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Global variability in fetal spina bifida surgery: a survey of neurosurgical strategies

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OBJECTIVE The aim of this study was to investigate the global variability in intraoperative neurosurgical management strategies for fetal spina bifida surgery.

METHODS All prenatal fetal spina bifida surgery centers identified through the International Society of Prenatal Diagnosis website and previous literature were invited to participate in an online survey addressing various aspects of the surgery, including fetal selection criteria, surgical technique, and common intraoperative challenges.

RESULTS Thirty-four centers (72%) responded to the survey, more than half of whom perform fewer than 10 surgeries annually (56%). The most common earliest gestational age (GA) for fetal surgery was 23 (36%, n = 12/33), ranging from < 21 weeks (9%, n = 3) to > 24 weeks (9%, n = 3). The latest GA for surgery varied from < 26 weeks (24%, n = 8) to 30 weeks (3%, n = 1), with the majority setting a cutoff at 26 weeks (50%, n = 17). Open fetal surgery is the predominant method in 76% of centers (n = 26), followed by a hybrid approach (laparotomy with fetoscopy on the uterus; 29%, n = 10) and fully percutaneous fetoscopic surgery (15%, n = 5). Filum terminale dissection is performed in 58% (n = 19/33) of centers and placode tubularization in 46% (n = 15/33). Myofascial flaps are routinely used in 55% of the centers (n = 18/33). When primary skin closure is not possible, 39% (n = 13/33) will use releasing side cuts and one-third of all centers will use acellular dermal matrix grafts (33.3%, n = 11/33). Extensive skin defects and suboptimal fetal access were commonly cited as the most significant intraoperative challenges.

CONCLUSIONS There is variability in the fetal inclusion criteria and intraoperative management of fetal spina bifida across centers. This variability emphasizes the need for more research on best practices as well as standardized outcome reporting (ideally through "core outcomes") to allow for comparison between centers. Identified challenges, such as difficulties in skin closure, highlight specific areas for future innovations in the field.

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KEYWORDS fetal surgery; fetoscopy; myelomeningocele; quality improvement; congenital; global surgery

The approach to the surgical management of spina bifida aperta, or myelomeningocele (MMC), has changed significantly since the Management of Myelomeningocele Study (MOMS) trial was published in 2011.[1–5] This trial showed that prenatal surgery improves infant motor function and decreases the need for ventriculoperitoneal (VP) shunting for hydrocephalus when compared with postnatal surgery for this common birth defect, affecting 4.63 per 10,000 births worldwide.[1,6] The results of the trial have led to an increased use of fetal surgery for spina bifida over the last decade. Forty to 50 centers now offer this intervention globally and hundreds of procedures are performed each year.[7–9]

The intraoperative neurosurgical technique of fetal spina bifida repair is often different from its postnatal management, as surgeons attempt to limit the duration of the surgery, tissues are more fragile, and complex procedures are more difficult due to the limited exposure of the fetus.[10]

ABBREVIATIONS ADM = acellular dermal matrix; GA = gestational age; IQR = interquartile range; MMC = myelomeningocele; MOMS = Management of Myelomeningocele Study; PDS = polydioxanone suture; VP = ventriculoperitoneal.

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TABLE 1. Survey questions and response options

Survey Question	Response Options
Does your center currently perform fetal SB surgery?	Yes, no
Approximately how many fetal SB surgeries does your center perform each year?	<10, 10–20, 21–40, 41–100, >100 cases, other (please specify)
In what year did your center perform its first fetal SB repair?	Open-ended year selection (e.g., 1996, 1997, …2023)
What is the minimum GA at which your center typically considers patients eligible for fetal SB surgery?	<21 wks, 21 wks, 22 wks, 23 wks, 24 wks, other (please specify)
What is the maximum GA at which your center typically considers patients to be eligible for fetal SB surgery?	<26 wks, 26 wks, 28 wks, 30 wks, 32 wks, other (please specify)
What is the highest level of spinal lesion for which your center offers fetal surgery for SB?	Lower cervical (C3–7), upper thoracic (T1–4), mid thoracic (T5–8), lower thoracic (T9–12), upper lumbar (L1–2), lower lumbar (L3–5), other (please specify)
What is the lowest level of spinal lesion for which your center offers fetal surgery for SB?	Upper lumbar (L1–2), lower lumbar (L3–5), upper sacral (S1–2), lower sacral (S3–5), other (please specify)
Is the presence of hindbrain herniation a requirement for fetal SB surgery at your center?	Yes, no, other (please specify)
What surgical approach does your center offer for fetal SB repair?*	Open fetal surgery, fully percutaneous fetoscopic surgery, hybrid fetoscopic surgery, other (please specify)
Is it common practice at your center to attempt to tubularize the placode during fetal SB surgery?	Yes, no, other (please specify)
Does your center routinely dissect the filum terminale during prenatal SB surgery?	Yes, no, other (please specify)
Is it common practice at your center to attempt to close the dura during fetal SB surgery?	Yes, no, other (please specify)
Does your center use dura patches or grafts as part of the standard intraoperative management in fetal SB surgery?	Yes, only if the dura cannot be primarily closed, no, other (please specify)
If your center uses dura patches/grafts, how many patches does your center routinely use?	One patch, two patches, other (please specify)
Does your center routinely perform paraspinal myofascial flaps for fetal SB surgery?	Yes, no, other (please specify)
If primary skin closure cannot be achieved, what alternative approach does your center utilize?*	Acellular dermal matrix (ADM), flap surgery, releasing side cuts, skin patch (non-ADM), other (please specify)
Does your center incorporate an ADM as an additional layer between the dura patch and skin during feasible primary skin closure?	Yes, no, other (please specify)
Any additional intraoperative techniques your center employs in prenatal SB repair?	Open-ended answer
What are the most significant challenges you face in the intraoperative management of fetal SB surgery?*	Skin closure w/ extended skin defects, fetal access during surgery, ensuring watertight closure, no significant challenges, other (please specify)

SB = spina bifida.
* Multiple options can be selected.

As is evident from published protocols, there is significant variability in neurosurgical techniques during open fetal surgery.[11–16] Additionally, some centers are now transitioning to exclusively or partially fetoscopic approaches as part of their standard of care.[17,18] While it has been demonstrated that fetoscopic repair results in lower maternal morbidity and possibly at least similar postnatal leg function compared with open fetal surgery, it is technically more challenging and further restricts the complexity of procedures that can be performed.[19,20] Despite the difference between pre- and postnatal surgical protocols, there has been a notable absence of studies directly comparing the (long-term) outcomes of different neurosurgical techniques used for prenatal MMC closure since the findings of the MOMS trial.

With this study, we aim to describe current practices and document the international variability in the prenatal neurosurgical approach to spina bifida closure as a first step toward identifying the most optimal closure technique.

Methods

Study Design

We developed an online survey to assess neurosurgical intraoperative strategies used during fetal spina bifida repair (Table 1). Study participants were requested to respond to the questionnaire describing their institutional protocols and routine, rather than focusing on personal preferences or occasional variations. Participants were

asked about institutional experience (start date of the fetal MMC surgery program and volume), as well as fetal selection criteria for surgery (lesion level, hindbrain herniation and gestational age [GA]). The core survey consisted of 22 questions regarding the surgical approach, defect management, closure techniques, and common intraoperative challenges. Ethical approval was not required for this study as personal (health) information was not collected.

Participating Centers

All centers identified as prenatal fetal spina bifida surgery centers through the International Society of Prenatal Diagnosis website as well as those that could be identified from previously published papers on fetal spina bifida surgery through a literature search (PubMed and citation chaining) were approached via email using the provided contact details for the neurosurgical or obstetric team members.[21] In cases in which contact information was not provided, additional contacts were retrieved through our research group's existing network. Respondents were given a period of 4 weeks for their initial response, after which a reminder was sent, followed by another reminder 2 weeks thereafter. Centers were excluded from the study when no response was received.

Statistical Analysis

For statistical analysis, the distribution of continuous data was initially assessed using a quantile-quantile (Q-Q) plot and a Shapiro-Wilk test. For dichotomous, ordinal, and categorical variables, data were summarized using absolute values and frequencies. Continuous variables were summarized using either means with standard deviations or medians with interquartile ranges (IQRs), depending on their distribution. In instances where responses were missing for a specific question, the percentage was calculated using only the subset of centers that provided a response, rather than the full cohort of centers. To analyze subgroup differences for dichotomous variables, Fisher's exact test was used. For ordinal or nominal dependent variables, a chi-square test of homogeneity was conducted to determine group differences. If the expected cell count was < 5, indicating a small sample size, Fisher's exact test was used instead. Outliers were identified through visual inspection of boxplots, considering values > 1.5 box-lengths from the edge of the box. Statistical significance was determined using a significance level of $p < 0.05$. All statistical analyses were performed using SPSS software (version 29.0, IBM SPSS Statistics for Windows).

Results

Baseline Center Characteristics and Selection Criteria

Of the 47 centers approached, 37 (79%) responded. Three (6%) were excluded from the study because they were not presently offering fetal surgical repair, leaving 34 centers (72%) for analysis. North American (44%), European (24%) and South American (24%) centers constituted the most prominent groups, with Oceania (3%), and Asian (6%) centers less represented (Table 2). More than half of all centers (56%) performed fewer than 10 fetal spina bifida surgeries per year. The median duration of surgical experience with the procedure was 9 (IQR 7, range 2–22) years. Open fetal surgery was the standard in 76% (n = 26) of the centers, followed by hybrid fetoscopic surgery (laparotomy with fetoscopy on the uterus; n = 10, 29%) and fully percutaneous fetoscopic surgery (n = 5, 15%).

TABLE 2. Baseline characteristics of the included centers (n = 34)

Variable	Value
Center location, n (%)	
North America	15 (44)
Europe	8 (24)
South America	8 (24)
Oceania	1 (3)
Asia	2 (6)
Case load/yr, n (%)	
<10 surgeries/yr	19 (56)
≥10 surgeries/yr	15 (44)
Yrs of experience, n (%)	
<10	16 (47)
≥10	17 (50)
Median starting yr (IQR)	2015 (7)
Median earliest GA required for surgery (IQR), wks	23 (2)
Median max GA to be eligible for surgery (IQR), wks	26 (2)

The most common minimal GA for surgery was 23 weeks (36%, n = 12/33), but some centers would offer surgery earlier than 21 weeks (9%, n = 3). Surgery was limited to pregnancies at fewer than 26 weeks' gestation in 24% of centers (n = 8), while 50% (n = 17) of centers set the upper GA limit to include 26 weeks (Fig. 1). One center (3%) extended the GA limit to include cases up to 30 weeks. Furthermore, 7 centers (21%) do not require hindbrain herniation for surgery.

When asked about the highest anatomical lesion level eligible for surgery, only 33% (n = 11) of centers reported they would perform fetal surgery for high thoracic lesions (T1–4; Fig. 2). Among these, 1 center (3%) also treats lesions at the low cervical level. Additionally, some centers have abandoned using anatomical levels as a criterion altogether (n = 3, 9%). Regarding the lowest anatomical levels eligible for surgery, the majority of centers (n = 21/33, 64%) indicated a willingness to operate on lesions starting at the upper sacral level (S1–2). However, some centers (n = 3, 9%) restricted their surgical interventions to lumbar lesions. Furthermore, 6 centers (18%) indicated they offer surgery to lesions starting below S2, with 2 centers (6%) specifying this consideration only in cases with coexisting hindbrain herniation.

Intraoperative Management

Nineteen centers (58%, 19/33) routinely dissect the filum terminale and 15 (46%, 15/33) tubularize the placode, typically with 6-0 or 7-0 polydioxanone sutures (PDSs). Approximately half (n = 18) of the centers use a patch or graft for dura repair, without attempting primary repair. Nine centers (27%) only use a dural patch if primary

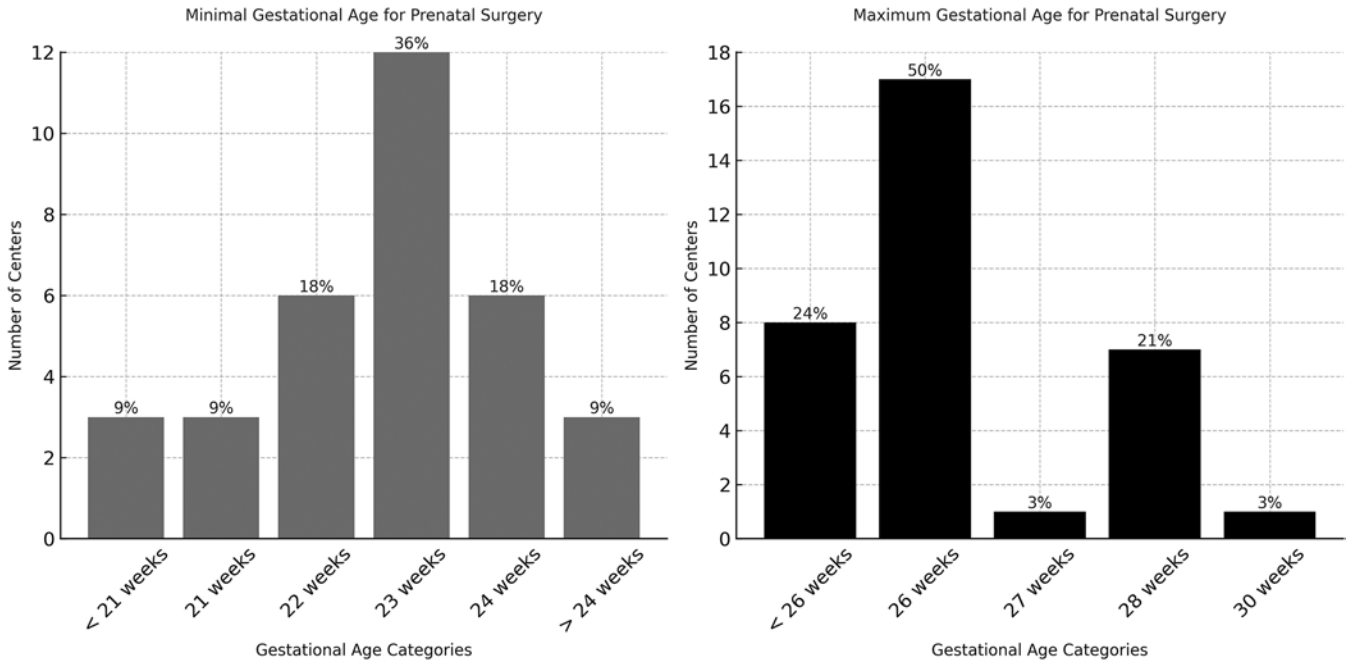

FIG. 1. Distribution of minimum and maximum GA for prenatal spina bifida surgery among centers in the study.

closure cannot be achieved. One center (3%) used a skin patch instead of a dural patch if the dural defect was too large for primary closure. Two centers (7%, 2/31) routinely use a double dural patch. Most centers perform paraspinal myofascial flaps (55%, 18/33), which are typically approximated with 4-0 PDSs, although a variety of resorbable suture materials (braided and unbraided) and thicknesses (ranging from 3-0 to 5-0) are used. If primary skin closure cannot be achieved, the preferred initial approach is to utilize releasing side cuts (39%, 13/33), followed by the application of an acellular dermal matrix (ADM; 33%, 11/33), with a minority resorting to more complex flap repairs (6%, n = 2). In cases in which primary skin closure is feasible, some centers (9%, n = 3) also incorporate an ADM as an additional layer positioned between the dural patch and the skin. The skin is typically closed with PDSs, yet a

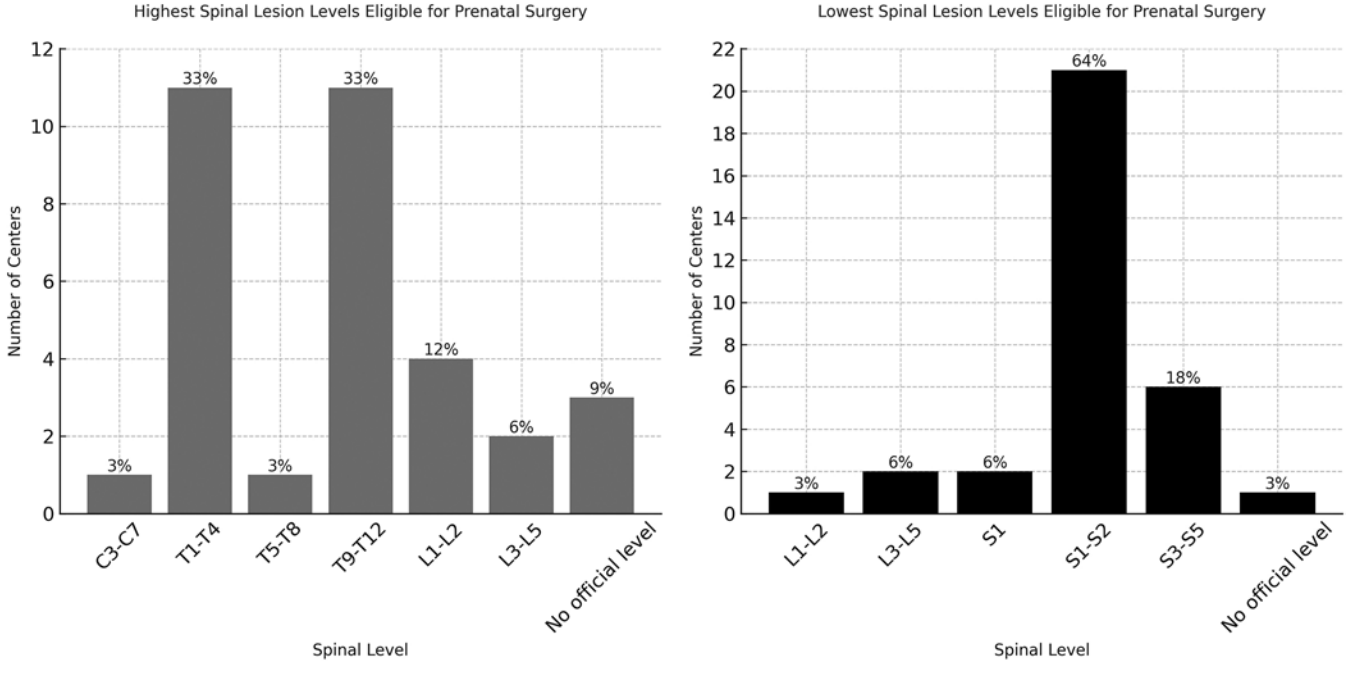

FIG. 2. Comparison of highest and lowest spinal lesion levels eligible for prenatal surgery.

TABLE 3. Subgroup analysis

Variable	Case Load/Yr, n (%)		p Value	Center Location, n (%)			p Value
	<10 Surgeries	≥10 Surgeries		North America	Europe	South America	
Uppermost location of spinal defect			0.433				**0.029**
Lower cervical (C3–7)	1 (5)	0 (0)		0 (0)	1 (17)	0 (0)	
Upper thoracic (T1–4)	7 (37)	5 (46)		8 (57)	4 (67)	0 (0)	
Middle thoracic (T5–8)	0 (0)	1 (9)		1 (7)	0 (0)	0 (0)	
Lower thoracic (T9–12)	6 (32)	5 (46)		4 (29)	1 (17)	5 (71)	
Upper lumbar (L1–2)	3 (16)	0 (0)		1 (7)	0 (0)	1 (14)	
Lower lumbar (L3–5)	2 (11)	0 (0)		0 (0)	0 (0)	1 (14)	
Surgical approach			**0.038**				0.976
Open fetal surgery	14 (74)	5 (33)		8 (53)	4 (50)	5 (63)	
Fully percutaneous fetoscopic surgery	2 (11)	2 (13)		1 (7)	1 (13)	1 (13)	
Hybrid fetoscopic surgery	3 (16)	8 (53)		6 (40)	3 (38)	2 (25)	
Routine dissection of filum terminale			**0.036**				>0.999
No	10 (59)	3 (20)		5 (36)	3 (43)	3 (38)	
Yes	7 (41)	12 (80)		9 (64)	4 (57)	5 (63)	
Routine tubularization of the placode			0.479				0.067
No	7 (41)	9 (60)		10 (77)	3 (38)	2 (25)	
Yes	10 (59)	6 (40)		3 (23)	5 (63)	6 (75)	

Boldface type indicates statistical significance.

wide variety of suture materials (braided and unbraided, resorbable and nonresorbable, barbed and nonbarbed) and thicknesses (ranging from 3-0 to 7-0) are used.

Challenges and Innovations

When asked about the most commonly identified challenges during procedures, surgeons mentioned extensive skin defects (53%, n = 18) and restricted fetal access during the procedure (29%, n = 10). Regarding directions for future research, participants indicated a need for investigating optimal methods for dura mater closure, the ideal timing for surgery, the outcomes of prenatal closure in patients without hindbrain herniation, and the potential reduction in the incidence of tethered cord syndrome through placode tubularization.

Subgroup Analysis

A subgroup analysis was conducted to examine the differences among groups in terms of annual case load, years of experience, and geographic location of the center. This analysis focused on lesion level for eligibility, the surgical approach used, the routine dissection of the filum terminale, and the tubularization of the placode (Table 3). A significant difference was observed in the surgical approaches between centers performing < 10 surgeries annually and those conducting ≥ 10. Specifically, 74% of centers with a lower annual caseload opted for open fetal surgery, compared with 33% of centers with a higher caseload ($p = 0.04$). Additionally, routine dissection of the filum terminale was more commonly performed in centers with < 10 surgeries per year (59%, $p = 0.04$). Fetal selection criteria varied significantly worldwide, with North American and European centers more likely to accept higher spinal defects for surgery compared with South American centers ($p = 0.03$).

Discussion

This study demonstrates that many centers have deviated from the standardized approach toward fetal selection for in utero surgery and the surgical methodology described in the MOMS trial.[1] As shown in Table 4, these deviations primarily involve differences in GA eligibility, inclusion criteria such as the presence of hindbrain herniation, and surgical techniques like placode tubularization and filum terminale dissection. These deviations are inherent to procedures being introduced clinically outside the rigid criteria of a trial. Newer centers will try to fit these advanced procedures within their center's routine methods, and this often results in small regional variations. Reassuringly, most of these variations have not impacted patient outcomes, as the reported short-term outcomes, such as the rates for VP shunt placement, hindbrain herniation reversal, and neonatal wound revision, are similar to those seen in the MOMS trial. While these outcomes were not directly self-reported in our questionnaire, we cross-referenced previously published data from centers in the respondents' geographic regions.[16,22,23] However, long-term outcomes from newer programs have only sparsely been reported, and that is exactly where neurosurgical variation may play a role: differences in management of the spinal cord can affect motor function, the occurrence of tethered cord, and inclusion cysts.[24–28]

The variation in methods demonstrated in this study highlights a need for research and consensus on optimal fetal selection criteria and surgical technique. Ideally, best practices would be derived from randomized trials com-

TABLE 4. Comparison of parameters between the MOMS protocol and current practices in fetal spina bifida surgery across 34 centers

Parameter	MOMS Trial	Current Study (n = 34 centers)
Hindbrain herniation	Required	Not required: 21% (n = 7)
Highest lesion level eligible for surgery	T1	T1–4: 33% (n = 11/33); C3–7: 3% (n = 1); no anatomical level criteria: 9% (n = 3)
Surgical approach	Open fetal surgery only	Open surgery: 76% (n = 26); hybrid fetoscopic surgery: 29% (n = 10); fully percutaneous fetoscopy: 15% (n = 5)
Filum terminale dissection	Not described	Routinely performed: 58% (n = 19/33)
Placode tubularization	Not described	Routinely performed: 46% (n = 15/33)
Use of dural patch	If primary closure cannot be achieved	If primary closure cannot be achieved: 27% (n = 9); always: 55% (n = 18/33); skin patch: 3% (n = 1); no: 12% (n = 4); other: 6% (n = 2)
Use of a double dural patch	Not described	Routinely performed: 7% (n = 2/31)
Paraspinal myofascial flaps	Not described	Routinely performed: 55% (n = 18/33)

paring different neurosurgical approaches. However, given that such trials are unlikely to happen, the next best approach would be intercenter comparison through natural experiments.[29] By "natural experiments," we refer to the variations in clinical practices across different centers, which naturally occur without experimental intervention. These variations allow for observational studies that can reveal the impact of different surgical strategies on outcomes in real-world settings. To facilitate such comparisons, centers should publish their surgical protocols as well as their short- and long-term outcomes. Ideally, a "core outcome" set should also be established as that would offer a standardized framework to uniformly evaluate and compare the outcomes of diverse surgical techniques. Our group is currently in the process of developing such a core outcome set.[30]

Compared to prenatally, postnatal protocols strongly recommend meticulously removing any dystrophic arachnoid remnants surrounding the placode to prevent secondary tethering of the spinal cord.[31] Additionally, they emphasize the importance of removing any epidermal or dermal remnants to avoid delayed formation of dermoid and/or epidermoid cysts.[31] Although our survey did not directly address these particular steps, our clinical experience suggests that the time constraints associated with prenatal closure may impact the thoroughness of the procedure compared with postnatal surgery. Moreover, postnatal protocols strongly recommend sectioning the filum terminale to prevent secondary tethering, yet in our cohort, only a small majority (58%) indicated they are routinely performing this procedure. It remains uncertain how many postnatal centers strictly adhere to the written protocol, as no new operative protocols for postnatal closure have been published in the last 15 years.[31] The most recent guideline on postnatal closure only states, "surgically re-approximate the pial edge of the neural placode and close the wound in sequential layers."[32] Therefore, a true comparison between daily protocols in pre- versus postnatal spina bifida closure remains difficult.

In terms of intraoperative management, our survey revealed that many centers try to protect the spinal cord as much as possible by dissecting the filum terminale, tubularizing the placode, and closing the dura (either primarily or with a graft). However, the variety of suture and graft materials used suggests that the field is still searching for the optimal approach that minimizes surgical complexity and maximizes fetal healing. Studies investigating the healing properties of experimental graft materials and stem cells are currently underway and will hopefully bring some objective evidence.[33,34]

Our study also highlights challenges faced during surgery, particularly skin closure in the presence of extensive defects and limited fetal access. The shift toward more minimally invasive procedures, with 44% of the centers participating in our study already offering a fetoscopic approach, stresses the need for further research in this field. Large skin defects are even harder to close fetoscopically than during open surgery. A lower threshold for the use of skin grafts or robotic assistance, which allows for the use of dexterous instruments, could be the way forward.

Furthermore, the results from the subgroup analysis illuminate how geographic location and institutional experience shape clinical patterns, especially regarding the surgical approach and eligibility criteria for surgery. This variation underscores the influence of local expertise, resources, and patient populations on surgical decision-making, suggesting that a one-size-fits-all approach may not be feasible in the global context of fetal spina bifida repair.

Strengths and Limitations of the Study

The study's strengths include the use of a global questionnaire, which achieved a good response rate from all continents, providing a comprehensive overview of current methods. However, the study also has several limitations. The generic nature of the questions and the grouping of findings did not allow for the identification of smaller, yet potentially significant, procedural differences. Additionally, while the study effectively describes the variability and identifies the most common approaches, it falls short of determining the best practices, which may differ from the most frequently reported methods.

Conclusions

While the field of fetal spina bifida repair has made significant progress since the MOMS trial, the journey toward optimizing neurosurgical surgical techniques and outcomes is ongoing. The diversity in practices revealed

by this study not only reflects the complex nature of these surgeries but also highlights the need for future research. Clinical studies informed by our findings, guided by animal work and supported by a core outcome set, will be critical in addressing the identified challenges, refining surgical techniques, and ultimately, improving the quality of life for patients with spina bifida and their families.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Van Mieghem, Kik, Kunpalin, Kulkarni, DeKoninck. Acquisition of data: Van Mieghem, Kik. Analysis and interpretation of data: Van Mieghem, Kik, Kunpalin, Kulkarni, DeKoninck. Drafting the article: Van Mieghem, Kik, Kulkarni, DeKoninck. Critically revising the article: Van Mieghem, Kunpalin, Kulkarni, DeKoninck, Spoor. Reviewed submitted version of manuscript: Van Mieghem, Kulkarni, DeKoninck, Spoor. Approved the final version of the manuscript on behalf of all authors: Van Mieghem. Statistical analysis: Kik. Administrative/technical/material support: Van Mieghem. Study supervision: Van Mieghem, DeKoninck.

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