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Early unfavorable outcomes of second-trimester selective feticide for complicated monochorionic twins: single-operator experiences

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Abstract

Objectives: This study reviews early unfavorable outcomes following selective *in-utero* cord occlusion in monochorionic twin pregnancies at risk of hemodynamic accidents by a single operator.

Methods: The study analyzed laser ablation (LA), laser transection (LT), radiofrequency ablation (RFA), and bipolar diathermy (BD) procedures performed between 14 and 22 weeks of gestation from 2006 to 2022. Outcomes included: (1) technical failure (abandonment before cessation of Doppler flow), (2) intraoperative events (hemodynamic instability in the woman or co-twin), and (3) complications (e.g., fluid leakage, infection, abruption, co-twin demise, or miscarriage) within 1 week post-procedure.

Results: Ten LAs were performed at 14–15 weeks for discordant anomalies, all without complications. Two LTs were conducted at 20 weeks for umbilical cord knotting; with one procedure experienced technical failure. All twin reversed arterial perfusion sequence (TRAPS) (n=55) received RFA, with one procedure experienced technical failure. All twin-to-twin transfusion syndrome (TTTS) (n=25) received BD, with one procedure experienced technical failure. Selective intrauterine growth restriction (sIUGR) (n=30) received RFA (n=5) and BD (n=25), with 1 RFA (25 %) and 1 BD (4 %) experienced technical failure. (p<0.01) All four technical failure cases had extensive anterior placenta. There were no intraoperative events. McDonald cervical cerclage was performed in 8/25 TTTS cases with pre-operative cervical length of ≤25 mm and/or funneling of the internal cervical os. Early procedure-related complications were experienced in two sIUGR cases receiving BD, both of which had extensive anterior placenta.

Conclusions: Early unfavorable outcomes were associated with sIUGR as an indication.

Keywords: monochorionic twins; umbilical cord occlusion; twin-to-twin transfusion syndrome; selective intrauterine growth restriction; twins reverse arterial perfusion sequence; discordant anomalies

Introduction

Deaths or major brain injuries in the co-twin occur in 15–25 % of monochorionic (MC) twin pregnancies following the demise of one twin. [1]. Sudden exsanguination through persistent placental vascular anastomoses into the deceased twin can be mitigated by selectively occluding the umbilical vessels *in-utero*. [2]. Selective *in-utero* cord occlusion is commonly indicated for twin reversed arterial perfusion sequence (TRAPS), selective intrauterine growth restriction (sIUGR) with absent-to-reversed end diastolic flow in the umbilical artery (sIUGR type 2 and 3), and discordant anomalies [3].

For severe twin-to-twin transfusion syndrome (TTTS), either selective fetoscopic laser photocoagulation (SFLP) or selective *in-utero* cord occlusion may be chosen and tailored to distinct clinical scenarios. SFLP is considered the standard of care for mid-trimester TTTS, as it directly targets and coagulates placental vascular anastomoses responsible for unbalanced blood flow between the twins, thereby restoring hemodynamic independence and improving survival rates of at least one twin in over 80 % of cases [4]. In contrast, cord occlusion is strictly reserved for situations where one twin is severely compromised (i.e. stage 3TTTS with significant myocardial dysfunction or stage 4TTTS with cardiogenic hydrops), and its continued survival threatens the co-twin through hemodynamic instability [5, 6]. This procedure sacrifices the affected twin in order to maximize survival

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and neurological protection of the healthy co-twin, and serves as a last-resource life-saving strategy for the remaining twin when dual survival cannot be achieved [3].

Procedures frequently employed include laser ablation (LA), laser transection (LT), bipolar diathermy (BD), and radiofrequency ablation (RFA) [7]. Prognostic factors following *in-utero* occlusion of umbilical vessels have been previously studied. A retrospective analysis of 48 cases demonstrated comparable overall survival and complication rates between RFA and BD [8]. RFA has gained preference over BD due to its technical simplicity [9]. A retrospective review of over 300 RFA procedures performed before and after 20 weeks of gestation showed similar co-twin loss rates (20.9 vs. 21.5 %), preterm premature rupture of membranes (PPROM) within 24 h (1.5 vs. 1.2 %), and gestational age at delivery (35.93 weeks [28–38] vs. 36 weeks [28.54–38.14], respectively) [10]. The use of multiple RF ablation cycles has been associated with unfavorable outcomes [11]. Post-procedure perinatal outcomes are influenced by various factors, including the operator's experience, chosen procedure, indication, gestational age at intervention, and the quality of neonatal care [8, 12, 13].

The choice of procedure for *in-utero* occlusion of umbilical vessels has largely depended on the operator's discretion, often influenced by the specific clinical indications [14]. Most published data come from single-center practices, and procedure-related outcomes vary significantly across centers [15, 16]. A single-center retrospective review of 143 RFAs reported better outcomes in cases of sIUGR and TRAPS compared to discordant anomalies [17]. Conversely, another single-center review of 268 cases identified the lowest survival rates in cases of TTTS stage 4, sIUGR type 3, and discordant anomalies [18].

Between 2006 and 2022, all selective umbilical vessel occlusions for complicated monochorionic twin pregnancies in this study were performed by a single operator. All patients underwent follow-up in our unit one week post-procedure. This setup provides a unique opportunity to assess the performance of different techniques with minimal inter-operator variability and reduced risk of missing data [19, 20].

Materials and methods

We conducted a retrospective review of electronic medical records for complicated MC twin pregnancies that underwent LA, LT, BD, or RFA (Figure 1) at the Siriraj Fetal Therapy Center, Faculty of Medicine Siriraj Hospital, Bangkok, Thailand. Inclusion criteria were: (1) gestational age between 14 and 22 weeks, (2) procedures performed between 2006 and 2022, and (3) a single operator (T.W.). Cases were assessed for: (1) technical failure, defined as abandonment of the procedure before complete cessation of color Doppler flow; (2) intraoperative events, defined as hemodynamic instability of the woman or co-twin; and (3) procedure-related complications, including fluid leakage, infection, placental abruption, co-twin demise, or miscarriage within one week post-procedure. Exclusion criteria were pregnancies involving triplets with MC twin pairs and procedures performed by operators other than T.W. The study protocol was approved by the Siriraj Institutional Review Board (SIRB 704/2, 559 [EC3]).

TTTS was classified using the Quintero staging system [21]. Oligohydramnios was defined as a deepest vertical pocket of ≤2 cm. TRAPS was diagnosed based on reversal of umbilical arterial flow toward the malformed twin. Selective termination for sIUGR was offered only for type 2 or type 3 cases, defined by: (1) an estimated fetal weight <10th percentile with absent or reversed end-diastolic flow in the umbilical artery Doppler of one twin, and (2) an intertwin weight discordance >25 %. It should be noted that selective feticide was not performed for cases of twin anemia polycythemia (TAP) sequence.

Instrumentation and techniques

All procedures were performed under fentanyl-based intravenous conscious sedation, combined with local anesthesia using 2 % xylocaine with adrenaline at the instrument insertion site extending to the myometrial wall. A small skin incision was made to allow for instrument insertion. Operative time was defined as the duration from instrument insertion to removal. The time required for cervical cerclage placement was excluded from this calculation.

Laser ablation (LA)

Under ultrasound guidance, an 18-gauge (G) UniPlex® needle (Pajunk Medical Systems, GA, USA) or an 18-G angiographic needle (Cook Medical, Bloomington, IN, USA) was percutaneously inserted into the intra-abdominal portion of the umbilical vessels of the targeted twin. A 600-micron (μm) diode laser fiber (Medilas®, Dornier MedTech, Wessling, Germany) was then inserted through the needle and advanced a few millimeters beyond its tip. Multiple laser impulses, each lasting a few seconds and starting at 10 W, were delivered. The process was repeated until the tissue surrounding the laser fiber became hyperechoic, and

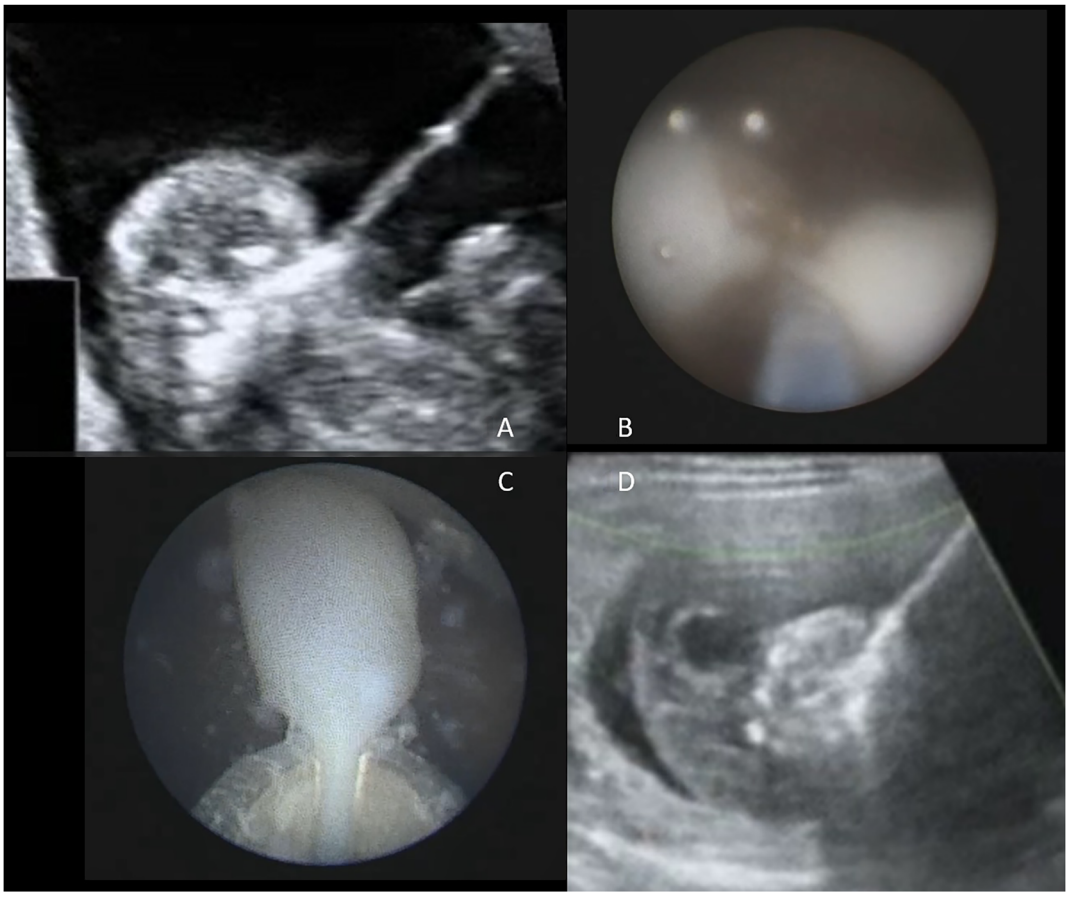

Figure 1: Selective feticide for complicated monochorionic twins, (1A) laser ablation, (1B) laser transection, (1C) bipolar diathermy, and (1D) radiofrequency ablation (RFA).

complete cessation of perfusion was confirmed using color Doppler [22].

Bipolar diathermy (BD)

Under ultrasound guidance, a 10-French (Fr) disposable cannula (Check-flo II, diameter 3.8 mm, Cook Medical, Bloomington, IN, USA) or a reusable rigid trocar (11519AS, diameter 3.6 mm, Karl Storz GmbH, Tuttlingen, Germany) was inserted into the amniotic cavity of the twin designated for termination. The Seldinger or direct puncture technique was employed for cannula insertion, with transplacental entry being avoided [23]. In cases of oligohydramnios, amnio-infusion was performed prior to cannula placement.

A 3-mm bipolar optical forceps (11540HLS, diameter 3 mm, Karl Storz GmbH, Tuttlingen, Germany) equipped with a mini straight-forward telescope 0 ° (11540AA, diameter 1.3 mm, Karl Storz GmbH, Tuttlingen, Germany) was introduced through the cannula. The forceps were guided into position using endoscopic and ultrasound visualization.

Once the umbilical cord of the targeted twin was grasped, coagulation was performed with power settings between 80 and 100 W for 30–60 s [24]. At least two separate coagulation applications were made at different sites along the cord. The thermal effects were monitored in real-time using ultrasound and endoscopic visualization to confirm full-thickness coagulation across the entire diameter of the cord. The process was repeated until color Doppler confirmed complete cessation of perfusion. For TTTS stage 4, the significant edematous nature of the cord can make visualization and effective grasping more challenging. BD in this situation required more precise techniques, more gentle handlings, and higher experiences to avoid complications such as cord rupture and hemorrhage [25].

Laser transection (LT) of the umbilical cord

Under ultrasound guidance, a 10-French (Fr) disposable cannula (Check-flo II, diameter 3.8 mm, Cook Medical, Bloomington, IN, USA) was inserted into the amniotic cavity of the twin designated for termination using the Seldinger

technique. BD was first performed as previously described until color Doppler confirmed complete cessation of perfusion.

Following BD, the 3-mm optical bipolar forceps with a mini straight-forward telescope (0°) were removed and replaced with one of two configurations: (1) A 3.3-mm curved operating sheath (11540KEK, Karl Storz GmbH, Tuttlingen, Germany) with a mini straight-forward telescope (0°, 11630AA, Karl Storz GmbH), equipped with a 3-Fr grasping forceps (11510C, 35-cm working length, Karl Storz GmbH) and a 400-µm diode laser fiber (Dornier MedTech, Wessling, Germany), or (2) A 9-Fr operating sheath (11630KF, Karl Storz GmbH) with a mini straight-forward telescope (0°, 11630AA, Karl Storz GmbH), equipped with a single working channel loaded with a 400-µm diode laser fiber (Dornier MedTech).

The laser fiber was advanced into contact with the pulseless umbilical cord. Grasping forceps were utilized for cords that were large or edematous. Laser energy at 20 W in cutting mode (Medilas®, Dornier MedTech) was applied to transect the cord from various angles, employing stepwise rotation until the ends were completely separated [26, 27].

Radiofrequency ablation (RFA)

Under ultrasound guidance, a 17-G (1.4 mm) Starburst® radiofrequency electrode and ablation system (Angiodynamics, Latham, NY, USA) was inserted into the fetal abdomen near the level of the umbilical cord insertion site. The tines were deployed, creating a 2-cm diameter sphere focused on the thermal effects. The procedure continued until the targeted area became hyperechoic, and complete cessation of perfusion was confirmed using color Doppler [28].

Peri-operative additional interventions

All patients received prophylactic antibiotics (intravenous cefazolin 2 g) and oral nifedipine (10 mg) for tocolysis half an hour before the procedure. For patients with a pre-operative cervical length of ≤25 mm and/or funneling of the internal cervical os, a McDonald cervical cerclage was performed. Uterine contractions following the procedure were managed with continuous intravenous infusion of either terbutaline or magnesium sulfate.

Statistical analyses

Descriptive statistics were applied as appropriate. Variables are presented as mean±standard deviation (SD) for normally distributed continuous variables, and as median with a 25–75 % interquartile range (IQR) for non-normally distributed variables. Statistical analysis was conducted using the two-tailed t-test or Wilcoxon rank sum test for continuous variables, depending on the distribution. Chi-square analysis was used for categorical variables. Survival analysis was employed to compare early unfavorable outcomes between groups. Multiple logistic regression was also performed. A p-value of ≤0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS 28.0.1 (Armonk, NY, USA).

Results

A total of 122 cases of *in-utero* occlusion of the umbilical vessels were identified during the study period, which included 10 LAs, 2 LTs, 60 RFAs, and 50 BDs. All LAs were performed at 14–15 weeks' gestation, with indications exclusively for discordant anomalies (8 cases of septated cystic hygroma with hydrops and 2 cases of limb-body wall complex). All LTs were conducted at 20 weeks' gestation, also for discordant septated cystic hygroma with hydrops, accompanied by knotting of the umbilical cords in monoamniotic (MA) twin pregnancies. RFAs and BDs were performed at 16–22 weeks' gestation. RFA was preferred in cases involving earlier gestation, smaller targets, oligohydramnios, and an extensive anterior placenta. The characteristics of these cases are summarized in Table 1. Transplacental placement of devices for selective reduction is a well-established risk factor for procedure-related fetal loss [29]. Therefore, there was a significant selection bias that smaller-caliber RFAs were more favored to larger-caliber BDs in cases with extensive anterior placenta (n=61) (p<0.01) (Table 1).

None of the LAs (0/10) experienced early unfavorable outcomes. One of the LTs (1/2) had technical failure, while the other (1/2) did not have any early complications. LAs and LTs were not compared with RFAs and BDs due to their relatively small sample sizes, different gestational ages, and indications for selective feticide.

All TRAPS (n=55) received RFA, with one procedure experienced technical failure. All TTTS (n=25) received BD, with one procedure experienced technical failure. Selective intrauterine growth restriction (sIUGR) (n=30) received RFA (n=5) and BD (n=25), with 1 RFA (25 %) and 1 BD (4 %) experienced technical failure (p<0.01). All four technical failure cases had extensive anterior placenta, resulting in intra-amniotic bleeding obscuring the view. There were no intraoperative events.

Pre-operative cervical length of ≤25 mm and/or funneling of the internal cervical os was observed in

Table 1: Characteristics of cases that received laser ablation (LA), laser transection of the umbilical cord (LT), radiofrequency ablation (RFA), and bipolar diathermy (BD).

Characteristics	LA (n=10)[a]	LT (n=2)[a]	RFA (n=60)	BD (n=50)	p-Value
MA (years) (median (min-max))	30 (23–35)	31 (30–32)	30 (18–42)	31 (19–40)	0.8
GA (weeks) (median (min-max))	14 (14–15)	20 (20)	20 (16–22)	20 (16–22)	0.8
Indications, %					
Discordant anomalies	10 (100)	2 (100)	0 (0)	0 (0)	N/A
TRAPS	0 (0)	0 (0)	55 (91.7)	0 (0)	<0.01*
sIUGR	0 (0)	0 (0)	5 (8.3)	25 (50)	<0.01*
TTTS	0 (0)	0 (0)	0 (0)	25 (50)	<0.01*
Extensive anterior placenta, %	5 (50)	1 (50)	45 (75)	10 (20)	<0.01*
Operative time (minutes) (min-max)	14 (10–20)	51.5 (35–68)	18 (11–40)	30 (22–50)	<0.01*
Cervical cerclage, %	0 (0)	0 (0)	0 (0)	8 (16)	<0.01*
Need for post-op intravenous tocolysis, %	0 (0)	2 (100)	5 (8.3)	35 (70)	<0.01*

∗The value means p-value ≤0.05. MA, maternal age; min, minimum; max, maximum; GA, gestational age; TRAPS, twins reversed arterial perfusion sequence; sIUGR, selective intrauterine growth restriction; TTTS, twin-to-twin transfusion syndrome; N/A, not available.

Table 2: Early procedure-related complications (exclude technical failure and pre-procedure shortening of the cervix) of cases that received radiofrequency ablation (RFA) and bipolar diathermy (BD) as per indications (sIUGR, selective intrauterine growth restriction; TTTS, twin-to-twin transfusion syndrome; N/A, not available).

	sIUGR (n=24)	TTTS (n=20)	p-Values
RFA	0	0	N/A
BD	2[a]	0	<0.01*

∗The value means p-value ≤0.05.

8/25TTTS cases; all of which received McDonald cervical cerclage. In BD cases, early complications occurred in 4/24 of TTTS (all of which had shortening of the cervix) and 2/24 of sIUGR type 2/3, respectively. After excluding technical failure and pre-procedural cervical shortening, early procedure-related complications were more prevalent among sIUGR cases ($p<0.01$) (Table 2). It was noted that both cases of sIUGR treated with BD, then suffered early procedure-related complications, had extensive anterior placenta. None of the technically successful RFA cases had early complications.

Overall, a total of 11 early unfavorable outcomes were observed during the study period, comprising 1LT, 2 RFAs, and 8 BDs. While a downward trend appears to be emerging over time, the limited sample size precluded statistical validation (Figure 2).

Discussion

The most effective procedure for *in-utero* occlusion of the umbilical vessels remains unclear. Perinatal outcomes from multi-center clinical trials are influenced by varying institutional practices. Even center-specific outcomes for *in-utero* umbilical cord occlusion are affected by differences in the proceduralists' levels of experience. The choice of selective termination procedures for complicated MC twin pregnancies is largely driven by technical considerations. Due to the smaller caliber of instruments, RFA is preferred over BD by many, especially in cases with lower amniotic fluid volume, smaller twin size, and shorter umbilical cords. Our data indicate a higher rate of technical failure in those undergoing RFA for sIUGR. Among successful procedures, early unfavorable outcomes were more frequent in cases treated with BD for sIUGR. The mechanics of the instruments and the pathophysiology of specific indications are examined to facilitate better and more personalized counseling. Even with selection bias, the negative impacts of extensive anterior placenta were observed. There was a chronological trend of improved performance, although this could not be statistically validated.

The outcomes of *in-utero* occlusion of the umbilical vessels vary across different reports, with significant differences in gestational age, indication, and procedure choice. Most commonly, BD and RFA are performed during the second trimester. A retrospective cohort of 36 RFAs and 17 BDs indicated more favorable outcomes for RFA in selective feticide cases involving sIUGR after 28 weeks of gestation [15]. Conversely, a retrospective comparison of 88 BDs and 58 RFAs showed no significant reduction in the overall complication rate with RFA [12]. Additionally, a review of 118 ultrasound-guided BDs demonstrated better outcomes when performed after 19 weeks [13]. Sun and colleagues reported that performing ≥2 cycles of RFA coagulation is the only independent risk factor for fetal death following RFA [30].

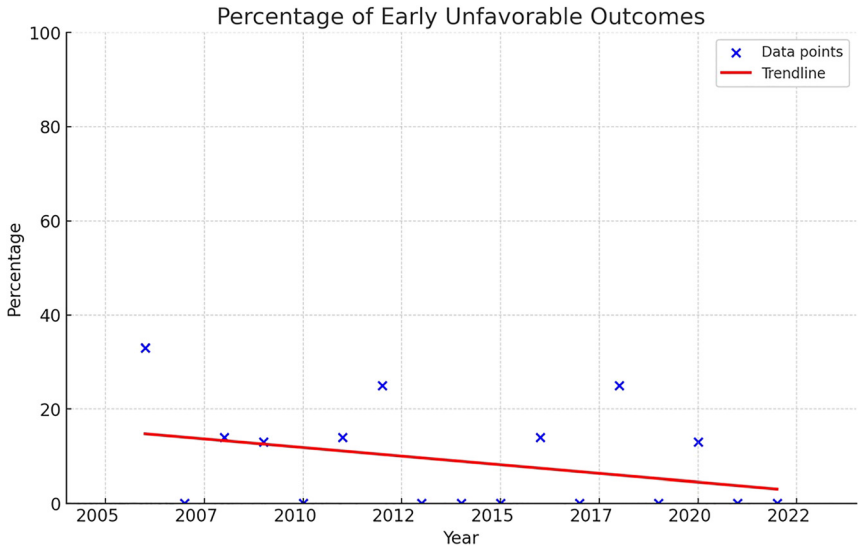

Figure 2: Trendline of early unfavorable outcomes observed during the study period.

RFA generates an alternating current at very high frequencies (200–1,200 kHz) between the tines of the probe. As the electric current alternates in different directions, tissue ions become agitated, attempting to align with the electrical field. This agitation produces frictional heat, resulting in a high tissue temperature that leads to tissue coagulation and necrosis, making RFA suitable for ablating tumors such as hepatic and thyroid. RFA has been utilized off-label to occlude the intrafetal portion of the umbilical vessels.

Bipolar diathermy, on the other hand, uses a high-frequency electric current to heat and coagulate tissue between forceps electrodes. This method eliminates energy dispersion, allowing for greater precision when treating smaller amounts of tissue, which is ideal for occluding the extrafetal portion of the umbilical vessels. However, due to the complexity of intrafetal vascular patterns, technical failure is more common in cases with branching intrafetal vessels [28]. Additionally, because the diameter of optical bipolar instruments is larger, early post-procedure complications tend to be higher [7, 14, 31].

The strength of this study lies in the single-operator setting, which eliminates interpersonal variation. However, the weakness of this study includes selection bias and limited generalizability of the outcomes. In general, all TRAPS cases were treated with RFAs, almost all sIUGR cases were treated with BDs, and early detection of discordant anomalies were treated with LAs. Due to the low complication rates of both BD and RFA in this cohort, we are unable to perform a meaningful analysis on other variables as predictors of early outcomes (insufficient power). While it is impossible to predict individual patient outcomes with certainty, these procedures should only be performed by experienced operators in the appropriate setting with the necessary tools available. The technique used for *in-utero* occlusion of the umbilical vessels should be guided by technical considerations and the individual discretion of the proceduralist. Patients should be informed of the practice-specific survival rates associated with each technique. Considering selection bias from a single-operator setting, early unfavorable outcomes of *in-utero* umbilical vessel occlusion were more commonly associated with RFA for sIUGR.

Research ethics: The study protocol was approved by the Siriraj Institutional Review Board (SIRB 704/2559 [EC3]).
Informed consent: Not applicable.
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Conflict of interest: The authors state no conflict of interest.
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Data availability: The data that support the findings of this study are available from the corresponding author [TW], upon reasonable request.

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