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Reducing perinatal complications and preterm delivery for patients undergoing in utero closure of fetal myelomeningocele: further modifications to the multidisciplinary surgical technique

Clinical article

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Object. As more pediatric neurosurgeons become involved with fetal myelomeningocele closure efforts, examining refined techniques in the overall surgical approach that could maximize beneficial outcomes becomes critical. The authors compared outcomes for patients who had undergone a modified technique with those for patients who had undergone fetal repair as part of the earlier Management of Myelomeningocele Study (MOMS).

Methods. Demographic and outcomes data were collected for a series of 43 delivered patients who had undergone in utero myelomeningocele closure at the Fetal Center at Vanderbilt from March 2011 through January 2013 (the study cohort) and were compared with data for 78 patients who had undergone fetal repair as part of MOMS (the MOMS cohort). For the study cohort, no uterine trocar was used, and uterine entry, manipulation, and closure were modified to minimize separation of the amniotic membrane. Weekly ultrasound reports were obtained from primary maternal–fetal medicine providers and reviewed. A test for normality revealed that distribution for the study cohort was normal; therefore, parametric statistics were used for comparisons.

Results. The incidence of premature rupture of membranes (22% vs 46%, $p = 0.011$) and chorioamnion separation (0% vs 26%, $p < 0.001$) were lower for the study cohort than for the MOMS cohort. Incidence of oligohydramnios did not differ between the cohorts. The mean (± SD) gestational age of 34.4 (± 6.6) weeks for the study cohort was similar to that for the MOMS cohort (34.1 ± 3.1 weeks). However, the proportion of infants born at term (37 weeks or greater) was significantly higher for the study cohort (16 of 41; 39%) than for the MOMS cohort (16 of 78; 21%) ($p = 0.030$). Compared with 10 (13%) of 78 patients in the MOMS cohort, only 2 (4%) of 41 infants in the study cohort were delivered earlier than 30 weeks of gestation ($p = 0.084$, approaching significance). For the study cohort, 2 fetal deaths were attributed to the intervention, and both were believed to be associated with placental disruption; one of these mothers had previously unidentified thrombophilia. Mortality rates did not statistically differ between the cohorts.

Conclusions. These early results suggest that careful attention to uterine entry, manipulation, and closure by the surgical team can result in a decreased rate of premature rupture of membranes and chorioamnion separation and can reduce early preterm delivery. Although these results are promising, their confirmation will require further study of a larger series of patients.
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Key Words • fetal surgery • in utero fetal repair of myelomeningocele • spina bifida repair • technique

Myelomeningocele is a congenital defect of the spine and spinal cord resulting from incomplete closure of the neural tube during the 4th week of fetal life. The spectrum and severity of deformities and neurological deficits correspond generally to the spinal level of the lesion. In most cases, myelomeningocele is associated with hydrocephalus, hindbrain herniation, motor and cognitive impairment, and bowel and bladder dysfunction.[14,15] Approximately 85% of infants with my-

Abbreviation used in this paper: MOMS = Management of Myelomeningocele Study.

elomeningocele will need a ventricular shunt soon after birth, and approximately 45% of these will need shunt revision within their 1st year of life.[3,9] Conventional management, to prevent further injury to the exposed neural elements, consists of prompt closure of the defect during the neonatal period.

During the late 1990s and early 2000s, results of nonrandomized clinical trials suggested that significant benefit might result from prenatal repair of myelomeningocele.[5] At the same time, it was appreciated that this procedure entailed significant risk to fetus and mother. In response to these benefits and risks, the National Institutes of Health elected to sponsor a multicenter, prospective, randomized clinical trial, the Management of Myelomeningocele Study (MOMS). This trial compared outcomes after prenatal and postnatal myelomeningocele closure.[2] The operations were performed at the 3 fetal surgery units that already had extensive experience with this procedure. After randomization of 183 of a planned 200 patients, enrollment was stopped in December 2010 by the Data Safety and Monitoring Board when it was found that for the prenatal repair cohort, the rate of ventricular shunt placement by 1 year of age was significantly reduced and motor function at 30 months of age was improved. MOMS also confirmed that fetal myelomeningocele repair increases the risk for chorioamnion separation, premature rupture of membranes, oligohydramnios, and preterm delivery, in addition to a 3% fetal mortality rate.

Because these risks were unacceptable to many, it therefore seemed prudent to seek methods that would reduce the risks and improve the benefits of intrauterine repair. To maximize the reliability of the MOMS results, a rigid set of inclusion criteria and surgical and postnatal management standards were adopted by the centers participating in the trial. These standards represented the best estimate of optimal practice at the time. It was to be expected that some of these standards would need modification in light of information gained from the study. In particular, MOMS criteria prescribed the use of a trocar for entering the uterus. The protocol states that "initial uterine entry is accomplished through a 1–2 cm hysterotomy which is made with a sharp instrument such as the Tulipan-Bruner trochar or a specially designed spear device which is attached to the lower limb of the uterine stapler." We postulated that trauma to the amniotic membranes caused by such devices might contribute to preterm labor and delivery. Thus, our group chose to modify the method of uterine entry and closure.

It should also be noted that the MOMS protocol prescribes that "all discharged patients (and their support person) will stay close to the MOMS Center in accommodations provided to permit standardized postoperative management, ultrasound evaluation, and delivery." Exceptions could be granted only in cases of extreme hardship. Before MOMS, the standard procedure at Vanderbilt had been to discharge patients to the care of their local maternal–fetal medicine specialist after approximately 5 days of hospitalization. After MOMS, that practice was resumed at Vanderbilt.

We describe preliminary results of the initial consecutive series of intrauterine myelomeningocele repairs performed at Vanderbilt during approximately the first 2 years after the conclusion of MOMS. These results suggest that a modified uterine surgical approach can achieve significant improvement in rates of premature rupture of membranes and chorioamnion separation and can achieve moderate improvements in gestational age at delivery.

Methods

Study Design and Statistical Analysis

This prospective cohort study reviewed outcomes for patients delivered at Vanderbilt between March 1, 2011, and January 31, 2013, who met previously published MOMS trial criteria and underwent prenatal repair of myelomeningocele.[2] The main outcomes evaluated included preterm delivery and delivery complications (in particular, premature rupture of membranes, chorioamnion separation, and oligohydramnios). These outcomes were then compared with those for the MOMS prenatal repair cohort (hereafter called the MOMS cohort). Consent was obtained to collect medical information about the parents and their neonates in a fetal surgery database approved by the Vanderbilt Institutional Review Board. Using the Shapiro-Wilk W test, we determined that distribution for our patient population was normal; therefore, we report means and standard deviations. Parametric statistics were used to compare our cohort with the previously reported MOMS cohort. A p value < 0.05 was determined a priori to indicate significance, and analysis was conducted by using StatPac (version 4.0, StatPac, Inc.) and SAS (version 9.3, SAS Institute, Inc.).

Surgical Technique

With a goal of improving pregnancy-related outcomes, we used a modified approach to uterine entry, fetus and membrane manipulation, and closure (Videos 1–4).

Video 1. Uterine opening. 1) Stay sutures are placed to stabilize the uterine wall and amniotic membrane. 2) Initial entry is performed with electrocautery. 3) Allis-Adair clamps are placed at the cut edges of the muscle exposing the amniotic membrane. Copyright Kelly A. Bennett. Published with permission. Click here to view with Media Player. Click here to view with Quicktime.

Video 2. Membrane binding. 1) Membrane is opened, and full-thickness running locked sutures are used to secure the membrane to the uterine wall. 2) Surgical stapler is used one time to enlarge the incision. 3) Fetus is visualized by ultrasonography and positioned by using extrauterine manipulation for access to the myelomeningocele sac. Copyright Kelly A. Bennett. Published with permission. Click here to view with Media Player. Click here to view with Quicktime.

Video 3. Lesion repair. 1) Lesion is closed in 2 layers in neurosurgical fashion; the neural placode is sharply dissected. The dura is identified and freed from the skin and lumbodorsal fascia and closed by using a running simple suture. 2) Skin is mobilized by spreading-scissor dissection and closed with a running simple suture. Copyright Kelly A. Bennett. Published with permission. Click here to view with Media Player. Click here to view with Quicktime.

Video 4. Uterine closure. 1) Uterus is closed with closely placed full-thickness running locked sutures supplemented

with figure-of-eight interrupted sutures; closure incorporates the absorbable staples to achieve accurate myometrial edge apposition. 2) Before the last sutures are placed, warmed sterile saline with antibiotics is used to restore amniotic fluid volume to preoperative level. Copyright Kelly A. Bennett. Published with permission. Click here to view with Media Player. Click here to view with Quicktime.

On the day of surgery, the patient was taken to a standard obstetrical operating room. Systemic broad-spectrum antibiotics were administered prophylactically. A 50-mg indomethacin suppository was administered per rectum, and the patient was anesthetized with a combination of general and epidural anesthesia. The indwelling epidural catheter also enabled administration of epidural narcotics for postoperative analgesia. The gravid uterus was exposed through a vertical infraumbilical midline laparotomy and exteriorized. The fetal position and placenta were then mapped using a sterile ultrasonography transducer. The primary surgeon chose the hysterotomy location according to the location of the placenta. In contrast to the operative procedure used for MOMS patients, initial uterine entry for our study cohort patients was accomplished without the aid of a trocar.

The initial entry into the myometrium was performed by using electrocautery with coagulative current, after placement under ultrasonography guidance of 2 full-thickness 0 chromic stay sutures for stabilization of the uterine wall and the amniotic membrane. A series of Allis-Adair clamps were then placed progressively on the cut edges of the muscle until the amniotic membrane was exposed. This technique allows for effective control of uterine bleeding, often resulting in negligible blood loss despite the gravid state of the uterus. The membrane was then opened under direct visualization; to avoid chorioamnion separation, the membrane was secured to the uterine wall with a full-thickness running locked suture of 0 chromic. For the duration of the procedure, most amniotic fluid remained in utero. Amniotic fluid that spilled from the amniotic sac was replaced with warmed normal saline. The footplate of a United States Surgical Corporation CS-57 auto-stapling device was then passed into the uterine cavity. To ensure that no fetal tissue was included, we examined the uterine wall in the stapler manually and with color Doppler ultrasonography. For creation of a 6-cm uterine incision, the stapler was then engaged one time.

Under ultrasonography guidance, the fetus was visualized and positioned by use of extrauterine manipulation through the uterine wall until the myelomeningocele sac was in the center of the hysterotomy. Careful attention was paid to minimizing direct handling of or trauma to the amniotic membrane. Proper positioning was maintained by gently holding the fetal trunk through the relaxed uterine wall while avoiding compression of the placenta, fetal head, and umbilical cord. The fetus was exposed to many of the same anesthetic agents given to the mother and, for additional analgesia during surgery, also received 20 μg/kg (estimated fetal weight) fentanyl by subcutaneous injection. During the procedure, fetal heart rate was monitored by continuous sonographic visualization. Fetal echocardiography was performed by our senior sonographer and supervised by our pediatric cardiologist.

The myelomeningocele was closed in 2 layers in routine neurosurgical fashion with the assistance of loupe magnification. The neural placode was sharply dissected from the surrounding arachnoidal tissue and allowed to drop into the spinal canal. The dura was then identified, freed from the skin and lumbodorsal fascia, reflected over the placode, and closed with a running 7-0 Vicryl (Ethicon) suture pattern. For patients in whom the dura could not reach over the entire defect, a small patch of dural substitute (Duraform, Codman & Shurtleff, Inc.) was sewn in a 360° fashion to cover the defect. Last, the skin was widely mobilized by spreading-scissor dissection in the subcutaneous plane and closed with a running simple suture of 5-0 PDS (Ethicon). For lesions in which excess tension on the skin edges prevented direct approximation, this approach was modified as follows. Vertical relaxing incisions were performed in one or both flanks, enabling elevation of 1 or 2 straight bipedicled skin and subcutaneous tissue flaps. These flaps were approximated centrally and closed over the spinal defect. Care was taken to maintain sufficient vascularity of the flaps. The secondary soft-tissue donor defects created by the transposition of the flaps were grafted with acellular cadaveric dermal allograft (Flex HD, Musculoskeletal Transplant Foundation).

The uterus was closed with full-thickness running locked 0 PDS suture, supplemented at intervals with full-thickness figure-of-eight interrupted sutures. Care was taken to achieve accurate apposition of the myometrial edges. The myometrial repair incorporated the absorbable polyglycolic acid staples left by the auto-stapling device and secured the amniotic membrane. To achieve a watertight secure closure, sutures were closely spaced. As the last of these sutures were placed, warmed sterile saline containing 500 mg nafcillin was returned to the uterus until ultrasonographic measurement of the deepest vertical pocket confirmed restoration of the amniotic fluid volume to the preoperative level. With the aim of preventing adhesion formation, the hysterotomy was then covered with a sheet of Interceed absorbable adhesion barrier (Johnson & Johnson Medical). The uterus was then returned to the abdominal cavity. The laparotomy was closed in standard fashion with 0 PDS suture, Scarpa's fascia with 3-0 PDS suture, and the dermis with INSORB staples (Incisive Surgical).

The patient was then transferred to the labor and delivery unit for postoperative care. The epidural catheter was removed on the 1st postoperative day, and prophylactic antibiotic therapy was administered for 2 days. Patients were discharged from the hospital when they were ambulating well, were eating a regular diet, and had achieved appropriate pain control. At the time of discharge, patients were free to return to their community of origin for continued prenatal care with their referring maternal–fetal medicine provider. Patients were monitored weekly with transabdominal ultrasonography for assessment of amniotic fluid index, cerebral ventricular dimension, position of the cerebellum in the posterior fossa, and fetal well-being. A dedicated coordinator maintained weekly telephone contact with patients and providers. Each patient was scheduled for elective cesarean delivery at 37 weeks of gestation or earlier for standard obstetric indications. Specific indications for delivery include the onset of labor or premature rupture of membranes, cho-

rioamnionitis, suspected uterine rupture, placental abruption, nonreassuring fetal status, or elective delivery at 34 weeks of gestation for severe hydrocephalus.

Results

Of 107 fetuses screened at Vanderbilt over the study period, 43 underwent intrauterine closure. Tables 1 and 2 detail the relevant demographic variables and outcomes for the study cohort and the MOMS cohort. For the study cohort, 43 patients were initially identified, but as a result of 2 fetal deaths, 41 patients are represented in all analyses except mortality rate.

The incidence of premature rupture of membranes, a major contributor to preterm labor and delivery, was 22% for the study group (9 of 41), which compared favorably with 46% for the MOMS cohort (36 of 78), ($p = 0.011$). An additional contributor to preterm delivery is chorioamnion separation. In the study cohort, no chorioamnion separation was seen, which compared favorably with the 26% (20 of 78) rate for the MOMS cohort ($p < 0.001$). The incidence of oligohydramnios did not differ statistically between the 2 cohorts.

The mean (± SD) gestational age at delivery was 34.4 ± 6.6 weeks, similar to that for the MOMS cohort (34.1 ± 3.1 weeks). However, a statistically significantly higher proportion of infants in the study cohort were born at 37 weeks or later: 16 of 41 (39%) in the study cohort and 16 of 78 (21%) in the MOMS cohort ($p = 0.030$). In addition, only 2 (4%) of 41 infants in the study cohort were delivered at less than 30 weeks, compared with 10 (13%) of 78 in the MOMS cohort. This comparison did not quite reach statistical significance ($p = 0.084$), but the trend is favorable and may reach significance as the study cohort grows. The mean (± SD) birth weight was 2487 ± 631 g versus 2382 ± 688 g in the MOMS cohort, a nonsignificant difference.

Of note, the distribution of lesion levels was statistically equivalent except at lesion level L3–4 (58% for the study cohort vs 38% for the MOMS cohort, $p = 0.038$). Although this difference might affect the need for ventricular shunting, it should not affect obstetrical outcomes. The mean (± SD) age of study cohort mothers at screening was 29 ± 5.5 years, consistent with that of MOMS cohort mothers, which was 29.3 ± 5.3 years. Among mothers, there were no surgical complications, no blood transfusions were administered, and no complete uterine dehiscence was reported for those who delivered. One patient was admitted to the intensive care unit for 1 day because of a postoperative diagnosis of pneumonia.

The fetus that died intraoperatively became asystolic and was unresponsive to resuscitative efforts. A diagnosis of placental abruption was presumed, and a rare thrombophilia was later diagnosed for the mother. This fetus figures in the calculation of total mortality but was not at risk for the other obstetrical primary outcome measures and was excluded from those calculations. Another fetus died after the mother experienced premature rupture of membranes 5 days postoperatively and is included in the analysis of premature rupture of membranes but not in other obstetrical primary outcome measures. Fetal mortality rates did not differ statistically between the cohorts (5% for the study cohort vs 3% for the MOMS cohort, $p = 0.533$). One infant died 18 days after delivery because of a complication from an umbilical line placement but is included in the analysis of obstetrical results because the death was not directly associated with the fetal repair. Two neonates underwent postnatal revision of the myelomeningocele repair, and the rate for ventricular shunt placement was 41% over 12 months, which is similar to the 40% reported for the fetal repair cohort in the MOMS trial ($p = 0.651$).

Discussion

Open fetal surgery for treatment of fetal anomalies

TABLE 1: Comparison of cohort demographics

Demographic	Value*		p Value
	Study Cohort (n = 43)	MOMS Fetal Repair (n = 78)†	
mothers			
race			
white	41 (95)	73 (94)	1.00
black	1 (2)	1 (1)	1.00
Hispanic	1 (2)	2 (2)	1.00
other	0 (0)	2 (2)	0.538
mean age at screening in yrs	29.4 ± 5.5	29.3 ± 5.3	0.922
neonates			
female	23 (53)	35 (45)	0.364
lesion level			
thoracic	0	4 (5)	0.296
L1–2	7 (16)	21 (27)	0.260
L3–4	25 (58)	30 (38)	0.038
L5–S1	11 (26)	23 (29)	0.647

* Values are presented as the number (%) unless noted otherwise. The mean value is presented as ± SD.

† Data from Adzick et al., 2011.

TABLE 2: Comparison of cohort outcomes

Outcome	Value*		p Value
	Study Cohort (n = 41)	MOMS Fetal Repair Cohort (n = 78)†	
mothers			
chorionic membrane separation	0	20 (26)	<0.001
oligohydramnios	10 (24)	16 (21)	0.708
premature rupture of membranes	9 (22)	36 (46)	0.011
spontaneous labor	10 (24)	30 (38)	0.125
blood transfusion at delivery	0	7 (9)	0.086
hysterotomy status at delivery			
intact	36 (88)	49/76 (64)	0.014
thinning	2 (4)	19/76 (25)	0.006
area of dehiscence	3 (7)	7/76 (9)	0.998
complete dehiscence	0	1/76 (1)	1.00
neonates			
perinatal death	2 (5)	2 (3)	0.533
mean gestational age at birth in wks	34.4 ± 6.6	34.1 ± 3.1	0.736
gestational age at birth in wks			
<30	2 (4)	10 (13)	0.084
30–34	12 (29)	26 (33)	0.651
35–36	11 (27)	26 (33)	0.466
>37	16 (39)	16 (21)	0.030
mean birth weight in g	2487 ± 631	2382 ± 688	0.418
dehiscence at repair site	3 (7)	10/77 (13)	0.538
shunt placement by 12 mos of age	14 (41)	31 (40)	0.651

* Values are presented as the number (%) unless noted otherwise. Mean values are presented as ± SD.
† Data from Adzick et al., 2011.

was first performed in the 1980s, after preliminary studies had been performed in animal models.[8,13] Because the potential risks were substantial and the likelihood of success was uncertain, these early open procedures were limited to the treatment of lethal malformations. As experience with the open technique improved and as the maternal and fetal risks became better understood, intervention for patients with nonlethal malformations was considered.[11] For fetuses who underwent prenatal myelomeningocele repair in MOMS,[2] placement of a ventricular shunt at 1 year of age was significantly reduced (prenatal repair group 40% vs postnatal repair group 82%, $p < 0.001$). These results were similar to those from earlier nonrandomized studies.[1,5,6,10,12] More recent studies using non-MOMS criteria have reported ventricular shunt rates as low as 52% and 65%.[4,7] MOMS also demonstrated improvement in overall neuromotor function in patients at 30 months of age by a variety of measures; for example, 42% of those who underwent fetal surgery but only 21% of those who underwent postnatal surgery were walking independently ($p < 0.01$). Finally, hindbrain herniation was significantly reversed by fetal surgery; no hindbrain herniation was observed for 36% of infants who underwent in utero repair and for only 4% of those who underwent postnatal repair. MOMS also revealed that fetal myelomeningocele repair increases the following risks: chorioamnion separation (26% with prenatal surgery vs 0% with postnatal repair, $p < 0.001$), premature rupture of membranes (46% vs 8%, respectively, $p < 0.001$), oligohydramnios (21% vs 4%, respectively), and preterm delivery (80% vs 15%, respectively, $p < 0.001$) and includes a 13% risk for extreme prematurity (delivery earlier than 30 weeks of gestation).

With these risks in mind, we set out to refine the technique of uterine entry. The surgical technique used at Vanderbilt was developed on the basis of our belief that shearing of the amniotic membrane away from the myometrium is a frequent complication when previously published operative techniques are used and that chorioamnion separation is a risk factor for premature rupture of membranes, preterm delivery, and oligohydramnios. We believe that shearing of the membrane may be a contributor to uterine irritability, especially when accompanied by membrane hematoma, and could predispose to placental abruption. It has been observed, and it is our belief, that trocar entry through the myometrium probably exerts substantial inward pressure on the membrane, tenting it on the trocar tip before perforation, which can lead to delamination over a variable area. We feel that prevention of amniotic membrane separation, membrane rupture, and oligohydramnios are critical aspects of maintaining pregnancy to term, although only 2 of these 3 outcomes were statistically significant in this study. Obtaining effective and watertight myometrial repair is essential and is ac-

complished by accurate apposition of the muscle edges with multiple closely spaced figure-of-eight sutures with a long-lasting absorbable suture material. Weak hysterotomy repair can also predispose a mother to risk for uterine rupture in the third trimester.

Uterine entry by use of the modified technique in this consecutive case series has led to substantial improvements in pregnancy-related outcomes. The 39% rate of term delivery (> 37 weeks of gestation) in this series is notably better than the 21% rate reported in MOMS. No chorioamnion separation was observed in our study cohort compared with 26% observed in MOMS. Thus, at least 2 of the 3 major determinants of preterm labor and delivery (premature rupture of membranes and membrane separation) were significantly improved by modification of the surgical technique. It is also interesting to note that the hysterotomy at delivery was more likely to be intact than in the MOMS fetal cohort (Table 2). At the same time, the risk for fetal death did not differ statistically.

The intraoperative death that occurred during this study was thought to have resulted from placental abruption, which probably resulted from a previously undiagnosed thrombophilia, caused by a factor V Leiden mutation. This diagnosis is known to cause complications associated with pregnancy. However, it is rare enough that patients applying for intrauterine repair are not routinely screened for this abnormality. The other fetal death resulted from premature rupture of membranes 5 days postoperatively, which resulted in preterm delivery 5 days after repair; the fetus was previable at that time. It should be noted that this patient was known to have endometriosis, which was said to be mild. However, at surgery it was found to be quite severe, resulting in extreme difficulty mobilizing the uterus. Positioning of the uterus and fetus were thus severely restricted, which made performing the procedure more difficult. From this episode, we concluded that care should be taken in the future to better assess the degree of involvement in patients with a history of endometriosis. Despite these 2 unfortunate outcomes, it still appears that the overall neonatal outcomes were not adversely affected by our modifications to the procedure; the overall mortality rate did not significantly differ from that of MOMS. Additional follow-up is ongoing to ascertain whether lower extremity motor function and cognitive development are also equivalent; we presently have no reason to suspect otherwise.

An additional point of discussion is postsurgical care. The reduced complications described above were seen in the setting of prenatal care provided in most instances by multiple maternal–fetal medicine providers outside our fetal surgical center, suggesting that the improvements are probably attributable to surgical techniques and anesthesia management rather than any specific fixed postoperative protocol. These practitioners comprise an extension of our Fetal Center team, and close communication is maintained with them by our Fetal Center coordinator and Fetal Center maternal–fetal medicine specialists. Accordingly, because of the varied and distributed nature of our subsequent pregnancy care, we recognize that changes in postoperative prenatal care regimen are a possible confounder in the interpretation of the results. The possibility that aspects of this coordinated extended network of maternal–fetal medicine care might contribute to the improved results seen in this series establishes, at a minimum, that provision of subsequent pregnancy care near home by patients' referring practitioners is a safe and effective strategy. This care will be critical as the intervention becomes more common. Anecdotal reports among our patient population also suggest that a home-based approach is preferred and is easier emotionally and financially on patients as well as their families.

Although several of the parameters that we measured demonstrated statistically significant improvements for the study cohort compared with those of the MOMS cohort, these results should still be considered preliminary. Our study cohort is half the size of the MOMS cohort; there is a possibility that adverse effects might appear in parameters that have not yet been measured in our cohort, such as lower-extremity or cognitive function. The incidence of ventricular shunt placement by 12 months of age was the same between groups, however. There was probably substantially better uniformity in the various evaluations in MOMS, given the small number of investigators involved in these evaluations. For the Vanderbilt group, many of the postsurgical evaluations were done by local maternal–fetal medicine specialists. We have considered whether the larger number of physicians involved might affect the results, although we believe that the outcome measures of interest, specifically premature rupture of membranes and membrane separation, are readily identifiable by maternal–fetal medicine specialists. We view the reported outcomes as being reliable.

Conclusions

Uterine access by use of the modified technique described in this report has led to improved pregnancy outcomes in our consecutive case series. When compared with the largest published studies of fetal myelomeningocele repair to date, these outcomes include reduced occurrence of premature rupture of membranes, chorioamnion separation, and early preterm delivery.[2,5] These early results, although promising, require further study in the ongoing growing series. It is hoped that these improvements will lead to further development or modifications of the technique of fetal myelomeningocele closure and to future additional improvements in outcomes for this challenging patient population. These data also point to the substantial value of a nationwide prospective registry of fetal myelomeningocele repairs and, indeed, all postnatal repairs, so that the effect of fetal intervention can continue to be studied in a manner similar to that of a phase IV postmarketing study. As pediatric neurosurgeons continue to partner with maternal–fetal medicine colleagues and others to implement the findings of MOMS, it is critical that we understand the entire team-based approach so that we can adequately analyze the results and create innovative solutions to barriers inhibiting the improvement of care.

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Disclosure

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References

1. Adzick NS, Sutton LN, Crombleholme TM, Flake AW: Successful fetal surgery for spina bifida. **Lancet 352:**1675–1676, 1998
2. Adzick NS, Thom EA, Spong CY, Brock JW III, Burrows PK, Johnson MP, et al: A randomized trial of prenatal versus postnatal repair of myelomeningocele. **N Engl J Med 364:**993–1004, 2011
3. Beeker TW, Scheers MM, Faber JA, Tulleken CA: Prediction of independence and intelligence at birth in meningomyelocele. **Childs Nerv Syst 22:**33–37, 2006
4. Bowman RM, Boshnjaku V, McLone DG: The changing incidence of myelomeningocele and its impact on pediatric neurosurgery: a review from the Children's Memorial Hospital. **Childs Nerv Syst 25:**801–806, 2009
5. Bruner JP, Tulipan N, Paschall RL, Boehm FH, Walsh WF, Silva SR, et al: Fetal surgery for myelomeningocele and the incidence of shunt-dependent hydrocephalus. **JAMA 282:**1819–1825, 1999
6. Bruner JP, Tulipan NE, Richards WO: Endoscopic coverage of fetal open myelomeningocele in utero. **Am J Obstet Gynecol 176:**256–257, 1997
7. Chakraborty A, Crimmins D, Hayward R, Thompson D: Toward reducing shunt placement rates in patients with myelomeningocele. **J Neurosurg Pediatr 1:**361–365, 2008
8. Crombleholme TM, Harrison MR, Langer JC, Longaker MT, Anderson RL, Slotnick NS, et al: Early experience with open fetal surgery for congenital hydronephrosis. **J Pediatr Surg 23:**1114–1121, 1988
9. Dennis M, Landry SH, Barnes M, Fletcher JM: A model of neurocognitive function in spina bifida over the life span. **J Int Neuropsychol Soc 12:**285–296, 2006
10. Farmer DL, von Koch CS, Peacock WJ, Danielpour M, Gupta N, Lee H, et al: In utero repair of myelomeningocele: experimental pathophysiology, initial clinical experience, and outcomes. **Arch Surg 138:**872–878, 2003
11. Harrison MR, Evans M, Adzick NS, Holzgreve W: **The Unborn Patient: The Art and Science of Fetal Therapy, ed 3.** WB Saunders, 2001
12. Kohl T, Hering R, Heep A, Schaller C, Meyer B, Greive C, et al: Percutaneous fetoscopic patch coverage of spina bifida aperta in the human—early clinical experience and potential. **Fetal Diagn Ther 21:**185–193, 2006
13. Langer JC, Harrison MR, Schmidt KG, Silverman NH, Anderson RL, Goldberg JD, et al: Fetal hydrops and death from sacrococcygeal teratoma: rationale for fetal surgery. **Am J Obstet Gynecol 160:**1145–1150, 1989
14. Rintoul NE, Sutton LN, Hubbard AM, Cohen B, Melchionni J, Pasquariello PS, et al: A new look at myelomeningoceles: functional level, vertebral level, shunting, and the implications for fetal intervention. **Pediatrics 109:**409–413, 2002
15. Tulipan N, Sutton LN, Bruner JP, Cohen BM, Johnson M, Adzick NS: The effect of intrauterine myelomeningocele repair on the incidence of shunt-dependent hydrocephalus. **Pediatr Neurosurg 38:**27–33, 2003

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