Fetoscopic Myelomeningocele Repair

- Benefits and complications of fetal and postnatal surgery for open spina bifida: systematic review and proportional meta-analysis
- Safety and Effectiveness of Fetal Myelomeningocele Repair: Case Series Analysis Using an Exteriorized Uterus and a Fetoscopic Approach
- Impact of Prenatal Repair for Fetal Myelomeningocele on Gastrointestinal Function
- Fetoscopic Robotic Open Spina Bifida Treatment (FROST): A Preclinical Feasibility and Learning Curve Study
- Outcomes Following Fetoscopic Repair of Myelomeningocele: A Prospective Single-Center Experience
- Fetoscopic Myelomeningocele (MMC) Repair: Evolution of the Technique and a Call for Standardization
- Two-dimensional Speckle Tracking Echocardiography and Fetal Cardiac Performance During Fetoscopic Repair of Myelomeningocele
- Fetoscopic repair of open spina bifida between 26 0/7 and 27 6/7 gestational weeks and postnatal cerebrospinal fluid diversion

The 2 types of maternal skin incisions for in utero spina bifida repair are low transverse (LT) incision perceived to be cosmetic benefit and midline longitudinal (ML) incision, typically associated with a reduction in surgical time and lower blood loss. Our objective was to compare short- and long-term outcomes associated with these 2 types of skin incisions following in utero spina bifida repair.

Methods: Prospective observational cohort of 72 patients undergoing fetal spina bifida repair at a single institution between September 2011 and August 2018. The decision for the type of incision was at the discretion of the surgeons. The primary outcome was total operative time. Secondary outcomes included an analog scale of wound pain score on postoperative day 3, duration of postoperative stay, and postoperative wound complications within the first 4 weeks. The Patient Scar Assessment Questionnaire, a validated questionnaire, was obtained for all patients (≥6 months from delivery) using 4 categories (appearance, consciousness, satisfaction with appearance and with symptoms), with higher scores reflecting a poorer perception of the scar.

Results: There were 43 women (59.7%) in the LT group and 29 (40.3%) in the ML group. In all patients, the same incision was used during cesarean delivery. The total operative time was higher in the LT group by 33 min ($p < 0.001$), primarily due to abdominal wall incision time (open and closure). No significant differences were found between the groups in pain score, length of postoperative stay, or the rate of wound complications. Fifty-three patients (73.6%) responded to the questionnaire, 36/43 from the LT group and 17/29 from the ML group. There was no difference in the scores of appearance, consciousness, and satisfaction with appearance and symptoms between the groups.

Conclusion: ML incisions shorten operative times without altering long-term incision-related satisfaction when compared to LT incisions [1)].

Lower extremity movement increases between POD 1 and POD 5 in fetuses after open fetal myelomeningocele repair. Knee and hip movement on ultrasound at 32 weeks correlates with ambulation at 30-36 months. These data may inform counseling, and direct therapy and spark prospective investigations [2)].

The Management Of Myelomeningocele Study (MOMS) trial demonstrated the safety and efficacy of open fetal surgery for spina bifida (SB).

Prenatal myelomeningocele (MMC) repair has significant advantages over postnatal repair, as was demonstrated by the Management of Myelomeningocele Study (MOMS) in 2011 [3].

Technique

Fetoscopic Myelomeningocele Repair Technique

Complications

Fetoscopic Myelomeningocele Repair Complications

Percutaneous Fetoscopic Spina Bifida Repair

Percutaneous Fetoscopic Spina Bifida Repair.

MOMS Trial

MOMS Trial.

The number of cases operated correlates with the outcome of SB fetal closure and ranges from 35 cases for standard-hysterotomy to ≥56-57 cases for minimally invasive modifications. The observations provide important information for institutions eager to establish a new fetal center, develop a new technique or train their team, and inform referring clinicians, potential patients and third-parties [4].

Early outcome urodynamic testing analyses demonstrated a lower incidence of high-risk bladders in Fetoscopic Myelomeningocele Repair patients with a trend toward clinically significant improvement compared to prenatal open in regard to all evaluated metrics. Larger, prospective, confirmatory studies are needed to further evaluate the potential benefits of Fetoscopic Myelomeningocele Repair on bladder safety and health [5].

Following fetoscopic closure of spina bifida, the MOMS MgSO4 regimen is associated with an increased risk of pulmonary edema than a more flexible regimen [6].

Case series

A cohort of fetuses with open spina bifida (OSB) who underwent open surgery in two fetal surgery centers (Argentina and Mexico). Two groups were defined based on the gestational age (GA) at intervention: MOMS time window group: GA 19+0 -25+6 , and late intervention group: GA 26+0 -27+6 .

Intrauterine OSB repair was successfully performed in 140 cases, either before (n=57) or after (n=83) 26 weeks, at on average 25.0 (22.9-25.9) and 26.8 (22.9-25.9) weeks, respectively. There were no significant differences in the rate of premature rupture of membranes, chorioamnionitis, oligohydramnios, preterm delivery, perinatal death and maternal complications. The late intervention group showed a significantly lower surgical times (112.6 vs. 124.2 min, p=0.01), lower interval between fetal surgery and delivery (7.9 vs. 9.2 weeks, p<0.01) and similar rate of hydrocephalus requiring treatment (30.6% vs. 23.3%, p=0.44) than the MOMS time window group.

Late fetal surgery for OSB repair between 26+0 -27+6 weeks is feasible and was associated with similar outcomes than that performed before 26 weeks. These findings may allow an extension of the proposed time window for cases with late diagnosis or referral [7].

All patients referred to the Trousseau Hospital in Paris for MMC were reviewed from July 2014 to June 2020. For all the patients who underwent fetal MMC repair, surgical details, maternal characteristics and data from the neonatal to the three-years-old evaluations were collected.

Among the 126 patients referred, 49.2% were eligible and 27.4% (n=17) of them underwent fetal MMC repair. Average gestational age at fetal surgery was 24+6 weeks. There was no case of fetal complication and the only maternal complication was one case of transfusion. They recorded 70% of premature rupture of membranes and 47% of premature labor. Average gestational age at delivery was 34+2 weeks and no patient delivered before 30 weeks. There was no case of uterine scar dehiscence or maternal complication during cesarean section. After birth, 59% of the children had a hindbrain herniation reversal. At 1-year-old, 42% were assigned a functional level of one or more better than expected according to the prenatal anatomic level and 25% required a ventriculoperitoneal shunt. At 3-year-old, all the children attended school and 75% were able to walk with orthotics or independently.

Open fetal surgery enables anatomical repair of the MMC lesion, a potential benefit on cerebral anomalies and motor function, with a low rate of perinatal and maternal complications [8].

An Institutional review board-approved retrospective analysis of all patients undergoing all forms of Myelomeningocele repair with inclusion criteria and exclusion criteria based on the MOMS trial was performed. Bladder safety assessment required initial urodynamic testing, renal bladder ultrasound (RBUS), and/or voiding cystourethrography (VCUG) within the 1st year of life. Follow-up analyses

within the cohorts required follow-up studies within 18 months after initial evaluations. Outcomes assessed included bladder-risk-categorization based on the CDC UMPIRE study (high, intermediate, and safe), hydronephrosis (HN), and vesicoureteral reflux (VUR). A single reader evaluated each urodynamic testing.

Initial urodynamic testing in 93 patients showed that the prevalence of high-risk bladders was 35% Fetoscopic Myelomeningocele Repair versus 36% traditional postnatal repair (PSTNR) and 60% prenatal open. Follow-up urodynamic testing showed only 8% of Fetoscopic Myelomeningocele Repair were high-risk compared to 35% prenatal open and 36% traditional postnatal repair. Change from initial to follow-up bladder-risk-category did not reach significance (p = .0659); however, 10% postnatal repair worsened to high-risk on follow-up, compared to none in either prenatal group. A subanalysis of follow-up urodynamic testing between the prenatal cohorts also was not significant (p = .055). Only 8% of Fetoscopic Myelomeningocele Repair worsened or stayed high-risk compared to 35% with prenatal open (p = .1). Hydronephrosis was significantly different at initial and subsequent follow-up between the groups with the least in the Fetoscopic Myelomeningocele Repair group.

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To evaluate if magnesium sulfate (MgSO4) titration following fetoscopic spina bifida closure is associated with fewer maternal complications than the Management of Myelomeningocele Study (MOMS) tocolytic regimen.

This prospective cohort study included 73 consecutive patients undergoing fetoscopic closure of spina bifida between 2015 and 2020. A policy of using the MgSO4 regimen per the MOMS trial was changed to a flexible one in which MgSO4 was titrated according to the frequency of the uterine contractions following surgery. The frequency of maternal pulmonary edema, low maternal oxygen saturation requiring oxygen supplementation, atelectasis, hypocalcemia and preterm delivery was compared before and after the policy was changed.

A higher proportion of women in the group that used the MOMS MgSO4 regimen had pulmonary edema compared to those in the flexible one [26.1% (6/23) vs. 6% (3/50); p= 0.024). Multivariate analysis showed that the MOMS tocolytic regimen was independently associated with a higher risk of pulmonary edema (aOR: 8.57; 95% CI: 1.54-47.7; p= 0.014) than a flexible one. There was no difference in the rate of preterm delivery.

Following fetoscopic closure of spina bifida, the MOMS MgSO4 regimen is associated with an increased risk of pulmonary edema than a more flexible regimen [10].

Fetal spina bifida repair (fSBR) has proven effective in the reversibility of hindbrain herniation, lower rate of shunt-dependent hydrocephalus, and independent ambulation. Besides distinct advantages, there are also concerns related to fSBR. One of these is the postnatal occurrence of inclusion cysts

(IC).

In a prospective study, 48 children who underwent fSBR were followed up in the University Children's Hospital Zurich, Switzerland.

Postnatal assessment included clinical examination, cystometry, and Spinal magnetic resonance imaging. Indication for IC resection was the evidence of a spinal mass on MRI in the presence of deteriorating motor or bladder function, pain, or considerable growth of the IC.

Fourteen children (30%) developed IC, all within the first 2 years of life. Six children underwent IC resection; 4 children due to deteriorating function, 2 children due to doubling of the mass on MRI within 1 year. Following IC resection, 4/6 children (67%) demonstrated altered motor function and 6 children (100%) were diagnosed with neurogenic bladder dysfunction.

Systematic follow-up of patients with a history of fSBR revealed a high incidence of IC. Whether these are of dysembryogenic or iatrogenic origin, remains unclear. Since both IC per se and IC resection may lead to loss of neurologic function, IC can be considered a “third hit.” [11].

Surgical management of spinal dysraphism often requires the use of dural substitutes. Amniotic membrane (AM) has drawn the interest of clinicians for its valuable concentration of cytokines and factors capable of promoting wound healing, re-epithelialization, inhibiting fibrosis and regulating angiogenesis. These beneficial qualities could make AM an interesting dural substitute for spina bifida repair. In this study, we describe the use of banked homologous AM as a dural substitute for the repair of spinal dysraphism in newborns. Our purpose is to test the mechanical characteristics, as well as the safety and effectiveness of AM in preventing postoperative complications and re-tethering.

The AM patch was carefully detached from the chorion of donors undergoing caesarean section, rinsed in saline solution, and cryopreserved in liquid nitrogen. Five newborns were treated using AM: three affected by open spinal dysraphism and two by spina bifida occulta. The AM patch was used as a dural substitute with two different positions and purposes: the amnion-side down covering the placode to prevent adhesions or placed extradurally facing the dura to avoid scarring and facilitating the sliding of the dural sac itself under the extradural tissue layers.

RESULTS: No adverse events occurred, and the surgical wounds healed without complications. MRI scans taken at 3 and 6 months after surgery showed a satisfying de-tethering of the spinal cord with no obvious evidence of new adherence formation.

CONCLUSIONS: We present a multimodal interposition technique using AM as a reconstructive and anti-adhesive tissue for the treatment of open myelomeningocele (MMC) and lipomeningocele (LMC) treatment. In our experience, AM proved its efficacy in restoring the dural sac integrity without complications. We support the use of AM as a promising dural substitute, speculating on how the use of AM could potentially change reconstructive strategies for spinal dysraphism [12].

Sepulveda et al. reported the experience with prenatal repair of open spina bifida (OSB) from 2 centers in Chile.

Women with a second-trimester fetus with OSB were offered intrauterine neurosurgical repair following the protocol from the Management of Myelomeningocele Study (MOMS) trial. Pediatric

follow-up with infants reaching 12 and 30 months of life was also reviewed.

Fifty-eight fetuses with OSB underwent intrauterine repair at an average (±SD) gestational age of 24.8 ± 0.9 weeks. There were 3 (5.1%) intrauterine deaths. The average gestational age at delivery of the remaining 55 cases was 33.3 ± 3.6 weeks, and the average birth weight was 2,172 ± 751 g. Delivery before 30 weeks occurred in 11 cases (20.0%). Two (3.6%) neonatal deaths (<28 days) occurred. At 12 months, a ventriculoperitoneal shunt or an endoscopic third ventriculostomy was required in 25% of the cases. At 30 months, 72.4% of the infants were able to walk.

Prenatal neurosurgical repair of OSB is a complex and challenging intervention. Major complications include perinatal death and severe prematurity. No major maternal complications occurred in our series. A reduction in the need for Cerebrospinal fluid shunt and an improved ability to walk seems to be the greatest long-term advantages of this procedure [13].

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