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Prenatal Repair of Spina Bifida: A 2-Center Experience with Open Intrauterine Neurosurgery in Chile

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Keywords
Fetal surgery · Fetal therapy · Intrauterine surgery · Myelomeningocele · Open neural tube defects · Spina bifida

Abstract

Objective: To report the experience with prenatal repair of open spina bifida (OSB) from 2 centers in Chile. ***Methods:*** 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. ***Results:*** 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. ***Discussion:*** 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 diversion and an improved ability to walk seem to be the greatest long-term advantages of this procedure.

Bulleted Statements

What's already known about this topic?

- The benefits of intrauterine versus postnatal neurosurgery repair of open spina bifida (OSB) are well established in clinical practice.
- Despite the large number of affected cases born every year and the fact that elective termination of pregnancy for OSB is not an option in Latin America, local ex-

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perience with open intrauterine surgery for OSB is still limited.

What does this study add?

- The experience with open intrauterine surgery for OSB at 2 fetal surgery centers in Chile is presented.
- Preliminary experience with a plastic retractor at the hysterotomy site appears to be promising in terms of reducing postoperative complications such as premature rupture of membranes, chorioamniotic membrane separation, and scar dehiscence.

Introduction

Since the publication of the Management of Myelomeningocele Study (MOMS) trial in March 2011 [1], there has been increasing interest in implementing programs for intrauterine repair of open spina bifida (OSB) at several centers across the world [2]. As the leading country in the development and implementation of this procedure, the USA has the most extensive clinical experience to date, with at least 13 centers performed this operation until June 2018 [2]. However, financial and social constraints make referral to American tertiary centers inaccessible for most patients. This is especially true for patients from developing countries and areas with limited resources, such as Latin America, where, in addition to the large number of cases that occur every year, elective termination of pregnancy in cases of OSB is illegal [3]. This has encouraged several centers in Latin America to offer intrauterine surgery for OSB in an effort to mitigate the devastating consequences of this condition for the individuals that are affected.

Very little experience with open surgery for OSB in Latin America has been published. Two centers in Brazil have recently reported their experience with 237 and 45 cases, respectively [4, 5]. In Chile, our group has reported the perinatal outcomes in 16 additional cases [6]. In Argentina, the experience with 25 cases has also been published in the Spanish literature [7]. The aim of the present study is to present our experience with cases of OSB undergoing open intrauterine surgery at 2 centers in Chile, 1 from the private sector (Clinica Las Condes, CLC) and the other from the public sector (Rancagua Regional Hospital, RRH). These fetal surgery programs started shortly after the results from the MOMS trial were published and followed the same intraoperative and postoperative protocols. This ensures that our experience is comparable to the MOMS trial, gathering information from a heterogeneous sample of Chilean patients.

Patients and Methods

This was a retrospective cohort study of women undergoing open intrauterine surgery for the prenatal repair of OSB at 2 tertiary referral centers in Chile. CLC is a large private hospital that started a fetal surgery program for OSB in September 2011. The first surgery was performed by a combined team led by specialists from Medellin, Colombia, who at that time had had performed 17 such interventions (J. Sanin-Blair, personal communication). The following operations were performed by the local medical team, which included 2 maternal-fetal medicine specialists (W.S. and J.L.A.), 1 neurosurgeon (F.O.), and 1 obstetric anesthesiologist (J.C.D.). In order to meet the demand from the public sector, a center for patients belonging to the Chilean National Health Service was set up at the RRH, a referral center located 85 km south of Santiago. This satellite program was developed in a similar fashion to the program at CLC and was coordinated by two of the authors (W.S. and E.C.). The first patient at this center was operated on in May 2012. After a combined CLC/RRH team worked together on the first 7 cases, the local team at RRH then started performing the operations on their own, following the same protocol. Both programs obtained institutional review board approval, and all patients undergoing surgery signed a written informed consent before the intervention.

Since the launch of these 2 fetal surgery programs, all pregnant women diagnosed as having a fetus with OSB in the second trimester of pregnancy have been considered potential candidates for open intrauterine surgery. Once the diagnosis was confirmed by ultrasound, any additional associated malformations not related to the OSB were then excluded by detailed prenatal ultrasound [8]. Following this, the parents received extensive and thorough counseling from the corresponding maternal-fetal medicine, neurosurgery, and anesthesiology specialists at each of the centers. All patients who met the entry criteria established by the MOMS trial [1] and agreed to open intrauterine repair underwent fetal magnetic resonance imaging. This was done in order to pinpoint the level and extent of the lesion, as well as to determine the intracranial features of the Chiari malformation [8]. Prenatal karyotyping was offered to all patients but was not considered compulsory in some cases due to late referrals. This decision was based on our previous experience of detecting all fetuses with OSB with an underlying chromosomal aneuploidy [9]. In some cases, a normal karyotype was subsequently confirmed by amniotic fluid collected at the time of the operation. A thorough clinical

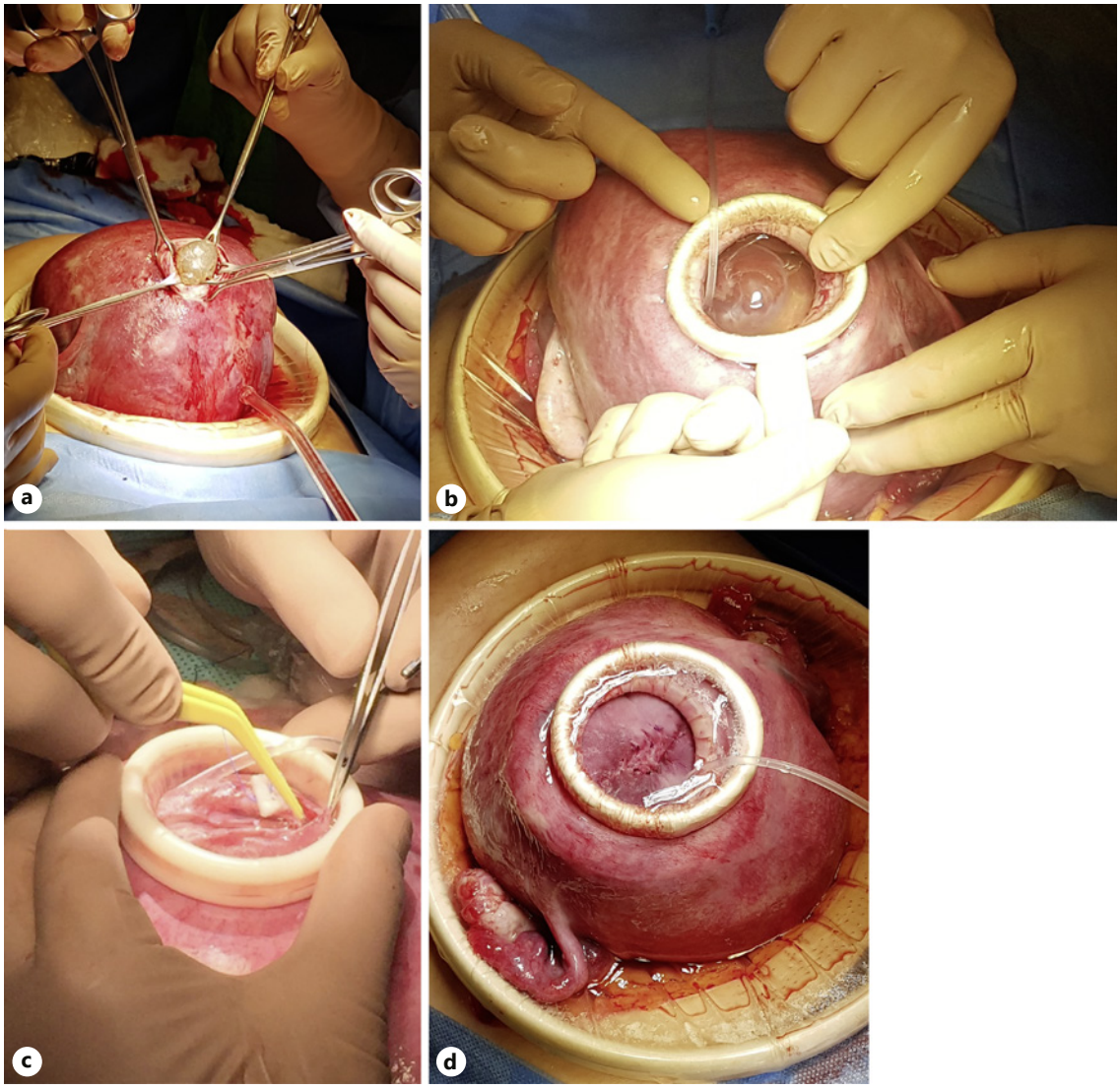

Fig. 1. a Exposure of the chorioamniotic membranes after hysterotomy. **b** Exposure of the spinal defect after amniorrhexis. **c** Neurosurgical repair of the spinal defect. **d** Final result after multilayer closure of the defect.

examination of the infants by a neonatologist and a clinical geneticist ruled out the presence of any associated non-chromosomal genetic conditions in all cases. Microarray analysis techniques were not available at the time of this study.

Intrauterine repair of OSB was performed under general anesthesia after an epidural catheter was placed for subsequent postoperative analgesia. Details of the anesthesiology protocol have been published elsewhere [10]. Just before the intervention, an ultrasound examination was performed in order to determine the exact position of the fetus and the placenta, with an emphasis on determining the best site of entry to access the fetal spinal lesion. If the fetus was in breech or transverse position, an external cephalic version was performed either before the laparotomy or before the hysterotomy once full uterine relaxation was achieved. Once the fetus was in vertex presentation, a Pfannenstiel incision was made and the uterus exteriorized. A longitudinal hysterotomy of about 3–4 cm was made with a surgical scalpel in the upper portion of the uterus opposite to the placental insertion site. Hemostasis was achieved using gauze compression combined with Allis or Babcock grasping forceps as needed. Once the chorioamniotic membranes were exposed (Fig. 1a), amniorrhexis was performed using a scalpel and scissors. In order to prevent further chorioamniotic

Table 1. Maternal-fetal characteristics and outcome

Variable	Study population (n = 58)	MOMS trial	
		prenatal surgery (n = 78)	postnatal surgery (n = 80)
Maternal age, years	29.9±5.0	29.3±5.3	28.8±4.9
BMI, kg/m^2	27.1±3.9	26.2±3.7	25.9±3.9
Parity (%)			
Nullipara	22/58 (38)	33/78 (42)	36/80 (45)
Multipara	36/58 (62)	45/78 (58)	44/80 (55)
Previous uterine surgery (%)	19/58 (33)	11/78 (14)	8/80 (10)
Upper level of the defect (%)			
Thoracic	5/58 (9)	4/78 (5)	3/80 (4)
Lumbar	53/58 (91)	74/78 (95)	77/80 (96)
GA at surgery, weeks[a]	24.8±0.9	23.6±1.4	23.9±1.3
CAS (%)	4/55 (7)	20/78 (26)	0/80 (0)
PROM (%)	14/55 (25)	36/78 (46)	6/80 (8)
GA at delivery (%)			
<30 weeks	11/55 (20)	10/78 (13)	0/80 (0)
30–34 weeks	22/55 (40)	26/78 (33)	4/80 (5)
>34 weeks	22/55 (40)	42/78 (54)	76/80 (95)
Perinatal mortality (%)	5/58 (9)	2/78 (3)	2/80 (3)
Birth weight, g	2,172±751	2,383±688	3,039±469
Dehiscence at repair site (%)	4/53 (8)	10/77 (13)	5/80 (6)
VPS or ETV at 12 months (%)	10/40 (25)	31/77 (40)	66 (82)
Ambulation at 30 months (%)	21/29 (72)	44/62 (71)	38/67 (57)

Results are expressed as mean ± SD or number of cases (percentage). MOMS, Management of Myelomeningocele Study; C/S, cesarean section; GA, gestational age; CAS, chorioamniotic separation; PROM, premature rupture of membranes; VPS, ventriculoperitoneal shunt; ETV, endoscopic third ventriculostomy. [a] The MOMS trial reported GA at randomization. Women assigned to have prenatal surgery were scheduled for surgery within 1–3 days after they were randomized.

membrane separation, the membranes were then sutured to the myometrium with a synthetic absorbable material (polyglactin 910, Vicryl®; Ethicon, Johnson & Johnson, Somerville, NJ, USA). A polyurethane circumferential plastic retractor was used at the hysterotomy site toward the end of the study. This technique has been described in detail elsewhere [6] and has subsequently been incorporated into our standard surgical protocol.

Once the back of the fetus was visualized, gentle manipulation was performed in order to position the fetal spine in line with the uterine incision and expose the full extension of the spinal defect (Fig. 1b). The fetus was then fixed in that position using external uterine compression, a maneuver that was facilitated by the relative oligohydramnios produced by the aspiration and leakage of amniotic fluid from the amniotic cavity. The neurosurgery team then started to repair the spinal defect under a microscope or using magnifying glasses (Fig. 1c). The procedure for neurosurgical repair was similar to the one used in the neonatal period and involved dissecting the placode and surrounding tissue. A multilayer closure of the defect was then performed, including tubularization of the spinal cord, duraplasty, closure of the muscular-aponeurotic layer, and, finally, closure of the skin (Fig. 1d). In the few cases where it was not possible to close the skin, a bovine collagen matrix patch (Duragen®; Integra LifeSciences Corp., Plainsboro, NJ, USA) was used to cover the subcutaneous tissue and fixed to the skin with absorbable stitches. Throughout the operation, the fetus was monitored intermittently with conventional and color Doppler ultrasound, as recommended [11, 12]. Following neurosurgery repair, local anesthesia was administered to the fetus (levobupivacaine 5 mg/mL), and the hysterotomy was closed in two layers with running Vicryl® sutures. In the very early part of the study, the amniotic fluid was partially aspirated at the time of amniorrhexis into 60-mL syringes and stored for reinfusion once the operation had been completed. Subsequently, the amniotic fluid volume was replaced with warmed

saline with antibiotics (cephazoline 2 g) through a Nelaton catheter at the end of the uterine closure. The uterus was repositioned in the abdominal cavity, and the maternal abdominal wall was closed in a conventional manner. Transabdominal ultrasound was used to check the fetal heart rate, umbilical artery Doppler, and the amount of amniotic fluid at the end of the operation.

The postoperative course was managed in an intermediate care obstetric unit, where the patient was monitored for maternal complications. Analgesics were administered intravenously and through the epidural catheter connected to a continuous epidural pump. In addition to this, prophylactic antibiotics (cephazoline, intravenously) and tocolytics (atosiban, intravenously for 48 h [13], followed by oral nifedipine until discharge) were also administered. Discharge from the hospital was considered on day 6 or 7, providing there were no uterine contractions (as determined by manual palpation and cardiotocography), no signs of chorioamnionitis, and no vaginal discharge. Oral and/or vaginal micronized progesterone was used for maintenance tocolysis until delivery. Clinical and ultrasound follow-up examinations were performed at the referring center as needed. A cesarean delivery was scheduled when labor started or the pregnancy reached at least 37 weeks.

Information on the patients' demographics, surgical details, subsequent antenatal course, perinatal outcome, and pediatric follow-up was obtained from the medical records, surgical protocols, interviews with the parents, and evaluations by a multidisciplinary team. This information was gathered until 30 months of age. The main pediatric variables that were studied included the need of postnatal intervention to cover the defect before neonatal discharge, need for ventriculoperitoneal shunt (VPS) or endoscopic third ventriculostomy (ETV) at 12 months, and ability to walk, with or without an orthosis, at 30 months.

Results

During the study period, from September 2011 to June 2019, 58 patients underwent intrauterine repair of OSB at our centers, of which 27 (46.5%) were performed at CLC and 31 (53.4%) at RRH. The operation was completed in 57 (98.2%) of the cases. In the remaining case, prolapse of a large segment of the umbilical cord occurred at the time of uterine entry and could not be reduced. This led to prolonged bradycardia and intraoperative fetal death before any attempt could be made to repair the spinal defect.

Table 1 displays the main clinical and surgical details from our cases. The average maternal age at the time of the operation was 29.9 ± 5.0 years (median 30; range, 18–40); 10 women (17.2%) were under the age of 25. Regarding parity, 22 (37.9%) women were primigravidas and 36 (62.1%) were multiparas of 1–3 previous deliveries, of which 19 (52.7%) had had at least 1 previous cesarean section. The average BMI was 27.1 ± 3.9 kg/m^2 (median 26; range, 20–37), with 3 (5.1%) women having a BMI ≥35 kg/m^2. The average gestational age at operation was 24.8 ± 0.9 weeks (median 25; range, 21–26). The placenta was predominantly anterior in 16 cases (27.5%), posterior in 39 cases (67.2%), and lateral in 3 cases (5.1%). The upper level of the spinal defect was lumbar in 53 cases (91.3%) and thoracic in the 5 remaining cases (8.6%), with the upper level located below L2 in 42 of the cases (72.4%). The spinal defect was classified as myelomeningocele in 43 cases (74.1%) and as myeloschisis in 15 cases (25.8%). Of the 57 cases that completed the operation, a collagen patch was used to reinforce the superficial layers of the defect in 9 cases (15.7%). A skin release incision was also made in 1 case (1.7%), in which there was a wide thoracolumbar myeloschisis. There was no maternal mortality or serious maternal complications during the intrauterine surgery or at delivery. None of the patients required a blood transfusion during or after the operation or at delivery. However, 2 patients (3.4%) presented with mild symptoms of pulmonary congestion shortly after the intervention, which were successfully treated with oxygen, a short course of diuretics, and fluid restriction.

In terms of perinatal outcomes, there were 3 intrauterine deaths in our series (5.1%). This included a case of intraoperative death as well as 2 other deaths that occurred within 24 h of surgery. In the 2 latter cases, several episodes of bradycardia were noted during the intervention. However, there was no evidence of umbilical cord compression or abruption placenta at the time of delivery. The parents did not grant permission for a postmortem examination in any of these 3 cases. Among the 55 remaining continuing pregnancies, chorioamniotic membrane separation was documented in 4 cases (7.2%) and prolonged rupture of the membranes in 14 cases (25.4%). Delivery occurred at an average gestational age of 33.3 ± 3.6 weeks (median 34; range, 24–38), of which 11 (20%) were delivered before 30 weeks, 22 (40%) at 30–34 weeks, and 22 (40%) after 34 weeks. The average birth weight was 2,172 ± 751 g (median 2,212; range, 850–3,980). All but one of the women delivered by cesarean section. In the remaining case, the patient presented with precipitous labor and delivered an 890-g infant vaginally 6 days after the

fetal surgery. Manual revision of the uterus after delivery ruled out a scar dehiscence or uterine rupture. An asymptomatic dehiscence at the surgical scar site was detected at the time of the delivery in only 1 case (1.8%).

Two neonatal deaths occurred during the first 28 days of life in our series, both attributed to complications of prematurity. Both women delivered within a week of the operation, one with a proven chorioamnionitis leading to neonatal death shortly after birth and the other due to precipitous labor leading to neonatal death on day 21. Overall, the perinatal mortality rate was 8.6% (5 of 58). Among the 53 perinatal survivors, there was an additional death after the neonatal period. In this case, a wide thoracolumbar myeloschisis could not be closed prenatally, despite skin release incisions, laminoplasty, and amniotic membrane coverage [14]. The fetus developed severe hydrocephaly following the operation, was born at 33 weeks, and died 30 days after birth due to complications developed from the severe hydrocephaly and Chiari malformation. An operation during the early neonatal period was needed due to dehiscence at the repair site in 4 of the 55 neonates (7.2%). Among the 40 infants that have reached 12 months of life, a VPS or an ETV was used to manage hydrocephaly in 10 cases (25.0%). Among the 29 infants that have reached 30 months of life, 21 (72.4%) are walking with or without an orthosis. At the time of writing, 5 women had subsequently delivered by cesarean section uneventfully.

Discussion

Intrauterine repair of OSB is a complex maternal-fetal intervention associated with severe perinatal complications. Although maternal safety is a major concern of any open fetal surgery, clinical experience has shown that this procedure is associated with a low rate of serious maternal complications [15, 16]. In our series, no maternal deaths or serious intraoperative or postoperative maternal complications were noted. Indeed, none of the patients required blood transfusion, during or after the intervention, and no cases of uterine rupture were reported. The rate of uterine dehiscence at the surgical site was also very low (1.8%). Nevertheless, 2 women presented with mild signs of pulmonary edema following the operation. Symptoms lasted only a few hours after the patients received prompt diagnosis and timely treatment.

In contrast, perinatal complications were both frequent and severe. These included perinatal death as well as severe prematurity with its associated consequences. Indeed, a perinatal death occurred in 8.6% of the cases and severe prematurity before 30 weeks in 20% of the cases. A particularly concerning issue was the high perinatal mortality rate in our series, which was 3 times higher than the one reported by the MOMS trial [1]. Although the differences between our study and the MOMS trial were not statistically significant in terms of perinatal mortality (5 of 58 [8.6%] vs. 2 of 78 [2.5%], respectively; $p = 0.1361$, Fisher's exact test), the majority of our perinatal deaths occurred in patients who were operated on during the first half of the program. In the second half of the program, there was a noticeable, although not statistically significant, reduction in the number of perinatal deaths in comparison to the first half (1 of 29 [3.4%] vs. 4 of 29 [13.7%], respectively; $p = 0.3525$, Fisher's exact test). It therefore seems clear that the experience gained from the learning curve may have played a role in this improvement. According to the MOMS trial (www.nejm.org/doi/suppl/10.1056/NEJMoa1014379/suppl_file/nejmoa1014379_protocol.pdf) [1], at least 234 patients were operated on at the 3 recruitment centers before the trial started. Their reported perinatal mortality rate before the trial was 7.6% (4 of 52) at the Children's Hospital of Philadelphia, 2.9% (5 of 170) at Vanderbilt University, and 25% (3 of 12) at the University of California, San Francisco, for an overall perinatal mortality rate of 5.1% (12 of 234). At the University of California, the perinatal mortality rate was significantly higher than the prevalence reported subsequently in the MOMS trial (3 of 12 [25%] vs. 2 of 78 [2.5%], respectively; $p = 0.0159$, Fisher's exact test). Nevertheless, in a series of 100 subsequent cases of open repair of OSB at the Children's Hospital of Philadelphia [17], the perinatal mortality rate increased to 6.1%, including 2 fetal deaths and 4 neonatal deaths. This evidence shows that factors other than the learning curve may influence the rate of perinatal deaths associated with intrauterine surgery, even at more experienced centers.

In our series, there was no clear explanation for 2 of the 3 intrauterine deaths. However, intraoperative factors such as fetal bleeding, hypoxemia, hypothermia, neurogenic shock and pain, and metabolic disorders during or shortly after the surgery may have played a role in the poor outcome in these cases. Although placental abruption has been recognized as a direct cause of fetal death during or after intrauterine surgery of OSB [4, 18], this was not the case in our population as careful examination of the placenta after delivery ruled out this possibility. In the remaining case, a completely avoidable cause of fetal death, that is, umbilical cord prolapse, was the cause of the intrauterine demise. This umbilical cord accident prompted us to induce full uterine relaxation and careful mapping of

the placental and umbilical cord position with color Doppler ultrasound before performing the hysterotomy in all following cases. In terms of neonatal deaths, prematurity was the leading cause in our series, which is similar to the experience at other centers [17]. In both cases, delivery occurred within a week of the operation; one newborn infant died shortly after delivery and the other in the late neonatal period. Premature labor in these cases was probably the result of intra-amniotic infection and chorioamnionitis, which was confirmed by amniotic fluid culture obtained by amniocentesis in one of the cases.

Severe prematurity as a complication of open intrauterine surgery was also a significant issue. Indeed, our prematurity rate below 30 weeks also seems high in relation to the results from the MOMS trial [1]. However, this difference was also not statistically significant (11 of 55 [20.0%] vs. 10 of 77 [12.9%], respectively; $p = 0.3369$, Fisher's exact test). In our series, the 2 neonatal deaths occurred in this subgroup of neonates, with the remaining neonates requiring prolonged admission to the neonatal intensive care unit. It is therefore clear from our series that the fetal mortality rate was highly dependent on intraoperative events. On the other hand, the neonatal mortality rate is probably dependent on the postoperative response of the host to the surgical injury to the myometrium and membranes, which can lead to chorioamnionitis, rupture of the membranes, and preterm labor. An important improvement to the surgical technique noted toward the end of the study was the incorporation of a plastic retractor at the hysterotomy site, which helped minimize mechanical trauma to the myometrium and membranes [6]. Preliminary experience with this technique was encouraging as the rate of obstetrical complications such as chorioamniotic membrane separation, premature rupture of the membranes, and preterm delivery was reduced, with a subsequent improvement in the perinatal outcome [6].

In our series, all cases, including those from the learning curve, have been included. This may explain some of the poor outcomes that occurred in our population. In the MOMS trial, the selection criteria were very strict and the surgical teams had performed at least 15 operations before the trial started (https://www.nejm.org/doi/suppl/10.1056/NEJMoa1014379/suppl_file/nejmoa1014379_appendix.pdf) [1]. We therefore expect that with increasing surgical experience, our results may soon be comparable to, or ideally better than, the ones reported by the MOMS trial, currently considered the gold standard for this type of surgery. In any case, our long-term results are encouraging. A significant advantage was the fact that only 25% of the infants required a VPS or an ETV at 12 months. This is lower than the 40 and 82% of ventriculoperitoneal shunting reported for the prenatal and postnatal surgery groups in the MOMS trial, respectively [1]. This is one of the main benefits of prenatal surgery [19–21] and is something that has clearly been achieved by our program. Furthermore, pediatric follow-up until 30 months also revealed that 72.4% of infants were able to walk, with or without an orthosis. A similar outcome was reported in the MOMS trial at 30 months, with 70.9 and 56.7% of children being able to walk with and without an orthosis, respectively [1].

In recent years, fetoscopic repair of OSB has become another alternative to open intrauterine surgery [22–25]. This so-called "minimally invasive" approach for intrauterine repair of OSB has been the subject of serious criticism [26]. Furthermore, it also requires special instruments, which are not needed for the open intrauterine approach. This is because the material required for open intrauterine surgery is already available at tertiary centers that are equipped for performing a classical cesarean section and neonatal neurosurgery. In addition to this, training to perform neurosurgical interventions using a fetoscope is challenging. Such interventions are obviously more complex than those performed by maternal-fetal specialists for twin-twin transfusion syndrome or fetal tracheal occlusion and, therefore, require additional expertise from the neurosurgeons [27]. The laboratory facilities required for experimental surgery and simulator training are also difficult to acquire and expensive to implement, especially in developing countries such as those in Latin America. To date, 2 fetoscopic approaches have been described in the literature. One of these is percutaneous [22–25], while the other involves exteriorization of the uterus through a laparotomy [28, 29]. As neither of these techniques has been tested in a randomized trial, there is still only limited information available on the short- and long-term outcomes, a requirement for this technique to be definitively included in clinical practice. From the information that is currently available, it is clear that the complication rate is higher with the percutaneous approach than with open intrauterine surgery [30–32]. This includes higher rates of rupture of membranes (91 vs. 36%, respectively; $p < 0.01$) and premature delivery (96 vs. 81%, respectively; $p < 0.04$) [32]. On the other hand, the fetoscopic approach after exteriorization of the uterus seems to be a promising alternative to open fetal surgery. A randomized clinical study is therefore desperately needed in order to determine whether this fetoscopic technique may provide a safer alternative to open fetal surgery, with improved short-term perinatal results and long-term

neurological outcomes. Evidence of such results may then encourage centers to implement this technique in the near future. The argument that the fetoscopic approach is less invasive to the myometrium than open surgery, therefore allowing for vaginal delivery in the current pregnancy [29], would seem to us to be a weak variable on which to base any decision. For example, it is clearly not an advantage for prospective patients who have had a previous cesarean delivery. In the meantime, we believe that, given the compelling scientific evidence that is currently available, open intrauterine surgery remains the best alternative for any mother carrying a fetus with an OSB.

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W.S. pioneered open intrauterine surgery for spina bifida in Chile and served as the Director of the Fetal Surgery Program at CLC until July 2014. Since then, he maintains affiliation to CLC as a maternal-fetal medicine specialist. The authors are grateful to the medical and paramedical personnel involved in the care of the patients described in this report. Special gratitude goes to (in alphabetical order) Chantal Diemer, RN; Silvana Echeverria, RM; Luis Medina, MD; Lia Muñoz, MD; Gonzalo Perez-Canto, MD; Ana Posso, MD; Mauricio Reascos, MD; Ana M. Rodriguez, MD; and Yemina Seijas, MD. The authors are also grateful to the Medical Directorate from both participating institutions, which have been instrumental in implementing the fetal surgery programs at our centers.

Statement of Ethics

The study complies with the guidelines for human studies and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The study protocol was approved by the institutional review board/ethics committee at the participating institutions (CLC-2011/RRH-2012). Written informed consent was obtained from all patients.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

W.S., E.C., F.O., J.M.M., and J.C.D.: study conception and design. W.S., E.C., F.O., J.M.M., and J.C.D: data acquisition. W.S.: manuscript writing. All authors participated in the intrauterine surgical procedures and postoperative care of the patients. All authors reviewed and approved the final version of the manuscript.

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