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Percutaneous minimal-access fetoscopic surgery for spina bifida aperta. Part II: maternal management and outcome

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KEYWORDS: fetal surgery; fetoscopy; fetus; outcome; spina bifida aperta

ABSTRACT

Objective *To assess maternal morbidity and outcome in women undergoing minimal-access fetoscopic surgery for spina bifida aperta.*

Methods *This was a retrospective study of 51 women undergoing minimal-access fetoscopic surgery to improve postnatal neurological outcome of spina bifida aperta, at a mean gestational age of 24 weeks, at our center between July 2010 and June 2013. We analyzed various perioperative complications of surgery, namely: maternal and fetal death, need for maternal blood transfusion, placental abruption, pulmonary edema, spontaneous labor, oligohydramnios, chorioamnionitis, chorioamniotic membrane separation, duration of hospitalization, amniotic fluid leakage, gestational age at delivery and status of hysterotomy site.*

Results *In none of the 51 women was there maternal demise, spontaneous labor, placental abruption or a need for maternal blood transfusion in the perioperative period. Chorioamniotic membrane separation occurred in one patient, mild pulmonary edema occurred in one and oligohydramnios occurred in seven. All fetuses survived surgery, but there was one very early preterm delivery 1 week after the procedure and this neonate died immediately, from early postoperative chorioamnionitis. Amniotic fluid leakage occurred in 43 patients, at a mean gestational age of 29.7 (range, 22.6–37.3) weeks; two of these patients developed chorioamnionitis. Duration of maternal hospitalization after surgery was 7.2 (range, 4–12) days. Mean gestational age at delivery was 33 (range, 24.6–38.1) weeks. All abdominal and uterine trocar insertion sites healed well.*

Conclusion *Minimal-access fetoscopic surgery for spina bifida aperta is apparently safe for most maternal patients. Despite the common occurrence of amniotic leakage, the majority of women deliver beyond 32 weeks of gestation.*

INTRODUCTION

Fetal surgery for spina bifida aperta (SBA) is a therapeutic approach to save motor and sensory function by protecting the exposed neural tissue from intrauterine mechanical and chemical damage[1]. Another goal is to reverse hindbrain herniation and ameliorate the progression of hydrocephalus by preventing cerebrospinal fluid leakage[2].

The randomized controlled 'Management of Myelomeningocele Study' (MOMS) compared maternal and fetal outcomes after open fetal surgery with those following standard postnatal care for SBA[3]. MOMS showed a statistically significant lower ventriculoperitoneal shunt rate, reduction in severity of hindbrain herniation and better leg motor function in the group which underwent prenatal surgery. Despite its encouraging potential to improve the quality of postnatal life in affected fetuses, the open operative approach may be criticized for the increased maternal risk and concerns over suboptimal neonatal outcome[4].

In contrast, minimal-access fetoscopic techniques promise a reduction of maternal and fetal morbidity. Pioneering fetoscopic procedures for SBA by Tulipan and Bruner and others, which preceded the introduction of the open operative approach, were abandoned due to technical difficulties and complications[5,6]. Following studies in inanimate models, sheep and postmortem

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human fetuses[7–9], over the past decade Kohl and colleagues introduced a fully percutaneous minimal-access fetoscopic approach at the German Center for Fetal Surgery & Minimally-Invasive Therapy (DFZT)[10]. The goal of this approach was to provide an alternative to open fetal surgery that had identical fetal benefits but largely reduced maternal morbidity. Between July 2010 and June 2013, 51 pregnant women underwent this procedure at our center. The aim of this retrospective study was to present the maternal morbidity and pregnancy outcome, as well as to provide information on the management of pregnancies undergoing this procedure.

PATIENTS AND METHODS

We reviewed retrospectively our data from 51 pregnant women whose fetuses had isolated SBA and apparently normal karyotype, and who underwent minimal-access fetoscopic surgery at our center between July 2010 and June 2013.

Patient referral and counseling

Pregnant women carrying fetuses with SBA, usually accompanied by their partners, were referred to our center by their local obstetrician or prenatal medicine specialist. Figure 1 presents the algorithm for minimal-access fetal surgery for SBA used at the DFZT. Following a detailed ultrasound examination at our unit, they were counseled about the malformation and its clinical significance. Counseling included the issues of termination of pregnancy or continuation of pregnancy followed by standard postnatal surgery, as well as the availability of open and fetoscopic fetal surgery. The fetoscopic operation was offered as standard of care at our hospital.

Pregnant women were also encouraged to meet other expectantly managed and/or operated mothers and their children with SBA, who are usually present at our hospital at some point throughout the year, in order to learn from their experience and obtain a first-hand impression of the condition. In addition, they were provided with a telephone list of previous patients in order to obtain first-hand information about their treatment as well as the outcome of children with spina bifida who were operated prenatally.

If a mother expecting a child with SBA decided to undergo minimal-access fetal surgery at our center, she was referred for more detailed counseling; among the issues presented were the impact of lesion level, brain anomalies, standard postnatal surgery and therapy, risks and benefits of the fetoscopic approach, perioperative and perinatal maternal and infant management, pregnancy care and mode of delivery.

Preoperative evaluations and maternal exclusion criteria

Prior to the procedures, all women underwent physical and laboratory evaluations, electrocardiography, echocardiography, magnetic resonance imaging and transvaginal assessment of their uterine cervical competence. As maternal safety is the primary concern during this evaluation phase, women with acute or chronic illness that would increase their surgical risk disproportionately were excluded. Some patients with an anterior placenta and/or very thick abdominal wall were not eligible for the percutaneous minimal-access operative approach or were informed that the procedure carried a higher risk of being technically unsuccessful. If no exclusion criteria applied, informed consent was obtained.

Maternofetal anesthesia and intraoperative monitoring

Our group has established an anesthetic protocol especially tailored to the needs of minimal-access fetoscopic interventions; it permits safe general maternofetal anesthesia with sufficient uterine relaxation and preservation of adequate uterine and fetoplacental blood flow throughout the procedure[11]. In addition, clinically relevant episodes of maternal pulmonary edema can be avoided almost entirely. Intra- and postoperative maternal monitoring include continuous electrocardiography, systemic arterial and central venous blood pressures, oxygen saturation, urine production, bispectral index, extravascular lung water and body temperature measurements.

Minimal-access fetoscopic surgery

All procedures were carried out under general fetomaternal anesthesia. Intraoperative maternal monitoring required over-the-wire insertion of a 7.5-French central venous catheter into the right jugular vein as well as insertion of a 4- or 5-French arterial catheter into the femoral artery (Figure 2). The initial punctures for insertion of the wire guides were performed with 18-gauge (1.2 mm) needles.

Employing maternal transabdominal ultrasound guidance, three trocars (external trocar diameter, 5 mm) were inserted percutaneously into the amniotic cavity using a Seldinger approach[12]. Similar to the insertion of the anesthetic catheters, the initial punctures for insertion of the guide wires were performed with an 18-gauge needle (diameter, 1.2 mm) (Figure 2). Trocar insertion was followed by partial evacuation of the amniotic fluid and carbon dioxide insufflation of the amniotic cavity for optimization of fetal visualization and manipulation. After closure of the defect, the insufflation was halted, the gas evacuated and the amniotic cavity refilled with warmed crystalline solution. Finally, the uterine and abdominal trocar insertion sites were closed, and mother and fetus were recovered from anesthesia.

Perioperative management

Perioperative antibiotic prophylaxis (Clindamycin, Ratiopharm GmbH, Ulm, Germany; 4 × 600 mg i.v./day) was administered, starting 1 hour before surgery until the third postoperative day. After surgery, the patients

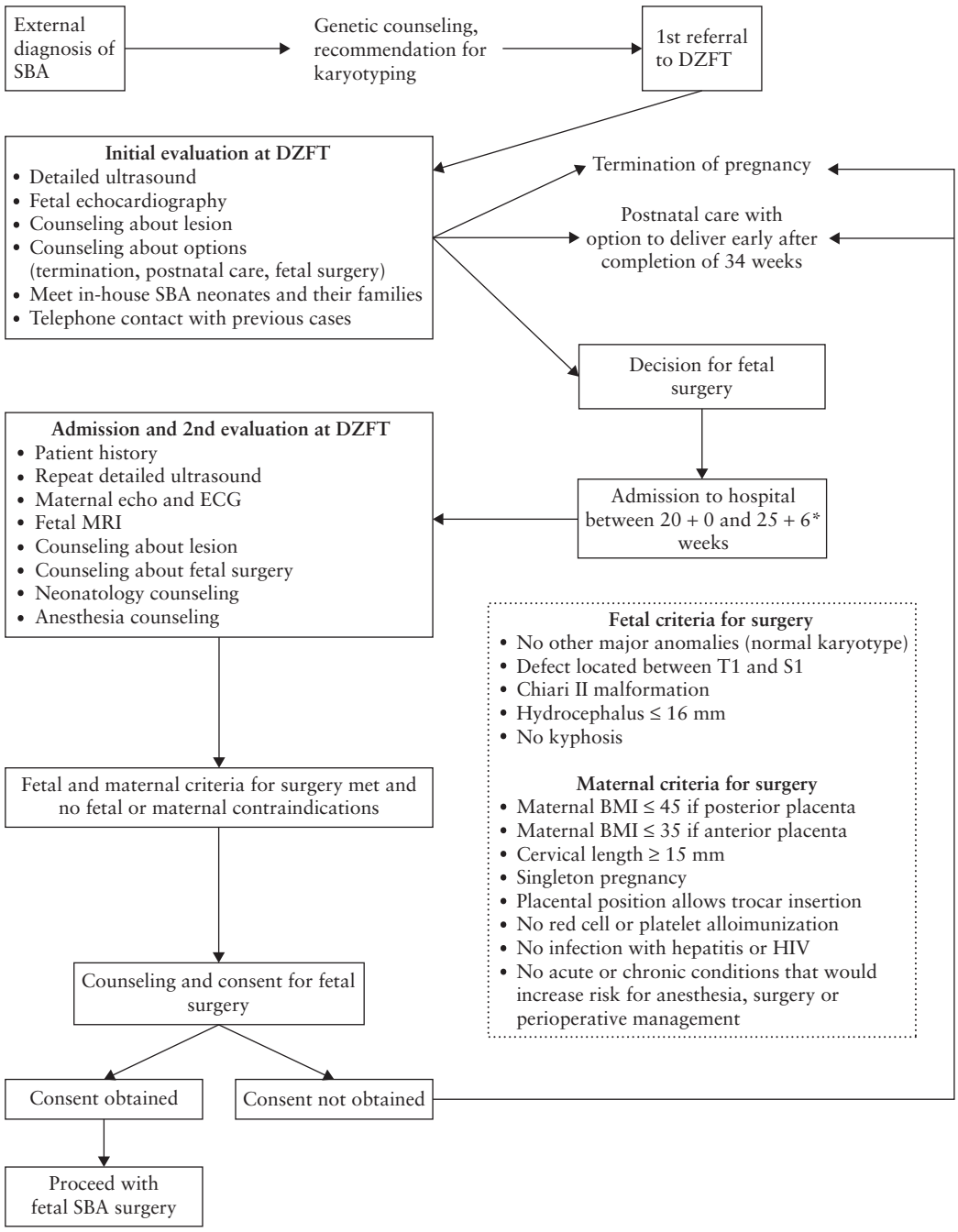

Figure 1 German Center for Fetal Surgery & Minimally Invasive Therapy (DZFT) algorithm for minimal-access fetal surgery for spina bifida aperta (SBA). *Later surgery, up to 29 weeks, performed only in rare cases with good leg function, Chiari-II malformation and mild hydrocephalus. BMI, body mass index; ECG, electrocardiography; HIV, human immunodeficiency virus; MRI; magnetic resonance imaging.

stayed in the intensive care unit for 24 hours. Tocograms were registered twice daily. Postoperative tocolysis was performed by infusion of the oxytocin antagonist atosiban (Ferring Pharmaceuticals, Malmö, Sweden) for 24 hours (bolus administration of 6.75 mg, then 300 µg/min over 3 h followed by 100 µg/min over 12 h). Chronic postoperative administration of tocolytic agents (e.g. nifedipine), as is done after open fetal surgery, was not required.

Postoperative fetal monitoring involved weekly ultrasound studies in order to assess the amount of amniotic fluid, the status of chorioamniotic membranes, fetal movements, fetoplacental and cerebral blood flow, patch position, brain ventricle and cisterna magna sizes as well as reversal of hindbrain herniation. Most pregnant women were discharged from hospital about 1 week after the procedure. Over the remainder of gestation, we recommended rest, a healthy diet and family support.

Following minimal-access fetoscopic surgery for SBA, fetal delivery was planned by elective Cesarean section. In cases with amniotic fluid leakage from iatrogenic membrane injury before 34 weeks, prophylactic antibiotics were given and Cesarean delivery was scheduled at completion of 34 weeks. If amniotic leakage occurred after this point, delivery was scheduled within the next 12 hours. If no amniotic fluid leak occurred, it was scheduled in the 39th week of gestation.

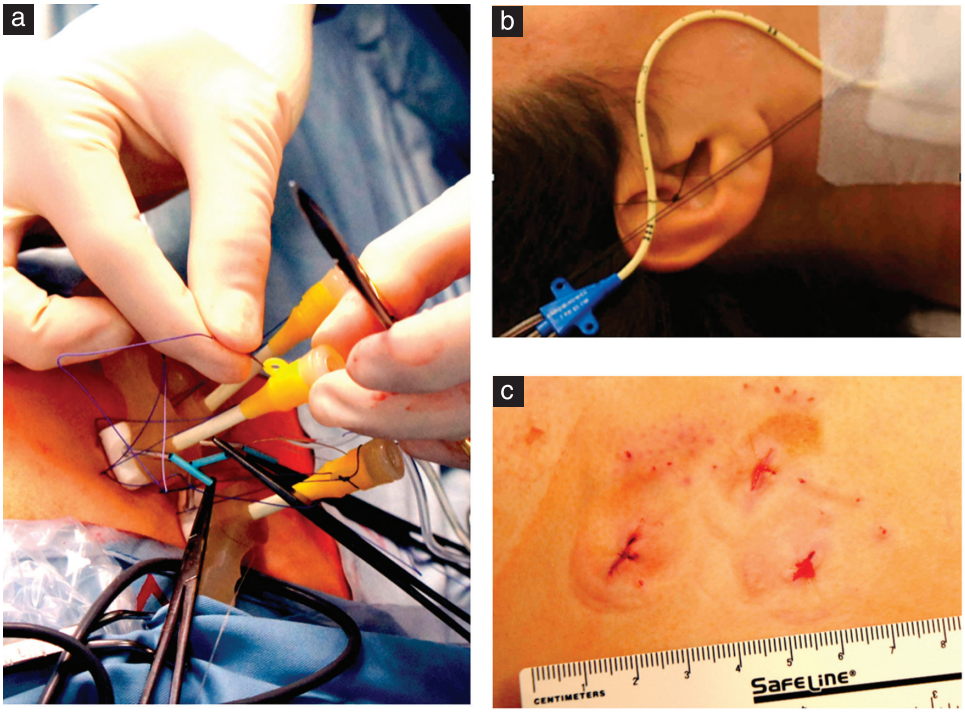

Figure 2 (a) Standard operative set-up for minimally invasive fetoscopic surgery for spina bifida aperta. Maternal percutaneous–transabdominal–transuterine–paraplacental–intra-amniotic access is achieved by three (rarely four) trocars with an external diameter of 5 mm. Following small skin incisions, all trocars are placed under ultrasound-guidance by a Seldinger approach via an 18-gauge needle (external diameter, 1.2 mm). A 5- or 6-French PICCO catheter (Pulsion Medical Systems, Munich, Germany; not seen in this image) placed into a femoral artery permits monitoring of extravascular lung water; in addition, a 7.5-French central venous catheter is inserted into the right jugular vein (b). Both catheters are also placed by a Seldinger approach via 18-gauge needles following small skin incisions. (c) The tiny skin incisions, seen following the removal of the trocars, are the hallmark of the minimal-access fetoscopic approach for spina bifida and are practically incomparable with the much larger abdominal and uterine incisions required for open fetal surgery.

Study variables

We studied patient charts for the peri- and postoperative occurrence of maternal and fetal death, need for maternal blood transfusion, placental abruption, pulmonary edema, spontaneous labor, need for chronic administration of tocolytics, oligohydramnios, chorioamnionitis, chorioamniotic membrane separation, length of hospitalization, amniotic fluid leakage, gestational age at delivery and wound healing complications, especially status of hysterotomy site. The Statistical Package for Social Sciences (SPSS) for Mac OS version 20.0 (IBM Corp., Armonk, NY, USA) was used for statistical calculations of means, SDs, ranges and percentages.

RESULTS

Of the 51 women in our study, 25 (49%) were nulliparous. There were 20 (39.2%) with an anterior placenta. Six (11.8%) had undergone previous uterine surgery, in the form of Cesarean section. Their mean ± SD body mass index was 26.6 ± 4.8 (range, 20.3–44.0) kg/m^2 and their mean ± SD cervical length was 43.5 ± 6.4 mm. At surgery, the mean maternal age was 31.5 (range, 19–41) years and the mean ± SD gestational age was 23.7 ± 1.8 (range, 21–29.1) weeks.

There were no maternal or fetal deaths, intolerance to anesthesia or partial amniotic carbon dioxide insufflation (PACI) or other complications of minimal-access fetal surgery for spina bifida, but there was one very early preterm delivery 1 week after the procedure, and this neonate died immediately, from early postoperative chorioamnionitis. In none of the 51 cases was there a need for maternal blood transfusion, placental abruption or spontaneous postoperative uterine contractions in the immediate perioperative period. A mild degree of postoperative pulmonary edema was observed in one (1.9%) patient and chorioamniotic membrane separation occurred in one (1.9%) patient. Perioperative oligohydramnios occurred in seven (13.7%) patients.

Postoperative uterine contractions on the day after surgery, despite atosiban-tocolysis, was observed in only one woman. This patient, operated at 22 + 4 weeks of gestation, developed amniotic fluid leakage 4 hours after surgery and was treated with atosiban for one additional day. She remained in hospital receiving prophylactic antibiotic treatment until the occurrence of chorioamnionitis required delivery at 27 + 6 weeks of gestation. Another case of chorioamnionitis was observed in a patient at 29.9 weeks of gestation. Following delivery on the same day, the baby required ventilation for 1 day because of respiratory distress syndrome. Early postoperative chorioamnionitis necessitating delivery within days after surgery at 24.6 weeks of gestation was observed in one case. Unfortunately, this neonate died

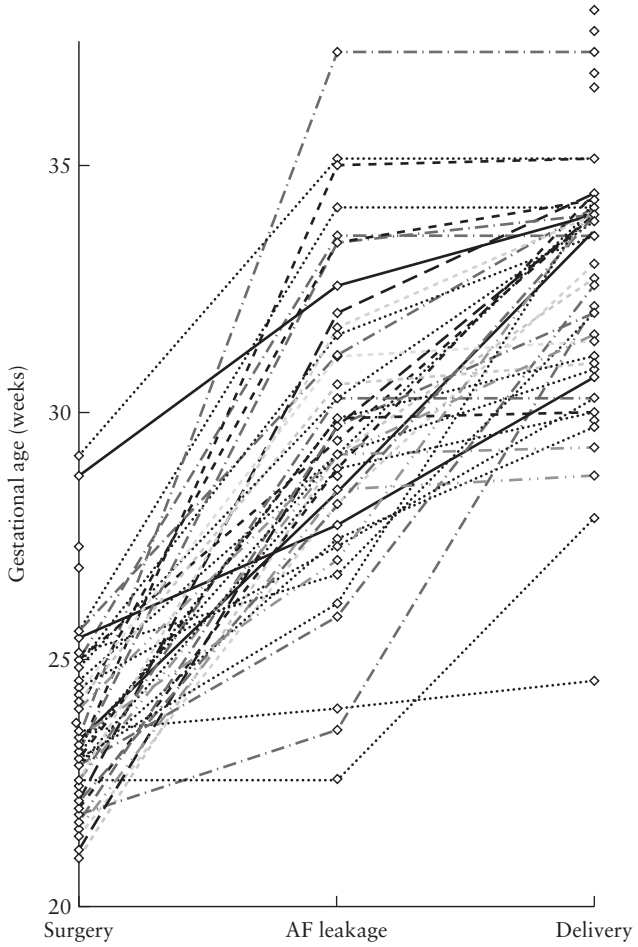

Figure 3 Postoperative course of 51 fetuses after minimal-access surgery for spina bifida aperta: individual plots of time following surgery to amniotic fluid (AF) leakage and delivery. Unconnected diamonds represent patients in whom amniotic fluid leakage did not occur.

from complications secondary to prematurity. All other fetuses survived gestation. In one case, the procedure could not be completed technically because of maternal obesity.

Local chorioamniotic membrane separation after the procedure that resolved within days after surgery was observed in two (4%) cases, operated in the 22nd week and delivered in the 33rd week of gestation. In one of these cases, only two of the three trocar insertion sites had been closed successfully at the end of the procedure and amniotic leakage began during the 27th week of gestation.

The mean postoperative duration of hospitalization was 7.2 (range, 4–12) days. Amniotic fluid leakage from iatrogenic membrane injury at some point after the procedure was observed in 43 (84.3%) patients; the mean ± SD gestational age at leakage was 29.7 ± 3.1 (range, 22.6–37.3) weeks (Figure 3). The mean ± SD gestational age at Cesarean delivery was 33.0 ± 2.8(range, 24.6–38.1) weeks. Forty-five (88.2%) infants were delivered at or beyond the 30th week of gestation and 25 (49.0%) after completing the 34th week of gestation (Table S1).

There were no blood transfusions needed during delivery. The uterine trocar insertion sites were intact and well-healed in all cases. Uterine wall thinning, dehiscence or rupture were not observed at delivery.

DISCUSSION

In our study of 51 pregnant women who underwent percutaneous minimal-access fetoscopic surgery for SBA, the surgical approach was safe and technically successful in almost all cases. The only maternal trauma from the minimal-access approach resulted from five small skin incisions and five punctures with 1.2 mm-needles for over-the-wire insertions of 5–11-French sheaths into the amniotic cavity, jugular vein and femoral artery. This limited amount of trauma stands in stark contrast to that of the open fetal surgical approach, which, in order to achieve the same fetal surgical goals, requires maternal laparotomy and hysterotomy.

Blood transfusions were not needed during minimal-access fetal surgery for SBA as no intraoperative placental abruptions or vascular injuries occurred in this series. The most serious complication was early postoperative chorioamnionitis in one patient, resulting in demise of the immature neonate.

In contrast to open fetal surgery, premature uterine contractions either did not occur or were short-lived during and after minimal-access fetoscopic surgery for SBA. This important management advantage permits use of both lower concentrations of inhalation anesthetics during surgery and lower doses and shorter courses of tocolytic agents: chronic administration of tocolytic agents was not required after fetoscopic surgery in our series. The benefits of this are two-fold. The risk of maternal pulmonary edema is largely decreased: in our series there was no clinically relevant maternal pulmonary edema in all except one patient after fetoscopy. This rare occurrence of maternal pulmonary edema suggests that monitoring of extravascular lung water, administration of lower dosages of volatile anesthetics and restriction of intravenous fluids to maintenance levels are effective in reducing the occurrence of this complication[11].

Additionally, the fetal and maternal risks of intraoperative maternal hypotension are decreased. As uterine blood flow is directly proportional to maternal blood pressure, it is not surprising that significant decreases in fetoplacental and uterine blood flow have been observed during open fetal surgery in humans and in animal studies in sheep, as higher drug doses are required in order to achieve sufficient maternal anesthesia and uterine relaxation[13–15]. This management problem was described recently in a case of severe intraoperative maternal hypotension during open fetal surgery for spina bifida[16]. During the procedure, the attending anesthetist maintained a maternal blood pressure around 80/50 mmHg in an attempt to avoid administration of catecholamines and intravenous fluid, as these may impair fetal hemodynamics or result in maternal pulmonary edema. Protracted maternal hypotension may explain why fetal bradycardia during

repair and postnatal periventricular leukomalacia have been observed in survivors in the MOMS trial and after open fetal surgery for other conditions[3,17,18]. In contrast, studies in human and ovine fetuses demonstrate that maternal blood pressure, fetoplacental blood flow and uteroplacental oxygen delivery are affected less by fetoscopic surgery[14,19].

Hospitalization and chronic tocolysis were not usually required after fetoscopic surgery. Most patients could be discharged from hospital within 1 week after surgery either until amniotic fluid leakage occurred or until elective readmission to our center for delivery. Chorioamniotic membrane separation may result from fetal surgery and is a risk factor for preterm prelabor rupture of membranes[20]. In our study this complication was observed in only two cases, probably as a result of pressure- and volume-controlled PACI as well as device-coverage of the membranes during trocar removal.

In early attempts at fetoscopic surgery in spina bifida, the time intervals from operation to delivery were short, exposing more than half of the operated fetuses to the risks of extreme prematurity before 30 weeks of gestation[21]. Preterm delivery is an important consequence of both open and minimal-access fetal surgery due to trauma to the chorioamniotic membranes from direct incision, trocar insertion or surgical manipulation. Yet, there has been a dramatic improvement in the prolongation of pregnancy. In our series, almost 90% of women delivered beyond the 30th week of gestation. Our mean gestational age at delivery of 33 weeks after minimal-access fetoscopic closure of spina bifida is similar to that reported for the MOMS trial fetuses[3], in whom neurodevelopmental tests showed significantly better results in patients undergoing prenatal surgery compared with those who did not, that were born about 4 weeks later.

Nevertheless, transvaginal amniotic fluid leakage still occurs in 85% of patients, albeit at a mean gestational age of 30 weeks. Fortunately, expectant management of leakage, with monitoring for early signs of infection, can be effective. Furthermore, leakage may be considered less detrimental than the obstetric complications of placental abruption and uterine dehiscence, or the potential complications when open fetal surgery is used. In contrast to open fetal surgery, after which dehiscence or thinning of the uterine wall is commonly observed at delivery, the uterine trocar insertion sites after minimal-access fetoscopic surgery were completely healed in our series. This finding may permit the avoidance of Cesarean section in future pregnancies and is one of the most important advantages of minimal-access fetoscopic surgery with regard to patient safety.

In conclusion, for almost all in our series of 51 pregnant women who underwent percutaneous minimal-access fetoscopic surgery for fetal SBA, the technique was safe. Technical failure, because of maternal obesity, was observed in only one case. In contrast to the pilot phase during development of this technique, the frequency of early preterm delivery prior to 30 weeks' gestation, fetal demise, technical failure and infectious maternal complications were reduced considerably[21], reflecting multiple improvements in the clinical and technical management of this complex procedure.

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SUPPORTING INFORMATION ON THE INTERNET

The following supporting information may be found in the online version of this article:

Table S1 Intervals from surgery to amniotic fluid leakage and/or delivery in 51 women undergoing minimal-access fetoscopic surgery for spina bifida aperta

