Chapter 4

Fetal surgery in complicated monoamniotic pregnancies: case series and systematic review of the literature

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ABSTRACT

Objective. This study aimed to analyze perinatal outcome in monoamniotic (MA) pregnancies that underwent antenatal surgical interventions for fetal complications.

Methods. Review of all MA pregnancies treated with antenatal surgical interventions in three fetal treatment centers between 2000 and 2013. Indications were twin–twin transfusion syndrome, twin reversed arterial perfusion sequence, discordant anomalies, or elective reduction. We analyzed associations between indication, type of intervention, perinatal survival, and gestational age (GA) at birth and compared our results with a systematic review of the literature.

Results. Fifty-eight MA pregnancies were included. Median GA at treatment was 18.0 weeks (range: 13.1–33.0). Procedures included cord coagulation plus transection (n= 42), cord coagulation without transection (n = 7), laser coagulation of placental anastomoses (n = 7), and one case each with interstitial laser and radiofrequency ablation. Median GA at birth was 34 weeks (range 16.0–41.0), and 75% (53/71) of fetuses intended to survive indeed survived. Literature review included 20 articles, reporting on a total of 45 cases of surgically treated MA pregnancies, showing similar outcome results.

Conclusion. We present the largest series concerning surgical interventions in complicated MA pregnancies. Despite being rare in experienced hands, a 75% survival is achieved. Collaboration between centers, data sharing, and benchmarking may further improve outcome.

INTRODUCTION

Monoamniotic (MA) twins account for approximately 1% of all monozygotic conceptions[1–3] and are the result of late splitting of the developing embryo, 8 to 9 days after fertilization. The perinatal loss rate in MA twins varies from 8% to as high as 42%.[4–6] High perinatal loss rates have been attributed mainly to umbilical cord entanglement, intertwin transfusion syndromes (including twin reversed arterial perfusion), discordant fetal abnormalities or growth, and preterm birth.[1,7,8]

Compared with complicated monochorionic–diamniotic cases, MA pregnancies carry additional risks, which should be taken into account when considering invasive interventions.[9,10] The most important factors being the presence of cord entanglement and the high incidence of proximate cord insertions.[11] So far, only a few small studies have specifically reported on treatment and clinical outcome in MA pregnancies requiring fetal surgical procedures during pregnancy, and all concerned only a single type of intervention.[12,13] Anecdotally, outcome in terms of survival and rate of prematurity appear disappointing.[13,14]

Fetal interventions performed in MA pregnancies mainly consist of laser coagulation of vascular anastomoses, selective feticide via interstitial laser, radiofrequency ablation (RFA), injection of vascular sclerosants, fetoscopic ligation, and umbilical cord occlusion. Cord transection has been proposed to improve the outcome of MA pregnancies by reducing the risk of fetal demise due to cord entanglement after cord occlusion.[14]

Specific series on technical details of these fetal interventions in relation to outcome are lacking. Therefore, we aimed to review relevant aspects of fetal surgical interventions in complicated MA pregnancies and to compare our experience with data obtained by a systematic review of the literature.

METHODS

Study population

All consecutive cases of fetal surgery in MA pregnancies performed at three major fetal treatment centers, the Leiden University Medical Center (The Netherlands), the University Hospitals, KU Leuven (Belgium), and the Jackson Fetal Therapy Institute, Miami (United States), between January 2002 and December 2012 were included in this retrospective study. All three fetal surgical centers have extensive experience in fetoscopic interventions. Chorionicity and amnionicity were established by ultrasound in the first

trimester of pregnancy. Detailed sonographic examination was performed in all fetuses at the treatment centers and continued on a weekly or biweekly basis. Indications for surgery included the following: twin reversed arterial perfusion sequence (TRAP), twin-to-twin transfusion syndrome (TTTS), MA pair discordant for fetal anomaly, or elective selective reduction on request of parents. Triplet pregnancies, consisting of a singleton and an MA twin pair requiring an antenatal surgical intervention, were also included in analyses. TTTS was diagnosed by the recognition of absent bladder filling in donor and/or polyuria in recipient and/or abnormal umbilical Doppler flows or signs of progressive TTTS. Iatrogenic MA pregnancies after fetal surgery in monochorionic diamniotic (MCDA) twin with (un)intentional perforation of the intertwin membrane that required additional antenatal intervention were also included in analyses.

Fetoscopic procedures

In MA pregnancies affected by TTTS, fetoscopic laser coagulation of the vascular equator was considered treatment of choice. The fetoscopic procedure was performed using (2 or 3.3 mm) fetoscope (Storz, Vianen, the Netherlands, or Richard Wolf Inc., Vernon Hills, IL, USA), for percutaneous introduction through a 3.3 or 3.8 mm shaft into the amniotic sac. Coagulation of the anastomoses was performed using a diode laser (Diomed Limited, Cambridge, UK) or ND: YAG laser (Dornier Medizin Technik, Germering, Germany) with an output of 15 to 70 W. In cases with discordant fetal anomalies or elective reduction on the parents' request, selective feticide was performed using the following techniques: Fetoscopic laser was used for coagulation and transection to cut the umbilical cord of the affected fetus; although in cases with hydropic cord or such advanced gestational age (GA, >18 weeks) where laser was expected to fail, bipolar coagulation of the umbilical cord was performed using either a disposable 3-mm forceps (Everest Medical Maple Grove, MN) or reusable 2.4-mm or 3-mm forceps (Karl Storz, Vianen). A portion of the umbilical cord was grasped under ultrasound guidance and occluded or ligated and transected with the laser fiber (400–600 μm), set in the cutting mode (40 W). Some operators used additional fetoscopic verification of the coagulation. Technical details on the procedure were also described in detail in previous publications.[14–16] Radiofrequency ablation and interstitial laser were only used in cases with TRAP at an early GA. The procedure used to arrest the flow toward the acardiac twin was performed by using a laser fiber through an 18G needle (Cook Medical, Limmerick, Ireland) or by a 17G radiofrequency needle (Cooltip RF ablation system; Valleylab, Boulder, CO, or Starburst SDE RFA Device, AngioDynamics Netherlands BV).

Operative technical data, including difficulties such as inability to transect the umbilical cord and suboptimal visualization due to bleeding, were recorded in all cases. After the procedure, patients remained in the hospital for 12 to 48 h. Ultrasound examination was performed within 24 h after surgery and then on a weekly or biweekly basis. After an initial follow-up in our centers, patients were often referred back to their local fetal-medicine specialist for further follow-up. Intact MA twins were planned to be delivered by elective cesarean, after steroid administration, at 32 to 34 weeks of gestation. Elective admission was preferred at 26–28 weeks to allow daily fetal monitoring. Pregnancies with one remaining viable fetus were managed as singletons, at the discretion of the local obstetrician. After delivery, macroscopic examination of the placenta was performed to confirm the diagnosis of monoamnionicity.

Information regarding postsurgical complications and perinatal outcome was retrieved prospectively in all cases from referring physicians and patients, and written medical reports were available in most cases. Complications including vaginal blood loss, hypotension, bleeding from uterine vessels, pre-labor premature rupture of membranes (PPROM), and maternal fever were recorded. Primary outcome variables were perinatal survival rate, defined as survival up to discharge from neonatal unit and GA at delivery. Secondary outcomes included technical complications during procedure, PPROM before 32 weeks of gestation and birth weight.

Systematic review of literature

Publications between 2000 and March 2013 reporting data on interventions and perinatal outcome in MA pregnancies were reviewed. An electronic literature search using MEDLINE, EMBASE, and Cochrane database was performed to find all relevant articles reporting perinatal outcome and fetal interventions in MA twin pregnancies, using the following keywords 'Twins, Monozygotic' OR 'Monoamnionicity' OR 'monochorionic' OR 'monochorionicity' AND 'Fetal Therapies' OR 'Obstetric Surgical Procedures' OR 'Electrocoagulation' OR 'electrocautery' OR 'thermocoagulation' OR 'diathermy' OR 'coagulation' OR 'coagulations' OR 'Laser Therapy' OR 'laser' OR 'Pregnancy Reduction, Multifetal' OR 'pregnancy reduction' OR 'selective fetal termination' OR 'fetal reduction' OR 'Selective feticide' OR 'Umbilical Cord/surgery' OR 'occlusion' OR 'transection' OR 'surgical' OR 'Ligation' OR 'ligation' OR 'photocoagulation'. No language restrictions were applied. We accepted original articles, short communications, letters to the editor, and case reports. In addition, a search was performed from the reference list of all identified articles. When needed, we contacted authors for additional, unpublished information. Articles were included irrespective to their primary objective.

We included all reported cases of MA twin pregnancies assessed by first-trimester ultrasound or iatrogenic MA due to perforation of the intertwine membrane during fetal surgery (confirmed during surgery or ultrasound and after delivery) in MCDA pregnancies with a second intervention in the MA sac. Exclusion criteria were as follows: termination of pregnancy <12 weeks gestation, pseudomonoamniotic cases, conjoined twins, and medical amnioreduction (using sulindac or indometacin). Two of the authors (S. P. and J. M.) initially screened all the titles and abstracts of papers, identified by the review search strategy, for relevance. Only studies that were obviously irrelevant were excluded at this stage. All other studies were assessed on the basis of their full text for inclusion versus exclusion by two reviewers independently (S. P. and J. M.) using the aforementioned criteria. Data extracted from each article included indication for intervention and type of intervention. Primary outcomes were similar to our case series: perinatal survival rate, defined as survival up to discharge from neonatal unit, and GA at delivery. Secondary outcomes included birth weight and PPROM before 32 weeks gestation. Statistical analysis was performed with SPSS version 21.0 (IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp.).

RESULTS

During the study period, 58 complicated MA pregnancies were treated with antenatal surgical interventions (15 in Leuven, 25 in Leiden, and 18 in Miami, respectively). Fifty-one cases (88%) were true MA pairs and seven cases (12%) were iatrogenic MA pregnancies due to unintentional septostomy in a MCDA pregnancy after a fetoscopic procedure for TTTS. Seven triplets, including an MA twin pair requiring antenatal surgical intervention, were included in this study. The main indications for surgery were discordancy for a severe fetal anomaly (N = 23, 40%), TRAP-sequence (N = 13, 22%), and TTTS (N = 16, 28%). In two cases (3%) TTTS occurred in combination with a severe fetal anomaly in one of the twins. In one case complicated with selective intrauterine growth restriction resulting in fetal demise, a cord transection was performed to prevent cord related accidents. In three cases (5%), selective reduction of one of the viable MA twins was performed for elective reasons to prevent cord accidents. A summary of indications for fetal intervention in MA pregnancies included in this study and review of literature is displayed in Table 1.

Characteristics	Current study n/total (%)	Literature n/total (%)
Monoamnioticity		
True MA	50/58 (88)	45/45 (100)
Iatrogenic MA after laser surgery	7/58 (12)	
Triplets	7/58 (12)	1/45 (2)
Indication for intervention		
TRAP	13/58 (22)	17/45 (38)
TTTS	16/58 (28)	4/45 (9)
TAPS		1/45 (2)
Discordancy for fetal anomaly	23/58 (40)	14/45 (31)
TTTS combined with discordant anomaly	2/58 (3)	1/45 (2)
Severe sIUGR	1/58 (2)	7/45 (16)
Elective to prevent cord accidents	3/58 (5)	1/45 (2)
Technical details		
Gestational age at intervention in weeks (median, range)	18.0 (13.1–33.0)	20.0 (12.0–33.0)
Fetoscopic laser coagulation of equator	7/58 (12)	1/45 (2)
Cord occlusion	7/58 (12)	4/45 (9)
Cord occlusion + transection	42/58 (72)	21/45 (48)
RFA	1/58 (2)	6/45 (13)
Interstitial laser	1/58 (2)	7/45 (15)
Alcohol injection		2/45 (4)
Serial amniodrainage		3/45 (7)
Cord ligation		1/45 (2)

MA, monoamniotic; TRAP, twin reversed arterial perfusion; TTTS, twin-to-twin transfusion syndrome; sIUGR, selective intrauterine growth restriction; RFA, radiofrequency ablation; TAPS, twin anemia polycythemia sequence.

Table 1 Characteristics and technical details

In almost all twin cases, there was a single intended survivor (due to for example congenital anomalies), except for seven cases of MCMA twins affected by TTTS, in which the aim was to save both twins. Of seven triplet pregnancies, one case of TTTS included three intended survivors, four triplets contained two intended survivors, and two triplets included a single intended survivor (one case with double TRAP and one case of selective reduction of both MA twins). Giving the characteristics of these pregnancies, the total number of intended survivors in this series adds up to 71.

In 42 cases, cord transection was attempted, and this was successful in 38/42 (90%). Cord occlusion alone was carried out in 7/58 (12%), and fetoscopic laser coagulation of the equator was performed in 7/58 (12%). In our series, only two cases of MA pregnancies complicated by TRAP were treated with RFA and interstitial laser therapy, respectively.

Postoperative PPROM before 32 weeks of gestation occurred in 16/58 cases (28%). Median (range) GA at treatment was 18.0 (13.1–33.0) weeks. Surgery was performed under local (N = 30, 52%), regional (N = 12, 21%), or general (N = 16, 27%) anesthesia using an ultrasound-guided single port procedure, except for one case where a second port was necessary for access. Introduction was performed percutaneously, except for one case in which the combined open laparoscopy and fetoscopy for completely anterior placenta procedure was used.17 The procedure was uncomplicated in 43/58 (74%) cases with a median duration of 60 min (range 20–142 min). Technical difficulties included decreased visibility due to bleeding or blurred amniotic fluid (N = 7, 12%), severe cord entanglement preventing successful procedure (N = 3, 5%), and inability to perform complete coagulation of the vascular equator (N = 4, 7%). This series included one case in which fetoscopic laser coagulation of the vascular anastomoses was performed, with intraoperative demise of the donor then followed by cord transection. In another case operated at 16 weeks of gestation because of a severe congenital anomaly in one twin, the wrong cord was sectioned because of severe entanglement limiting visibility.
Furthermore, the procedure was complicated by perioperative rupture of membranes, and the parents decided to terminate the pregnancy.
In this study, 55/71 (77%) of fetuses were live-born, and 18/71 (23%) pregnancies were complicated by intrauterine fetal demise. Two of the 55 live-born babies died in the neonatal period (4%). Therefore, perinatal survival in this series was 53/71 (75%). Median GA at delivery was 34.0 weeks (range 16.0–41.0 weeks). The median birth weight of live-born children was 2475 g (range: 745–4044 g). In none of the cases, maternal morbidity occurred. Details on pregnancy outcomes are summarized in Table 2. This study includes a few cases that were previously published.[14,15,18–21]

	Current study n/total (%)	Literature n/total (%)
No. of pregnancies/no of fetuses (incl. TRAP)	58/123	49/91
No. of triplet pregnancies	7	1
No. of intended survivors	71	49
Perinatal survival at 28 days	55/71 (77)	41/49 (84)
IUFD	17/71 (23)	8/49 (16)
NND	2/55 (4)	4/41 (10)
Gestational age at birth in weeks (median, range)	34.0 (16.0–41.0)	33.5 (13.0–39.0)
Birth weight in grams* (median, range)	2475 (745–4044)	1890 (648–3050)
PPROM < 32 weeks	16/58 (28)	9/45 (20)
Preterm birth between 24 and 32 weeks	17/58 (29)	14/45 (29)

*Live births.

TRAP, twin reversed arterial perfusion; IUFD, intrauterine fetal demise; NND, neonatal death within 28 days after birth; PPROM, preterm prelabor rupture of membranes.

Table 2 Pregnancy outcomes

Systematic review of the literature

Combination of the four search strategies revealed 820 references in MEDLINE, 964 in EMBASE, 647 references in ISI Web of Science, and none in the Cochrane library. A manual search revealed no additional studies for consideration. In total, after removal of duplicates, 32 relevant published reports were screened. Figure 1 provides a flow diagram with the number of studies screened, assessed for eligibility, and included for review according to our search strategies. Unfortunately, 12 articles failed to discuss amnionicity or included cases without surgical interventions. Because unpublished information could not be obtained, these cases were excluded from this study. To obtain the full range of research to date, we accepted case series (n= 5) and case reports (n = 13) as well. A total of 20 articles met the inclusion criteria, and we identified 50 cases of MA pregnancies that underwent surgical interventions.[4,7,13,22–38]

Baseline characteristics of the study population and indications for surgery are summarized in Table 1 and clinical outcome in Table 2. Combination of our data and review of literature showed perinatal survival rates (of intended survivors) of 78% (25/32) in 20 cases of TTTS, 77% (24/31) in 30 cases of TRAP, 72% (28/39) in 37 cases of twins discordant for anomalies, 63% (5/8) in eight cases of IUGR, and 80% (4/5) in four cases in which selective reduction was performed only to prevent cord accidents. We pooled the data from the MA pregnancies treated with selective feticide (n = 74), and we compared cases that underwent umbilical cord occlusion without transection with cases in which the cord was successfully transected after occlusion. Survival and GA at birth tend to increase after transection compared with cases having intact cords. Perinatal survival of 56/64 (88%) and median GA at birth of 36 weeks was reached after transection of the cords compared with 9/15 (60%) and 28 weeks after cord coagulation alone. Analysis of these pregnancies outcomes is shown in Table 3.

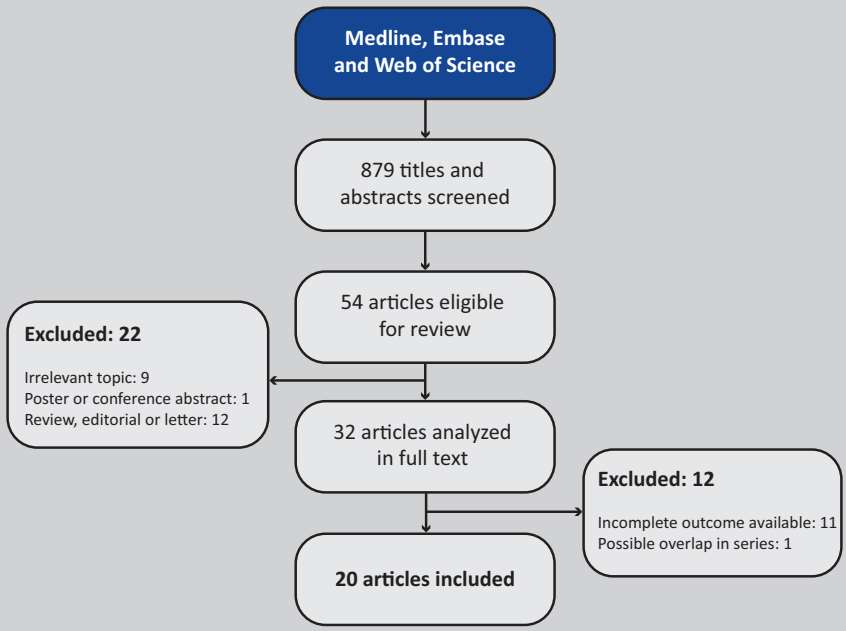

Figure 1 Flow with number of studies screened, assessed for eligibility, and included for review with exclusion criteria according to our search strategies.

Pregnancy outcomes in cases of selective feticide	Successful transection	Selective feticide with intact cords
n=74	n/total (%)	n/total (%)
No. of pregnancies	60	14
No. of triplet pregnancies	5	2
No. of intended survivors	64	15
Perinatal survival at 28 days	56/64 (88)	9/15 (60)
IUFD	8/64 (12)	6/15 (40)
NND	3/56 (5)	2/9 (22)
Gestational age at birth in weeks (median, range)	36.0 (16.0–40.0)	28.0 (16.0–41.0)
Birth weight in grams* (median, range)	2775 (796–4044)	2150 (745–3325)
PPROM < 32 weeks	16/60 (27)	4/14 (29)
Preterm birth between 24 and 32 weeks	8/60 (13)	4/14 (29)

*Live births.
IUFD, intrauterine fetal demise; NND, neonatal death within 28 days after birth; PPROM, preterm prelabor rupture of membranes

Table 3 Pooled data on pregnancy outcome intact versus transected cords

DISCUSSION

This paper reports on the largest series to date of antenatal surgical procedures in complicated MA pregnancies. Combining our data with the published literature, we can conclude that these complex procedures in this rare and highly complicated group of pregnancies, performed in highly specialized fetal treatment centers, can lead to good outcome in the majority of cases.

In case of a single intended survivor, our results suggest improved pregnancy outcomes in cases treated with cord transection. Diversity in indication and intervention makes it difficult to arrive at a consensus for an optimal strategy regarding fetal surgery in MA pregnancies. Individualization of cases is critical when determining the timing and type of intervention. Operator's experience, preferences, and pregnancy details – such as an anterior placenta, a triplet pregnancy, or signs of TTTS – may all influence options and choices.

A few other studies reported on surgical interventions in MA pregnancies. If anomalies affect only one twin, selective feticide is frequently offered as an intervention. The option of cord occlusion and transection in MA twin discordant for fetal anomalies to prevent fetal demise due to cord accidents was already proposed by Middeldorp et al.[14] and Quintero et al.[18] Valsky et al. showed that cord occlusion and transection in MA twins resulted in similar perinatal outcomes compared with those of diamniotic discordant twins treated with cord occlusion.[13] Perinatal outcome after selective feticide was also reported by van den Bos et al.[19] Preterm birth and adverse perinatal outcome appeared to occur more frequently with use of the fetoscopic laser coagulation compared with bipolar cord coagulation. However, authors stated that their population was inhomogeneous and therefore difficult to compare, and these results may be influenced by the GA at which the procedure is performed – before 18 weeks versus after 18 weeks gestation.

Although often performed with technical success, surgical procedures in MA pregnancies can be technically challenging. Especially, cord entanglement can be hazardous during fetoscopic interventions. Multiple loops of entanglement make identification of the correct cord difficult. Although rare, accidental coagulation of the wrong cord does occur, as presented in our series and previously reported.[30]

Another dilemma is the management of MA pregnancies diagnosed with TRAP. In addition to the threatened compromise of the pump twin, the risk of cord pathology seems to justify surgical intervention. Our data combined with literature data showed 30 cases treated using several surgical approaches, but predominantly cord coagulation and transection, with perinatal survival rates of 77%. Previously published series of

a combination of MA and diamniotic TRAP pregnancies undergoing prophylactic surgery at 16–18 weeks showed survival rates from 74% up to 90%.[15,39,40]

Analysis of published studies over the last 20 years reported a lower but non-negligible incidence of TTTS in MA twins (6%), compared with MCDA pregnancies (10–15%).[9] This is most likely due to the protective effect of arterio–arterial placental anastomoses.[8,41,42]

The combined outcome from our series and the literature shows that perinatal survival using fetoscopic laser in MA twins with TTTS is 78%, similar to recent outcomes in MCDA twins.43 In addition, a case of twin anemia polycythemia sequence (TAPS) in an MA pregnancy was successfully treated with laser coagulation by Diehl et al.[33]

A remarkable discordance in the prevalence of TTTS (28% vs 9%) and selective intrauterine growth restriction (2% vs 16%) in MA twins could be noted when comparing the results of current study with previously published literature. This effect may be due to the matter how diagnoses were made. In addition, these numbers may reflect some degree of referral and publication bias.

Our study does have some limitations. Reports on MA pregnancies mainly consist of case reports or small case series; therefore, conclusions drawn from the literature are limited. Amnionicity is underreported in literature, perhaps under documented, especially in earlier years. Even though authors were personally approached to gain more data, the number of cases that could be included for this paper was limited. Because our centers are acknowledged as regional or national tertiary institutions for complex fetoscopic interventions, cases may reflect some degree of referral bias, and this may influence pregnancy outcomes. Our data should be interpreted with care due to the retrospective nature of this study, the relative small number of cases in each subgroup, and varying GAs at diagnosis and interventions.

In summary, all surgical interventions in MA twins, despite being minimally invasive techniques, carry a high risk of complications and require highly skilled operators. Survival and short-term morbidity were similar to rates reported in MCDA pregnancies. However, as in other areas of fetal intervention, there is a growing awareness that it is also essential to evaluate long-term outcome in survivors. The limited numbers and variety in pathology make prospective comparative studies, let alone randomized trials, extremely difficult to perform within a reasonable timeframe. To improve outcomes in these rare, high-risk pregnancies, international collaboration, sharing data on techniques and protocols, benchmarking, and setting standards for indications and interventions are more achievable and still very valuable goals.

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