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Incidence and clinical implications of early inadvertent septostomy after laser therapy for twin–twin transfusion syndrome

R. CRUZ-MARTINEZ*, T. VAN MIEGHEM†, L. LEWI†, E. EIXARCH*, T. COBO*, J. M. MARTINEZ*, J. DEPREST† and E. GRATACOS*

**Department of Maternal-Fetal Medicine, Institute Clínic of Gynecology, Obstetrics and Neonatology, Hospital Clinic-IDIBAPS, University of Barcelona and Centre for Biomedical Research on Rare Diseases (CIBERER), Barcelona, Spain; †Department of Obstetrics and Gynecology, University Hospitals Leuven, Leuven, Belgium*

KEYWORDS: amniotic band syndrome; fetal therapy; septostomy; TTTS; twin-twin transfusion syndrome

ABSTRACT

Objective *To evaluate the incidence and clinical outcome of inadvertent septostomy after fetoscopic laser therapy for twin–twin transfusion syndrome (TTTS) and, particularly, to explore its association with the risk of developing pseudoamniotic band syndrome (PABS).*

Methods *In a cohort of 414 consecutive monochorionic twin pregnancies with confirmed TTTS treated with laser, the incidence of postoperative septostomy within 1 week of the procedure was recorded prospectively. Rates of preterm delivery, preterm premature rupture of membranes (PPROM), intrauterine fetal demise (IUFD) and PABS were compared among cases with and without septostomy.*

Results *The mean gestational age at laser therapy was 20.4 (range, 15.3–27.6) weeks. Postoperative septostomy occurred in 30 (7.2%) cases. Pregnancies complicated with septostomy had a significantly higher proportion of preterm delivery before 32 weeks (76.7% vs. 30.2%, $P < 0.001$), PPROM before 32 weeks (46.7% vs. 19.0%, $P < 0.001$), IUFD (43.3% vs. 25.8%, $P < 0.05$) and PABS (13.3% vs. 1.0%, $P < 0.001$), compared with pregnancies without septostomy.*

Conclusions *Inadvertent septostomy occurred in 7% of cases after fetoscopic laser therapy and was associated with a substantially increased risk of adverse perinatal outcome and PABS.*

INTRODUCTION

Twin–twin transfusion syndrome (TTTS) is a complication affecting 6–17% of all monochorionic twin pregnancies and, with expectant management, is associated with a mortality rate of about 80–100%[1,2]. The first-line treatment of severe TTTS is fetoscopic laser photocoagulation of placental intertwin anastomoses, which is associated with survival rates of at least one twin ranging from 75% to 85%[3,4]. However, as with any invasive fetal procedure, laser treatment is associated with an increased risk of preterm premature rupture of membranes (PPROM), which may occur in up to 12–28% of cases, and of preterm labor, with about 30.5% of cases delivering before 32 weeks[5–7].

Occasionally, fetoscopic therapy is also associated with other complications that may increase further the risk of adverse outcome. Clinical experience suggests that a proportion of cases treated with fetoscopy are complicated by septostomy, as a consequence of inadvertent perforation of the donor's collapsed membrane at uterine trocar insertion or due to the need to coagulate some of the placental anastomoses through the intertwin membrane[5,8]. This complication leads to creation of a monoamniotic twin pregnancy and entails significant risks of intrauterine fetal demise (IUFD) resulting from cord entanglement, preterm labor and PPROM[8–12]. In addition, septostomy has been suggested to increase the risk of pseudoamniotic band syndrome (PABS)[8,13,14] and consequently of limb amputation[14,15]. Indeed, PABS has been reported to occur in up to 3% of cases of TTTS treated with laser[5,16], but its potential association with the occurrence of post-laser septostomy has not been investigated.

The aim of this study was to assess the prevalence and clinical implications of inadvertent septostomy after laser therapy for TTTS and, particularly, to explore its association with the risk of developing PABS.

Correspondence to: Dr E. Gratacos, Maternal-Fetal Medicine Department, Hospital Clinic, University of Barcelona, Sabino de Arana 1, 08028 Barcelona, Spain (e-mail: gratacos@clinic.ub.es)

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SUBJECTS AND METHODS

Subjects

Included in the study was a cohort of 414 consecutive monochorionic diamniotic twin pregnancies with confirmed TTTS which were treated with laser coagulation in the period between June 2006 and December 2009 at Hospital Clinic, Barcelona, Spain and the University Hospitals Leuven, Belgium. The inclusion criterion for fetal surgery was: monochorionic diamniotic pregnancy with TTTS defined according to the Eurofoetus criteria[17], which includes polyuric polyhydramnios in the recipient twin, with a deepest vertical amniotic fluid pocket of at least 8.0 cm before 20 weeks of gestation and at least 10.0 cm thereafter, together with oligohydramnios in the donor twin, with a deepest vertical amniotic fluid pocket of less than 2.0 cm. Exclusion criteria were: IUFD, congenital malformations, chromosomal abnormalities, and echographic evidence of septostomy prior to laser therapy. TTTS was classified according to the severity staging system proposed by Quintero *et al.*[18]. The surgical protocol was approved by the hospital ethics committee and women provided written informed consent to participate (IRB 2008/4584).

Fetoscopic laser therapy

Selective laser coagulation of the placental anastomoses on the chorionic plate was performed as described previously[4]. This involved percutaneous insertion under local anesthesia of 1.2–2.0-mm fiber semi-rigid endoscopes with remote eyepiece through operative fetoscopic sheaths and trocars with maximum external diameter of 8 or 10 French. Intertwin anastomoses were identified and coagulated systematically along the intertwin vascular equator with a non-touch technique using an Nd/YAG or diode laser. Amniotic fluid was subsequently drained until the deepest amniotic fluid pocket was < 8 cm on ultrasound examination.

Ultrasound examination

Following fetoscopic laser ablation, septostomy was searched for prospectively by ultrasound examination at the laser center every 24 h during the first 3 days and then 72 h later. Septostomy was diagnosed in the presence of a free-floating intertwin membrane flap on ultrasound examination. After initial follow-up at the laser center, patients were referred back to their local obstetrician or fetal medicine specialist for further follow-up. In all cases, we collected information regarding perinatal outcome, including PPROM before 32 weeks of gestation, IUFD of one or both fetuses, gestational age at delivery, and identification of PABS either on ultrasound examination or after delivery.

Statistical analysis

Student's *t*-test and Pearson's chi-square test were used to compare quantitative and qualitative data, respectively, within the study group. All tests were two-tailed and $P < 0.05$ was considered statistically significant. The odds ratio of adverse perinatal outcome between cases with and those without septostomy was calculated using a 2×2 table. Statistical calculations were performed using the Statistical Package for the Social Sciences (SPSS 17.0, SPSS Inc., Chicago, IL, USA) software.

RESULTS

In all 414 monochorionic twin pregnancies fulfilling the inclusion criteria for surgery laser coagulation was performed successfully. The overall survival rate of at least one twin was 92% (381/414) and of both twins was 73% (302/414). According to the Quintero staging system, there were 78 (18.8%) Stage I cases, 130 (31.4%) Stage II, 179 (43.2%) Stage III and 27 (6.5%) Stage IV.

The baseline characteristics of the study population are shown in Table 1. The mean gestational ages at therapy and at delivery were 20.4 and 32.7 weeks, respectively. Septostomy occurred within the first week postoperatively in 30 (7.2%) cases, of which 11 were identified within 24 h after surgery. Eight (1.9%) cases were complicated with PABS, all of which presented as limb constrictions and were diagnosed postnatally. There were no cases of limb amputations.

Table 2 displays data on the surgical procedure comparing patients with and those without septostomy. There were no significant differences in terms of gestational age at therapy, anterior location of the placenta, total fluid drained on amnioreduction, or duration of surgery. The rate of septostomy was no different between cases operated on with an 8-French and those operated on with a 10-French cannula (7.8% (4/51) vs. 7.2% (26/363), $P = 0.86$). The rate of septostomy was also similar between the severity stages of TTTS (5.1%, 8.5%,

Table 1 Maternal characteristics, procedure data and perinatal outcome of 414 monochorionic diamniotic twin pregnancies with confirmed twin–twin transfusion syndrome treated with laser coagulation

	Value
Maternal age (years)	31.4 (17.3–42.9)
Primiparous	44.7
Non-Caucasian ethnicity	13.0
Anterior placenta	44.9
Gestational age at surgery (weeks)	20.4 (15.3–27.6)
Duration of surgery (min)	44.7 (10–150)
PPROM before 32 weeks	21.0
Gestational age at PPROM (weeks)	27.9 (20.1–36.7)
Preterm delivery before 32 weeks	33.6
Septostomy	7.25
Cesarean section	34.3
Gestational age at delivery (weeks)	32.7 (24.0–41.0)
Survival of at least one twin	92.0
Survival of both twins	72.9
Pseudoamniotic band syndrome	1.9

Results expressed as mean (range) or %. PPROM, preterm premature rupture of membranes.

Table 2 Procedure data of monochorionic diamniotic twin pregnancies with confirmed twin–twin transfusion syndrome treated with laser coagulation according to whether postoperative septostomy occurred

	Septostomy (n = 30)	*No septostomy (n = 384)*	P*
Gestational age at surgery (weeks)	21.1 (2.9)	20.3 (2.6)	0.15
Anterior placenta	44.5	50.0	0.87
Duration of surgery (min)	41.1 (15.2)	44.9 (25.9)	0.42
Total amniotic fluid drained (mL)	673 (232)	601 (289)	0.18

Results expressed as mean (SD) or %. *Student's *t*-test or Pearson-χ^2-square test.

Table 3 Individual risk of different adverse perinatal outcomes and development of pseudoamniotic band syndrome (PABS) in monochorionic diamniotic twin pregnancies with confirmed twin–twin transfusion syndrome treated with laser coagulation which then developed septostomy ($n = 30$)

Dependent variable	*OR*	*95% CI*	P
PPROM < 32 weeks	3.73	1.74–7.98	< 0.001
PTD < 32 weeks	7.59	3.17–18.2	< 0.001
With PPROM	5.29	2.38–11.7	< 0.001
Without PPROM	2.46	1.13–5.41	0.024
IUFD (one or both fetuses)	2.20	1.03–4.69	0.030
PABS	14.6	3.46–61.8	< 0.001

IUFD, intrauterine fetal demise; OR, odds ratio; PPROM, preterm premature rupture of membranes; PTD, preterm delivery.

7.3% and 7.4% in Stages I–IV, respectively ($P = 0.85$)). Figure 1 illustrates the frequency of adverse perinatal outcome and PABS in cases with and those without septostomy. Pregnancies complicated with septostomy had a significantly higher proportion of preterm delivery before 32 weeks (76.7% vs. 30.2%, $P < 0.001$), PPROM before 32 weeks (46.7% vs. 19.0%, $P < 0.001$), IUFD (43.3% vs. 25.8%, $P < 0.05$) and PABS (13.3% vs. 1.0%, $P < 0.001$) than did pregnancies without septostomy. Septostomy accounted for half of the cases complicated with PABS in this clinical series. Table 3 shows the odds ratio (OR) for each of these complications in pregnancies in which septostomy occurred.

DISCUSSION

This study reports the incidence of inadvertent septostomy after laser therapy in a large multicenter series, and provides evidence that this complication is associated with poorer perinatal outcome due to a substantially increased incidence of preterm delivery, preterm premature rupture of membranes, stillbirth and PABS.

The 7.2% rate of septostomy observed in our series was higher than the 1.3% (2 in 152 cases) reported by

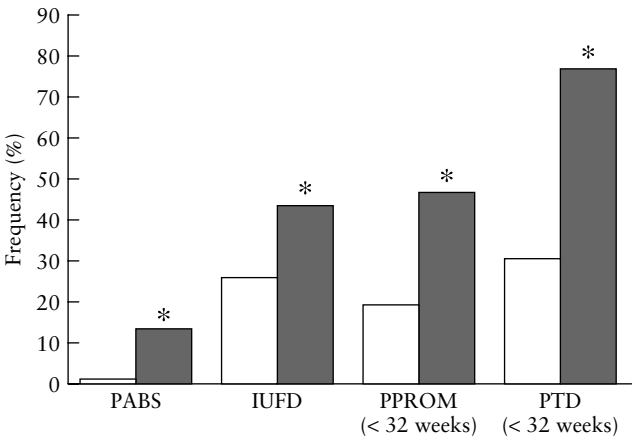

Figure 1 Frequency of pseudoamniotic band syndrome (PABS) and adverse perinatal outcome in 414 monochorionic diamniotic twin pregnancies with confirmed twin–twin transfusion syndrome treated with laser coagulation, according to whether postoperative septostomy occurred (septostomy, ■; no septostomy, □). Adverse perinatal outcome was significantly different between the groups (*$P < 0.05$). IUFD, intrauterine demise of either one or both fetuses; PPROM, preterm premature rupture of membranes; PTD, preterm delivery.

Habli *et al.*[5] in a single-center series, a difference that we believe might be due to the prospective nature of our study. Otherwise, the results of our study are in line with previous reports. Several small case series of monochorionic twins have reported the perinatal outcome of septostomy, occurring either spontaneously[8–10] or unintentionally after amniocentesis[11,14], or cordocentesis[12]. In these studies, septostomy was associated with a risk of cord entanglement[8–12] similar to that reported in monoamniotic twins[19–21], and with an increased risk of preterm rupture of membranes and preterm delivery[8,10]. In comparison with non-complicated cases, pregnancies in our series with inadvertent septostomy were associated with remarkable increases in the risk of these complications. This illustrates the fact that, once septostomy occurs, virtually all cases end up being effectively monoamniotic pregnancies, with additional risks created by free-floating intramniotic membrane flaps.

This study is in agreement with previous reports which found that PABS occurred after fetoscopic laser ablation for TTTS in 2–3% of cases[5,16]. The association between PABS and invasive procedures has also been described after minimal procedures such as amniocentesis[15], and it is possibly related to the occurrence of iatrogenic membrane detachment. Our findings suggest that the risk of PABS is further increased by the occurrence of septostomy, which accounted for 50% of cases complicated with PABS. An association between septostomy and PABS had already been suggested in a series of eight cases of spontaneous septostomy in monochorionic twins[8] and in a previous case report of TTTS managed with planned septostomy[13]. Even if the defect is initially small and well-defined, septostomy often leads to complete tearing of the intertwin membrane, resulting in free-floating flaps which may evolve to fibrous strings (Figure 2a) of considerable

strength, capable of trapping and damaging fetal limbs (Figure 2b), or the umbilical cord[16].

From a clinical perspective, our findings suggest that septostomy occurs even in experienced hands. Operations were performed by experienced surgeons, each having performed 200–400 such procedures previously. Therefore, signs of septostomy should be actively sought in the follow-up after laser therapy and, if identified, limb integrity should be confirmed on sonographic follow-up. Septostomy may occur due to unintentional perforation of the intertwin membrane that remains invisible due to folding and redundancy as the donor twin becomes stuck[5], but this event is rare when the insertion site is chosen carefully by experienced operators. A more common reason for iatrogenic septostomy may be the occasional need to coagulate vessels that lie beneath or very close to the intertwin membrane (Figure 3). The relatively high rate of septostomy observed in our study could be a reason to consider performing the vessel coagulation outside the intertwin membrane whenever this is possible.

Amniotic microseptostomy in combination with amniodrainage was proposed as a therapeutic option for the management of TTTS more than 10 years ago[22]. However, addition of septostomy has failed to demonstrate any benefit in comparison with amniodrainage alone[23,24], and there have been reports suggesting that it could be associated with risks including PPROM and amniotic bands[25]. Our study further supports the notion that septostomy should not be offered under any circumstances in complicated monochorionic twins.

Strengths of our study include its prospective design, the inclusion of a large cohort of patients and the combination of results from two fetal medicine centers. As a limitation we acknowledge that, although cases were followed up with serial ultrasound examinations until delivery and the utmost care was taken to record all complications occurring, it is still possible that a number of cases complicated with septostomy were missed (since the complication was searched for at the laser center during the week following laser), in which case, the proportion of septostomies would have been underestimated slightly. However, if this were the case it would have biased the results against our hypothesis concerning the association between septostomy and adverse perinatal outcome; we therefore believe that this possible limitation does not substantially affect the main conclusions to be drawn from this study.

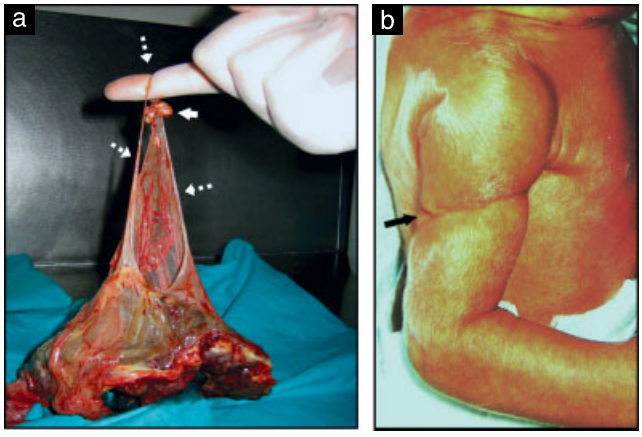

Figure 2 Images of a case diagnosed with septostomy later complicated with pseudoamniotic band syndrome. (a) On placental examination, the intertwin membrane appears with large fenestrations. Some membrane flaps have evolved into a fibrotic nodule (solid arrow) and strings (dotted arrows) of considerable strength. (b) The fetal arm presents a significant cleft.

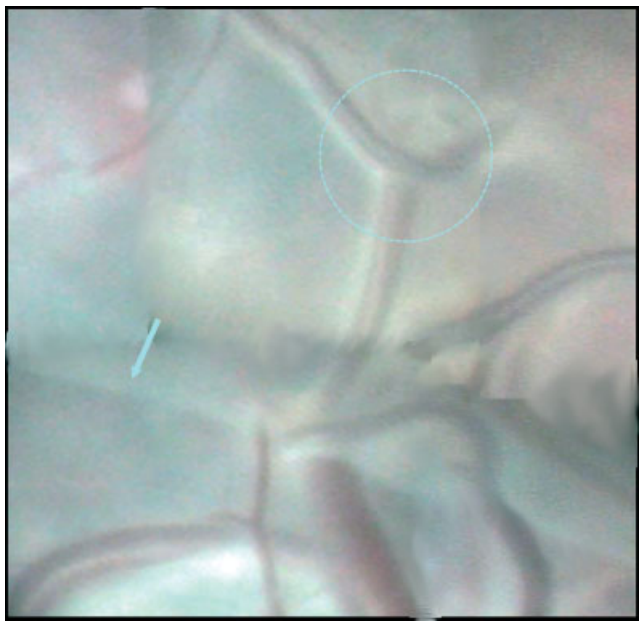

Figure 3 Fetoscopic image of an arteriovenous anastomosis (circle) located in the sac of the donor, and consequently covered by the intertwin membrane (arrow). Coagulation of this anastomosis must be done through the intertwin membrane.

In conclusion, septostomy occurred in 7% of cases after laser coagulation for TTTS and was associated with a substantial increase in the risk of adverse perinatal outcome and PABS. Planned septostomy should be avoided in clinical practice. After fetoscopic procedures in twins, careful evaluation of the intertwin membrane should be performed at every follow-up ultrasound examination.

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