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Original Article

Foetal Heart Rate Pattern after Complete Cord Occlusion by Radiofrequency Ablation for Selective Reduction in the Complicated Monochorionic Twin Pregnancies

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Abstract

Background: The purpose of the present study was to assess foetal heart rate (FHR) pattern after complete cord occlusion by radiofrequency ablation (RFA) for selective reduction in the complicated monochorionic twin pregnancies. **Materials and Methods:** A prospective cohort study was done at an Iranian Hospital in 2016–2017 on 85 pregnant women candidate for selective reduction by RFA. Umbilical vein was cauterised two times (power 100 Watt) for 2 min. Cease of blood flow was confirmed by colour Doppler and FHR was recorded. Then, the pattern of FHR after cord blood occlusion was assessed and recorded with certain intervals until cardiac asystole. **Results:** Of all 85 participants who entered the study, 59 cases with normal heart echocardiography were eligible. After about 4-min post-RFA, FHR steeply dropped to <80 beats/min. In 10 min, FHR deceased to about 60 beats/min, and in 20 min, it reached to 40 beats/min. At the 15th min after RFA, the majority of foetuses and at 85th min, all the foetuses showed cardiac asystole. **Conclusion:** We found that about 4 min after complete cord occlusion by RFA, FHR steeply decreased to problematic ranges. Our results indicated that in similar conditions such as foetal hypoxia and time for rescuing of foetus was too limited. Moreover, it is supposed that such a pattern of heart rate in preterm foetuses may be presented in terms, so tight monitoring of FHR trend, presence of an expert surgery team and advanced hospital facilities seems necessary.

Keywords: Asystole, foetal heart rate, radiofrequency ablation, selective reduction, twin pregnancy

Introduction

Monochorionic-diamniotic twin pregnancy as a high-risk condition affects twin and high-order pregnancies. The perinatal mortality and morbidity in these types of pregnancies were reported extremely high due to vascular anastomoses and connections between foetal circulations. Twin-to-twin transfusion syndrome (TTTS) with frequency of 9% is responsible for the main cause of foetal death (90%). Foetal growth restriction, severe malformations, twin anaemia-polycythaemia sequence, twin reverse arterial perfusion, early preterm labour and premature delivery are other causes of mortality and morbidity in monochorionic-diamniotic twin pregnancy.[1-5]

Intrauterine foetal death (IUFD) of one twin in the first and second trimesters threatens co-twin's life by 12%–15%. Selective termination of a single foetus in monochorionic twins protects surviving co-twin from back-bleeding through the vascular anastomoses and significant hypotension resulting neurologic injuries and precipitate death.[6] These findings demonstrate unique challenges for the performance of selective foetal reduction by ablating blood flow, usually in the umbilical cord and achieve asystole in the selected monochorionic pregnancy.[3,7]

Compression of the umbilical cord with a thin wall-flexible umbilical vein (stimulating sympathetic response) and two thick wall-resistive arteries (stimulating parasympathetic response) causes autonomous system imbalance resulting marked acidosis, hypercapnia, progressing hypotension, cerebral hypoperfusion and pronounced tissue hypoxia. These

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profound alterations injury vital organs such as heart resulting recurrent heart rate decelerations, loss of accelerations and decreased variability.[8,9]

There are some effective procedures for selective feticide in complicated monochorionic twin pregnancies with a survival rate of 70%–83% and a normal development rate in 92%. Bipolar cord coagulation, laser cord coagulation, cord ligation and radiofrequency ablation (RFA) were performed that can effectively occlude blood supplying the targeted twin to survive and protect the co-twin.[5,10-12] RFA has been used recently in selective foetal reduction as a minimally invasive and percutaneous treatment technique, safe and efficient with good outcomes.[11,13,14]

There have been some studies over the past few years looking at selective reduction procedures, their own surgical techniques, outcomes and other cons and pros. On the other hand, there remains a crucial paucity on information regarding foetal heart rate (FHR) pattern after such procedures. The purpose of the present study was to assess FHR pattern after complete cord occlusion by RFA for selective reduction in the complicated monochorionic twin pregnancies.

Materials and Methods

A pilot, cohort, prospective study was done at Yas Hospital affiliated to Tehran University of Medical Sciences (Tehran-Iran) from December 2016 to August 2017. Our hospital is a referral centre for complicated monochorionic twin pregnancy in Iran. The study population consisted of 85 pregnant women with complicated monochorionic pregnancies who referred from all over the country as candidates for selective reduction by RFA.

The inclusion criteria were gestational age of 16–26 weeks, monochorionic complicated pregnancies with severe TTTS (Stages 2 and 3), selective intrauterine growth restriction (IUGR) Type II and III; foetal growth less than 10th percentile for weight of foetuses or difference in foetuses' weight > 25% and to persistent and intermittent absent or reversed end-diastolic flow in the umbilical artery Doppler waveform pattern, foetal major structural anomaly in each twin, as well. In TTTS cases, RF was performed for the twin with lower weight. Exclusion criteria included monochorionic acardiac foetuses and any heart abnormality diagnosed by echocardiography.

After performing all prenatal care and tests including ultrasound examination, aneuploidy screening test, amniocentesis (if there was its indication), anomaly scan and echocardiography, pregnant women who met inclusion criteria underwent selective reduction using RFA. All demographic and clinical data related to maternal age, gravid, parity, underlying diseases, gestational age, foetal weights, echocardiographic results and doppler indexes were recorded.

Technique

Before any procedure, all steps and related risks including miscarriage, preterm labour, the probability of any morbidity and mortality in co-twin were explained for eligible participants, then written consent forms were obtained. The day before operation another ultrasound examination was performed by an expert perinatologist to confirm RFA indication, biometric assessment including estimation of foetal weight, amniotic fluid volume and Doppler study. One-hour pre-operation medications including 50 mg indomethacin suppository, 1 g oral amoxicillin and 50 mg promethazine were prescribed. Before RFA procedure, another ultrasound examination was done to monitor and record FHR and Doppler study.

RFA procedure was performed by the same perinatologist using radiofrequency (RF) generator; RF um 2004 (manufactured by RF Medical Co., South Korea). Using lidocaine solution, the site of RF needle insertion was locally disinfected and anaesthetised. Under continuous ultrasound and colour Doppler guidance, the site of intra-abdominal umbilical vein was determined, then the RF simple needle (Gage 17 and 2 cm exposed tip) was inserted [Figure 1]. Umbilical vein was cauterised (power 100 Watt) for 2 min [Figure 2]. Cease of blood flow was confirmed by colour Doppler and FHR was recorded. If the blood flow was not stopped, the procedure was repeated and FHR was recorded as zero point. Then, the pattern of FHR was assessed with certain intervals (2 min in the first 10 min then every 5 min) until cardiac asystole. All patients were followed up for 24 h. The perinatologist evaluated remained co-twin by ultrasound examination the day after procedure; FHR was checked and foetal middle cerebral arterial peak systolic velocity measurements were also performed.

The study protocol was approved by the Ethics Board of the Tehran University of Medical Sciences (Registration number: IR. Tehran University of Medical Sciences [TUMS]. MEDICINE. REC.1396.4229).

Statistical analyses

All statistical analyses were conducted using Stata 12 software. Data cleaning and data exploration were performed. Results were presented as mean ± standard deviation for continuous

Figure 1: Radiofrequency simple needle.

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variables and n (%) for categorical variables. Spearman's, Mann–Whitney and Pearson Correlation tests were used to analyse the relationships between variables. $P < 0.05$ was used as statistical significance. With the proposed sample size of 59, the study had a power of 80% and an alpha error of 0.05.

Results

Of all 85 participants who entered the study, 4 cases were excluded due to foetal acardia and 9 nine cases were excluded due to heart abnormality. Moreover, 9 other cases exited due to post-RF procedure co-twin's anaemia (2 cases) and IUFD (7 cases). Of 7 IUFD cases, two of them were triplet gestations. Of dichorion-triamniotic triplets, one case, who was monochorionic, entered the study as an RF candidate (selective IUGR).

The mean age of 59 multifoetal pregnant women was 28.57 ± 5.28 (minimum 20 and maximum 42) years and the most of them were nuli and primipara (77.8%). The mean of gestational age was 20.54 ± 2.23 weeks. Detailed demographic data are shown in Table 1. Indications of RF procedure were as shown below: foetal anomaly in 16 cases (25.4%), selective IUGR in 24 (38.1%) and TTTS Stage 2 and 3 in 19 (30.2%). Except for 4 cases with missing data, all 59 foetuses had normal heart echocardiography, mean weight was 275.89 ± 133.52 g. Thirty-three cases (55%) had absent and reversed umbilical artery pattern (selective IUGR and TTTS).

The mean asystole time was 32.19 ± 21.84 min. FHRs follow-up with certain intervals after RFA was done (22 times for the longest cardiac asystole occurrence). Based on the results, after about 4 min, FHR steeply dropped to <80 beats/min. In 10 min, FHR deceased to about 60 beats/min and after 20 min, it reached to 40 beats/min. Trend of FHR declined until cardiac asystole is shown in Figure 3. At the 15th min, the majority of foetuses and at 85th min, all the foetuses showed cardiac asystole; the trend of cardiac asystole is also shown in Figure 4. Mean time of asystole was not significantly different between cases with normal and abnormal umbilical cord Doppler (39.00 ± 19.81, 35.09 ± 22.13; $P = 0.417$). Moreover, no relationship was observed between the time of asystole and MCA in remained twin that was evaluated after 24 h by ultrasound examination.

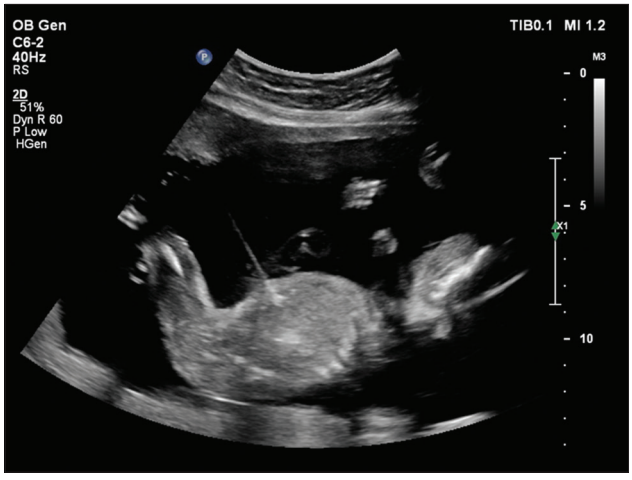

Figure 2: Needle of Radiofrequency in fetal abdomen cross umbilical vein.

Discussion

In the present study, we performed RFA for selective foetal reduction in complicated monochorionic pregnancies with

Table 1: Demographic data of participants and their foetuses

Variables	Minimum	Maximum	Mean±SD
Gravida			
1; 18 (28.65%)	1.00	5.00	2.1525±1.04739
2; 23 (36.5%)			
3; 10 (15.9%)			
4; 7 (11.1%)			
5; 1 (1.6%)			
Para			
0; 22 (34.9%)	0.00	3.00	0.8475±0.82657
1; 27 (42.9%)			
2; 7 (11.1%)			
3; 3 (4.8%)			
Abortion			
0; 45 (71.4%)	0.00	3.00	0.2881±0.58871
1; 27 (42.9%)			
2; 7 (11.1%)			
3; 3 (4.8%)			
AC* (cm)	87.00	195.00	135.8644±27.16264
Weight (g)	110.00	712.00	275.8966±133.52057
Before RF** MCA	20.00	37.00	26.4915±2.96748
Before RF FHR	125.00	165.00	147.2712±9.52462
After RF MCA	22.00	29.00	25.2000±3.11448

*Abdominal circumference; **RF. SD: Standard deviation, FHR: Foetal heart rate, Middle cerebral arterial, RF: Radiofrequency

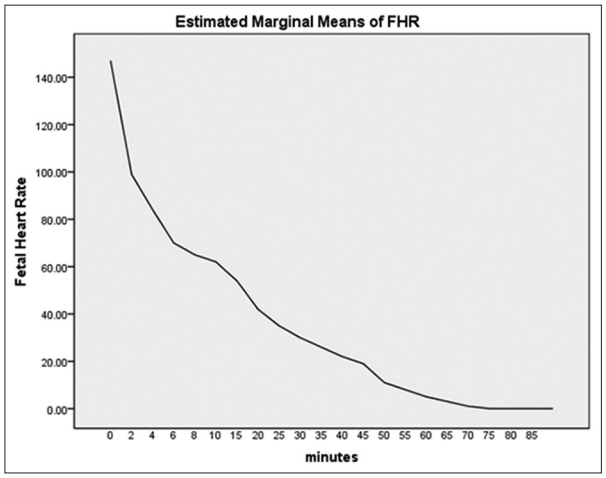

Figure 3: Pattern of foetal heart rate after radiofrequency ablation with certain intervals until cardiac asystole is shown; at the beginning of radiofrequency ablation procedure, the mean foetal heart rate started to decline and after 4 min, it reached to 80 beats/min and continued to zero at 85th min post-procedure initiation.

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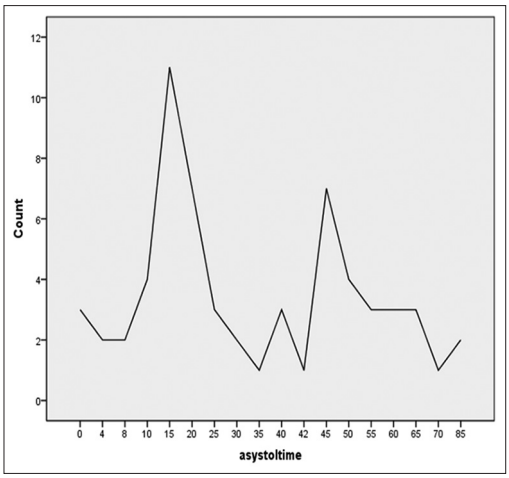

Figure 4: Trend of cardiac asystole in participants after radiofrequency ablation; at 15th and 50th min, the majority of patients and at 85th min, all the participants showed cardiac asystole.

survival rate 78%–86% as the most successful and reasonable option.[12,15,16] Although few studies have investigated effects of cord compression and hypoxia on foetal circulation in animal models, our study is the first study from Iran which assessed the heart rate pattern in the human model of the preterm foetus, after RFA for selective reduction. To the best of our knowledge, very few studies from other countries have also focused on this subject.[13]

Evaluation of FHR pattern after umbilical vessels occlusion in complicated monochorionic pregnancies provided a unique opportunity to predict and generalise foetal physiologic responses to some real high-risk situations such as foetal hypoxia, cord compression, umbilical cord hematomas, true cord knots and cord stricture resulting FHR abnormalities. Prolonged FHR deceleration was also imitated with some maternal complications including uterine rupture, placenta abruption maternal apnoea during a convulsion, cardiac arrhythmia, maternal cardiac arrest and cessation of maternal circulation.[6] It is notable that the induction of hypoxic conditions and assessment of its long-lasting effects in human subjects, particularly in the term foetuses were not possible and ethic; consistent to our finding, Cunningham *et al*. showed similar pattern of the FHR (abrupt, jagged-appearing and constant deceleration) in experimental animal models after complete occlusion of the umbilical cord.[17] Another main strength of our study was recording foetal heart pattern after cord blood occlusion. We supposed that in term foetuses such as the preterms, this trend of bradycardia during complete cord blood occlusion may demonstrate a limited golden time from decision to delivery for supportive measures and improvement foetal surveillance in such critical conditions. Based on the results, we found that in preterm foetuses after about 4 min, FHR steeply dropped to <80 beats/min. In 10 min, FHR deceased to about 60 beats/min and after 20 min, it reached to 40 beats/min [Figure 3]. Cunningham *et al*. confirmed that FHRs <80 beats/min are associated with problematic conditions such as loss of beat-to-beat variability, foetal acidaemia and inevitable foetal compromise.[17] This finding was also confirmed by Gabbe *et al*., they proposed that perimortem caesarean delivery should be performed before 4 min after maternal cardiac arrest, if resuscitation procedure was not successful and maternal circulation was not restored.[6] It seems that tight monitoring of FHR trend for foetuses that are vulnerable to hypoxia and its related complication (such as uterine rupture condition) helps in sooner diagnosis and timely treatment.

In the present study, we assessed and recorded the trend of cardiac asystole in 59 cases after RFA procedure; success rate in using RFA for foetal reduction was 100%. Repeated RFA procedure disrupts normal foetal circulation and oxygenation resulting inefficient oxidative phosphorylation, anaerobic metabolism, lack of adenosine triphosphate reserves, inadequate energy state, accumulation of lactic acid, acidosis, failed sodium–potassium pumps, cell injury, vital organ failure and finally foetal death.[18] In accordance to our finding, Paramasivam *et al*. demonstrated 100% success rate with no maternal morbidity in using RFA for 35 monochorionic pregnant patients who underwent selective foetal reduction.[3] On the other hand, Smok *et al*. demonstrated some potential of failure rate in occlusion of the umbilical vessels and bleed-back phenomenon after RFA procedure. Distorted cord insertion site and incorrect needle placement due to the enlarged foetal bladder were reported as responsible factor for increasing failure rate.[19]

The mean intrauterine asystole time was 32.19 ± 21.84 min. At 15th min, many of the foetuses (18.64%) and at 85th min, all the foetuses (100%) showed cardiac asystole [Figure 4]. An investigation by Li *et al*. indicated that stopped heart beating in 1, 3 and 2 cases were observed after 10, 35 and 3–7 min, respectively, after RFA.[13] It seems that this difference between the times of RFA procedure and cardiac asystole may relate to the numbers of sample size.

It was notable that after RFA, we excluded all IUFD or anaemic survivor co-twins from the study. It seems that IUFD patients were cases with stuck twin or cases who exposed to some technical complications due to foetal malposition and cord accessibility. We supposed that incomplete closure of the umbilical vein and blood leakage to selected foetus for RFA can affect on trend of cardiac asystole. Foetuses with heart abnormality, patients with TTTS Stage 4 as well as twins with higher weights were also excluded to omit the influences of such complications on cardiac asystole.

Our study had some limitation. Foetal age at the time of selective foetal reduction could be a confounder[20] due to its strong correlation with the maturation of cardiac neurohumoral control mechanisms. On the other hand, we were not able to evaluate our participants in narrower ranges of gestational age because of small sample size. Therefore, these points are strongly suggested in the future research. Moreover, with a larger sample size, it is possible to investigate the correlation

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between FHR alteration of a single foetus in monochorionic twins and the probability of anaemia and IUFD occurrence in surviving co-twin. Although in the present study, we did not report results related to survived co-twin's outcome, we followed our participants and relevant information will be provided in the future study.

Conclusion

We found that in preterm foetuses, about 4 min after complete cord occlusion by RFA, FHR steeply decreased to problematic ranges (<80 beats/min). After 10 min, FHR deceased to 60 beats/min and 20 min later, it reached to 40 beats/min. Our results may indicate that for rescuing foetus in hypoxic conditions such as cord compression, maternal foetal circulation arrest and complete placenta abruption; time was too limited. Hence, tight monitoring of FHR trend, presence of an expert surgery team and advanced hospital facilities seem necessary. This sooner diagnosis, decision-making and treatment can also protect the physician from consequent legal complications.

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Conflicts of interest

There are no conflicts of interest.

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