinements and team experience have enhanced neurosurgical performance within acceptable surgical times. Moreover, the benefits of fetoscopy, particularly in preserving future reproductive potential, provide significant advantages for patients.

However, this technique is not suitable for all patients. As inclusion criteria expand, more complex cases will probably arise, making anatomical reconstruction increasingly challenging. Prepared alternative solutions will be critical to ensure optimal outcomes. Additional limitations include the small annual number of patients, which extends the learning curve, and patient loss to follow-up, complicating data collection and analysis. Advances in neurosurgical techniques, especially in achieving placode neurulation and dural closure, are essential.

Clinical and research implications

Efforts to enhance closure quality and membrane fixation, combined with ongoing advances in cell therapies, may be pivotal for improving outcomes for these patients and their mothers. In this study, we have delivered high-quality data for comparison with other viable techniques, enabling clearer insights into optimal treatment options.

Conclusion

The hybrid two-layer closure of ONTD is a safe procedure with obstetric and perinatal outcomes comparable with those of open surgery. However, it may not be suitable for all types of defect. Long-term data are needed to enable comprehensive comparisons and assess whether this technique should be recommended over other surgical options.

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REFERENCES

1. Sanz Cortes M, Chmait RH, Lapa DA, et al. Experience of 300 cases of prenatal fetoscopic open spina bifida repair: report of the International Fetoscopic Neural Tube Defect Repair Consortium. *Am J Obstet Gynecol*. 2021;225(6):678.e1-678.e11.

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2. Belfort MA, Whitehead WE, Shamshirsaz AA, Ruano R, Cass DL, Olutoye OO. Fetoscopic repair of meningomyelocele. *Obstet Gynecol*. 2015;126(4):881-884.
3. Giné C, Arévalo S, Maíz N, et al. Fetoscopic two-layer closure of open neural tube defects. *Ultrasound Obstet Gynecol*. 2018;52(4):452-457.
4. Friszer S, Dhombres F, Morel B, Zerah M, Jouannic JM, Garel C. Limited dorsal myeloschisis: a diagnostic pitfall in the prenatal ultrasound of fetal dysraphism. *Fetal Diagn Ther*. 2017;41(2):136-144.
5. Gine C, Maiz N, Arévalo S, Rodó C, López M, Carreras E. Ruptured saccular limited dorsal myeloschisis: good indication for fetal repair. *Ultrasound Obstet Gynecol*. 2024;63(1):113-115.
6. Vande Perre S, Guilbaud L, de Saint-Denis T, et al. The myelic limited dorsal malformation: prenatal ultrasonographic characteristics of an intermediate form of dysraphism. *Fetal Diagn Ther*. 2021;48(9):690-700.
7. Carreras E, Maroto A, Illescas T, et al. Prenatal ultrasound evaluation of segmental level of neurological lesion in fetuses with myelomeningocele: development of a new technique. *Ultrasound Obstet Gynecol*. 2016;47(2):162-167.
8. García I, Suárez E, Maiz N, et al. Fetal heart rate monitoring during fetoscopic repair of open spinal neural tube defects: a single-centre observational cohort study. *Int J Obstet Anesth*. 2021;48:103195.
9. Manrique S, Maiz N, García I, et al. Maternal anaesthesia in open and fetoscopic surgery of foetal open spinal neural tube defects: a 6-year observational study. *Eur J Anaesthesiol*. 2019;36:175-184.
10. Maiz N, Arévalo S, García-Manau P, et al. Presurgery motor level assessment for prediction of motor level at birth in fetuses undergoing prenatal repair of open spina bifida: time to abandon the anatomical level for counseling. *Ultrasound Obstet Gynecol*. 2023;61(6):728-733.
11. Heuer GG, Adzick NS, Sutton LN. Fetal myelomeningocele closure: technical considerations. *Fetal Diagn Ther*. 2015;37(3):166-171.
12. Belfort MA, Whitehead WE, Shamshirsaz AA, et al. Fetoscopic open neural tube defect repair: development and refinement of a two-port, carbon dioxide insufflation technique. *Obstet Gynecol*. 2017;129(4):734-743.
13. Sanz-Cortes M, Whitehead WE, Johnson RM, et al. Laparotomy-assisted, two-port fetoscopic myelomeningocele repair: infant to preschool outcomes. *J Neurosurg Pediatr*. 2025;35(1):10-21.
14. Peralta CFA, Botelho RD, Romano ER, et al. Fetal open spinal dysraphism repair through a mini-hysterotomy: influence of gestational age at surgery on the perinatal outcomes and postnatal shunt rates. *Prenat Diagn*. 2020;40(6):689-697.
15. Lapa Pedreira DA, Acacio GL, Gonçalves RT, et al. Percutaneous fetoscopic closure of large open spina bifida using a bilaminar skin substitute. *Ultrasound Obstet Gynecol*. 2018;52(4):458-466.
16. Lapa DA, Callado GY, Catissi G, Trigo L, Faig-Leite F, Sevilla APAB. The impact of a biocellulose-based repair of fetal open spina bifida on the need to untether the cord: is it time to unify techniques for prenatal repair? *Einstein (Sao Paulo)*. 2024;22:eAO0557.
17. Joyeux L, De Bie F, Danzer E, et al. Learning curves of open and endoscopic fetal spina bifida closure: systematic review and meta-analysis. *Ultrasound Obstet Gynecol*. 2020;55(6):730-739.
18. Kohl T. Minimally invasive fetoscopic surgery for spina bifida aperta: learning and doing. *Ultrasound Obstet Gynecol*. 2020;56(4):633.
19. Joyeux L, Danzer E, De Bie F, et al. Reply. *Ultrasound Obstet Gynecol*. 2020;56(4):634-635.
20. Prytkova V, Ali S, Greves CD, Elbabaa SK. The effect of using synthetic vs. biological dural substitutes during prenatal and postnatal repair of spina bifida on spinal cord tethering—a review of literature. *Childs Nerv Syst*. 2024;40(11):3629-3639.
21. Chmait RH, Monson MA, Pham HQ, et al. Percutaneous/mini-laparotomy fetoscopic repair of open spina bifida: a novel surgical technique. *Am J Obstet Gynecol*. 2022;227(3):375-383.
22. Adzick NS, Thom EA, Spong CY, et al. A randomized trial of prenatal versus postnatal repair of myelomeningocele. *N Engl J Med*. 2011;364(11):993-1004.
23. Moldenhauer JS, Soni S, Rintoul NE, et al. Fetal myelomeningocele repair: the post-MOMS experience at the Children's Hospital of Philadelphia. *Fetal Diagn Ther*. 2015;37(3):235-240.

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