Isolated ascites in a monochorionic twin after fetoscopic laser ablation is not necessarily secondary to recurrence or anaemia

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Abstract
Abstract

Background/Purpose: We report a case study of jejunal atresia and the results of a systematic literature review of all reported cases of bowel complications occurring after fetoscopic laser ablation (FLA) for the treatment of twin-to-twin transfusion syndrome (TTTS). **Methods:** A systematic literature review was performed of bowel complications after FLA for TTTS according to PRISMA guidelines. **Results:** There are 11 published cases of small bowel atresia, 5 cases of necrotising enterocolitis (NEC), and 2 cases with foetal bowel perforations. Recipient twins were more likely to be affected by small bowel atresia (7 recipient and 4 donor cases) and NEC (3 recipient and 2 donor twins). Prenatal ultrasonographic abnormalities were demonstrated in 7/9 of all cases with bowel atresia and both cases of bowel perforation. The overall survival rate for neonates with bowel complications after FLA is 72%, but at 22%, it is much lower for co-twins. The survival rates for jejunoileal atresia and NEC are 91 and 40%, respectively. **Conclusions:** It is uncertain as to whether these bowel anomalies are due to bowel ischaemia associated with TTTS, the treatment with FLA, or a combination of both. Cases with prenatal abdominal ultrasonographic abnormalities after FLA should have close prenatal and postnatal assessment to detect bowel complications.

Abstract Second Language

Abstract Third Language

Key Messages

Body

Introduction

Twin-to-twin transfusion syndrome (TTTS) complicates up to 15% of all monochorionic (MC) pregnancies and carries a high mortality rate (80–100%) if untreated [1]. Fetoscopic laser ablation (FLA) improves the survival of at least one foetus in up to 85–90%, and FLA using the "Solomon technique" produces the best outcomes in reducing complications of twin anaemia polycythaemia sequence [2]. There are various post-fetoscopic laser complications in foetuses associated with ischaemia, including neurological handicap (secondary to strokes), bowel atresia, necrotising enterocolitis (NEC), and skin necrosis [3]. It is uncertain whether these are associated with the TTTS itself, its treatment, or a combination of the two. Bowel complications in MC twins complicated by TTTS with or without treatment by FLA are uncommon, and the underlying aetiology is poorly understood.

We report a single case study of jejunal atresia in a foetus whose twin pregnancy was complicated by TTTS and treated by FLA, and we also present the results of a systematic literature review of all reported cases of bowel complications associated with this condition.

Case Report

A 26-year-old nulliparous woman with a MC diamniotic twin pregnancy was diagnosed with Quintero stage III (recipient) TTTS and selective intrauterine growth restriction of the donor twin (sIUGR) at 16 weeks and 5 days of gestation and was referred to our tertiary centre for treatment. The "donor" twin had severe oligohydramnios (deepest vertical pool = 1 cm) with absent end diastolic velocimetry on umbilical artery (UA) Doppler velocimetry. The recipient twin had polyhydramnios (deepest vertical pool = 9 cm) with ultrasound evidence of a distended foetal bladder, tricuspid regurgitation, and abnormal intra-foetal Doppler flow (raised pulsatility index on UA Doppler and absent velocity during atrial contraction in the ductus venosus [DV] Doppler waveform). The percentage difference in estimated foetal weight was 32%, and no

structural anomalies were visualised on ultrasound scan for both foetuses.

FLA was performed on the day after diagnosis under sedation and local anaesthesia. A trocar and 2 mm fetoscope was inserted under ultrasound visualisation into the recipient sac. The placenta was located anteriorly on the uterine wall, and direct visualisation of the inter-twin membrane was achieved. Chorionic plate vasculature was mapped from the cord insertions between the donor and recipient cords. Aberrant vascular anastomoses were then ablated by employing a selective sequential technique and the "Solomon technique" using diode laser at a power of 30–60 W. A total of 9 anastomoses (all arterio-venous) were identified and coagulated, followed by amniodrainage with 1,500 mL of amniotic fluid removed to achieve a maximum pool depth of 6 cm. The duration of the procedure was 30 min. Transabdominal sonography 2 h after FLA revealed viable foetuses, and there were no septostomies or chorioamniotic separations.

Sadly, the donor foetus died within one week from FLA. Serial ultrasound sonography was performed for the surviving recipient twin at weekly intervals. The first follow-up scan one week after FLA revealed normal UA and middle cerebral artery Doppler scans but an elevated peak velocity index for veins of the DV Doppler, which normalised during a repeat scan the week after. In utero scan of the foetal brain using magnetic resonance imaging (MRI) was performed at 24 weeks demonstrating no foetal brain anomaly in the surviving twin (ex-recipient). The surviving foetus showed no anomaly on ultrasound examination until 22 weeks and 6 days of gestation (6 weeks after FLA), when isolated ascites (free fluid in the abdominal cavity) was detected, and the measured peak systolic velocimetry of the middle cerebral artery was <1.5 MoM (indicating a low probability of foetal anaemia). The UA Doppler was normal, but the peak velocity index for veins of the DV Doppler was again elevated. Serial ultrasound scanning noted the disappearance of the ascites within 5 days with normalisation of DV Doppler, and ultrasonography follow-ups were unremarkable subsequently until delivery.

At 27 weeks of gestation, the pregnancy was complicated by preterm premature rupture of membrane but managed conservatively. A repeat MRI scan again demonstrated no foetal

brain pathology at 29 weeks. At 32 weeks, there were associated uterine contractions that were persistent, and therefore, an emergency Caesarean delivery was performed (birth weight of 1,975 g). The baby girl was diagnosed with respiratory distress syndrome and was intubated in the Neonatal Intensive Care Unit. Neonatal haemoglobin on day 1 was 148 g/dL, and platelet count was normal at 330×10^9/L.

An abdominal X-ray performed to confirm the placement of the endotracheal tube position raised suspicions of bowel obstruction, and jejunal atresia was diagnosed subsequently. Laparotomy was performed on day 3 of life, which revealed a malrotation of the small bowel with evidence of a re-sealed jejunal perforation just proximal to the area of jejunal atresia. The atretic segment was resected with an end-to-end anastomosis, and a Ladd's procedure for malrotation was done. The baby made an unremarkable recovery following the surgery and was discharged home on normal feeds at the equivalent of 38 weeks of gestation.

Methods of Systematic Review of the Literature

A systematic literature review of bowel complications after FLA for TTTS was performed according to the PRISMA guidelines. The PubMed database was searched electronically with a combination of keywords for "twin-to-twin transfusion syndrome," "jejunal atresia," "bowel ischaemia," "necrotising enterocolitis," "laser," and "fetoscopic." A manual check of the reference list was performed, and there was no restriction of language used. The predefined criterion for study inclusion was bowel complications in twin pregnancies complicated with TTTS after FLA. The titles and abstracts were screened to identify articles fulfilling the criteria. Full text review of these articles was performed, and the reference lists of relevant articles were searched manually to identify additional reports. Because of the rarity of this diagnosis, we accepted single case studies or cohorts of <5 cases. Two reviewers (L.N.T. and K.W.C.) performed the searches for articles fulfilling the inclusion and exclusion criteria independently, and any differences were resolved by a third reviewer (M.D.K.).

We extracted the following data from each report: author, publication year, other associated anomalies, karyotyping results, stage of TTTS at diagnosis, gestational age at FLA, antenatal imaging abnormalities, weight differences at birth, haemoglobin at birth for both donor and recipient, site of affected bowel, outcome of donor and recipient twins, gestational age at delivery, mode of delivery, and postpartum management.

Results

The search resulted in the review of 88 articles, 9 papers (10.2%) of those 88 met the final inclusion criteria. Figure 1 is an algorithm of the selection process and inclusion of studies in this review. A total of 18 cases (together with our present case) are included in our study. Cases number 6 and 7 as well as 11 and 12 are donor and recipient twins from the same pregnancies, where both twins suffered from bowel complications; therefore, these 18 cases are reported from 16 MC pregnancies (Table 1).

The Quintero stage of TTTS at diagnosis and FLA was mostly severe (≥ Quintero stage II) in 13 cases; whereas in 1 case, FLA was done for TTTS stage 1, and stage was not mentioned for the remaining 2 cases (Table 1). The median gestational age at development of TTTS was 18 weeks (ranging between 16 and 20 weeks), while the median gestational age at the time of FLA was also 18 weeks (ranging between 16 and 25 weeks). There is no mention of additional structural anomalies in 6 pregnancies, and 3 neonates out of the remaining 10 pregnancies (30%) have additional anomalies: pulmonary stenosis in 2 cases and congenital cystic adenomatoid malformation of the lung in 1 case (Table 1).

There are 11 reported cases of small bowel atresia (8 ileal, 3 jejunal), 5 cases of NEC, and 2 cases with foetal bowel perforations after FLA for TTTS (Table 2). Recipient twins are affected by small bowel atresia in 7 and donor twins in 4 cases. Similarly, there is a predominance of recipient twins being affected by NEC, with 3 recipients versus 2 donor twins

(Table 2). For cases 11 and 12, both twins are from the same pregnancy and had ascites and echogenic bowel from prenatal scans. The donor twin had transverse colon perforation leading to meconium peritonitis without requiring bowel resection. Similarly, the recipient twin had meconium peritonitis, but this was secondary to small bowel perforation at the jejunum and required resection and double stoma. No atretic segments were found in the intestinal tract of the recipient, but there were necrotic patches scattered throughout the jejunum with microemboli seen.

In more than half of the cases (9 out of 14 cases; no findings reported for 3 other pregnancies), imaging abnormalities of the abdomen were seen on prenatal scans. The features seen were dilated loops of bowel (6 cases, resolved prior to delivery in 1 case), ascites (5 cases, resolved prior to delivery in 1 case), calcification (1 case), and echogenic bowel (2 cases). Prenatal abdominal sonographic anomalies were more commonly seen in cases with bowel atresia (7 out of 9 reported cases) but not reported for NEC (out of 3 reported cases). For cases 11 and 12 with isolated bowel perforation, ascites and echogenic bowel suggestive for meconium peritonitis were detected antenatally.

All neonates with NEC were born prematurely, with one at 34 weeks (moderate to late preterm), one at 31 weeks (very premature), and three cases born before 28 weeks (extremely premature). In the postnatal life, the timing of clinical manifestation for NEC is mostly late, with 1 case diagnosed within the first 2 days of life, and the remaining 4 cases presented later with surgery performed more than a week after birth (between day 9 to day 18 after delivery). For neonates with small bowel atresia, most surgeries (9 out of 11 cases) were performed within the first 3 days of life, except for 2 cases who were operated on day 14 and day 23 after birth. Almost all cases with bowel complications had surgery done (17 out of 18) except for the case reported by Huisman et al. [6], where the baby had severe pulmonary stenosis requiring dilatation at day 1 and subsequently died at day 4 with severe NEC.

The overall survival rate in neonates with bowel complications after FLA is 72%, whereas

it is much lower for the co-twin at 22% (however, there are no details of pre- or post-FLA sonographic findings to suggest reasons for the lower survival rate of the co-twins). The survival rates decrease with gestational age at birth (Table 3). The outcomes are more favourable for neonates with jejunoileal atresia compared to NEC, with survival rates of 91 and 40%, respectively (Table 3). Complete data about survival outcomes (both for case and co-twin) for each pregnancy are available for 11 out of 16 pregnancies: with survival of both twins in 2 pregnancies (18%; 1 bowel atresia and 1 NEC), 1 twin in 8 pregnancies (73%; 5 bowel atresia, 2 NEC, and 1 bowel perforation), and neither twin in 1 pregnancy (9%; NEC) (Table 2). In the remaining 5 pregnancies (all cases had bowel atresia), 4 neonates affected by bowel complications survived but no information was available for their co-twins.

Weight differences at birth was reported in 8 pregnancies in whom both twins survived to birth, and 3 of these pregnancies had weight discrepancies of >20% (Table 2): these are cases 6 and 7, where both twins from the same pregnancy had NEC and died; case 9 (donor, smaller twin), who had jejunal atresia and both case and co-twin survived; and case 15 (donor, smaller twin), who was diagnosed with ileal atresia and survived but no information was available for co-twin. For the remaining 5 pregnancies with birth weight differences of <20%, 2 neonates died (case 5 with ileal atresia in the heavier recipient twin and case 12 with bowel perforation in the smaller recipient twin). Among the 4 neonates who survived, 3 were donor twins (cases 10, 11, and 13), who were born heavier than their co-twins, and 1 was a recipient twin (case 14), who weighed less at birth than the co-twin.

Haemoglobin results were extracted from 5 pregnancies, and the differences in haemoglobin levels between donor and recipient twins are 0.3 g/dL (both case and co-twin survived), 1.5 g/dL (both had NEC and died), 2.0 g/dL (affected donor with higher haemoglobin level survived, affected recipient died), 2.8 g/dL (affected recipient with lower haemoglobin died, outcome of co-twin unknown), and 6.3 g/dL (both donor with higher haemoglobin and co-twin survived) (Table 2).

Most of these cases were delivered by Caesarean section (12 out of 13 reported pregnancies) (Table 2).

Discussion

Our case study is important as it reminds foetal medicine and neonatal specialists that isolated ascites noted on ultrasound after treatment for TTTS is not necessarily secondary to either recurrence or foetal anaemia but may be secondary to in utero bowel perforation.

The total prevalence of jejunoileal atresia in singleton pregnancies with normal karyotype is 0.7 per 10,000 live births from the EUROCAT registers between 1990 and 2006 [13]. In this study, 21 cases out of 423 with jejunoileal atresia were twins, although the chorionicities of these pregnancies were not known [13]. In 1994, the study by Cragan et al. [14] has suggested an association between small intestinal atresia and monozygotic twinning, where monozygotic twins are at increased risk of having small bowel atresia compared to singletons.

Based on our results, small bowel atresia occurs more commonly in the ileum compared to the jejunum in MC twins complicated by TTTS and treated by FLA, which is similar to the prevalence of small intestinal atresia in all births, with a predominance for ileal atresia [15]. Mesenteric ischaemia in MC twins is postulated to be due to hypoperfusion and/or hyperviscosity associated with vascular anastomoses in TTTS, haemodynamic alteration where there is demise of a co-twin, or a thromboembolic phenomenon after laser ablation of the vascular anastomoses [4, 5, 9]. There is no report of duodenal atresia after FLA in the literature, probably because the aetiology for duodenal atresia is attributed to developmental failure of recanalisation rather than ischaemia [16].

Chiang et al. [17] reported that donor twins are at increased risk of hypoperfusion to the gastrointestinal tract and hypoxaemic damage leading to bowel complications. Differences in haemoglobin levels between donor and recipient twins have been suggested to be the cause of

bowel complications, especially in donor twins and those with anaemia [17]. On the contrary, our results have shown that recipient twins are at a higher risk of having bowel complications following FLA compared to donor twins, both from small bowel atresia and NEC. Donor twins also have higher haemoglobin levels than recipient twins in 4 out of 5 cases, which makes anaemia a less likely explanation for bowel complications (although haemoglobin levels are not reported for most cases, presumably because most co-twins died before delivery and, therefore, no blood samples would be available for analysis).

Marcellin et al. [10] reported that the recipient twin showed evidence of microthrombi and microemboli both in post-operative and post-mortem specimens. However, the mechanism of this extensive bowel thromboembolic event confined to the jejunum is unknown. Due to the small number of cases available currently, more in-depth studies are required to ascertain the exact underlying pathologies of bowel complications after FLA.

Prenatal sonographic findings (dilated foetal bowel loops, enlarged stomach, echogenic bowel, polyhydramnios) are seen in 34–87% of all cases with postnatal diagnosis of jejunoileal atresia [18, 19]. Most of the cases in our systematic review (64%) with jejunoileal atresia after FLA had prenatal sonographic evidence of bowel abnormalities, which was described as transient in some foetuses. Consideration could be given to perform in utero MRI in cases with abnormal post-operative prenatal sonography to aid in diagnosing bowel atresia and possibly the underlying cause such as thromboembolism. Huisman et al. [6] has demonstrated the utility of foetal MRI in the year 2005 to evaluate post-operative changes in the placenta in addition to changes in the central nervous system, as MRI is not limited by maternal bowel gas or overlying bony structures compared to ultrasonography. This is further supported by reports regarding the superiority of foetal MRI in overcoming the limitations associated with sonography, such as operator dependence, inherent inferior image contrast, patient factors such as obesity and small field of view, and non-specific US findings which may relate to transient normal variants [20–22]. The detection of jejunal and ileal atresia with US alone is low with detection rates of 66.3 and

25.9%, respectively, and MRI has been shown to improve detection of small and large bowel obstructions, malrotations, and perforations resulting in meconium peritonitis or pseudocyst [20–23]. Although jejunoileal atresia is associated with a good survival rate, surgical therapy should be expedited; hence, cases with prenatal suspicions warrant careful postnatal assessment with plain abdominal radiograph or enema studies, even if the prenatal ultrasonographic differences have resolved prior to delivery [24].

A prospective multicentre cohort study showed that the incidence of NEC requiring surgical management and spontaneous intestinal perforation (SIP) is approximately 11% in the most premature babies at extremely low gestational age (<25 weeks), and this risk is similar in singleton and multiple pregnancies [25]. The risk of developing NEC which can be managed medically (without the need for surgical intervention), however, is higher for singleton compared to multiple pregnancies [25]. For the general population, over 90% of all neonates with NEC are born prematurely, and NEC is associated with a high mortality rate of 70–80% [26–28]. Survivors may have significant long-term morbidity including short gut syndrome and neurodevelopmental delay [26]. Despite efforts to establish clear diagnostic criteria for NEC, the condition is thought to encompass more than one disease entity, such as isolated intestinal perforation and ischaemic bowel disease due to cardiac anomalies [26]. These emphasise the complexity of diagnosing and managing NEC [26]. The aetiology of NEC is multifactorial and is largely related to the immaturity of the gastrointestinal tract [26]. For neonates with NEC after FLA for TTTS, all were delivered prematurely and, therefore, the most likely aetiology is prematurity rather than a direct consequence of FLA. In our study, none of the neonates with NEC had prenatal sonography abnormalities, and most of them had late presentation of the complication, which makes antenatal detection unlikely and close postnatal monitoring for signs of NEC necessary, especially in neonates born prematurely.

Bowel perforation can be caused by atresia, stenosis, volvulus, internal hernia, intussusception, Meckel's diverticulum, meconium ileus, a peritoneal band, or may be idiopathic

[29]. Multiple pregnancy has also been found to be associated with a higher risk of developing SIP although the cause is unknown [25, 27]. SIP is considered a separate clinical entity from NEC and affects neonates earlier in life, particularly neonates with a very low birth weight [31–33]. Therefore, we analysed cases 11 and 12 separately from cases with atresia and NEC because meconium peritonitis in these cases resulted from bowel perforation without evidence of obstruction, and the authors did not classify them as NEC [10]. Tsukimori et al. [31] reported a similar case of SIP in their recipient twin, but the intervention for TTTS was amnioreduction instead of FLA. The authors hypothesised that the perforation in their case was due to an ischaemic event which occurred in utero, based on the surgical and histopathological findings [31]. Tiwari et al. [32] reported that unlike NEC, SIP has no long-term gastrointestinal sequelae and is associated with good outcome (100% survival rate in their series), and thus it is important to distinguish this condition from NEC for prognostic reasons [33].

Based on our results, it is interesting to note that for neonates with birth weight discrepancies of <20% compared to their co-twins, most donor twins weighed more than their recipient co-twins at birth after treatment with FLA. Although there is no data available regarding weight discrepancies prior to FLA for the cases in our report, Chmait et al. [34] have demonstrated that donor twins have lower estimated foetal weight compared to recipient twins at the time of diagnosis of TTTS prior to treatment with FLA. Our findings are in concordance with the results from another study by Chmait et al. [35] whereby donor twins exhibit catch-up growth in utero after FLA for TTTS, which continues until 2 years of age. However, MC pregnancies complicated with sIUGR, which is present in our case, have additional risks of intrauterine demise of the growth-restricted twin, especially in the presence of abnormal UA Doppler (20–40% increased risk) [36]. The normally grown twin is also at risk of concomitant intrauterine death, sequelae of prematurity, and neurological damage [36]. Having stage III TTTS posed additional risk of perinatal death (70–100% for advanced TTTS) to our recipient twin, if no antenatal treatment was instituted [37].

The main limitation of this review is the small number of cases reported in the literature for intestinal complications after FLA, thereby limiting the interpretation of the values in inter-twin discordances. All publications are case reports or case series, which means there is a publication bias due to the absence of control groups. It is also difficult to conclude whether these bowel complications are due to complications of prematurity, multiple pregnancy, monochorionicity, TTTS, or true iatrogenic consequences from FLA. Given the scarcity of reported cases of bowel complications after FLA in the literature, there is no data about its prevalence, and attempts to collect this information would ideally require a worldwide collaboration from all centres performing FLA for TTTS. In addition, to our knowledge, there is currently no epidemiological study looking at bowel complications in other subgroups of MC pregnancies, such as uncomplicated TTTS, twin anaemia polycythaemia sequence, sIUGR, or early/untreated TTTS, hence comparison of bowel complications after FLA against these foetuses is not possible. It is pertinent to comprehensively record and report cases with bowel complications after FLA, including prenatal and postnatal investigation findings to ascertain the underlying pathology and ascertain if these complications are direct complications from FLA. The use of advanced imaging modalities including serial Doppler studies, in utero foetal or postnatal MRI as well as judicious histopathological examination of placenta and resected bowel specimens may provide further clues regarding this condition. Maternal factors such as race, anaemia, smoking status, obesity, and consumption of aspirin have also been found to be associated with increased risks of NEC and SIP and may, therefore, also affect the outcomes of these pregnancies [25].

Conclusion

Although bowel complications following FLA for TTTS are increasingly detected and reported, it is still a rare complication, and the underlying aetiology remains unknown. Cases

with prenatal gastrointestinal sonographic abnormalities should be followed up with postnatal imaging to exclude bowel abnormalities, and neonates, especially those born prematurely, should be monitored closely for signs of bowel perforations.

Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Study conception and design, data acquisition, analysis and data interpretation, drafting of the manuscript, critical revision: all authors.

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Appendix after References (Editorial Comments)

Legend(s)

Fig. 1. Flow chart for systematic literature search of bowel complications after fetoscopic laser ablation for twin-to-twin transfusion syndrome (up to July 2018).

Table(s)

Footnote(s)

Table 1. Publication details and characteristics of the cases

Case No.	First author	Publication year	Type of study	Stage of TTTS	GA at		Karyotyping	Other associated anomalies (case; co-twin)
					diagnosis	FLA		
1	Arul [4]	2001	Case series	N/A	20 w	N/A	N/A	N/A; N/A
2	Arul [4]	2001	Case series	N/A	19 w	N/A	N/A	N/A; N/A
3	Schnater [5]	2005	Case report	Severe	20 w	21 w	N/A	N/A; N/A

4	Huisman [6]	2005	Case report	III	N/A	20 w		N/A	Severe pulmonary stenosis; N/A
5	Morikawa [7]	2008	Case series	II	18 w	19 w		46XX	No; No
6, 7†	Detlefsen [8]	2008	Case series	III	N/A	25 w		N/A	N/A; N/A
8	Saura [9]	2010	Case series	III	18 w	18 w		N/A	Pulmonary stenosis; N/A
9	Saura [9]	2010	Case series	II	16 w	16 w		N/A	No; No
10	Saura [9]	2010	Case series	II	17 w	17 w		N/A	CCAM; No
11, 12††	Marcellin [10]	2012	Case report	II	17 w	18 w		46XY	N/A; N/A
13	Sanchez-Galan [11]	2017	Case series	III	N/A	18 w		N/A	N/A; Pulmonary stenosis
14	Sanchez-Galan [11]	2017	Case series	I	N/A	19 w		N/A	No; No
15	Sanchez-Galan [11]	2017	Case series	III	N/A	20 w		N/A	N/A; Hypertension and septal hypertrophy
16	Sanchez-Galan [11]	2017	Case series	II	N/A	21 w		N/A	N/A; No
17	Piek [12]	2018	Case report	II	N/A	18 w		N/A	N/A; N/A
18	Current case	2018	Case report	III	16 w 5d	16 w 6d		N/A	N/A; N/A

TTTS, twin-to-twin transfusion syndrome; GA, gestational age; FLA, fetoscopic laser ablation; N/A, not available; w, weeks; d, days; CCAM, congenital cystic adenomatoid malformation. † Case 6 is donor and Case 7 is recipient in the same pregnancy. †† Case 11 is donor and Case 12 is recipient in the same pregnancy.

Table 2. Clinical characteristics, outcomes, and management of bowel complications

Case No.	Case (affected twin)	Antenatal imaging abnormalities	Type of bowel problems	Outcome		Weight difference at birth, g or % (case/co-twin)	Hb at birth, g/dL			GA at delivery	Mode of delivery (indication)	Postpartum management
								donor	recipient			
			case	co-twin								

1	R	N/A	Ileal atresia and meconium cyst	Alive	Died at 26 w		N/A	N/A	N/A		33 w	N/A	R: Intestinal obstruction at 3 h of life; laparotomy: large meconium cyst associated with distal ileal atresia; resection and stoma
2	R	N/A	Ileal atresia	Alive	Died at day 3 of life		N/A	N/A	N/A		27 w	N/A (abruption)	R: Intestinal obstruction at day 2 of life; laparotomy: necrotic mass of ileum 8 cm from ileocaecal valve; resected and stoma done
3	R	Post FLA – progressive intestinal distension from 24 w	Ileal atresia	Alive	Died 2 w after laser		N/A	N/A	N/A		35 w	C-sec (fetal distress during labour)	R: MRI: no anastomosis seen between 2 circulations of placental vessels; laparotomy soon after birth: V-shaped ileal atresia with adhesion to liver; partial resection of distended ileum and enterostomy
4	R	Case: pre-FLA – abnormal venous Doppler Co-twin: IVH 48 h after op, confirmed with MRI	NEC	Died	Fetocide for IVH at 27 w		1,490/?	N/A	N/A		34 w	C-sec (mild pre-eclampsia)	R: Severe pulmonary stenosis which was dilated successfully at day 1 of life; severe NEC from day 2 of life and died at day 4 of life
5	R	Post FLA – USG and MRI at 28 w: ascites and dilatation of stomach and duodenum	Ileal atresia and meconium peritonitis	Died	N/A		1,802/1,542	13.1	10.3†		30 w	C-sec (maternal generalised oedema)	R: Ileal atresia and meconium peritonitis; resection and ileostomy at day 23; died at day 63 from septic shock and multi-organ failure
6, 7†	D and R	D: Pre-FLA – Doppler demonstrated TTTS	D: NEC with sigmoid and ileal perforation R: NEC with ileocaecal perforation	D: Died R: Died	–		>20%	16.5†	15†		25 w	C-sec	D: Radiologically pneumoperitoneum at day 10 of life; laparotomy: sigmoid perforation seen; sigmoidoscopy and Hartmann pouch done; persistent septicaemia and thrombocytopenia, relaparotomy done on day 25 of life, not successful due to severe bleeding, died 1 day later; autopsy: covered perforation of distal ileum and severe peritonitis R: NEC on day 12 of life; unstable cardiac condition, therefore only percutaneous abdominal drainage performed; day 24 of life: exploratory laparotomy showed ileocecal perforation; HPE: NEC; ileostomy done; developed cardiomyopathy, cerebral convulsion, osteopenia and died at 4 months
8	R	Post FLA – USG: 25.4 w: intestinal dilatation, resolved before 33 w	Ileal atresia and perforation	Alive	Died within 24 h of FLA		3,090/N/A	N/A	18.8†		39.4 w	Eutocic – normal	R: Abdominal distension with several enlarged intestinal loops and air fluid levels after birth; laparotomy: severe intestinal dilatation proximal to ileal atresia and perforation; resection and end-to-end anastomosis
9	D	Post FLA – USG: Intestinal dilatation at 26.2 w to delivery	Jejunal atresia (multiple sites)	Alive	Alive		1,910/2,760	21.3†	15		38.4 w	C-sec	D: Abdominal distension with severe enlarged intestinal loops after birth; laparotomy: multiple jejunal atresia; resected and end-to-end anastomosis

10	D	Nil	NEC with ileocaecal wall ischeamia	Alive	Alive	1,320/1,280	15.2†	14.9	31 w	C-sec	D: Bloody stool at day 9 of life, distended and firm abdomen with dilated bowel loops; low platelets, leukocytosis, metabolic acidosis; resection and ileostomy at day 17 of life; intestinal transit 4 months later
11, 12††	D and R	Post FLA – USG at 25 w: hyperechogenic bowel and ascites in both twins Normal fetal Doppler examinations	D: Tranverse colon perforation R: Jejunal perforation with necrosis and adhesions	D: Alive R: Died	–	1,025/925 (D/R)	11.1†	13.1†	27 w and 6 d	C-sec (deceleration in D)	D: Clinical ascites, peritoneal puncture done 15 min after delivery; 55 mL green meconium-like fluid aspirated; surgery: meconium peritonitis secondary to transverse colon perforation; stoma without bowel resection R: Clinical ascites; surgery at 24 h of life: copious meconium and distended jejunum upstream of jejunal perforation with adhesion and necrosis. 29 cm bowel resection and double stoma done; HPE: fibrosis of wall with oedematous vessels, amassed pigmented macrophages, several sub-mucosal capillaries with microthrombi and microemboli; died 24 h after surgery from multi-organ failure. Post-mortem: no bowel atresia; necrotic patches scattered throughout jejunum, with microemboli or microthrombi in the submucosal capillaries. Histological examination of jejunum: old microthrombi not found in other organs Maternal viral infection and cystic fibrosis screen were negative
13	D	Nil	Jejunal atresia and sigmoid perforation	Alive	N/A	910/750	N/A	N/A	25 w and 3 d	C-sec (PPROM)	Iatrogenic sigmoid perforation, laparotomy at day 14 of life: type I jejunal atresia; resection of atretic zone, jejunostomy, closure of perforation
14	R	Post FLA – USG and MRI: dilated loops and ascites, later on developed intra-abdominal calcifications suggestive of meconium peritonitis	Ileal atresia and volvulus	Alive	N/A	1,690/1,940	N/A	N/A	34 w	C-sec (PPROM + first twin breech)	Surgery at 24 h of life: segment of atretic ileum with volvulus, which was ischaemic; resection of atretic loop and intestinal bypass performed; stoma closed at 2 months, re-operated 4 months later due to intestinal obstruction
15	D	Post FLA – USG: hyperechoiec bowel with dilatation of intestinal loops	Ileal atresia with perforation	Alive	N/A	972/1,484	N/A	N/A	31 w and 3 d	N/A (placental insufficiency)	Surgery at first 24 h of life: perforated type II ileal atresia; resection of atretic segment and ileostomy
16	R	Post FLA – USG: TAPS	NEC with caecal perforation	Alive	Died at 23 w	800/N/A	N/A	N/A	26 w and 4 d	C-sec (PPROM)	Surgery at day 18 of life: NEC of right colon and caecal perforation; small segment at terminal ileum resected and ileo-colostomy performed; at 6 months; resection and anastomosis of 2 stenotic segments (due to previous NEC) and closure of stoma

17	D	Post FLA – USG: severe IUGR	Ileal atresia with perforation	Alive	N/A		625/N/A	N/A	N/A		30 w and 5 d	C-sec (abnormal Doppler on USG and decelerations on CTG in D)	Placenta injection with color dye after delivery: no anastomoses seen; day 3 of life: increasing abdominal distension and free air on abdominal radiography; laparotomy: mid-ileum atresia complicated by blowout proximal to the obstruction; 6 cm resection of atretic ileal segment and ileostomy performed
18	R	Pre FLA – tricuspid regurgitation, raised PI on UA Doppler, absent a-wave in DV Doppler Post FLA – USG at 1 w: normal UA and MCA Dopplers, raised PVIV of DV Doppler, normalised 1 w later; transient ascites at 22 w with raised PVIV of DV Doppler, which normalised 1 w later until delivery. MRI: no brain anomaly at 24 w	Jejunal atresia with perforation	Alive	IUD within a week of FLA		1,975/N/A	N/A	14.8 †		33 w	C-sec (PPROM from 27 w+ in labour)	R: Jejunal atresia at day 3 of life; laparotomy: malrotation of small bowel with evidence of re-sealed jejunal perforation just proximal to the area of jejunal atresia; atretic segment removed and end-to-end anastomosis performed

Hb, haemoglobin; GA, gestation age; N/A, not available; w, weeks; d, days; D, donor; R, recipient; FLA, fetoscopic laser ablation; IVH, intraventricular haemorrhage; USG, ultrasound; MRI, magnetic resonance imaging; NEC, necrotising enterocolitis; HPE, ■■■; C-sec, Caesarean section; PPROM, preterm premature rupture of membranes; TAPS, twin anaemia-polycythaemic sequence; IUGR, intra-uterine growth restriction; CTG, cardiotocography; PI, pulsatility index; IUD, intra-uterine demise; UA, umbilical artery; DV, ductus venosus; MCA, mid cerebral artery; UA, umbilical artery; PVIV, peak velocity index for veins. † Case.

Table 3. Survival rates for fetuses affected by bowel complications

	Survivors, *n*	Cases where data is available	Survival rate, %
Case (overall)	13	18	72
Case (according to gestational age at birth)			
Term (>37 weeks)	2	2	100
Moderate to late preterm (32–37 weeks)	4	5	80
Very preterm (28–32 weeks)	3	4	75
Extremely preterm (<28 weeks)	4	7	57
Co-twin (overall)	2	9	22
Survivors in each pregnancy (no data available for co-twins in 5 pregnancies)			
Both twins	2	11	18
One twin	8	11	73
No survivor	1	11	9
Survival according to type of bowel complications (Cases)			
Jejunoileal Atresia	10	11	91

NEC	2	5	40
Spontaneous bowel perforation	1	2	50

Total number of pregnancies: 16. Total number of cases: 18 (cases 6 and 7 as well as cases 11 and 12 are donor and recipient twins from the same pregnancies).

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