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Patient empowerment improves follow-up data collection after fetal surgery for spina bifida: institutional audit

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CONTRIBUTION

What are the novel findings of this work?

In a fetal surgery program whereby the referring unit provides the obstetric and neonatal care after discharge, spontaneous return of outcome data by referring centers was low, yet patient empowerment improved data collection. We first used the Maternal and Fetal Adverse Event Terminology, and it ranked complications in a clinically more relevant way.

What are the clinical implications of this work?

Patient involvement allows them to play an active role as co-researchers, which improved outcome data acquisition for this audit. The Maternal and Fetal Adverse Event Terminology is a useful tool to report on complications after fetal surgery and should be considered in future reports.

ABSTRACT

Objectives: To define and grade fetal and maternal adverse events following fetal surgery for spina bifida and to report on the impact of engaging patients in collecting follow-up data.

Methods: This prospective single-center audit included one hundred consecutive patients undergoing fetal surgery for spina bifida from the first onwards. In our setting, patients return to their referring unit for further pregnancy care and delivery. On discharge, referring hospitals were requested to return outcome data. For this audit, we prompted patients and referring hospitals for missing outcomes. Outcomes were categorized as missing, returned spontaneously or following additional request, and as either provided by the patients or referring center. Postoperative maternal and fetal complications until delivery were defined and graded according to the Maternal and Fetal Adverse Event Terminology (MFAET) and the Clavien-Dindo classification.

Results: There were no maternal deaths and seven (7%) severe maternal complications (anemia in pregnancy, postpartum hemorrhage, pulmonary edema, lung atelectasis, urinary tract obstruction, and placental abruption). No uterine ruptures were reported. Perinatal death occurred in 3% and other severe fetal complications in 15% (perioperative fetal bradycardia/cardiac dysfunction, fistula-related oligohydramnios, and preterm rupture of membranes <32 weeks). Preterm rupture of membranes occurred in 42% and overall, delivery took place at a median gestational age of 35.3 weeks [IQR 34.0-36.6]. Information following additional request, both from centers, but mainly through patients reduced missing data by 21% for the gestational age at delivery, by 56% for the uterine scar status at birth, and by 67% for the shunt insertion at 12 months. Compared to the generic Clavien-Dindo classification, the Maternal and Fetal Adverse Event Terminology ranked complications in a clinically more relevant way.

Conclusions: The nature and rate of severe complications were similar to those reported in other larger series. Spontaneous return of outcome data by referring centers was low, yet patient empowerment improved data collection.

INTRODUCTION

Open spina bifida has a prevalence of approximately 4.9 and 3.2 per 10,000 births in Europe and the USA, respectively.[1, 2] Patients suffer variable degrees of lifelong neurodevelopmental delay, bowel and bladder dysfunction, and orthopedic disabilities.[3]

The Management of Myelomeningocele Study (MOMS) demonstrated that, in selected cases, fetal spina bifida repair reduces the need for a cerebrospinal fluid shunt at 12 months of age (40% vs 82%) and improves the composite score for mental development and motor function at 30 months compared to postnatal repair.[4, 5] These differences persist into school age.[6] However, fetal surgery comes with substantial maternal and fetal risks. In the MOMS, the average gestational age at delivery following fetal surgery was 34.1 weeks, and 13% of women delivered before 30 weeks.[4] Uterine dehiscence, chorioamniotic membrane separation, placental abruption and preterm premature rupture of membranes (PPROM) are typical complications. Since the MOMS, some cohort studies have reported on complications of prenatal repair, some using the generic Clavien-Dindo classification for surgical interventions.[7-12] Recently, the Maternal and Fetal Adverse Event Terminology (MFAET[13]) has been proposed as a tool to aid classification of maternal and fetal adverse events, using a well-defined list of pregnancy-related complications. However, to our knowledge this classification has not yet been clinically applied.

In 2012, The University Hospitals Leuven established a clinical fetal surgery program for spina bifida following an off- and on-site training program[14]. In that program, subsequent obstetric and neonatal care are well defined (Appendix S1 and Figure S1) but provided by the patient's referring unit after discharge rather than at the fetal surgery center. Such *decentralized* fetal surgery program hampers the collection of follow-up data needed to audit a clinical service and ensure optimized care.[14]

The first objective of this study was to collect and assess maternal and fetal complications of patients undergoing fetal surgery for spina bifida in our unit, using the purpose-designed MFAET classification. The second objective was to report on the spontaneous return of follow-up data and the impact of engaging patients in collecting outcomes.

METHODS

Study design

This single-center study at the University Hospitals Leuven, Belgium, included the first 100 patients undergoing fetal surgery for spina bifida between January 2012 and December 2021.

Population and patient flow

Our eligibility criteria for fetal surgery were largely in line with the MOMS-criteria, except for an update of the upper limit of body mass index (from 35 to 40) and the inclusion of women with well-controlled diabetes or previous caesarean sections (Appendix S2).[15] Fetal repair was done under general anesthesia, through laparotomy, uterine exposure and entry to the amniotic sac via an initial small hysterotomy with further expansion using a stapler after crushing of the myometrium.[4] Initially, a 6–8 cm stapled hysterotomy was made which we were able to reduce to 3-4 cm over the years. Through the hysterotomy, ideally a three-layered repair (dura, myofascia, skin) was performed to provide watertight closure.[16] Eventually the uterus was closed in two watertight layers: the first running, the second interrupted and inverting. The first ten patients received magnesium sulfate as tocolysis, the following 90 had atosiban. Details on the postoperative management can be found in Appendix S1 and Figure S1. In December 2019, our center was assigned by the National Health Service England as a highly specialized commissioned service, and a modified leaflet with postoperative and postnatal instructions was added (Appendix S1).

Data collection

Available data were first retrieved from the electronic clinical records. These were entered into a purpose-designed Research Electronic Data Capture (REDCAP) database[17, 18], covering maternal demographics, pre-existing conditions, prenatal fetal findings, operative and postoperative complications, and pregnancy and infant outcomes. For missing data, we contacted patients and referring centers. For this audit, outcomes after discharge were again requested via patients and referring centers via e-mail through the REDCAP platform. In case of a bounce back or missing contact details, patients and referring centers were contacted by telephone, and in the absence of a response, through a letter and telephone support was offered.

Classification of outcomes

Complications were first graded according to the MFAET (Table 1, Appendix S3).[13] Maternal complications not included were graded according to the Common Terminology Criteria for Adverse Events (CTCAE).[19] Complications were first assigned to categories by an experienced fetal surgeon (JDP). After that, these were recategorized by four physicians engaged in the fetal surgery program (SV, JDP, EV, SM,) and the lead authors of the MFAET classification (RS, AD) in a consensus meeting. Prior to that, all were trained by grading 20 complications in 5 practice cases (Appendix S4). To enable comparison with earlier studies[12, 20], complications were also categorized by two observers (SV, JDP) according to the Clavien-Dindo classification (Table S1).[7] Complications are reported as early (≤7 days) or late postoperative (>7 days until delivery).

Information exchange

We compared the availability of data on three empirically chosen outcome measurements we considered essential to assess the quality of care: (1) uterine scar status at delivery; (2) gestational age at delivery; (3) shunt rate at 12 months. We recorded whether this data was returned *spontaneously* following the instructions issued at discharge or *upon additional request* and whether this information was provided by the referring center and/or the patient.

Statistical analysis

We performed descriptive statistics, reporting numbers, percentages, and, where appropriate, medians and interquartile ranges; using SPSS (version 28; IBM Software, Inc, Armonk, NY) and GraphPad Prism for Windows V.9.3.1 (GraphPad Software, San Diego, CA, USA). The Pearson χ^2 test was used to compare response rates. To assess the variability in the reporting accuracy between patients and centers, we performed a Bland-Altman analysis of the continuous variable gestational age at birth.

RESULTS

Demographics

Table 2 displays maternal and pregnancy characteristics and operative details. All but three patients were from Europe; one out of four patients were UK citizens referred as part of the NHS England Highly Specialised Commissioned Services.

Complications

We identified 265 maternal and 55 fetal complications. All complications were reviewed, and of the 24 severe to life-threatening, 21% were recategorized (four downgraded, one upgraded). The recategorization rate for mild and moderate ones was 0% and 1%, respectively (two upgraded). Therefore, 2% of complications were recategorized at the review stage. Four types of complications (amnio-peritoneal fistula, oligo- to anhydramnios, uterine dehiscence, PPROM grade 1) lacked a precise MFAET definition. Hence, they were labelled as difficult to categorize and they may be revised in a future MFAET edition.

Taking only the highest graded complication for each woman into account, mothers had a variety of mild (15%), moderate (77%), severe (6%), life-threatening (1%) and no lethal complications (0%). Along the same lines, in fetuses, mild complications occurred in 21%, moderate in 10%, severe in 14%, life-threatening in 1% and lethal in 3%, respectively. There was no trend in the occurrence of complications over time (Table S2).

Early complications

Maternal complications are detailed in Table 1. There were no maternal deaths (grade 5). Five (5%) patients had severe complications, including two women who received postoperative blood transfusions due to a low postoperative hemoglobin but without an obvious active bleeding site. Both patients had already a low hemoglobin (<10 g/dL) pre-operatively. One patient developed pulmonary edema, which resolved after a single course of furosemide. One dyspnoeic patient was diagnosed with lung atelectasis on X-ray, which improved after oxygen supplementation and physiotherapy. One patient had flank pain on day four. On ultrasound scan, she had unilateral hydronephrosis without demonstrable urolithiasis. A similar pain episode occurred before the index pregnancy. She received a double-J stent on postoperative day six, which was removed three months later.

Eighty-three patients (83%) had mild or moderate early maternal complications. Of note, in two patients, there was severe oligohydramnios on postoperative day two and seven, respectively, and an amnio-peritoneal fistula was confirmed on MRI. The first patient, early in our experience, was managed conservatively as an in-patient for 55 days (grade 2). The second patient was managed as an out-patient (grade 1). One patient developed acute lower abdominal pain on day four, and because of an initial epoch of hematuria, we suspected and eventually confirmed on MRI urinary leakage at the bladder dome. An indwelling catheter was inserted for ten days which resolved the symptoms (grade 2). Two out of our first ten patients, who still received magnesium sulfate rather than atosiban for tocolysis, experienced lethargy or hallucinations.

Five (5%) grade ≥3 fetal complications occurred. One fetus developed bradycardia and decreased cardiac contractility during surgery, requiring resuscitation. Although the fetus recovered, intrauterine fetal death was diagnosed the following day (grade 5). Two additional fetuses required intra-operative resuscitation: one for bradycardia (heart rate <100 beats per minute) without hypo-contractility, and one for hypo-contractility without bradycardia. Both recovered after a single dose of atropine. For the two mothers with amnio-peritoneal fistulas, the associated oligohydramnios was categorized as a grade 3 fetal complication. Five fetuses (5%) had mild to moderate complications, including one with bradycardia <100 beats per minute, which resolved by maternal repositioning.

Late postoperative complications

We obtained post-discharge outcome details on 95 patients. Delivery occurred at a median gestational age of 35.3 weeks [IQR 34.0-36.6]. Twenty-one women delivered prior to 34 weeks (24%); including six who delivered prior to 30 weeks (6%). Grade ≥3 maternal complications were present in three (3%), including one placental abruption at 35 weeks (grade 4) and two blood transfusions due to postpartum hemorrhage (grade 3). Mild or moderate complications developed in 73 patients (77%). The majority were instances of PPROM at a median of 34.1 weeks [IQR 32.3-35.5]. The median interval from PPROM to delivery was 0 days [IQR 0-3]. Of the 17 women who had PPROM <34 weeks, two delivered before 30, thirteen between 30-34 weeks and two after 34 weeks. There were no instances of uterine rupture, yet nine patients (9%) were diagnosed with scar dehiscence without symptoms. At caesarean section, eleven (12%) women underwent uterine scar repair, including two of the ten patients who were described to have a thin scar. One patient presented with anhydramnios at 31 weeks, went into preterm labor at 33 weeks, and an amnio-peritoneal fistula was diagnosed at the time of birth. One patient presented with contractions at 26 weeks, an elevated CRP, and amniocentesis demonstrated chorioamnionitis, prompting preterm delivery (maternal grade 2; fetal grade 4). Both mother and baby recovered following antibiotics, and at the time of writing, the child is healthy and five years old. Chorioamnionitis was demonstrated on pathology in one asymptomatic patient who delivered at 29 weeks (grade 1).

Regarding fetal complications, we observed two perinatal deaths: one was an intra-uterine demise at 29 weeks with an umbilical cord knot shown at post-mortem examination; the other was a neonatal death from complications of prematurity following delivery at 29 weeks. Other fetal complications are displayed in Table 1.

Clavien-Dindo classification

Complications were also categorised using the Clavien-Dindo classification (Table S1). We categorised three maternal complications as severe, one early (urinary tract obstruction) and two late (placental abruption and chorioamnionitis). Five fetal complications were classified as severe (two fetal bradycardias, two perinatal deaths and one fetal cardiac dysfunction).

Shunt rate at 12 months

At the closure of the audit, 69 children had reached the age of 12 months. Of those, 32 (46%) had a ventriculoperitoneal shunt (n=29) or endoscopic ventriculostomy (n=3). Fetuses with no, mild to moderate (10-15mm), or severe ventriculomegaly (>15mm) at preoperative ultrasound were eventually shunted in 32% (n=6/19), 47% (n=17/36) and 57% (n=8/14), respectively.

Information exchange

Two patients (2%) declined to provide further follow-up. Seventy patients (70%) and forty-six referring centers (46%) returned follow-up data upon additional request. The response rate among patients operated before or after the start of the NHS-commissioned service was comparable (36/56 vs 34/44; P= .15), but the response rate among referring centers increased (18/56 vs 28/44; P= .002). Additional feedback following additional request, both from centers but mainly through patients, reduced the missing information on gestational age at delivery from 26% to 5%, uterine scar status from 61% to 5%, and shunt rate at 12 months from 89% to 22% (Table 3 and Figure 1). In 32 patients, both the local center and the patient reported on outcomes at delivery. Gestational age and scar status were identical in 94% (n=30). In two patients, there was a difference of one day. According to the Bland–Altman method, the limits of agreement within a 95% confidence interval was one day. In two other patients, a discrepancy arose in scar status. Of the 31 replies on the shunt rate at 12 months, all were concordant.

DISCUSSION

Main findings

In 100 consecutive patients undergoing fetal surgery for spina bifida, seven severe maternal and 18 severe fetal complications occurred (MFAET grade 3-5). Using the Clavien-Dindo classification, only three (3%) maternal complications would be considered severe. The spontaneous outcome reporting was poor, particularly for outcomes to be reported at one year (11%). Direct engagement with patients and repeated requests to the referring centers resulted in additional information. However, despite all efforts, we still lacked information on essential outcomes such as scar status in 5%, and shunt rates in 22%.

Interpretation

One goal was to compare the MFAET and Clavien-Dindo classification, which differ in some respects. MFAET adds a specific dimension of *pregnancy-related* complications and discriminates between fetal and maternal complications. For instance, MFAET assesses the maternal and fetal impact of complications separately, e.g., in case of chorioamnionitis and PPROM. Also, in our data set, MFAET ranks certain adverse events higher (e.g., pulmonary edema, lung atelectasis, urinary tract obstruction and postpartum hemorrhage) than the Clavien-Dindo system, reflecting their clinical impact. Also, MFAET has a low interobserver variability for moderate and mild complications (only 1% reclassification), but a higher variability for severe complications (20% reclassification). Therefore, some MFAET definitions may need further refinement. Finally, some typical fetal spina bifida surgery-related complications are not captured, such as the uterine scar status, the occurrence of an amnioperitoneal fistula and the presence oligo- or anhydramnios.

For benchmarking our outcomes, we compared the rate and nature of complications, including PPROM rate and gestational age at delivery to other series.[4, 8, 10, 21] As in previous trials, there were no symptomatic uterine ruptures in the index pregnancy[4, 8, 10]. Unfortunately, there is no *precise* definition of uterine dehiscence and thinning, which may need to be addressed in future editions of the MFAET classification. Herein, we referred for dehiscence to a myometrial defect that was covered by peritoneum. We also reported on 92 mothers (92%) experiencing mild to moderate complications (MFAET grade 1-2). At first glance, this is dramatically higher than the 16% in our systematic review.[12] For that, however, the Clavien-Dindo classification was used, which, again, rates complications lower, and most included studies were retrospective chart reviews. Conversely, the rate we observed is close to what was reported by Vonzun *et al*.[21] in a similar prospective single-center audit in Zurich, Switzerland. However, the nature of complications differed. In the Swiss audit, seroma formation and chorioamniotic membrane separation were more frequent, whereas we observed more patients with anemia, oliguria and hypotension. The clinical impact of these complications and the difference between both cohorts are limited.

We had nine patients (9%) with early *fetal* complications. The nature and rate of complications, as well as the shunt rate (46%) at 12 months of age, are comparable to previous reports.[4, 8-10]

According to the American College of Obstetrics and Gynecology, fetal surgery units must collect and benchmark their outcomes.[22] In a *decentralized* program, we observed an impressive lack of return of outcomes despite precise instructions on discharge. Delivery data were missing in 26% for the gestational age at delivery to 61% for uterine scar status and missing infant outcome was as high as 89% for shunt placement at 12 months. Additional requests to patients and centers significantly reduced the amount of missing data. Although good reference data are lacking, the problem of missing outcomes on patients not delivering at the fetal surgery center is not new.[4, 8, 9] The second observation is that, logically, the amount of missing data increases as time after fetal surgery proceeds, e.g., up to 22% for one-year shunt rates. Finally, patients were more responsive to our additional requests than referring centers (approximately 75% versus 45%) and patients' answers aligned remarkably well for the three selected key parameters (94-100%). Although discrepancies may occur more frequently for other, more sophisticated neurologic outcomes, our experience illustrates that patient involvement increases data acquisition in a *decentralized* setting. To improve data quality and accuracy, one could combine efforts and ask patients to urge caregivers at the follow-up unit to fill out standardized reports. Involving patients in research moves them from a passive to an active role and expands their role as co-researchers, thereby promoting patient empowerment.[23, 24]

Strengths and Limitations

This study reports "real world" data on a reasonably sized consecutive case series of patients managed in a standardized way. We have maximized data completeness through contact with patients and referring centers. Our study is one of the few to quantify the impact of patient engagement on data collection and assess concordance with hospital-provided data, which is effective. Finally, we first used the MFAET classification to categories complications of a complex feto-maternal intervention. Our study is limited by its sample size, which precludes a reliable estimate of rare complications. Furthermore, we do not have complete outcomes for all cases, including the two women who declined to participate. This means benchmarking outcomes remains difficult and complications may have been underestimated. Although there was good concordance between patient and hospital-provided data, the delay in providing data and the self-reported nature of patient data may limit the accuracy and quality.

Conclusion

In a cohort of 100 consecutive patients undergoing fetal surgery for spina bifida, similar rates and types of severe maternal and fetal complications were observed as in other large series. The MFAET was first applied and aided in clinically relevant classification of maternal and fetal complications. While spontaneous return of outcome data by referring centers was low, patient empowerment improved data collection.

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Details of Ethics Approval

Auditing of the fetal surgery program for spina bifida was approved by the Ethics Committee for clinical studies (S63598) of the UZ Leuven. All patients gave informed consent for the surgery as well as for data-collection. This study was conducted in compliance with the principles of the Declaration of Helsinki (2013), the principles of Good Clinical Practice (GCP) and in accordance with all applicable regulatory requirements.

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Table 1: Consensus categorization of maternal adverse events from surgery until delivery, categorized by the MFAET classification. [13] [13]

	Early complications (day 0-7), n=100				**Late complications (day 8 - delivery), n=95**			
	Maternal		**Fetal**		**Maternal**		**Fetal**	
Grade 5: *death*	-	-	Fetal bradycardia: non-labor	1 (1%)	-		Perinatal death	2 (2%)
Grade 4: *life-threatening consequences needing urgent intervention*	-	-	-	-	Placental abruption	1 (1%)	Chorioamnionitis	1 (1%)
Grade 3: *severe, but not immediately life-threatening*	Anemia in pregnancy (transfusion) Pulmonary edema Lung atelectasis Urinary tract obstruction	2 (2%) 1 (1%) 1 (1%) 1 (1%)	Oligo-to anhydramnios due to fistula Fetal bradycardia: non-labor Fetal cardiac function abnormalities	2 (2%) 1 (1%) 1 (1%)	Postpartum hemorrhage	2 (2%)	PPROM[‡] Oligo-to anhydramnios due to fistula	9 (9%) 1 (1%)
Grade 2: *moderate or needing local or non-invasive interventions*	Oliguria Anemia in pregnancy (iron supplementation) Hypotension Infection[*] Premature labor Dysesthesia Bladder perforation Wound complication[†] Amnio-peritoneal fistula Cerebrospinal fluid leakage	24 (24%) 14 (14%) 12 (12%) 7 (7%) 6 (6%) 2 (2%) 1 (1%) 1 (1%) 1 (1%) 1 (1%)	Fetal bradycardia: non-labor	1 (1%)	PPROM[‡] Premature labor Uterine dehiscence[§] Postpartum hemorrhage Wound complication[†] Amnio-peritoneal fistula Chorioamnionitis Hemorrhage in pregnancy	40 (42%) 28 (29%) 11 (12%) 5 (5%) 4 (4%) 1 (1%) 1 (1%) 1 (1%)	PPROM[‡]	10 (11%)

Grade 1: *no or mild symptoms not leading to an intervention*	Anemia in pregnancy Rash maculo-papular Wound complication[†] Hemorrhage in pregnancy Amnio-peritoneal fistula Lethargia Hallucinations	64 (64%) 3 (3%) 2 (2%) 1 (1%) 1 (1%) 1 (1%) 1 (1%)	PPROM[‡]	4 (4%)	Postpartum hemorrhage Uterine dehiscence[§] Wound complication[†] Chorioamnionitis Hemorrhage in pregnancy	10 (11%) 8 (8%) 5 (5%) 1 (1%) 1 (1%)	PPROM[‡]	21 (22%)

Note: patients could report multiple complications

[*]Infections other than wound infection, requiring antibiotic treatment: urinary tract infection (n=2), vaginal infection (n=1), e causa ignota (n=2)

†Wound complications were either early [grade 1: seroma (n=1), hematoma (n=1); grade 2: wound infection (n=1)] or late [grade 1: seroma (n=4), dehiscence (n=1); grade 2: wound infection (n=4)]

‡These patients had chorioamniotic membrane separation without confirmed rupture of membranes

§ Definition for uterine dehiscence was agreed upon during the consensus meeting: a myometrial defect, covered by peritoneum. Grade 1: asymptomatic scar thinning without repair at delivery. Grade 2: asymptomatic partial scar dehiscence or scar thinning which was repaired at delivery. Grade 3: scar dehiscence associated with symptoms, yet not perceived as life-threatening. Grade 4: life-threatening symptomatic scar dehiscence.

‡ PPROM is categorized as a maternal (grade 2) as well as a fetal complication and then further subdivided (grade 1: CMS; grade 2: PPROM from 32-33+6 weeks; grade 3: PPROM between 22-32 weeks; grade 4: PPROM <22 weeks)

Table 2: Demographic and operative characteristics of the condition on ultrasound prior to surgery.

Characteristics	Study cohort
Number of patients	100
Maternal findings	
Maternal age (years)	31 [27-36]
Body-mass index at first visit	25 [22-30]
Nulliparous	42 (42%)
History of uterine surgery	
Cesarean section	13 (13%)
Myomectomy	0 (0%)
Country*	
Belgium	10 (10%)
Other European countries	87 (87%)
Non-European	3 (3%)
Findings in the index fetus	
Ventriculomegaly (diameter >10.0 mm)	69 (69%)
Type of lesion	
Myeloschisis	35 (35%)
Myelomeningocoele	65 (65%)
Talipes	23 (23%)
Anatomical level of lesion (ultrasound)	
T12 or higher	6 (6%)
L1-L2	17 (17%)
L3-L4	42 (42%)
L5-S1	35 (35%)
Lower limb movement– n (%)[†]	68/82 (83%)
T12 or higher	3/6 (50%)
L1-L2	15/15 (100%)
L3-L4	27/32 (73%)
L5-S1	23/29 (79 %)
Operative characteristics	
Gestational age at surgery (weeks)	25.3 [24.8-25.7]
Neurulation placode	41 (41%)
Skin repair technique	

Primary closure	77 (77%)
Skin substitute	23 (23%)
Skin-to-skin time (min)‡	200 [175-225]
Neurosurgery time (min)§	74 [60-90]
Length of hospital stay (days)	6 [6-7]

Data are given as n, median [interquartile range], n (%) or n/N (%).

* European: excluding Belgium and including UK Non-European: USA (n=1), Australia (n=2)

† Preserved lower limb movement was defined as movements in hip, knee and ankle joints of both lower limbs. Total number of observations was 82 patients.

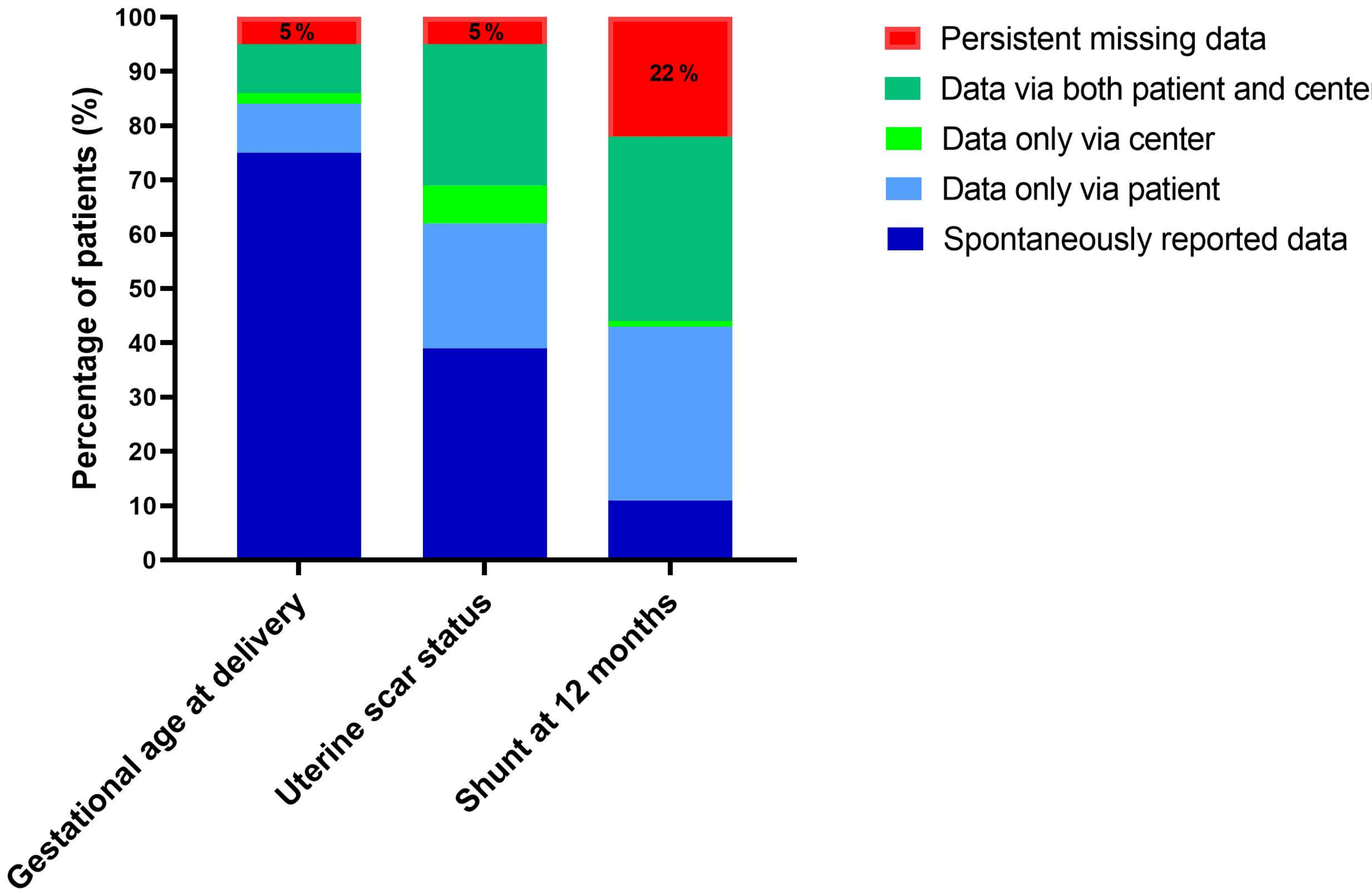
‡ Data of 73 patients available.

§ Data of 79 patients available.

Table 3: Missing data before and after information request.

Reported outcome (n)	Missing data prior to invite	Response by patients following invite	Response by centers following invite	Persistent missing data
Gestational age at delivery (n=98)	25/98 (26%)	18/25 (72%)	11/25 (44%)	5/98 (5%)
2012-2019 (n=54)	11/55 (20%)	6/11 (55%)	1/11 (9%)	4/55 (7%)
2020-2021 (n=44)	14/43 (33%)	12/14 (86%)	10/14 (71%)	1/43 (2%)
Uterine scar status at birth (n=98)	60/98 (61%)	48/60 (80%)	32/60 (53%)	5/98 (5%)
2012-2019 (n=54)	33/55 (60%)	24/33 (72%)	11/33 (33%)	4/55 (7%)
2020-2021 (n=44)	27/43 (63%)	24/27 (89%)	21/27 (78%)	1/43 (2%)
Shunt rate at 12 months (n=88)*	78/88 (89%)	58/75 (77%)	31/75 (41%)	19/88 (22%)
2012-2019 (n=53)	45/53 (85%)	29/45 (64%)	12/45 (27%)	15/53 (28%)
2020-2021 (n=35)	33/35 (94%)	29/33 (88%)	19/33 (58%)	4/35 (11%)

Data are given as n/N (%). *Three had perinatal deaths, seven had not reached 12 months of age at the time of writing



Percentage of patients (%)
0
10
20
30
40
50
60
70
80
90
100
5 %
5 %
22 %
Gestational age at delivery
Uterine scar status
Shunt at 12 months
Persistent missing data
Data via both patient and center
Data only via center
Data only via patient
Spontaneously reported data