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Original Article

Radiofrequency ablation for selective reduction in complex monochorionic multiple pregnancies: A case series

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ABSTRACT

Objective: To determine the safety and efficacy of radiofrequency ablation (RFA) for selective fetal reduction in complex monochorionic multiple pregnancies.
Materials and methods: From July 2011 to January 2015, data on all cases treated with RFA were collected prospectively in our hospital. Indications, procedure details, cause of fetal demise and pregnancy outcomes were analyzed. Sonography and magnetic resonance imaging were performed to detect fetal brain damage. Information regarding development after birth was collected according to the Gesell Development Schedule®.
Results: There were 22 cases of twins (6 presenting with twin-twin transfusion syndrome, 10 with malformations, 4 with selective intrauterine growth restriction, and 2 with twin reversed arterial perfusion sequence); and 11 cases of triplets (9 dichorionictriamniotic, 2 monochorionictriamniotic). All surgeries were completed with one puncture. No maternal complications presented during RFA procedure, and the PPROM rate before 32 w was 9% (3/33). There were 3 cases of intrauterine fetal demise and 4 twin cases where pregnancy was terminated. The fetal survival rate was 77% (17/22) in twins, 91% (20/22) in triplets. Total fetal survival rate was 84% (37/44). The neurodevelopmental follow-up investigations showed no abnormalities in any of the survivors.
Conclusion: RFA for selective fetal reduction in complex monochorionic multiple pregnancies is effective, minimally invasive, and safe.

Introduction

In twin pregnancies, 20% are monochorionic (MC) [1]. Several complications can arise in MC pregnancies such as twin-to-twin transfusion syndrome (TTTS), twin reversed arterial perfusion sequence (TRAP), twin anemia-polycythemia sequence (TAPS) and selective intrauterine growth restriction (sIUGR), due to the vascular anastomosis on the placental surface. As a result, the perinatal morbidity and mortality in MC twins are significantly higher than in dichorionic (DC) twins [1]. In MC twins presenting with complications, selective fetal reduction has been used as a method to reduce perinatal mortality [2,3].

Injection of potassium chloride (KCl) into the fetal heart is used as a method of feticide for termination of pregnancy. However, this method is not suitable for fetal reduction in MC twins due to the transplacental passage of KCl into the co-twin and potential hypotensive damage to the brain of the surviving fetus. Therefore, the preferred method of fetal reduction in MC twins is the immediate and complete occlusion of cord blood flow. Several methods have been clinically explored to occlude cord blood flow such as: laser cord coagulation [4], cord ligation [5], bipolar cord coagulation (BCC) [6], radiofrequency ablation (RFA) [7], and recently two new methods, microwave ablation [8], and high intensity focused ultrasound [9]. A systematic review analyzing different fetal reduction techniques reported that the overall survival rate was higher using RFA (86%) and BCC (82%) compared to laser cord coagulation

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(70%) and cord ligation (72%) [3]. While BCC potentially induces a faster and more complete occlusion of umbilical vessels by the compression of bipolar forceps, compared with RFA, the procedure is more technically complicated and requires the use of an instrument with a larger diameter, resulting in higher rates of preterm premature rupture of membranes (PPROM) in BCC (28.2%) compared to RFA (17.7%) [10].

RFA works with alternating current at very high frequencies (200–1200 kHz) between the electrodes, resulting in high tissue temperatures that cause tissue coagulation and necrosis inside the targeted area. In fetal reduction, RFA can be performed using a 17 gauge (1.4 mm) needle to ablate tissue within a diameter of 2 cm, and is reported to be a safe and effective procedure with lower procedure-related risks such as PPROM and preterm delivery [11–13].

Herein we report a prospective analysis of 33 consecutive cases of RFA performed in our center on complicated MC pregnancies. We analyze indications, procedure details, and pregnancy outcomes to determine the safety and efficacy of RFA as fetal reduction technique.

Methods

Between July 2011 and January 2015 at our hospital, 33 consecutive MC multiple pregnancy cases were treated with RFA. A detailed ultrasound examination was performed to determine the status of chorionicity, placental position, malformations or abnormal growth, amniotic fluid volume, cervical length, as well as the umbilical artery and middle cerebral artery blood flow. Indications for RFA included complicated twin pregnancies such as TTTS (stage III and IV) [14], malformations, sIUGR (type II and III) [15], and TRAP (exceeding 50% of the abdominal circumference of the donor). RFA was also performed in one of the MC twins in DCTA and MCTA triplet pregnancies to reduce potential risk of preterm labor and TTTS. Patients and their families underwent detailed counseling regarding the risks of the RFA procedure, including miscarriage, preterm labor, co-twin demise and neurological or thermal injury to the surviving fetus, fetal brain MRI and the Gesell Development Schedule® [16,17] would be used for follow-up and a signed consent before RFA was obtained. The research was proved by the Hospital Ethics Committee.

To minimize the risk of procedure-related loss, oral indomethacin (25 mg) [18] and dydrogesterone (10 mg) [19] were administered prior to the RFA procedure. All RFAs were performed by the same operator and sonographer under local anesthesia. The Starburst Radiofrequency Ablation System (Angiodynamics, Latham NY) with the 1500X RF generator and 17G Starburst SDE RFA needle were used for all procedures. Under ultrasound guidance, a 17G RFA needle (12 cm in length) was used to puncture to get near to the abdominal segment of the fetal umbilical cord, avoiding placenta and amniotic sac of other fetus(es). Once the needle tip was positioned, the three electrodes were ejected to surround the abdominal segment of the cord vessels. Thermal energy with a diameter range of 2 cm was applied using the RF generator (target temperature = 110 °C, power = 30–50 W). In each 3 min long ablation cycle, all three electrode lines reached an average temperature of 100–110 °C for the duration of the cycle. If the temperature in all three electrode tines did not increase synchronously, they were retracted and the position was adjusted. During the ablation, color Doppler was used to confirm cessation of blood flow in the cord vessel (Fig. 1). In the case where multiple ablations were required, there was a cool-down interval of 1 min between ablation cycles. Ultrasonography was performed to confirm cardiac asystole in the targeted fetus.

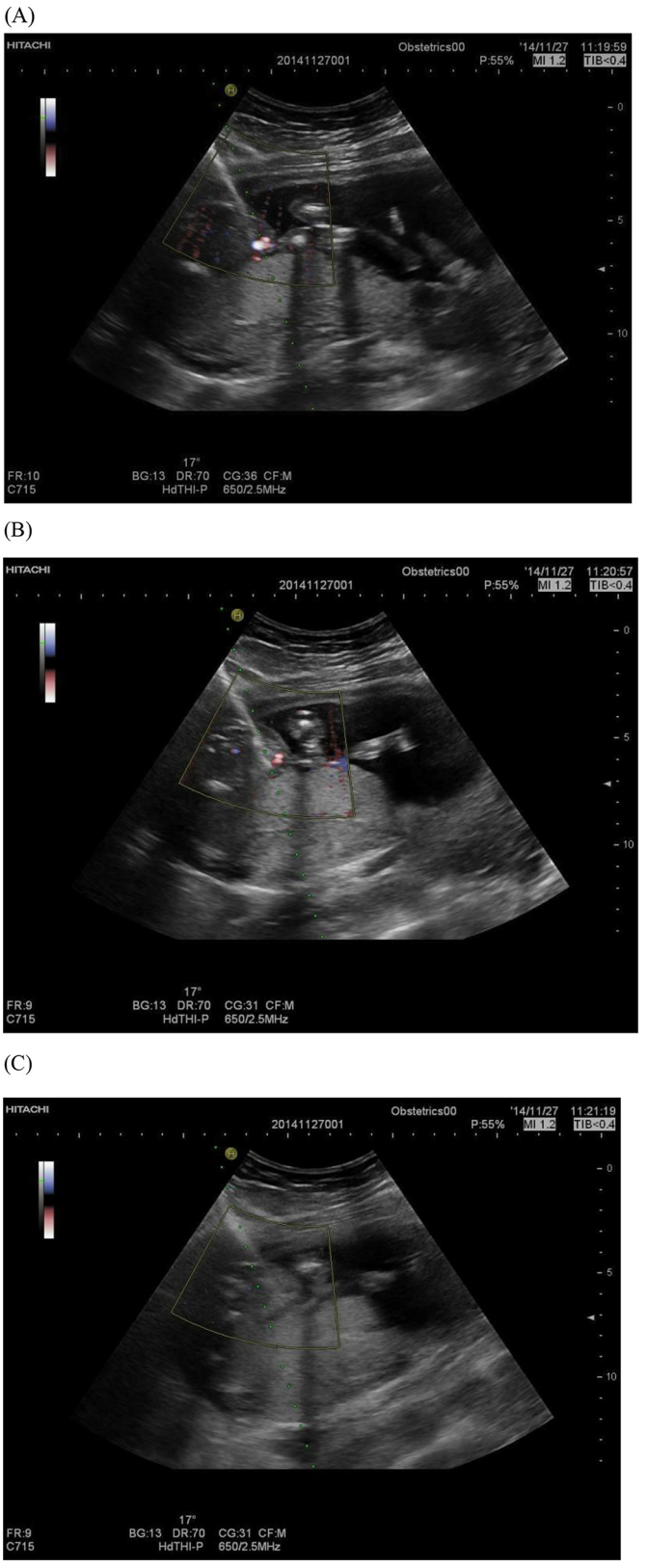

Fig. 1. Color Doppler flow change of the umbilical vessels showing at the beginning (A), during (B), and after (C) RFA procedure.

Following the RFA procedure, patients were administered 10 ml of 25% magnesium sulfate intravenously to prevent uterus contraction and kept in the hospital for further observation. An ultrasound scan was performed 24 h after the procedure to evaluate the surviving fetus, placenta, amniotic fluid volume, S/D of the umbilical artery and middle cerebral artery peak systolic velocity (MCA-PSV). Further ultrasounds were performed every two weeks following the RFA. Hypotensive brain damage such as porencephaly, ventriculomegaly, leucomalacia were investigated via MRI 4 weeks after the procedure, or at 24 w in the cases where RFA was performed earlier than 20 w. A 1.5-T MR scanner (Magnetom A Tim+Dot system, Siemens, Germany) with an 8-channel phased-array body coil and respiratory gating was used to examine all fetuses. Scanning protocols included: standard three-plane location of the fetal brain, three orthogonal planes T2-weighted imaging (T2W1) using a half-fourier acquisition single-shot turbo spin-echo sequence with fat suppression, and axial T1-weighted imaging (T1W1) using a fast low angle shot sequence with fat suppression. The follow-up interview was carried out using the Gessel Development Schedule revised by the Beijing Intelligence Development Group [16,17] at 6th month, 12th month or 36th month by a neonatologist. The information of adaptive behavior, gross motor performance, fine motor movement, language development and individual social behaviors were collected. Scores of 70–84 indicate moderate delay; scores of <70 indicate severe delay. A score of 84 is the cutoff point for determining normal and developmental delay.

Results

The patient characteristics and pregnancy outcomes following RFA are detailed in Table 1. RFA was performed in 22 cases of twins presenting with complications, including 6 TTTS cases (4 stage III and 2 stage IV), 10 malformation cases (9 MCDA, 1 MCMA), 4 sIUGR cases (type II constant absent/reverse end-diastolic flow and type III, intermittent absent/reverse end-diastolic flow in the umbilical artery), and 2 TRAP cases. RFA was also performed on 9 cases of DCTA triplets and 2 cases of MCTA triplets. All procedures were completed at an average gestational week of 20.2 ± 3.8 w (ranging 14^{+5}w to 27^{+2}w) with one surgical puncture. Only one ablation cycle was needed for complete cessation of blood flow in 26 cases, two ablation cycles were needed in 6 cases (26^{+2}w and 20^{+6}w TTTS, 27^{+2}w TRAP, 23w sIUGR, 14^{+5}w and 16^{+4}w DCTA), and three cycles were needed in a DCTA case (16^{+4}w at intervention and experienced IUFD of the co-twin within 24 h). In one TRAP case, drainage of 200 ml of fluid inside the body cavity was performed prior to RFA, otherwise, no additional procedures such as amnioreduction or amnioinfusion were performed. No maternal complications were reported during the procedure.

Intrauterine fetal demise (IUFD) of the co-twin occurred in three patients postoperatively. One co-twin IUFD case was determined 10 h after the RFA in a MCMA gastroschisis case. The other two co-twin IUFD cases were found in two DCTA triplet cases at 24 h and 6 weeks post procedure respectively. Four twin cases underwent termination of pregnancy (TOP), which decided by the parents for

Table 1
Characteristics and pregnancy outcomes of 33 radio frequency ablation (RFA) cases.

Case	Age	Mode of conception	Amnionicity	Indication	GA(w) at RFA	Ablation cycles	Delivery (VD/CS)	GA(w) at delivery	Outcome birth weight	Gessel score of survivors (age of test)[b]
1	25	natural	MCDA	TTTS III	23^{+1}	1	CS	31^{+6}	2200 g[a]	90 (3y)
2	26	natural	MCDA	TTTS III	25^{+2}	1	VD	38^{+3}	2200 g	85 (3y)
3	33	natural	MCDA	TTTS III	20^{+6}	2	CS	39^{+1}	2700 g	87 (1y)
4	34	IVF-ET	MCDA	TTTS III	18^{+2}	1	TOP for PROM and fever at 30^{+4}w			
5	31	natural	MCDA	TTTS IV	25^{+3}	1	CS	32^{+1}	1750 g[a]	80 (1y)
6	28	natural	MCDA	TTTS IV	26^{+2}	2	VD	39	3240 g	92 (6m)
7	24	natural	MCDA	sIUGRII	24^{+2}	1	CS	37	3120 g	98 (1y)
8	27	natural	MCDA	sIUGRII	26^{+1}	1	CS	36^{+2}	2600 g	77 (6m)
9	25	natural	MCDA	sIUGRII	18^{+5}	1	VD	39^{+2}	3500 g	96 (6m)
10	31	natural	MCDA	sIUGRIII	23	2	TOP for PROM at 26 w			
11	27	natural	MCMA	gastroschisis	17^{+3}	1	IUFD (within 10 h postprocedure)			
12	25	natural	MCDA	anencephalus	16	1	VD	34^{+2}	2850 g	90 (3y)
13	25	IVF-ET	MCDA	anencephalus	17^{+4}	1	CS	38^{+5}	2900 g	88 (3y)
14	29	natural	MCDA	anencephalus	17^{+5}	1	VD	41^{+1}	3650 g	100 (3y)
15	27	natural	MCDA	anencephalus	20^{+3}	1	VD	39^{+2}	3350 g	96 (1y)
16	35	natural	MCDA	anencephalus	21^{+4}	1	TOP for continuous bleeding at 25w			
17	30	natural	MCDA	muti-deformities	16^{+5}	1	VD	38^{+3}	3200 g	89 (1y)
18	26	natural	MCDA	muti-deformities	20	1	CS	39^{+3}	3100 g	94 (1y)
19	32	natural	MCDA	Limb deficiency	24^{+3}	1	VD	36	2840 g	103 (6m)
20	30	natural	MCDA	Limb deficiency	26^{+5}	1	VD	35^{+5}	2300 g	90 (6m)
21	30	natural	MCDA	TRAP	22^{+4}	1	TOP for maternal asthma at 25^{+4}w			
22	25	natural	MCDA	TRAP	27^{+2}	2	VD	31	1350 g[a]	89 (3y)
23	24	IVF-ET	DCTA	DCTA	14^{+5}	2	CS	37^{+3}	3170/2930 g	92/97 (3y)
24	33	IVF-ET	DCTA	DCTA	15^{+2}	1	CS	36^{+4}	2500/3000 g	95/97 (3y)
25	36	IVF-ET	DCTA	DCTA	16^{+3}	1	VD	37w	1 IUFD (within 9w)/3050 g	95 (3y)
26	30	IVF-ET	DCTA	DCTA	16^{+4}	3	VD	37^{+6}w	1 IUFD (inside 24 h)/2900 g	88 (1y)
27	21	natural	DCTA	DCTA	18^{+4}	1	CS	37^{+1}	2400/2160 g	86/88 (yy)
28	30	Ovulation induction	DCTA	DCTA	18^{+4}	1	CS	38^{+6}	2800/2500 g	88/92 (1y)
29	30	natural	DCTA	DCTA	18^{+6}	1	CS	39	2950/2000g	92/90 (1y)
30	38	IVF-ET	DCTA	DCTA	17^{+5}	1	VD	37^{+5}	1950[a]/1700 g[a]	93/88 (1y)
31	33	IVF-ET	DCTA	DCTA	16^{+4}	1	CS	37^{+1}	2650/2450 g	103/93 (1y)
32	24	natural	MCTA	MCTA	18^{+1}	1	VD	35^{+2}	2250/2300 g	96/90 (6m)
33	33	Ovulation induction	MCTA	MCTA	18^{+4}	1	CS	38^{+6}	2800/2500 g	90/85 (6m)

GA, Gestational age; MCMA, monochorionicmonoamniotic; DCTA, dichorionictriamniotic; MCDA, monochorionic diamniotic; MCTA, monochorionictriamniotic; TRAP, twin reversed arterial perfusion; TTTS, twin-to-twin transfusion syndrome; TOP, termination of pregnancy; sIUGR, selective intrauterine growth restriction; CS, cesarean section; VD, vaginal delivery.

[a] Neonates hospitalized for preterm birth or low birth weight.

[b] Children were tested at 3 years old, or at 1 year old or 6 months old if younger than 3.

Table 2
Indications and fetal survival rate following radiofrequency ablation (RFA).

Indications	Number of cases	PROM	Delivery<32 w	Delivery32-35^{+6}w	Fetal loss	Fetal survival rate
Twins	**22**	**3**	**2**	**4**	**5**	**77% (17/21)**
MCDA TTTS	6	2	1	1	TOP	83% (5/6)
MCDA sIUGR	4	1			TOP	75% (3/4)
MCDA malformation	9			2	TOP	89% (8/9)
MCMAmalformation	1				IUFD	0% (0/1)
TRAP	2		1		TOP	50% (1/2)
Triplets	**11**	**0**	**0**	**1**	**2**	**91% (20/22)**
DCTA fetal reduction	9				2 IUFD	89% (16/18)
MCTA fetal reduction	2			1	0	100/100% (4/4)
Total	**33**	**3**	**2**	**5**	**7**	**84% (37/44)**

MCMA, monochorionicmonoamniotic; DCTA, dichorionictriamniotic; MCDA, monochorionic diamniotic; MCTA, monochorionictriamniotic; TRAP, twin reversed arterial perfusion; TTTS, twin-to-twin transfusion syndrome; TOP, termination of pregnancy; IUFD, intrauterine fetal demise.

fear of the negative prognosis of the fetus. One case presenting with sIUGR underwent TOP at 26 weeks due to PPROM. One MCDA anencephalus case underwent TOP at 25 weeks due to continuous vaginal bleeding. One case of TTTS underwent TOP at 30^{+4}w due to PPROM and high fever. One TRAP patient underwent TOP 17 days following RFA due to the exacerbation of maternal bronchial asthma at 25 w.

All patients with ongoing pregnancies were examined for MCA-PSV 24 h post RFA procedure, and 28 patients were recruited for fetal brain MRI to detect fetal brain damages. One case of mild ventriculomegaly (1.2 cm) was found in a sIUGR case, and appeared to be stable at 0.6–0.7 cm in a follow up ultrasound. Otherwise, no abnormalities in the MCA-PSV or the fetal brain MRI were detected.

The survival rates following RFA are detailed in Table 2. Twenty eight cases (85%) reached delivery with at least one survivor, and the average gestational age at the time of birth was 36.9 ± 2.6 w (range 31–41^{+1}w). In twins, the fetal survival rate was 77% (17/22), whereas in triplets it was 91% (20/22). Twenty one cases underwent delivery after 36 w, five cases delivered between 33 and 35^{+6}w, and 2 cases delivered between 31 and 32 w (1 TTTS case and 1 TRAP case). The overall fetal survival rate for all fetuses was 84% (37/44). There was no neonatal death and five neonates (born before 34 w) were hospitalized for preterm birth or low birth weight. According to the follow-up interview, no abnormalities or retardation were observed in all survivors.

Discussion

RFA has been used for selective fetal reduction in complicated multiple pregnancies, Kumar et al. reported a live birth rate of 78% following RFA in monochorionic pregnancies [11]. RFA is the preferred method of fetal reduction for TRAP cases presenting with a larger volume (>50% of the abdominal circumference of the donor). Lee et al. reported a survival rate of 92% in 98 TRAP cases using RFA [20,21]. Advantages of RFA include its procedural simplicity, reduced trauma to the membranes, and fewer additional intraoperative procedures such as amnioinfusion or amnioreduction, all while providing similar pregnancy outcomes as bipolar cord coagulation [18,22,23]. A meta analysis by Gaerty analyzed 17 publications with 481 cases of bipolar cord occlusion and 320 cases of RFA treatment in MC twin pregnancies, and the overall survival rate was found to be similar, 76.8% and 79.1% respectively [10]. In this study, the overall survival rate after RFA was 84%, 77% in complicated MC twins, and 91% in DCTA and MCTA triplets. The reason of a better performance may lie in two points: experiences of the operators with hundreds of fetal reduction with potassium chloride [24]; and the triplet cases without complications took a greater proportion of 33% (11/33) in this series, which is 14.4% (46/320) in Gaerty's analysis [10].

Fetoscopic laser coagulation is the primary choice for treatment in cases presenting with stage II-IV TTTS, and it also provides improved long-term neurological outcomes [24]. Since fetoscopic laser surgery was not available in our center, six cases of TTTS (stage III-IV) received RFA treatment to save one fetus and were included in this series. Although the literature reported that selective termination of donors *versus* recipients does not affect neonatal outcomes of the co-twin [3], we chose to terminate the smaller and Oligohydramnios donor twin due to its thinner umbilical cord and ease of access.

More than one ablation cycle was needed to achieve total blood flow occlusion in 7 cases. In the 27^{+2}w TRAP case, thick umbilical cord accounted for the reason. While in other cases, due to the thick abdominal wall and movements of the fetus, the position of the three electric tines was difficult to be perfect to surround the target vessels, and was then readjusted when one ablation cycle failed.

Following invasive fetal interventions, PPROM and preterm delivery are the most common complications and major risk factors for adverse perinatal outcome [24]. Thermal injuries to the mother or fetus have also been reported following RFA [7,13,21]. In the present study, no maternal or fetal thermal damage was observed and the PPROM rate before 32 w was 9% (3/33).

Rates of IUFD of the co-twin following RFA treatment has been reported to be 15%, and to occur more frequently within the first two postoperative weeks [3,10] In the present study, the IUFD rate was 7% (3/44), with two cases presenting within 24 h. Typically during RFA, the heartbeat of the fetus disappears approximately 30 min after cessation of umbilical blood flow [6]. However, in the case of MCMA gastroschisis, the heartbeat ceased simultaneously with the cord blood flow after one ablation cycle, and the co-twin died within 10 h. For MCMA cases, cord transection was suggested to avoid cord entanglement [5], but this technique was not available in our center. Due to the protrusion of abdominal contents, the distance from the RFA needle tip to the fetal heart was much closer than normal in the MCMA case. We speculate that the cardiac arrest was induced by ablation energy before the cessation of the cord blood flow, and subsequent exsanguination through the cord vessel lead to the co-twin demise thereafter. In a DCTA case that required three ablation cycles to achieve complete blood flow cessation, IUFD at 18^{+2}w occurred within 24 h after RFA treatment. This IUFD case supports the hypothesis that slower occlusion of the umbilical vessel may increase the risk for IUFD by altering blood flow patterns [5,10], which need to be testified by large scale research. More ablation cycles are typically needed at later gestation or when the umbilical cord is thick [13]. There was another case of a DCTA co-twin IUFD, however the cause was not determined since the parents refused autopsy following delivery.

Ultrasound and fetal brain MRI can identify hypotensive brain injury, such as porencephaly, ventriculomegaly, leucomalacia, and necrosis of the corpus callosum [5]. Kumar et al. reported three

cases of brain damage following RFA: schizencephaly, bilateral pseudocysts adjacent to the lateral cerebral ventricles, and severe ventriculomegaly [11,13]. In our study fetal brain MRI following RFA only showed mild ventriculomegaly in one case, which turned to be 0.6–0.7 cm in follow up scans. In the developmental follow-up, no abnormalities or retardation was found in all survivors and the parents were satisfied with the outcome. However, long-term follow-up using a controlled and standardized developmental scoring system should be implemented [25,26].

In this study, we achieved a delivery rate with at least one survivor of 85% and total fetal survival rate of 84% following RFA, without developmental retardation after birth. We conclude that RFA is a minimally invasive, safe, and reliable technique for selective fetal reduction in complex MC multiple pregnancies especially in a center without fetoscopy.

Conflicts of interest

The author(s) have no conflicts of interest relevant to this article.

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