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Percutaneous minimally invasive fetoscopic surgery for spina bifida aperta. Part I: surgical technique and perioperative outcome

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KEYWORDS: Chiari-II malformation; fetal surgery; fetoscopy; fetus; hydrocephalus; spina bifida

ABSTRACT

Objectives *To analyze the current technical approach of percutaneous minimal-access fetoscopic closure of spina bifida aperta (SBA) and provide an overview of its development in ovine and human fetuses.*

Methods *Minimal-access percutaneous fetoscopic closure of SBA was performed at the German Center for Fetal Surgery & Minimal-access Therapy (DZFT) in 51 human fetuses at 21.0–29.1 weeks of gestation (mean age, 23.7 weeks). Various parameters of surgical relevance for the success and safety of the procedure and the early perioperative outcome were analyzed retrospectively. In addition, information from the early clinical cases was examined to determine how this shaped development of the approach.*

Results *Percutaneous minimal-access fetoscopic closure of SBA was performed with a high rate of technical success, regardless of placental or fetal position. 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. Of the 50 surviving fetuses, 44 (88%) were delivered at or beyond 30 weeks and 25 (50%) at or beyond 34 weeks of gestation. There was one neonatal death from an uinsuspected case of trisomy 13 and two infant deaths from Chiari-II malformation.*

Conclusions *Following an adequate learning curve, minimal-access fetoscopic surgery for fetal spina bifida can be performed with a high rate of technical success, regardless of placental position.* *Copyright © 2014 ISUOG. Published by John Wiley & Sons Ltd.*

INTRODUCTION

Open fetal surgery for spina bifida aperta (SBA) has been performed in hundreds of human fetuses. The 'Management of Myelomeningocele Study' (MOMS) provided level-I evidence that prenatal SBA closure may preserve leg function and reduce the severity of hindbrain herniation and hydrocephalus in affected fetuses[1]. Yet, the open surgical approach is associated with significant maternal morbidity, as it requires maternal laparotomy and hysterotomy for fetal access. In a significant proportion of cases, the hysterotomy scar becomes a weak spot, prone to uterine wall dehiscence or even rupture after fetal surgery or in future pregnancies.

As the clinical consequences of SBA can be far-reaching, including the possibility of life-long disabilities and requirements for therapy, maternal trauma resulting from the open surgical approach has been accepted by many pregnant women and prenatal specialists as a price worth paying when weighed against the clinical benefits. Yet, even the earliest prenatal procedures in the mid-1990s aimed at reducing maternal injury: in order to avoid maternal hysterotomy, Drs Bruner and Tulipan performed their pioneering surgery by fetoscopy, securing skin grafts to the malformation[2,3]. Their technique, however, still required maternal laparotomy followed by transuterine trocar placement, and was quickly abandoned in favor of the open approach because of technical difficulties and unfavorable outcomes. A few other attempts at fetoscopy were performed at The University of California, San Francisco (UCSF), but were also subsequently abandoned for similar reasons[4].

During studies in inanimate models, sheep and postmortem human fetuses, I have developed a fetoscopic approach for prenatal closure of SBA that is less invasive, access being fully percutaneous[5–10]. This paper provides an overview of its development and presents technical data as well as perioperative outcomes from 51 cases that underwent the percutaneous minimal-access fetoscopic surgical procedure for SBA at the German Center for Fetal Surgery & Minimal-access Therapy (DZFT) over the past 3 years. With this paper and a sister paper, also in this issue of the Journal, presenting maternal management

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and outcome[11], I aim to promote the dissemination and further development of this technique.

PATIENTS AND METHODS

Various parameters of relevance to the surgical success of percutaneous minimal-access fetoscopic spina bifida closure were analyzed retrospectively in 51 cases that underwent the procedure at our center between July 2010 and June 2013. Analysis of these data was approved by the local committee on human research (#158/13). The procedure has been offered as standard of care at the DZFT since July 2010, following: (1) completion of a pilot study, approved by the Committee of Human Research, in 30 patients at the University of Bonn, Germany; (2) the finding by an independent study in 13 of the pilot study patients that postnatal leg function was significantly better and the rate of shunt-dependent hydrocephalus was significantly lower than that in lesion-level-matched controls that did not undergo surgery prenatally[12]; and (3) substantial improvement in the technical success rate and maternal and fetal safety, and increase in gestational age at delivery, compared with the early pilot phase experience.

Fetal selection

The preferable gestational age for percutaneous fetoscopic patch coverage of SBA ranges between 20 + 0 and 25 + 6 weeks. The procedure can be carried out later but only when the degree of hydrocephalus is still mild and stool soiling of the lesion can be anticipated from characterization of the surgical anatomy by ultrasound[13,14]. For the fetus to be eligible for the procedure, the defect should be located between vertebrae T1 and S1. Fetuses with a gibbus are excluded. Further requirements are hindbrain herniation and a diameter of the lateral brain ventricles < 16 mm as assessed by ultrasound and magnetic resonance imaging (MRI). The fetuses should be free from other major organ abnormalities on ultrasound. They should present a normal karyotype, although some pregnant women, following counseling, elect to forgo preoperative amniocentesis. In these cases, fetal surgery is offered when ultrasound and MRI studies do not raise suspicion of any other major fetal malformations or chromosomal anomalies.

Intraoperative ultrasound monitoring

In addition to identification of the correct fetal patient, pre- and intraoperative multimodal ultrasound provides information critical for the safety and success of minimal-access fetoscopic closure of SBA: it provides surgically relevant information about the lesion that helps in planning the procedure and selecting safe and suitable trocar sites during intra-amniotic access, it enables monitoring of uterine closure and allows collection of hemodynamic information. Doppler ultrasound interrogation of the fetoplacental circulation as well as determination of fetal heart rate and contractility are performed regularly at defined times: before and after induction of anesthesia, after placement of maternal central venous and arterial lines, before intra-amniotic access, after amnioinfusion, before insufflation and at the end of the procedure. This hemodynamic information helps the anesthesiologist to adjust the depth of anesthesia and to optimize maternal and fetal hemodynamics by maternal administration of a crystalline solution, Ringer's solution (B. Braun Melsungen AG, Melsungen, Germany), catecholamines and other drugs according to the requirements of the procedure and in dosages safe to both mother and fetus.

Only when maternal and fetal hemodynamics remain stable after induction of anesthesia and, if required for achieving sufficient intra-amniotic work space, after amnioinfusion, will the first trocar be placed. If maternal or fetal hemodynamics or fetoplacental blood flow deteriorate after induction of anesthesia or amnioninfusion, and attempts at their normalization fail, the procedure is abandoned. Fortunately, this situation is rare, having been encountered only once over the past 3 years.

Surgical approach

Percutaneous minimal-access fetoscopic surgery for SBA is performed via three (or four) trocars, with an external diameter of 5 mm, that are placed into the amniotic cavity under continuous ultrasound monitoring by a Seldinger approach (Figure 1). Following partial removal of the amniotic fluid, partial amniotic carbon dioxide insufflation (PACI) is performed, as described previously[4,6], in order to maintain visibility of intra-amniotic contents. Using fetoscopic instruments (Karl Storz, Tuttlingen, Germany), fetal posturing is then carried out to maneuver the fetus into a position in which the malformation can be reached for the purposes of surgery.

The lesion is dissected with a needle electrode and the neural tissue is carefully freed from surrounding tissues (Figures 2 and 3). Depending on the anatomy of the lesion, the neural cord is covered with one or more collagen and teflon patches. Regardless of the closure technique, succesful watertight coverage is demonstrated at the end of the procedure by observing bulging of the patch as well as lack of cerebrospinal fluid leakage when its surface is compressed with an instrument.

Once the lesion has been closed, the insufflated carbon dioxide is removed with simultaneous refilling of the amniotic cavity with warm Ringer's solution. Following percutaneous coverage of the chorioamniotic membranous defects, the abdominal trocar insertion sites are closed with non-absorbable 5-0 surgical sutures.

Study variables

The following parameters were analyzed: maternal age, gestational age at surgery and at delivery, fetal demise during surgery, placental position, success of percutaneous amniotic access, number of trocars, incidence and consequences of trocar dislodgment, success of fetal posturing, pressures and duration of partial amniotic carbon dioxide

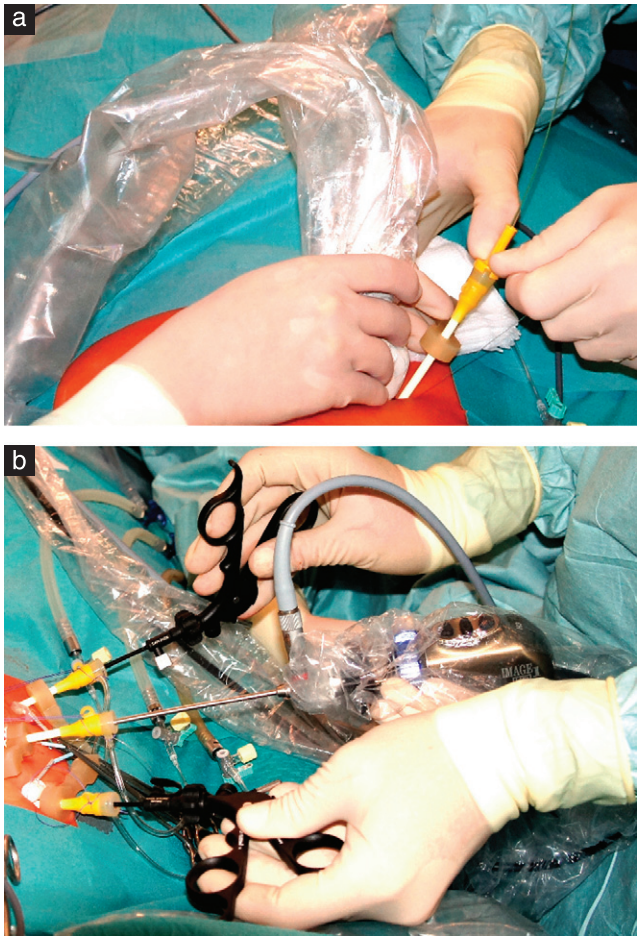

Figure 1 Percutaneous minimal-access fetoscopic surgery for spina bifida aperta: external aspect of the set-up. The procedure is performed via three (or four) trocars, each with an external diameter of 5 mm, that are placed into the amniotic cavity under continuous ultrasound monitoring by a Seldinger approach (a). Following partial amniotic carbon dioxide insufflation and fetal posturing, surgical dissection of the malformation is carried out using fetoscopic instruments (b).

insufflation (PACI), need for additional venting of insufflation gas from the maternal abdomen, type of lesion (flat, cystic), lesion size, lesion level, type of fetoscopic closure (single patch, double patch, triple patch, direct closure, direct closure with patch), overall technical success of the procedure defined as patch coverage of the neural tissue, success of uterine closure, and skin-to-skin-time of fetoscopic procedure.

RESULTS

Maternal age at surgery ranged between 19 and 41 (mean, 31.5) years and gestational age at surgery ranged between 21.0 and 29.1 (mean, 23.7) gestational weeks (Table 1). Gestational age at delivery in survivors ranged between 27.9 and 38.1 (mean, 33.0) weeks. All fetuses survived surgery, but there were four infant deaths: one early neonatal death after severe preterm birth at 24.6 weeks (Case 5) and two more infant deaths from severe brain-stem dysfunction attributed to Chiari II malformation in the first few months following delivery (Cases 3 and 7). One fetus, whose parents had opted against preoperative karyotyping, underwent technically successful surgery and was delivered at 35.1 weeks of gestation, but died from trisomy 13 (a diagnosis which was unexpected given the finding of isolated SBA prior to fetal surgery) after delivery (Table 1, Case 51). Further details of surgical outcome are given in the sister paper in this issue[11].

There were 20 procedures performed in the presence of an anterior placenta and 31 in the presence of a posterior placenta (Table 1). Skin-to-skin time ranged between 45 and 315 min. The 45-min case was abandoned because maternal obesity in combination with an anterior placenta made completion of the procedure technically impossible. The shortest successful case took 140 min, in a fetus with a flat lesion that could be dissected easily and covered by a single patch. Sixteen procedures took 140–200 min to perform, 22 procedures took 201–250 min and 11 procedures took 251–301 min. In the case which underwent the longest procedure (315 min), the surgical anatomy was highly complex and triple patch coverage was performed.

Ultrasound-guided percutaneous intra-amniotic access with ports with an external diameter of 5 mm was established in all cases. Three trocars were inserted into the amniotic cavity during 49 procedures and four trocars were required during two (Cases 5 and 7); in these cases, the additional trocar was necessary for maintaining a stable fetal position throughout the procedure. In one case, dislodgment of one trocar occurred at the end of the procedure, such that closure of the trocar insertion site could not be performed (Case 24). In another case, which had to be abandoned, dislodgment of two trocars occurred, as a consequence of maternal obesity, immediately after initiation of insufflation (Case 32); this case was also the only one in which favorable percutaneous fetal posturing was not achieved.

Opening pressures for PACI ranged between 9 and 30 (mean, 15.6) mm Hg and duration ranged between 10 and 275 (mean, 183) min (Table 1). PACI was well tolerated by both mother and fetus and permitted clear visualization throughout the entire fetoscopic procedure. Additional venting of insufflation gas from the maternal peritoneal cavity was required in 17 cases.

There were 36 flat and 15 cystic lesions. Measured at skin level, their areas ranged between 3 and 12 cm^2. Overall technical success of the procedure, defined as complete patch coverage of the exposed neural tissue at the end of fetal surgery, was achieved in all except the one case in which early dislodgment of two trocars occurred in an obese patient (Case 32). Single-patch coverage was performed in 31 fetuses, double-patch coverage in 14 (Figure 2), triple-patch coverage in two and direct closure of the lesion in three. In two fetuses in the latter group, the skin was closed immediately above the neural cord without interposition of patch material (Cases 35 and 44); in the other two, as recommended by our local neurosurgeon, direct skin closure was performed after covering the neural cord with a collagen patch (Case 48) (Figure 3).

Coverage of all membranous defects at trocar removal was achieved in 47 cases. Coverage of only two of three

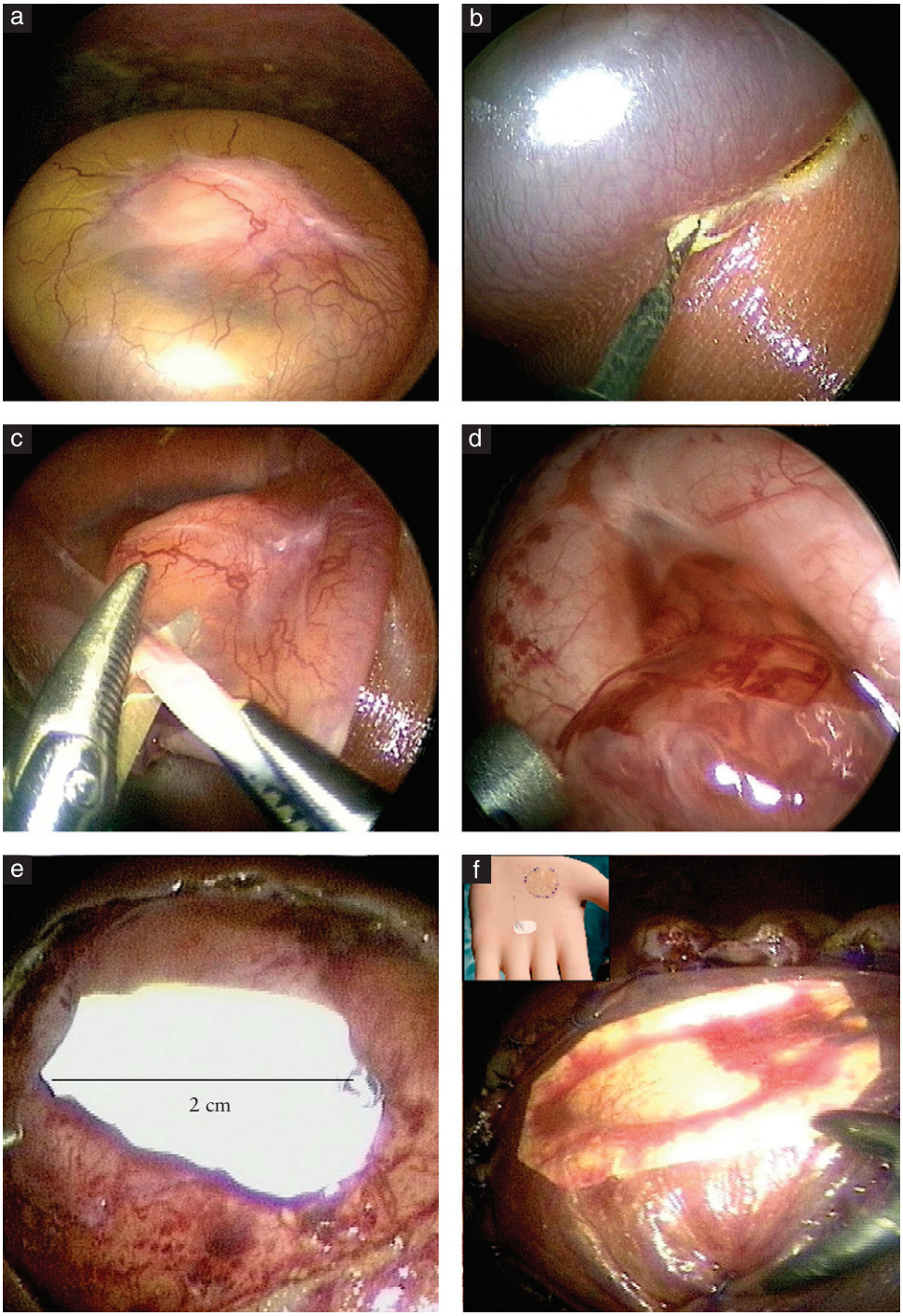

Figure 2 Minimal-access fetoscopic double patch closure of a large L3-myelomeningocele at 23 + 2 weeks of gestation: fetoscopic views. (a) The large myelomeningocele before surgical dissection; the exposed neural tissue can be visualized clearly in the gas-insufflated amniotic cavity. (b) The malformation is dissected with a needle electrode. (c) Note the high degree of precision that can be achieved within a range of < 1 mm during manual dissection of the placode using micrograsper and microscissors. (d) Neural tissue after removal of surrounding pathological tissues; note clear visualization of the spinal cord nerves in the high-powered fetoscopic field, employing a 3.3-mm-30° rod-lens fetoscope. (e) View after protecting the neural tissue with an inert Gore-polytetrafluoroethylene patch (Gore Preclude Pericardial Membrane, Flagstaff, AZ, USA), with the aim of preventing tethering. (f) Definitive coverage of the entire surgical field is achieved with a collagen patch (inset). Successful watertight coverage is demonstrated at the end of the procedure by bulging of the patch as well as lack of cerebrospinal fluid leakage on compression with an instrument.

access sites was achieved in the remaining four cases, because of trocar dislodgment in two cases, to avoid the risk of umbilical cord compromise in one case and because two trocar insertion sites were situated too close to each other in one case.

DISCUSSION

This retrospective analysis shows that percutaneous minimal-access fetoscopic surgery for SBA in human fetuses can be performed with a high rate of technical

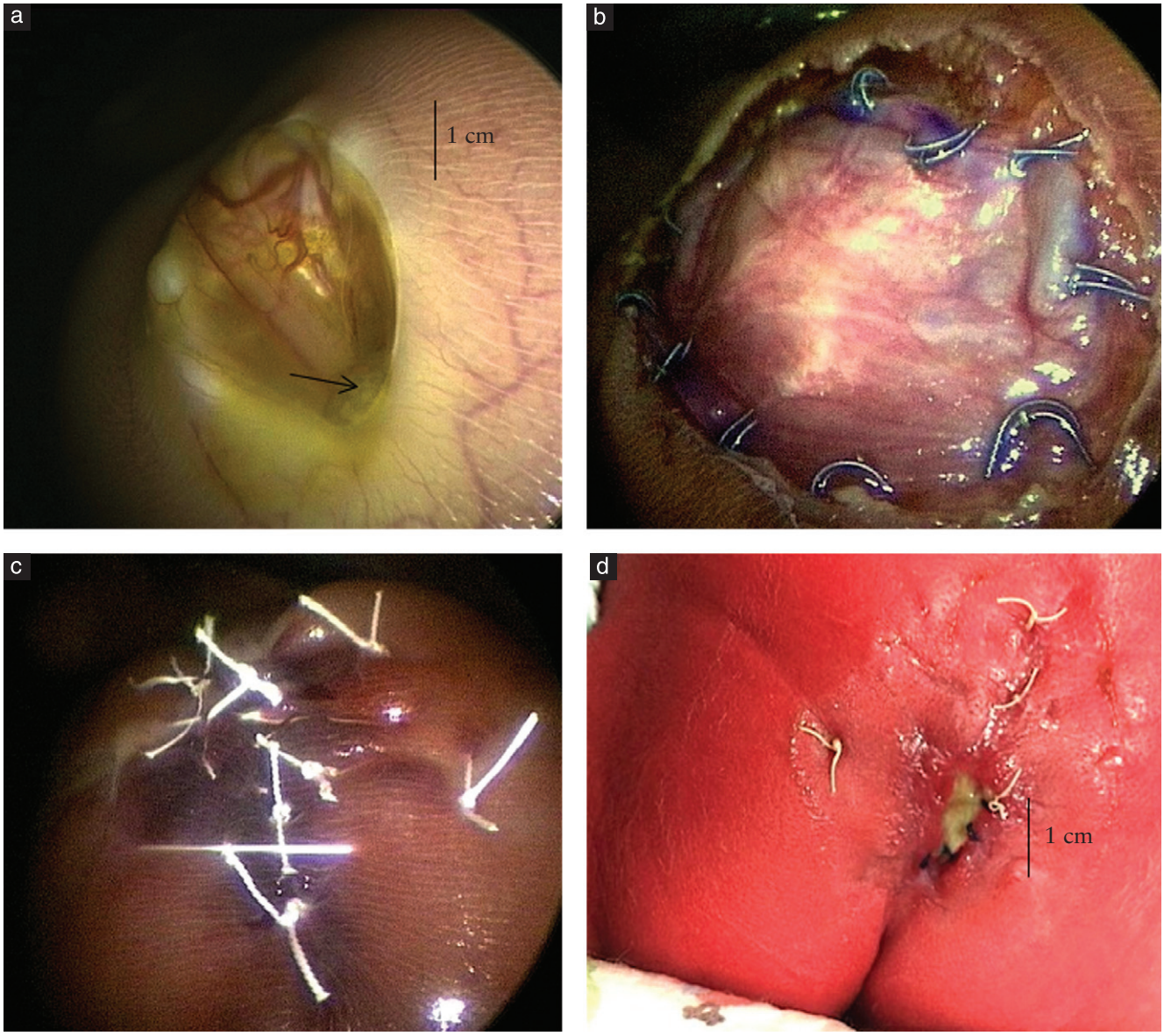

Figure 3 Minimal-access fetoscopic direct closure of a sacral myeloschisis at 23 + 6 weeks of gestation. (a) The sacral myeloschisis before surgical dissection. A small amount of stool (arrow) can be visualized over the opening of the central canal at the rostral end of the neural tissue. (b) Following surgical dissection, the malformation has been covered with a collagen patch. (c) Complete skin closure. (d) After delivery, a very small part of the collagen patch can be seen as a result of dehiscence of one of the skin sutures; in this case the skin overgrew the patch, without need for further intervention.

success, regardless of placental position, and with a low rate of perioperative mortality. Like the open fetal surgical approach, percutaneous fetoscopic patch coverage of the malformation aims at protecting the spinal cord tissue, reversing hindbrain herniation and reducing the need for postnatal ventriculoperitoneal shunt insertion. Compared with open fetal surgery for SBA, however, the percutaneous minimal-access fetoscopic approach reduces considerably the risk of maternal injury by avoiding laparotomy and hysterotomy. Hence, maternal pain and discomfort are usually minimal beyond the second day after surgery. In addition, most pregnant women can be discharged home from hospital within a week. Adhering to the fundamental ethical principle of *primum non nocere*, further exploration and dissemination of the minimal-access fetoscopic technique seem worthy goals and may eventually lead to replacement of the open operative approach.

Employing ultrasound guidance, percutaneous fetal access with three trocars can be achieved in essentially all cases. Rarely, a fourth trocar is required for securing a favorable fetal lie throughout the procedure. As each trocar is inserted over a guide wire, the initial puncture hole for maternal percutaneous–transabdominal–transuterine–paraplacental–intra-amniotic trocar insertion has a diameter of only 1.2 mm. This method of intra-amniotic access is the hallmark of percutaneous minimal-access fetal surgery and is practically beyond comparison with the much larger incisions in the maternal abdomen and uterus that are required for open fetal surgery (Figure 4). My growing clinical experience showed that fetoscopic surgery can be performed

Table 1 Characteristics of 51 pregnancies undergoing percutaneous minimal-access fetoscopic closure of spina bifida aperta

			GA (weeks)			Lesion				Trocar		PACI					
ID	MA (yrs)	Plac. loc.	Surg.	Deliv.	SSS time (min)	Level	Type	Size* (cm)	Amnio. access	n	Disl. (n)	OP (mmHg)	Duratn (min)	Mat. ab.vent.	Fetal post.	Closr tech.	Surg. succ.	Surv.
1	31	Post	24 + 0	34 + 0	230	L4	Flat	3	+	3	–	13	190	–	+	SP	+	+
2	30	Ant	22 + 6	29 + 5	240	L1	Flat	4 × 3	+	3	–	16	195	–	+	SP	+	+
3	23	Ant	25 + 0	34 + 0	240	L5	Flat	4 × 3	+	3	–	22	265	–	+	SP	+	– (Chi.)
4	31	Ant	24 + 0	36 + 6	255	L4	Flat	4 × 3	+	3	–	14	210	–	+	DP	+	+
5	36	Ant	23 + 4	24 + 4	270	L3	Flat	4 × 3	+	4	–	24	220	–	+	DP	+	–
6	36	Post	21 + 1	34 + 0	240	L2	Flat	4 × 3	+	3	–	20	195	+	+	SP	+	+
7	22	Ant	25 + 0	33 + 4	290	L2	Flat	4 × 2	+	4	–	30	240	–	+	SP	+	– (Chi.)
8	34	Post	24 + 6	30 + 0	300	L5	Flat	3	+	3	–	14	240	–	+	SP	+	+
9	29	Ant	25 + 3	30 + 5	260	L5	Cyst.	2	+	3	–	16	220	–	+	DP	+	+
10	38	Ant	21 + 5	32 + 0	195	L4	Flat	2 × 1.5	+	3	–	20	220	–	+	SP	+	+
11	35	Ant	25 + 3	30 + 5	265	L3	Flat	3.5 × 3	+	3	–	16	215	+	+	SP	+	+
12	30	Post	27 + 2	36 + 4	270	S 1	Flat	3 × 2	+	3	–	13	215	+	+	TP	+	+
13	19	Post	22 + 0	34 + 3	180	L4	Cyst.	3	+	3	–	16	180	+	+	SP	+	+
14	36	Post	23 + 3	34 + 1	210	L4	Cyst.	3	+	3	–	14	170	+	+	SP	+	+
15	30	Post	25 + 1	32 + 0	315	L4	Cyst.	3	+	3	–	12	275	–	+	TP	+	+
16	30	Post	24 + 4	38 + 1	255	L5	Flat	2 × 1.5	+	3	–	12	215	–	+	DP	+	+
17	30	Post	22 + 1	34 + 3	270	L1	Flat	4 × 3	+	3	–	15	240	–	+	SP	+	+
18	19	Post	24 + 1	31 + 0	240	L4	Flat	3 × 1.5	+	3	–	16	210	–	+	DP	+	+
19	41	Post	22 + 6	30 + 0	300	L1	Flat	3 × 3.5	+	3	–	18	250	–	+	DP	+	+
20	40	Ant	22 + 4	34 + 3	210	L4	Flat	2.5 × 3	+	3	–	16	165	–	+	DP	+	+
21	38	Ant	24 + 6	33 + 4	210	L5	Flat	3 × 2	+	3	–	12	180	–	+	SP	+	+
22	36	Ant	21 + 4	28 + 5	215	L3	Flat	2 × 1.5	+	3	–	9	185	–	+	SP	+	+
23	29	Post	23 + 0	30 + 0	210	L4	Flat	2	+	3	–	15	135	–	+	SP	+	+
24	34	Ant	21 + 3	33 + 0	190	L3	Flat	2.5	+	3	1	10	150	–	+	SP	+	+
25	40	Post	23 + 3	37 + 2	210	L5	Flat	2.5	+	3	–	15	150	+	+	SP	+	+
26	25	Post	25 + 4	34 + 1	225	L3	Cyst.	4.5 × 3	+	3	–	24	190	+	+	SP	+	+
27	28	Post	22 + 2	34 + 0	225	L4	Flat	4 × 2.5	+	3	–	17	175	+	+	SP	+	+
28	28	Post	22 + 4	37 + 5	225	L4	Cyst.	4	+	3	–	16	180	+	+	DP	+	+
29	33	Post	24 + 2	31 + 3	245	L3	Flat	3 × 2.5	+	3	–	13	210	–	+	SP	+	+
30	36	Post	23 + 1	29 + 6	245	L5	Flat	3 × 2.5	+	3	–	11	205	–	+	DP	+	+
31	34	Post	24 + 0	29 + 2	205	L1	Flat	3 × 2.5	+	3	–	17	170	–	+	DP	+	+
32	23	Ant	24 + 4	32 + 5	45	L3	Flat	NA	+	3	2	16	10	–	–	NA	–	+
33	30	Ant	23 + 6	35 + 1	240	L5	Flat	3 × 2.5	+	3	–	16	195	–	+	DP	+	+
34	40	Ant	21 + 0	31 + 1	165	L4	Cyst.	3 × 2.5	+	3	–	14	120	–	+	DP	+	+
35	33	Post	26 + 6	38 + 1	160	L5	Flat	3 × 2	+	3	–	12	130	–	+	DC	+	+
36	29	Post	21 + 4	34 + 2	150	L5	Cyst.	2	+	3	–	18	150	+	+	SP	+	+
37	26	Post	22 + 4	33 + 6	155	L5	Flat	3 × 2.5	+	3	–	14	130	+	+	SP	+	+
38	23	Post	22 + 6	32 + 4	200	T11	Flat	4 × 3	+	3	–	20	155	+	+	SP	+	+
39	37	Ant	24 + 3	30 + 2	225	L5	Cyst.	4 × 3	+	3	–	14	205	–	+	DP	+	+
40	25	Ant	23 + 1	34 + 2	180	L2	Flat	5 × 3	+	3	–	15	150	–	+	SP	+	+
41	26	Post	28 + 5	34 + 0	140	L5	Flat	4 × 3.5	+	3	–	12	110	–	+	SP	+	+
42	32	Ant	21 + 6	32 + 1	220	L5	Flat	3.5	+	3	–	18	190	–	+	SP	+	+
43	32	Post	24 + 0	30 + 6	200	T11	Flat	5 × 4	+	3	–	10	140	–	+	SP	+	+
44	30	Post	29 + 1	35 + 0	210	L4	Flat	4 × 3	+	3	–	18	170	+	+	DC	+	+
45	38	Post	22 + 3	34 + 2	185	L4	Cyst.	5 × 4	+	3	–	15	175	+	+	SP	+	+
46	37	Post	23 + 0	34 + 4	190	L3	Cyst.	5 × 4	+	3	–	14	150	+	+	SP	+	+
47	32	Post	23 + 2	31 + 4	190	L3	Cyst.	3.5 × 3	+	3	–	15	150	+	+	DP	+	+
48	28	Post	23 + 6	34 + 0	225	S 1	Flat	3.5 × 3	+	3	–	16	190	–	+	DCP	+	+
49	32	Ant	22 + 4	27 + 6	280	L2	Cyst.	4 × 3.5	+	3	–	16	240	–	+	SP	+	+
50	30	Post	23 + 1	35 + 1	175	L5	Cyst.	3 × 2	+	3	–	16	130	–	+	SP	+	+
51	34	Ant	21 + 1	35 + 1	180	L4	Cyst.	4 x 3.5	+	3	–	10	150	+	+	SP	+	– (Tris.)

*Lesion size given as diameter for circular lesions and mean length and width for oval lesions. +, Yes; –, No; Amnio. access, amniotic access achieved; Ant, anterior; Chi, Chiari; Closr tech., closure technique; Cyst., cystic; DC, direct closure; DCP, direct closure over patch; Deliv., at delivery; Disl., dislodgement; DP, double patch closure; Duratn, duration; Fetal post., fetal posturing achieved; GA, gestational age; ID, case number; L, lumbar; MA, maternal age; Mat. ab.vent., venting of insufflation gas from maternal abdomen required; NA, not applicable; OP, opening pressure; PACI, partial amniotic carbon dioxide insufflation; Plac. loc., placental location; Post, posterior; S, sacral; SP, single patch closure; SSS time, surgical skin-to-skin time; Surg., surgery; Surg. succ., technical success of surgery; Surv., survival; T, thoracic; TP, triple patch closure; Tris., trisomy; yrs, years.

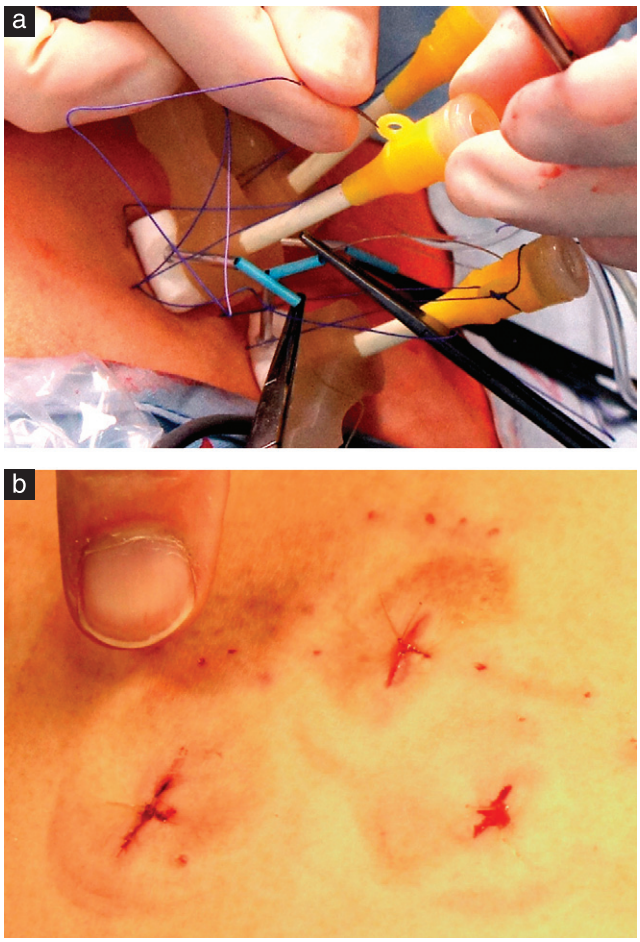

Figure 4 (a) Employing ultrasound guidance, percutaneous fetal access with three trocars can be achieved in essentially all cases. As each trocar is inserted over a guide wire, the initial puncture hole for maternal percutaneous–transabdominal–transuterine–paraplacental–intra-amniotic trocar insertion has a diameter of only 1.2 mm. (b) The tiny incisions and punctures for trocar insertion during the minimal-access approach are barely comparable to the much larger incisions in the maternal abdomen and uterus that are required for open fetal surgery.

in most cases regardless of placental position. During ultrasound-guided trocar insertion in cases with an anterior placenta, a safety margin of about 3 cm away from the placental edge suffices in preventing placental injury.

Trocar dislodgement was rare in this clinical series. It was usually sufficient to advance each trocar about 3–5 cm into the amniotic cavity. Yet, as seen in two of our cases, trocar dislodgment may occur during instrument manipulation or in adipose patients, in whom the trocar tip can sometimes be advanced into the amniotic cavity only 2 cm or less. Trocar dislodgment can also be a consequence of too much traction between the abdominal and uterine walls, of sudden uterine volume changes due to intraoperative uterine contractions, or of the amniotic cavity gradually collapsing due to unattended gas loss along the trocars into the maternal abdomen[5]. In cases with an anterior placenta, trocar dislodgment requires abandonment of the procedure since amniotic gas insufflation precludes ultrasound-guided reinsertion of another trocar. Unmonitored or in the presence of impaired ultrasound imaging quality, trocar insertion in cases with an anterior placenta carries a high risk for placental or maternal bowel injury. In contrast, in cases with a posterior placenta, reinsertion can be achieved easily through the original opening, guided by fetoscopy.

Successful fetal posturing with endoscopic instruments can be achieved in most cases, although the more obese a patient, the more difficult posturing maneuvers can become. In this situation, the fragile instruments and endoscopes often bend to critical degrees. In obese patients with a posterior placenta, we have found postponing the procedure until the fetus lies in a more favorable position to be a helpful strategy. Alternatively, in cases involving more severe obesity in combination with an anterior placenta, maternal laparotomy and transuterine trocar placement or even open fetal surgery may be considered.

Due to the small trocar size, continuous pressure- and volume-controlled exchange of large volumes of crystalline solutions throughout the procedure in order to manage complications of bleeding or provide a clear field of view for dissecting and closing the malformation may be difficult or impossible to achieve. In order to overcome the disadvantages of operating in fluid, management principles and safety measures for percutaneous gas insufflation of the amniotic cavity were defined from animal studies in sheep and early clinical experience[5–7,15,16]. PACI over a mean period of 3 h permitted clear visualization throughout all 51 fetoscopic procedures and did not result in any critical or unmanageable maternal cardiovascular effects as assessed by arterial blood gas analyses and continuous maternal electrocardiography, blood pressure, oxygen saturation and end-expiratory carbon dioxide concentration monitoring. Encouragingly, postnatal clinical examinations as well as ultrasonography and MRI in the infants, did not reveal any evidence of chronic brain injury that could be attributed to the fetoscopic set-up. These clinical findings were supported by our group's previous insufflation studies in sheep[16,17].

During the earliest clinical cases, it was not clear how well and for how long mother and fetus would tolerate anesthesia and PACI in particular. Years earlier, Bruner *et al.*[2] were the first to insufflate an exteriorized uterus in humans during four fetoscopic procedures and they encountered placental abruption in one of these. PACI has never before been used in a percutaneous fetoscopic set-up in humans and, furthermore, previous studies of other investigators on exteriorized sheep suggested that carbon dioxide and/or insufflation pressures > 15 mmHg would lead to dangerous degrees of fetal acidosis[18–20]. During our own studies in sheep, we observed that insufflation of the amniotic cavity when the maternal abdomen was closed was tolerated at much higher insufflation pressures than was previously thought possible, without interfering with fetoplacental blood flow. Nevertheless, the first human procedures were kept as short and as simple as possible. Whenever a minor bleeding complication or some membrane detachment was detected, the procedure was abandoned for reasons of maternal safety. As a result

of this caution, three of the first 19 procedures in the pilot study were not completed[12].

In order to keep the procedure short in the initial cases, we simply covered the lesion using inert patch material and left the malformation itself untouched[9]. However, due to the strong traction forces on the patch rim from fetal growth, the patches often partially dehisced and coverage of the entire lesion until delivery was seldom achieved. As a consequence, during this early phase of the pilot study, all operated fetuses had to undergo standard postnatal repair of the lesion. Encouraged by the observation that our protocol for maternofetal anesthesia and amniotic carbon dioxide insufflation were well tolerated by both mothers and fetuses over periods of hours, surgical dissection of the lesion followed by closure with a collagen patch was introduced in subsequent cases[7,21].

At that time, we believed that the collagen patch employed for watertight coverage of the lesion would be overgrown by skin until delivery. However, the surface of the patch did not overgrow at all or did so only to some degree, when the procedure was performed prior to 22 weeks of gestation. Therefore, in almost all of our operated fetuses, patch overgrowth with skin still had to happen within the first postnatal weeks of life (Figure 5). Nevertheless, in fetuses with relatively narrow malformations, direct skin closure above the patch is also possible (Figure 3).

Further advances in handling the fetoscopic set-up and increasing experience with the surgical anatomy of the malformation have helped us to adapt the fetoscopic approach to lesions of various sizes and surgical complexities: single-patch closure with a collagen patch is now the technique most commonly performed. It is preferred in those cases in which the spinal canal is sufficiently deep such that cerebrospinal fluid can reaccumulate between spinal cord and patch, reducing the risk of tethering of the neural cord to the patch in the postoperative period. In more shallow lesions that do not allow for a sufficient cerebrospinal fluid cushion between spinal cord and patch, or in cases in which small skin remnants may sometimes not be removed completely during fetoscopy, double-patch closure is performed: the spinal cord tissue is first covered with a small inert teflon patch, then the entire defect is covered with an additional collagen patch (Figures 2 and 3).This approach is chosen in order to facilitate the conditions for postnatal neurosurgical procedures. The technically more simple fetoscopic closures have been critisized by surgeons who believe that fetal repair must adhere to the postnatal standards of repair[22]. This non-evidence based practice was recently challenged by Pedreira and colleagues from Sao Paulo[23]. They developed and recently introduced clinically a simplified fetoscopic spina bifida closure technique in sheep, which resulted in better preservation of nerve tissue and less adherence of the spinal cord to the scar when compared with the classic technique performed by a neurosurgeon. Their findings prompted them to suggest that 'the use of the current (classic neurosurgical 3-layer) repair technique (during open fetal surgery) may need to be reassessed'.

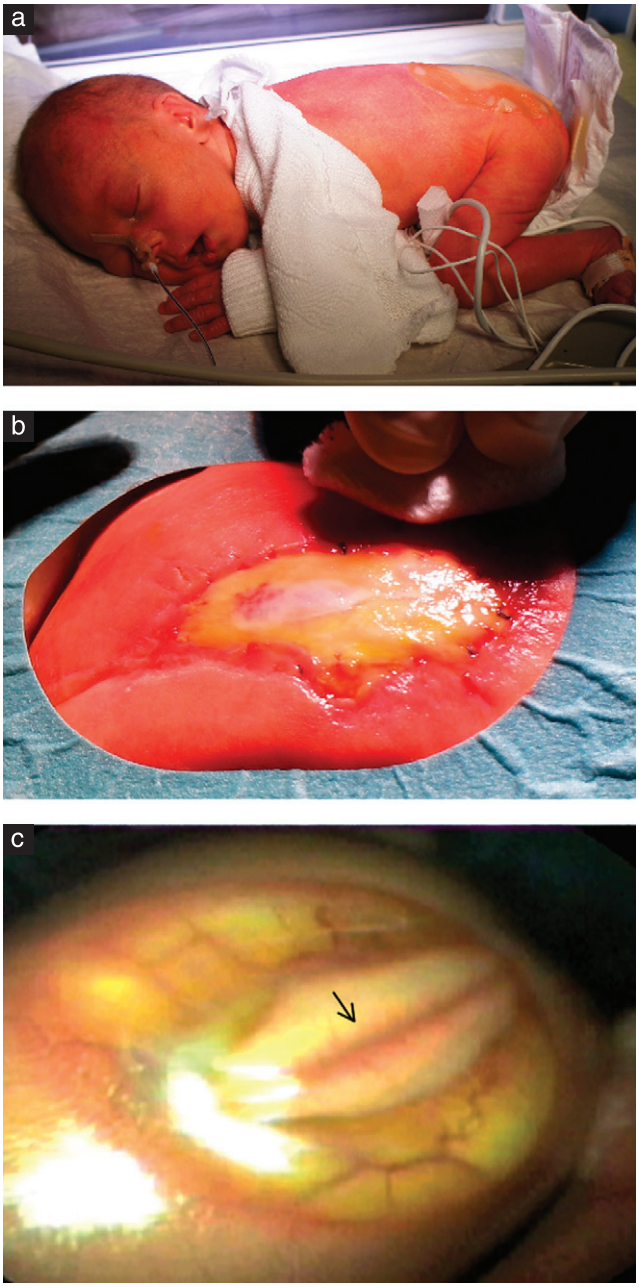

Figure 5 (a) Newborn with spina bifida, at 35 weeks of gestation, following double-patch closure at 22 + 4 weeks of an L4 defect extending over the entire sacrum. Because, in human fetuses, the surface of the patch does not overgrow with skin over the remainder of gestation, this occurs within the first few postnatal weeks. (b) Perfectly ingrown upper patch after removal of the surgical clips. (c) Fetoscopic image of the large malformation with a long segment of exposed placode (arrow) before closure. Note that, at the time of surgery, many malformations are almost as wide as the entire fetal back.

Clearly, the future will show to what extent this fetal malformation can or should be addressed surgically *in utero*. In order to facilitate surgical dissection during more complex procedures (Figure 6), we and others have suggested and tested the incorporation of surgical robotics for minimal-access fetal SBA repair in sheep[8,24]. The results

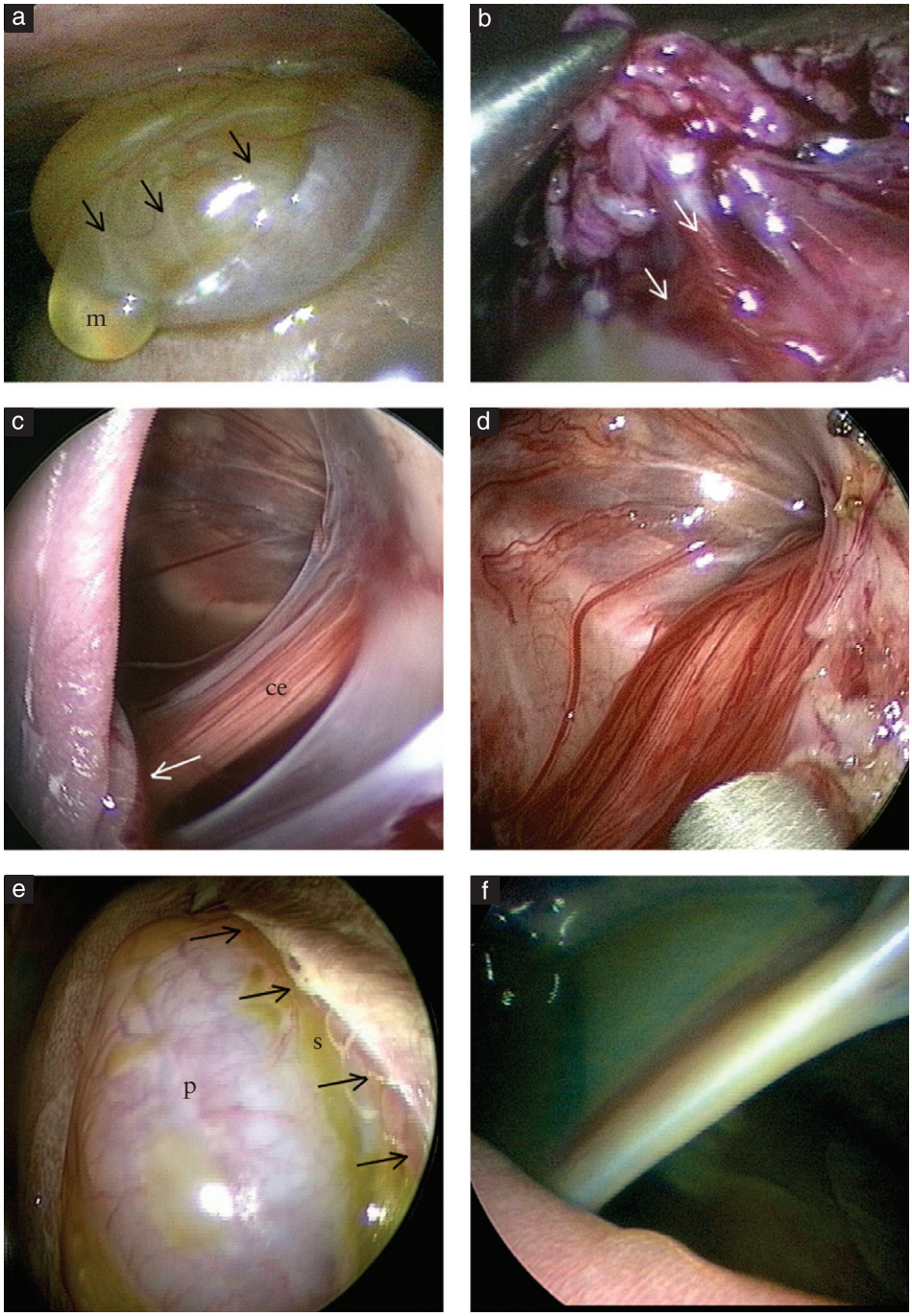

Figure 6 Surgically challenging set-ups for minimal-access fetoscopic surgery of spina bifida that may benefit from the incorporation of surgical robotics. (a,b) Large L4 myelomeningocele with a terminal myelocystocele (m) at 25 + 1 weeks of gestation. The main surgical difficulty resulted from sparing the spinal nerves (a, arrows), that were attached along the inner surface of the sac, from injury during resection of the sac tissue. (b) After removal of most parts of the sac, the intact nerves (arrows) can be seen still adherent to a part of the inner layer of the sac that was preserved. (c,d) Large L5 myelomeningocele. (c) The delicate nerves of the cauda equina (ce) were found attached (arrow) to the far sturdier pathological skin at 24 + 3 weeks of gestation. (d) Fetoscopic image after removal of all sac tissue. (e) L5 myelomeningocele with pathologic skin adjacent to the neural placode (p) at 26 + 6 weeks of gestation. Beige-colored stool can be seen along the placode and also on its surface. As in the case depicted in (b) and (c), the surgical difficulty here results from the dissection of the delicate neural tissue from the far sturdier pathological skin. (f) In this case, a firm strand of amniotic tissue divides the amniotic cavity into two compartments. This problem makes posturing maneuvers more difficult and in itself poses a risk factor for preterm rupture of membranes.

of these feasibility studies did not provide any evidence for superior patch coverage of experimental skin lesions by a robot compared with what can be achieved by a manual approach. Yet, in order to facilitate fetoscopic dissection of the placode and achieve the precision of tissue handling that would be needed for a fetoscopic 'classic three-layer approach', surgical robotics may be desirable.

Coverage of the trocar insertion defects within the chorioamniotic membranes has been one of the most important accomplishments during the development of

the fetoscopic technique. Since its introduction, nearly 90% of affected fetuses have been delivered at or beyond 30 weeks of gestation, enabling avoidance of the serious complications associated with prematurity[25,26].

In conclusion, percutaneous minimal-access fetoscopic surgery for SBA in human fetuses can be performed with a high rate of technical success regardless of placental position. Despite its potential for important benefits in patients with SBA, there is still a low risk for perioperative fetal demise or significant chronic morbidity from prematurity.

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