Outcome of Twin Reversed Arterial Perfusion Sequence: 15-Year Experience in a Tertiary Hospital in Hong Kong

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Objective: To evaluate our local experience of twin reversed arterial perfusion sequence.
Methods: This was a retrospective cohort study of all twin pregnancies complicated by twin reversed arterial perfusion sequence that were managed at a university teaching hospital in Hong Kong from 1 January 1998 to 31 December 2012.
Results: Of 16 cases identified, two were excluded and 14 were analysed. The median (range) gestation at diagnosis was 16.0 (10.8-24.3) weeks. Seven cases were treated conservatively and seven were treated with surgical intervention. Comparison of surgical and conservative treatment showed that the former was associated with a trend for better survival (71% vs. 43%), and less miscarriage (14% vs. 43%), preterm delivery (20% vs. 33%), and small for gestational age (0 vs. 33%), although these were not statistically significant. There was no significant difference in median gestation at delivery (37.0 vs. 37.4 weeks). Two cases (28.6%) with treatment failure and one other case (14.3%) had procedure-related complications. In the small-size acardiac twin subgroup (acardiac-to-pump twin size ratio <50%), both surgical and conservative treatments had excellent survival (100%). Of the six cases diagnosed in the first trimester, three (50%) ended in miscarriage before 16 weeks of gestation, and all were associated with a large-size (i.e. acardiac-to-pump twin size ratio ≥50%) acardiac twin.
Conclusions: Surgical intervention for twin reversed arterial perfusion sequence tended to improve survival with few adverse events. Our surgical intervention results were comparable with other studies. Conservative management appears to be safe for twin reversed arterial perfusion with a small acardiac twin. Diagnosis of twin reversed arterial perfusion sequence in the first trimester was associated with a high miscarriage rate at or before 16 weeks, especially with a large-size acardiac twin.
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Introduction

Twin reversed arterial perfusion (TRAP) sequence is a rare condition unique to monochorionic (MC) twin pregnancy, occurring in approximately 1 in 35,000 pregnancies, 1 in 100 MC twin pregnancies, and 1 in 30 MC triplet pregnancies[1,2]. Twin reversed arterial perfusion sequence is a condition in which one twin (termed the acardiac twin) has a non-functioning or absent heart and receives all of its perfusion from its structurally normal co-twin (termed the pump twin). The acardiac twin has no placental share and perfusion occurs through a superficial arterial-arterial placental anastomosis between the structurally normal pump twin and the acardiac twin. Blood flows in a retrograde fashion from the pump twin towards, rather than away from, the acardiac twin through the umbilical artery and then back towards (but not into) the placenta through the umbilical vein. The returning blood bypasses the placenta and returns to the pump twin through vein-vein anastomosis[3]. The overall perinatal mortality rate

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of the pump twin without any intervention ranges from 35% to 55%[4,5]. Contributors to perinatal death of the pump twin are congestive heart failure, preterm delivery due to polyhydramnios, and mass effect of the acardiac twin. Intrauterine growth restriction and development of fetal hydrops may further complicate the wellbeing of the pump twin. In case of monoamniotic (MA) twins, the umbilical cord of the pump twin may become entangled with that of the acardiac twin[6].

The goal of treating TRAP sequence is to maximise the likelihood of term delivery and survival of the pump twin in a safe and effective manner. The definitive treatment of this condition is obliteration of the arterial-arterial and vein-vein anastomoses via fetal intervention. However, fetal intervention has significant risks of preterm delivery (PTD), preterm prelabour rupture of membranes (PPROM), miscarriage, intrauterine death (IUD), and treatment failure. As a result, conservative management, with a survival rate of 90%, has been advocated[7]. There are many issues regarding the management of TRAP sequence, such as whether to intervene and, if so, when to intervene, and which method of intervention, such as cord occlusion or intrafetal ablation, to use.

This study aimed to review the local experience of twin pregnancies complicated by TRAP sequence managed by conservative treatment or surgical intervention.

Methods

This retrospective cohort study was conducted at the Fetal Medicine Unit, Tsan Yuk Hospital, and Queen Mary Hospital, The University of Hong Kong. The unit provides tertiary hospital care and manages high-risk pregnancies that are referred from other local hospitals in Hong Kong. There are around 4000 deliveries annually. More than 90% of the patients are ethnic Chinese. Ethical approval for this study was obtained from the local institutional human research ethics committee. All consecutive cases of TRAP sequence that were managed between 1 January 1998 and 31 December 2012 were identified by reviewing the departmental database. Details of all identified cases were obtained from the case notes and hospital electronic systems (Clinical Management System and Obstetrics Clinical Information System). The data were collected from prenatal records, ultrasound (USG) reports, operation records, delivery charts, and neonatal records.

All cases underwent detailed USG examination by maternal fetal medicine subspecialists to confirm the diagnosis of TRAP sequence. Women were counselled regarding the prognosis of the pump twin. The various options were offered, namely, termination of pregnancy (TOP), conservative management, or surgical intervention. For women who opted for conservative management, the pregnancies were followed up weekly until there was no growth and no blood flow in the acardiac twin. Thereafter, the pregnancies were evaluated every 2 to 3 weeks to monitor the growth of the pump twin. Surgical intervention was not recommended until after at least 16 weeks of gestation (up to 2007) and 12 weeks of gestation (after 2007) or when there was a significant risk of death for the pump twin, such as increase in size of the acardiac twin, acardiac-to-pump twin size ratio of ≥50%, abnormal Doppler or cardiac decompensation of the pump twin, or polyhydramnios[8]. Surgical intervention was also recommended for monochorionic monoamniotic (MCMA) cases to prevent the death of the pump twin from cord entanglement[9]. The acardiac-to-pump twin size ratio was calculated by comparing abdominal circumferences or estimated fetal weights, or by comparing the upper pole-rump length of the acardiac and the crown-rump length of the pump twin[10]. Estimated fetal weight of the acardiac twin was calculated by measuring in three dimensions (anteroposterior, transverse, and longitudinal) and using the equation for a prolate ellipsoid to estimate volume (in mL); fetal weight was then obtained by assuming that 1 mL is equal to 1 gm[11]. All women gave written informed consent prior to treatment.

Intrafetal monopolar thermocoagulation was performed under local anaesthesia. An 18-gauge needle was introduced transabdominally under USG guidance targeted near to the major intra-abdominal vessel of the acardiac twin. The stylet was then removed. A 1-mm wire electrode, which was insulated along most of its length with 3 mm of wire left bare at the tip, was passed through the lumen of the needle until the 3-mm length of bare wire had passed the end of the needle. The wire electrode was connected to a standard monopolar diathermy machine. Thermocoagulation was applied several times at 30 to 40 W for 5 to 15 seconds until cessation of blood flow in the acardiac twin was demonstrated by colour Doppler USG[12].

Fetoscopic laser cord coagulation was performed under general anaesthesia. A 1-mm mini-fetoscope (Karl Storz, Tuttlingen, Germany) was used. The trocar was inserted into the amniotic cavity under USG guidance. The fetoscope was passed through the trocar and the umbilical cord insertion of the acardiac twin was identified. Neodymium-doped yttrium aluminium garnet laser fibre was then passed through the operative channel of the

fetoscope. Laser coagulation pulses of 30 W for 3 seconds each were delivered until arrest of flow was detected by colour Doppler USG.

Bipolar cord coagulation was performed under general anaesthesia. A 3.5-mm laparoscopic trocar and 3-mm bipolar forceps (Karl Storz, Tuttlingen, Germany) were used. After the trocar was inserted into the amniotic cavity under USG guidance, the bipolar forceps was passed through the trocar and the umbilical cord insertion to the acardiac twin was identified and grasped under USG guidance. Bipolar coagulation of 20 to 55 W for 15 seconds each was applied until arrest of flow was detected via colour Doppler USG.

Treatment failure was defined as incomplete cessation of blood flow, a second procedure needed to achieve complete occlusion, procedure abandoned, or death of the pump twin within 24 hours of the procedure. Procedure-related miscarriage, PTD, and PPROM were defined as occurring within 4 weeks of the procedure.

After fetal intervention, patients were discharged either on the same day or the next day. Ultrasound was performed before discharge to ensure that there was no blood flow in the acardiac twin and that the pump twin was normal. The pregnancies were followed up weekly until stable and then every 2 to 3 weeks to monitor the growth of the pump twin. Patients were referred back to their local hospitals to continue antenatal care and for delivery if their condition was stable.

Statistical analysis was performed using the Statistical Package for the Social Sciences Windows version 16.0 (SPSS Inc., Chicago [IL], US). Variables were expressed as median and range for non-normally distributed variables. Comparison between the outcome groups was by Mann-Whitney *U* test for continuous variables and Fisher's exact test for categorical variables. A p value of ≤0.05 was considered statistically significant.

Results

There were 16 cases of TRAP sequence diagnosed in the study period. Two cases were excluded due to missing case notes for one and TOP at the patient's request for the other. Therefore, 14 cases were included in the analysis. Of these, 12 (85.7%) cases were Chinese. Thirteen (92.8%) cases involved spontaneous conception. There were 13

Table 1. Clinical characteristics of twin reversed arterial perfusion sequence with conservative management

Case No.	Year	Type of twinning	Median gestational age at diagnosis (weeks)	Size ratio (%)	Sign of pump twin compromise	Progress	Outcome	Median gestational age at delivery (weeks)	Mode of delivery	Birth weight (g)
1	1998	MCDA	22+1	166	Hydrops, oligohydramnios	-	IUD at 24+4 weeks	25+3	-	-
2	2002	MCDA	10+6	63	-	-	Miscarriage at 13 weeks	-	-	-
3	2004	MCDA	24+2	28	-	Pump twin SGA, oligohydramnios	Live birth	32+0	LSCS	1260
4	2005	MCDA	14+0	14	-	Acardiac twin without blood flow at 14+6 weeks	Live birth	38+0	NSD	2610
5	2005	MCDA	13+3	73	Sinus bradycardia, UA REDF	-	Miscarriage at 13+5 weeks	-	-	-
6	2009	MCDA	11+2	64	-	-	Miscarriage at 12+5 weeks	-	-	-
7	2012	MCDA	12+4	34	-	Acardiac twin without blood flow at 15+4 weeks	Live birth	37+3	LSCS	2550

Abbreviations: IUD = intrauterine death; LSCS = lower segment Caesarean section; MCDA = monochorionic diamniotic; NSD = normal spontaneous delivery; SGA = small for gestational age; UA REDF = umbilical artery Doppler reversed end-diastolic flow

Table 2. Clinical characteristics of twin reversed arterial perfusion sequence with surgical management

Case No.	Year	Type of twinning	Median gestational age at diagnosis (weeks)	Size ratio (%)	Sign of pump twin compromise	Progress
8	1999	MCDA	16+0	20	-	Increased size of acardiac twin
9	2001	MCDA	20+2	94	Polyhydramnios	-
10	2001	MCDA	16+0	22	-	Increased size of acardiac twin, polyhydramnios
11	2003	MCDA	20+1	21	-	Increased size of acardiac twin
12	2004	MCDA	17+1	93	Cardiomegaly, polyhydramnios	-
13	2007	MCMA	16+0	151	-	-
14	2007	MCDA	12+2	52	-	Increased size of acardiac twin

Abbreviations: IUD = intrauterine death; LSCS = lower segment Caesarean section; MCDA = monochorionic diamniotic; MCMA = monochorionic monoamniotic; NSD = normal spontaneous delivery; PPROM = preterm prelabour rupture of membranes; VE = vacuum extraction

(92.8%) pairs of MC diamniotic twins and one (7.2%) pair of MCMA twins. There were no high-order pregnancies. The median (range) maternal age was 31.5 (23-42) years. Six (42.9%) patients were nulliparous. The overall median (range) gestational age at diagnosis was 16.0 (10.9-24.3) weeks. In eight cases the pump twin survived, for an overall survival rate of 57.1%. The overall median (range) gestation at delivery was 37.0 (25.4-39.7) weeks. Fetal karyotypes were available in eight (57.1%) cases and all were normal. In eight (51.7%) cases, USG revealed that the acardiac twin had acardius acephalus, which was the most common morphology. The remaining six cases had acardius anceps (n=5) or acardius amorphous (n=1). Seven cases were managed conservatively and seven underwent fetal intervention.

In the conservative management group (Table 1), the median (range) gestational age at diagnosis and delivery were 13.4 (10.9-24.3) weeks and 37.4 (32.0-38.0) weeks, respectively. Three of the seven cases had live birth of the pump twin, achieving a survival rate of 42.9%. The median birth weight was 2550 (range, 1260-2610) g. Among the pump twins that survived, one had both PTD before 34 weeks and small for gestational age (SGA), and two had spontaneous cessation of blood flow of the acardiac twin during follow-up, with both having small acardiac-to-pump twin size ratios of <50%. Three (42.9%) cases had miscarriage, all of which had large acardiac-to-pump twin size ratios of ≥50%. Two cases, which occurred before 2007, presented in the first trimester with acardiac-to-pump twin size ratio of ≥50%; at the time, departmental policy was to delay intervention until ≥16 weeks in such cases, and the miscarriages happened at <16 weeks. One case, which was diagnosed at 11.3 weeks, presented after 2007 when the departmental policy had changed to allow earlier surgical intervention at ≥12 weeks, although miscarriage occurred at 12.7 weeks. One case had IUD at 24.5 weeks, and that the TRAP sequence was first diagnosed at 22.1 weeks with a large acardiac-to-pump twin size ratio of >100% and signs of compromise of the pump twin. However, the patient declined fetal intervention or TOP.

In the surgical intervention group (Table 2), the median (range) gestational age at diagnosis, time of procedure, and time of delivery of live births were 16.0 (12.3-20.3) weeks, 18.0 (14.1-25.0) weeks, and 37.0 (33.0-40.3) weeks, respectively. Five of the seven cases had live birth of the pump twin, achieving a survival rate of 71.4%. The median (range) birth weight was 2815 (2045-3075) g. The median treatment-to-delivery interval for live birth cases was 16.0 (range, 11.0-26.2) weeks. Among the surviving pump twins, one (20.0%) case underwent PTD before 34 weeks but none were SGA. There was one

Median gestational age at treatment (weeks)	Method	Complication	Outcome	Median gestational age at delivery (weeks)	Mode of delivery	Birth weight (g)
17+1 (First attempt); 17+3 (second attempt)	Intrafetal monopolar thermocoagulation	Partially successful after second attempt	Live birth	39+5	VE	3075
21+0	Intrafetal monopolar thermocoagulation	Successful	Live birth	37+0	LSCS	2950
17+0	Intrafetal monopolar thermocoagulation	Successful	Live birth	33+0	NSD	2045
25+0	Intrafetal monopolar thermocoagulation	Successful	Live birth	36+0	LSCS	2700
19+4 (First attempt); 20+0 (second attempt)	Intrafetal monopolar thermocoagulation	Successful after second attempt	PPROM, miscarriage at 23+2 weeks	-	-	-
18+2	Bipolar cord coagulation	Successful	IUD at 24 weeks	-	-	-
14+1	Laser cord coagulation	Successful	Live birth	40+2	VE	2815

(14.3%) miscarriage and one (14.3%) IUD, at 3 and 6 weeks after the procedure, respectively. Four cases had acardiac-to-pump twin size ratios of ≥50% at the time of diagnosis. Of these, two had polyhydramnios and one of them had cardiomegaly of the pump twin. The remaining three cases had small initial acardiac-to-pump twin size ratios (<50%), but serial monitoring showed that the acardiac twin size was increasing. Thus, treatment was indicated in these cases. For the treatment modality, five (71.4%) cases underwent intrafetal monopolar thermocoagulation, one (14.3%) underwent bipolar cord coagulation (BCC), and one (14.3%) underwent fetoscopic laser cord coagulation. In five cases successful cessation of blood flow was achieved after a single procedure. The case of BCC involved MCMA twins with acardiac-to-pump twin size ratio of 150%; the procedure was smooth and dislodged of cord of the acardiac twin, but it was complicated by IUD 6 weeks after the procedure. Two of the cases undergoing intrafetal monopolar thermocoagulation needed a second procedure to achieve cessation of blood flow; the treatment failure rate was therefore 28.6%. One of the two cases still had low blood flow after the second attempt, but with spontaneous cessation 5 weeks after the second procedure resulting in the live birth of the pump twin. Although the other case had successful complete occlusion after the second procedure, the case was complicated by PPROM and miscarriage 3 weeks after the procedure (14.3%).

When comparing surgical to conservative management, there was a trend for the surgical group to have a better survival rate of the pump twin, and less chance of PTD, SGA, miscarriage, and IUD, although these did not reach statistical significance. When comparing only the small acardiac-to-pump twin size ratio (<50%) subgroups, both surgical and conservative management had excellent survival rates of the pump twin (100%) [Table 3].

In subgroup analysis, six cases of TRAP sequence were confirmed in the first trimester. Four of the six cases had acardiac-to-pump twin size ratios of ≥50%. Three (50%) ended in miscarriage with fetal death before 16 weeks of gestation. One case underwent surgical treatment at 14.1 weeks and survived. The other two cases had acardiac-to-pump twin size ratios of <50%, and both had spontaneous cessation of blood flow during follow-up and underwent term live birth deliveries (Table 4).

Discussion

Since Van Allen et al[3] reported the pathophysiology of TRAP sequence in 1983, numerous types of intervention have been described to interrupt the vascular supply of the acardiac twin in order to improve the outcome of the pump twin. These techniques target the umbilical cord vessels, the intrafetal vessel or the vascular anastomoses on the placental surface, and include cord occlusion by

Table 3. Outcomes of conservatively and surgically managed cases*

Characteristic	Conservative (n=7)	Surgical (n=7)	p Value
Gestation at diagnosis (weeks)	13.4 (10.9-24.3)	16.0 (12.3-20.3)	0.38
Pump twin survival rate	3 (43%)	5 (71%)	0.59
Gestation at delivery for live birth (weeks)†	37.4 (32.0-38.0)	37.0 (33.0-40.3)	0.79
Adverse outcome	6 (86%)	3 (43%)	0.27
Preterm delivery ≤34 weeks†	1/3 (33%)	1/5 (20%)	1
SGA (<10th centile)†	1/3 (33%)	0	0.38
Miscarriage	3 (43%)	1 (14%)	0.56
IUD	1 (14%)	1 (14%)	1
Survival in cases with small acardiac twin‡	3/3 (100%)	3/3 (100%)	1

Abbreviations: IUD = intrauterine death; SGA = small for gestational age

* Data are shown as median (range) or No. (%)

† For live births only (3 conservative cases and 5 surgical cases)

‡ Defined as an acardiac-to-pump twin size ratio of <50% (3 conservative cases and 3 surgical cases)

Table 4. Clinical characteristics of twin reversed arterial perfusion sequence diagnosed in the first trimester

Case No.	Year	Type of twinning	Median gestational age at diagnosis (weeks)	Size ratio (%)	Sign of pump twin compromise	Progress	Treatment	Outcome	Median gestational age at delivery (weeks)	Mode of delivery	Birth weight (g)
Large-size acardiac twin*											
2	2002	MCDA	10+6	63	-	-	-	Miscarriage at 13 weeks	-	-	-
5	2005	MCDA	13+3	73	Sinus bradycardia, UA REDF	-	-	Miscarriage at 13+5 weeks	-	-	-
14	2007	MCDA	12+2	52	-	Increased size of acardiac twin	Laser cord coagulation	Live birth	40+2	VE	2815
6	2009	MCDA	11+2	64	-	-		Miscarriage at 12+5 weeks	-	-	-
Small-size acardiac twin†											
4	2005	MCDA	14+0	14	-	Acardiac twin without blood flow at 14+6 weeks	-	Live birth	38+0	NSD	2610
7	2012	MCDA	12+4	34	-	Acardiac twin without blood flow at 15+4 weeks		Live birth	37+3	LSCS	2550

Abbreviations: LSCS = lower segment Caesarean section; MCDA = monochorionic diamniotic; NSD = normal spontaneous delivery; UA REDF = umbilical artery Doppler reversed end-diastolic flow; VE = vacuum extraction

* Defined as acardiac-to-pump twin size ratio of ≥50%

† Defined as acardiac-to-pump twin size ratio of <50%

coil[13], ligation[14], cord coagulation with bipolar diathermy[15], or laser[16], or intrafetal ablation by alcohol[17], monopolar[12], laser[18], radiofrequency ablation (RFA)[19] or, most recently, high-intensity focused USG[20]. Laser coagulation of the vascular anastomoses on the placental surface has also been proven to be a safe and effective alternative[21]. However, no single technique has been shown to be unequivocally optimal[9,22].

Our study shows that surgical intervention has a trend for better survival of the pump twin, and less chance of PTD, SGA, and miscarriage, although these advantages did not reach statistical significance. The pump twin survival rate with surgical intervention in our cohort was 71%, which is comparable with large systematic reviews and meta-analyses of individual types of interventions (65-85%)[16,18,19,21-24]. Our results also have similar treatment failure rate (28.6% vs. 0-35%), procedure-related complication rate (14.3% vs. 19-30%), and PTD rate (20% vs. 11%-71.4%)[16,18,19,21-24].

In our study, five cases underwent intrafetal ablation and two underwent cord occlusion. Because of the small number of cases, we cannot draw any conclusion about which intervention had the better outcome. A systematic review by Tan and Sepulveda[22] suggests that the intrafetal technique was preferred because of significantly later gestational age at delivery (37 weeks vs. 32 weeks, p=0.04), lower technical failure rate (13% vs. 35%, p=0.03), lower rate of PTD or PPROM before 32 weeks (23% vs. 58%, p=0.003), and higher clinical success rate (77% vs. 50%, p=0.02). On the basis of recent publications, it appears that the most commonly used techniques are RFA, intrafetal laser, and BCC[25]. These techniques all have survival rates for the pump twin ratio of >80% in large systematic reviews and meta-analyses with TRAP sequence diagnosed and treated at or after 16 weeks of gestation[14,15,17,18,19,23,25,26]. Two studies comparing RFA and BCC for a variety of complications in MC twins reported similar rates of survival for the two techniques[26,27]. Our department had stopped using intrafetal monopolar thermocoagulation for the most recent cases, after 2007, as it is less effective than the other treatments.

There are ongoing discussions regarding the decision to intervene and the timing of such intervention. Some authors propose conservative treatment, waiting for evidence of compromise in the pump twin before undertaking any intervention. The advantage of such an approach is possible avoidance of an adverse outcome from the intervention (e.g. miscarriage, PPROM). Other authors favour prophylactic intervention at 16 to 18 weeks, after obliteration of the coelomic cavity, to reduce the risk of miscarriage and to preclude the difficulty of achieving cessation of blood flow in a large, and often hydropic, acardiac twin in advanced gestation[10,16]. The results of this latter approach were promising, with 80% to 90% survival rates in most of the large series[11,16,28]. This approach is still popular in many fetal therapy centres.

In recent years, however, with increasing introduction of universal first trimester Down syndrome screening worldwide as well as in Hong Kong, TRAP is increasingly being diagnosed in the first trimester. This was also observed in our study. Despite the trend for earlier diagnosis, surgical intervention is still often delayed until after 16 weeks. Reluctance to perform surgical intervention before 16 weeks primarily stems from the concern that the persistence of the coelomic cavity before this gestation time may lead to higher risks of membrane rupture and miscarriage. However, studies have shown high miscarriage rates reported in the pump twin between 12 and 16 weeks[10,18,29]. Lewi et al[10] demonstrated that eight of 24 (33%) TRAP sequences diagnosed in the first trimester resulted in spontaneous death of the pump twin before 16 weeks. Other authors reported fetal mortality following diagnosis in the first trimester of 83% to 100%, with all losses occurring at or before 16 weeks[18,29]. Our study was consistent with these findings — when TRAP sequence was diagnosed in the first trimester, fetal mortality was high (50%), and all fetal deaths occurred at or before 16 weeks. The actual incidence of fetal death following diagnosis in the first trimester might have been higher because of referral bias, with a subset of cases possibly having miscarried at local hospitals without referral. Also, some authors found that there are no USG features that could help to distinguish between pregnancies resulting in death of the pump twin from those that will survive until prophylactic intervention after 16 weeks[10,25]. Moreover, there have been reports of successful results of minimally invasive intervention for TRAP sequence before 16 weeks utilising intrafetal laser[18], RFA[19], mini-fetoscopic laser coagulation[16], as in our study or, most recently, non-invasive high-intensity focused USG[20]. Furthermore, a recent meta-analysis by Chaveeva et al[25] demonstrated that in 104 TRAP sequence cases treated with intrafetal laser, the pump twin survival rate was unrelated to the gestational age at surgical intervention, so there is no benefit to delaying intervention. The same study[25] also showed that there was an inverse association between gestational age at treatment and gestational age at birth, so early intervention may have the additional benefit of reducing the risk of preterm delivery. These observations have led to a tendency to recommend earlier prophylactic intervention from 12 weeks[10,18,25,30].

Our study showed that all the fetal deaths occurring at or before 16 weeks had a large acardiac-to-pump twin size ratio (≥50%). The only case with large acardiac twin size and in which the pump twin survived had undergone surgical intervention. So large acardiac twin size could

possibly be a poor predictor for pump twin death when TRAP sequence is diagnosed in the first trimester, and this could constitute a group with a particular need for early prophylactic treatment from 12 weeks.

The technique of choice for early intervention is likely to be intrafetal laser or RFA rather than BCC because both intrafetal laser and RFA employ smaller instruments. Intrafetal laser was more commonly used as more clinical evidence was available to support its favourable outcome. In a recent meta-analysis of 51 cases of intrafetal laser therapy, including cases from 10 studies and a large cohort from the authors, the overall neonatal survival rate was 80% with the preterm birth rate before 32 weeks being 11%. For the subgroup with treatment before 16 weeks, the outcome was significantly better, with survival of 16 of 18 (88.9%) cases, with two IUDs and two preterm births before 32 weeks[18]. However, there is a scarcity of data on the use of RFA before 16 weeks. A large multicentre study reported that the rate of IUD of the pump twin was significantly higher in cases undergoing RFA at 15 to 19 weeks than that in those treated after 19 weeks (33.3% vs. 10.7%)[23].

Our study found that for a small-size acardiac twin (<50%), both conservative and surgical management had excellent survival rates for the pump twin, reaching 100%. All small-size acardiac twins diagnosed in the first trimester (≤14 weeks) had spontaneous cessation of blood flow during follow-up and delivery of a healthy pump twin at term. This concurred with previous studies that suggested conservative management with close monitoring to be safe in pregnancies in which the acardiac twin was <50% the weight of the pump twin. Jelin et al[31] showed that in a retrospective cohort of 18 cases of small acardiac twin, 11 underwent conservative management and seven underwent surgical management by RFA; pump twin survival was 91% for the overall conservative management group, 88% for the conservative management group that had blood flow, and 100% for RFA. In their cohort there were no statistically significant differences in gestational ages at delivery, birth weights, and survival rates between these groups, even after stratification by blood flow[31].

The retrospective design of the current study only allowed categorisation of cases by the final treatment modalities (observation vs. in-utero intervention). Together with the sample size, bias was potentially introduced. It is difficult to make definitive conclusions based on our finding. Despite these limitations, our study adds some evidence that surgical intervention had a trend for better survival rates for the pump twin, and less chance of PTD, SGA, and miscarriage. Our local data showed that the outcomes of surgical intervention were comparable with other studies. In cases with small acardiac-to-pump twin size ratio (<50%), conservative management with close monitoring appeared to be a safe option. However, when TRAP sequence was diagnosed in the first trimester, it was associated with high fetal mortality (50%) at or before 16 weeks, especially for those with large acardiac-to-pump twin size ratios, which could be a possible predictor for pump twin death when TRAP sequence is diagnosed in the first trimester. Early prophylactic intervention from 12 weeks may benefit this group. A larger study will be necessary to examine whether prophylactic intervention at 12 weeks can prevent the deaths of those who would have died before 16 weeks as well as to explore the optimal early surgical intervention technique in such gestations.

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