Radio frequency ablation in complicated monochorionic multiple pregnancy: prediction of perinatal outcome and comparison of two different needle insert angles

Qian Liu[1], Xiaomei Shi[1], Liyuan Fang[2], Tengzi Rao[2], Lishuang Shi[3], and Jing Wu[1]

[1]Guangdong Women and Children Hospital
[2]Guangdong Women and Children Hosplital
[3]Guangdong Women and Children Hosplital

April 28, 2020

Abstract

Objective To assess the risk factors for adverse pregnancy outcome in the RFA selective reduction procedure for complicated multiple pregnancies and to compare the pregnancy outcomes between two radio frequency needle insert angles, abdominal and dorsal insert angle. Methods In order to retain at least one fetus, 145 pregnant women with complicated monochorionic multiple pregnancy chose radio frequency ablation to do selective reduction. Compare the procedure characteristics and pregnancy outcomes of the two different needle insert angles groups by SPSS 21.0. Results The RFA procedure in 145 complicated monochorionic multiple pregnancies were all conducted successfully, 116 cases through abdominal insert angle, and 29 cases through dorsal insert angle. Cox regression analysis indicated that the survival curve of fetal survival time interval after the procedure between the two needle insert angles were statistically different(P<0.001), with two significant predictors, cervical length (RR=0.969, P=0.043) and the gestational age before the procedure (RR=1.205, P<0.001) . Multivariable logistic analysis showed that compared to live birth at term, the risk of miscarriage,termination and IUFD were statistically higher when the cervical length was less than 35mm(P<0.001).Even though the survival rate was non-significant different within the indications(P=0.623), the pregnancy with live born fetus showed a higher trend in IUGR &TTT(90.9%) than other indications. Conclusion The interval between RFA to delivery specific survival curve showed a significant improvement with the abdominal needle insert angle compared with dorsal insert angle. The cervical length and gestational age before RFA procedure were two risk factors about the adverse pregnant outcome.

Introduction

Monochorionic(MC) multiple pregnancies especially twin pregnancies, may be complicated by specific and serious complications, such as selective intrauterine growth restriction(sIUGR), twin-twin transfusion syndrome(TTTS), twin reversed arterial perfusion(TRAP), discordance for structural anomalies and twin anemia polycythemia sequence(TAPS). Untreated complicated MC multiple pregnancies disease may result in higher perinatal morbidity and mortality[1].It is still controversial about whether selective reduction or laser ablation of placental anastomoses is preferred for MC twins complicated with sIUGR or TAPS, while fetoscopic laser ablation was recognized as first-line treatment for stage II to IV TTTs diagnosed before 26 weeks gestational age[1]. However ,in some situation, selective reduction is not a bad option due to few hospitals can perform laser ablation but fetal intrauterine condition are critical, especially in our country. Moreover, it can save one of the twin with a low risk of neurodevelopment impairment[2].

During the recent years, radio frequency ablation has been widely used in many clinical therapies, such as neoplasm ,some heart disease[3], human liver lesion, fetal congenital cystic adenomatoid (CCAM) [4], human fetal sacrococcygeal teratoma [5], and complicated monochorionic twin pregnancies [6, 7].While, it seemed that

RFA is more minimal invasive to fetus and pregnant women than other methods for selective reduction used in multiple pregnancies. RFA was the most common technique for monochorionic multiple pregnancies selective reduction[8].

The inserted angle is one of key points in the procedure of RFA. Usually, the procedure was conducted under direct real-time sonographic guidance, RFA needle was percutaneously inserted through the maternal abdomen wall into the intrauterine fetal abdomen at the level of the cord insertion site of the complicated twin[7]. However, fetus were positioned prone and remained throughout the whole procedure. Fetal back may can be alternative needle insert angle. However, the needle needs to pass through fetal spine which may obviously increases the difficulty and extended the procedure time of RFA. We hypothesis that the prenatal and postpartum outcome were worse in the cases through fetal dorsal insert angle.

In our study, the aim was to assess the risk factors for adverse pregnancy outcome in the RFA selective reduction procedure due to the complicated MC twin pregnancies and to compare the pregnancy outcome of two different needle insert angles in the RFA procedure.

Materials and Methods

Study population

We conducted a retrospective study of patients with complicated MC multiple pregnancies who underwent selective reduction by RFA in single fetal therapy center between 2015 Jan and 2018 Dec. According to the difference of the needle insert angle, the study subjects were divided into two groups, abdominal insert angle group (n=116) and dorsal insert angle group(n=29). those who underwent dorsal needle insertion were all due to being positioned prone continuously throughout the procedure.

Prior to the procedure, a comprehensive ultrasound examination was performed in order to confirm the gestational age and chorionicity, and also to confirm the diagnosis and staging of complicated MC multiple gestation. RFA was one option of fetal therapy methods for all case of complicated MC multiple pregnancies such as triplets, quadruplets, TTTS, sIUGR, TRAP, TAPs, and discordance for structural anomalies. Since more than one intrauterine treatment options were available for each case, all pregnant women and their husbands received a thorough consultation prior to the procedure of RFA.

All pregnant women rolled in the study have given their written informed consent and that the study protocol was approved by the committee of local hospital on human research.

Radiofrequency ablation (RFA)

All patients were admitted to the hospital in a day before the day of the procedure of RFA after undergoing a comprehensive assessment before fetal therapy procedure. All procedures were conducted by the combination of one fetology specialist and one interventional ultrasound specialist in the intrauterine therapeutic room of Medical Genetics Center.

All patients were treated using the RF-1500 RFA system (MedSphere international (Shanghai) CO., Ltd, China). According to RFA protocol[9], local anesthesia was conducted at the planned puncture site on the maternal abdomen (2% lidocaine hydrochloride administered subcutaneously).Under continuous sonographic guidance, a 15cm or 20cm 17-gauge RFA electrode needle was inserted form fetal abdomen or back to adjacent to the area of the umbilical cord insertion, after confirmation of the location, the umbrella Electrode were deployed.RFA energy was applied start from 20 watts, increasing 10W per minute, until the impedance exceeds the critical value, when the host stop active output. If the impedance don't exceed, maintain ablation 2-3min after reaching target temperature of 100 . The procedure was repeated for an additional one or two cycles using the same heating algorithm, until cessation of cord blood flow was confirmed using color and power Doppler velocimetry.

Follow-up was organized locally through multiple contact methods, such as telephone and some internet contact. All surviving fetuses underwent a head MRI after 28 weeks of gestation to assess fetal neurological development and to determine if there was a brain injury. Pregnancy and neonatal outcome data were

obtained from the clinical notes or from referring physicians, and missing data were collected by telephone interview with the patients.

Definition

Post-procedural complication included the things happened within two weeks following the procedure: intrauterine fetal death(IUFD) of the co-twin, miscarriage, pregnancies were terminated due to abnormal ultrasound findings such as hydrops of the co-twin.

Adverse perinatal outcome included any of the following: IUFD or miscarriage after two weeks following the procedure, termination of the pregnancy and preterm delivery before 28 weeks of gestation.

sIUGR was defined as an estimated fetal weight $<$ 10th percentile in one twin and estimated fetal weight discordance [?]25%. Cases were classified into one of three types according to UA Doppler flow[10].

Statistic

Data analysis was performed with SPSS 21.0 software(IBM SPSS Statistics for Windows, IBM, USA). Student's t -test and Mann-Whitney U -test were used to compare continuous variables with and without normal distribution between the two group. The Chi-square and Fisher's exact tests were used for categorical variables. Cox survival regression was conducted to compare the proportion of women undelivered after the procedure.We used logistic regression to analyze risk factors associated with adverse pregnancy outcomes. Differences were considered significant when $P < 0.05$.

Results

Characteristics of the study groups

Total 145 selective termination of complicated monochorionic multiple pregnancies were conducted successfully, 116 through fetal abdomen and 29 through fetal back. 133 procedures were carried out in MC twins and 11 in triplets with a MC pair and 1 MC quadruplet.Figure 1 shows the Color Doppler before and after ablation of the two needle insertion angles. Table 1 shows the obstetric characteristics of the pregnant women in the two groups. Maternal age and gestational age at procedure were similar between the two groups.TTTS was the most common indication for the selective reduction in the two groups.

Operative characteristics and pregnancy outcome

The operative characteristics and pregnancy outcomes were showed in table 2. There was no significant difference between the two groups in the operative characteristics. The cervical length before procedure and the total ablation time were non-significant. The rate of preterm birth before 37 weeks, before 34 weeks, before 32 weeks ,before 30 weeks and before 28weeks were similar between the two groups. The complication after the procedure in the two group were non-significant different, including post-procedural complication and perinatal complication. Termination of pregnancy(TOP) due to fetal serious oligohydramnios or structural anomaly of the co-twin. TOP occurred in 8 cases in fetal abdomen group and 3 cases in fetal back group. The TOP rate was non-significant different in the two group(6.9% vs 10.3,p =0.53). The characteristics about delivery were non-significant different between the two groups too, including the neonatal gestational age and the rate of cesarean section.

The relation of RFA technique was assessed by means of survival analysis. Multivariate Cox regression analysis indicated that the survival curve of fetal survival time interval after the procedure between the two needle insert angles were statistically different, while set several related variables as covariates, including gestational age at the procedure, cervical length, indications and total ablation time. (P <0.001)(Figure 2). The model characteristic was showed in table 3, cervical length and the gestational age before the procedure were significant predictors for the period between RFA procedure and delivery(table 3).

Risk of adverse outcome of the RFA procedure: multivariable analysis Multivariable logistic analysis was conduct to assess the relation of the risk of perinatal adverse outcome and several factors, include different RFA needle insert angle, gestational age at the RFA procedure cervical length before the procedure,

the overall ablation time, while controlling for maternal age and indication for RFA as potential confounders. The result showed that compared to live birth at term, the risk of miscarriage,termination and IUFD were statistically higher when the cervical length was less than 35mm(Table 4). The model revealed that the subject cervical length less than 27mm were 33.416 times to report adverse perinatal outcome than those whose cervical length more than 35mm. While other factors were non-significantly related with a higher rate of adverse perinatal outcome, including miscarriage, IUFD, termination and preterm birth.**Factors associated with risk of advertise outcome**We further assessed the association between the indication for RFA and the risk of adverse post-procedure complication. Overall, 49(33.8%) RFA were conducted due to TTTS, 30(20.7%) due to anomalous co-twin, 23(15.9%) due to sIUGR, 19(13.1%) due to TRAP, 12(8.3%) due to excessive number of fetuses, 11(7.6%) due to TTTS accompanied by sIUGR, 1(0.7%) due to TAPS. Table 5 showed the outcome variables stratified by indication. Table 5 showed the outcome variables stratified by indication.The gestational age at the procedure was significantly different within the indications, those who underwent RFA for TRAP and excessive number of fetuses were lower than monochorionic twin pregnancy complications. Women who underwent RFA for TTTS had a similar gestational age at the procedure as who underwent RFA for TTTS, TTTS & sIUGR. The interval between RFA procedure and delivery was statistically different within the indications, the interval of those who underwent RFA for excessive numbers of fetuses was longer than other indications. The preterm labor(<37weeks) rate was statistical different within the indications, those who underwent RFA for TTTS was later than any other indications. Even though there was non-significantly different during the indications, the gestational age at delivery of TTTS was lower than other indications.Even though there was non-significant difference within the indications, the pregnancy with live born fetus showed a higher trend in IUGR &TTTS and excessive number of fetuses than other indications. In order to assess the impact of gestational age at the RFA procedure on perinatal outcome, we conduct a subgroup analysis, according to whether the procedure was performed before 24weeks or after 24 weeks, the age of viability[2].(table 6) Overall, 117 RFA procedures were performed before 24 weeks gestational age, and 28 RFA procedures were performed after 24 weeks gestational age. In order to avoid serve preterm birth, the RFA procedure were conducted before 28 weeks. There was no significant difference between the subgroups with regard to total ablation time, alive rate, adverse perinatal outcome rate, gestational age at delivery and preterm labor. The interval between RFA procedure and delivery was statistically shorter in post-viability group than in pre-viability group.

Discussion

The aim of this study was to assess the risk factors for adverse pregnancy outcome in the RFA selective reduction procedure due to the complicated MC twin pregnancies and to compare the pregnancy outcome of two different needle insert angles in the RFA procedure. We found that both needle insert angles were equal in terms of the fetal neonatal survival rate and the adverse perinatal outcomes of the monochorionic multiple pregnancies. Selective reduction due to the indication of TTTS accompanied with sIUGR was associated with more favorable pregnancy outcome, regardless of the procedure technique. There was similar survival rate in those whom selective reduction was performed through fetal dorsal insert angle by comparison with abdominal insert angle. Even though there was no significant difference, the survival rate was lower in patients in whom RFA procedure was performed at a pre-viability gestational age in comparison to post-viability.

Usually, the radio frequency needle was inserted percutaneously into fetal abdomen to the intra-fetal portion of umbilical cord[7, 11]. Our study found that when the fetus stay in prone position, the needle need to be inserted into fetal back and then the umbrella Electrode were deployed, electrical energy was transferred to fetal tissue with heat as usual insert angle, needle abdominal insertion [3, 7, 12]. In our series, technique success was obtained in all cases by inserting the needle once in both groups, abdominal and dorsal needle insert angle.

Previous studies have explored the pregnancy outcome of selective reduction in complicated monochorionic multiple pregnancies as a function of the technique used[2, 13, 14], especially in complicated MC twin pregnancies. Our research showed similar perinatal survival rates and adverse perinatal outcome rates for both

needle insertion. The overall survival rate was 73.4% and the overall gestational age at labor was 31.09±6.04 weeks. Even though there was no significant difference between the two groups, our finding indicated a trend towards earlier gestational age among the needle dorsal insertion group(one week earlier than the needle abdominal insertion). Such a difference in gestational age at delivery may be clinically significant in terms of the adverse perinatal outcome, such as neonatal morbidity and mortality.

In respect of the effect of the indications of RFA selective reduction on the perinatal outcome, we found that TTTS accompanied with sIUGR was associated with a predominant outcome with a survival rate of more than 90%, obviously higher than other studies[15]. A probable explanation was that in the cases suffered TTTS accompanied with sIUGR, the smaller twin present a obvious disadvantage status due to the uneven placental share[16] and imbalance of placental arteriovenous anastomosis[17], after fetal reduction, the intrauterine environment of the co-twin was closer to a singleton pregnancy than other indications.

It is well known that cervical length can be a good predictor of spontaneous preterm birth in asymptomatic twin pregnancy[18]. Our study found that the survival curve of fetal survival time interval after the procedure between the two needle insert angles were statistically different(P <0.001), with two significant predictors, cervical length (RR=0.969, P =0.043) and the gestational age before the procedure (RR=1.205, P <0.001) . Moreover, multivariable logistic analysis showed that compared to live birth at term, the risk of miscarriage,termination and IUFD were statistically higher when the cervical length was less than 35mm. Therefore, we recommend that cervical length and gestational age should be attentively evaluated before the clinical decision making about RFA selective reduction.

The preterm delivery outcomes were chosen due to their clinical importance. Neonates delivered prior to 28 weeks gestational age were acknowledged as "extremely preterm" and have a significantly lower survival rate compared to "very preterm"(28-32 weeks) and "moderate to late preterm" (32-36 weeks) neonates[19]. Gestational age specific survive curve showed a significant improvement with delivery later than 32 weeks gestational age across the world[20, 21]. In our study, the overall rate of preterm delivered before 32 weeks gestational age within the indication was lower than some research but higher than someones[22, 23], this may due to the severity of the disease or cervical length or gestational age or other reasons.

The main limitations of this study are its retrospective study design and short follow-up time, which meant lack of the long-term follow-up outcome assessments of neurodevelopment of surviving fetuses. Second, our study was performed and followed at an fetal therapy center. Besides, after our team became more proficient and confident in the operation of selective fetal reduction, we began to perform fetal reduction with unconventional needle insertion angles such as dorsal side needle insertion. We will prospectively investigate the long-term follow-up outcomes of surviving fetuses with RFA procedure at two different needle insertion angles.

Statements

A cknowledgement

The authors thank the Department of Department of Children Inherited Metabolism and Endocrine and Medical Genetics Center staff members of Guangdong Women and Children Hospital; and the parents and their children who participated.

Disclosure Statement

The authors have no conflicts of interest to declare.

Contributions to Authorship

The version to be published was approved by all the authors.all authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Author Jing Wu was responsible for research design and management. Author Qian Liu was responsible for

case collection, data analysis, and article writing. Author Xiaomei Shi, Liyuan Fang and Tengzi Rao were responsible for case collection. Author Lishuang Shi was responsible for follow-up work of all cases .

Details of Ethics Aprroval

All pregnant women rolled in the study have given their written informed consent and that the study protocol was approved by the Guangdong Women and Children Hospital Medical Ethics Committee on October 19,2017. The Ethics Review Resolution Number is 20171048.

Funding

There was no funding for this research.

.

References:

1. Prefumo F, Jauniaux E. Twin-to-twin-transfusion syndrome: from amniodrainage to laser. BJOG 2018;125(9):1163. 2. Yinon Y, Ashwal E, Weisz B, et al. Selective reduction in complicated monochorionic twins: prediction of obstetric outcome and comparison of techniques. Ultrasound in Obstetrics & Gynecology 2015;46(6):670-677. 3. Cabassa P, Fichera A, Prefumo F, et al. The use of radiofrequency in the treatment of twin reversed arterial perfusion sequence: a case series and review of the literature. Eur J Obstet Gynecol Reprod Biol 2013;166(2):127-32. 4. Milner R, Kitano Y, Olutoye O, et al. Radiofrequency thermal ablation: A potential treatment for hydropic fetuses with a large chest mass. Journal of Pediatric Surgery 2000;35(2):386-389. 5. Paek BW, Jennings RW, Harrison MR, et al. Radiofrequency ablation of human fetal sacrococcygeal teratoma. American Journal of Obstetrics and Gynecology 2001;184(3):503-507. 6. Paramasivam G, Wimalasundera R, Wiechec M, et al. Radiofrequency ablation for selective reduction in complex monochorionic pregnancies. BJOG: An International Journal of Obstetrics & Gynaecology 2010;117(10):1294-1298. 7. Tsao K, Feldstein VA, Albanese CT, et al. Selective reduction of acardiac twin by radiofrequency ablation. Am J Obstet Gynecol 2002;187(3):635-40. 8. Weichert A, Kalache K, Hein P, et al. Radiofrequency ablation as a minimally invasive procedure in the treatment of twin reversed arterial perfusion sequence in twin pregnancy. Journal of Clinical Ultrasound 2013;41(4):245-247. 9. Moise KJ, Johnson A, Moise KY, et al. Radiofrequency ablation for selective reduction in the complicated monochorionic gestation. Am J Obstet Gynecol 2008;198(2):198.e1-5. 10. Gratacos E, Lewi L, Munoz B, et al. A classification system for selective intrauterine growth restriction in monochorionic pregnancies according to umbilical artery Doppler flow in the smaller twin. Ultrasound Obstet Gynecol 2007;30(1):28-34. 11. Peng R, Xie HN, Lin MF, et al. Clinical Outcomes after Selective Fetal Reduction of Complicated Monochorionic Twins with Radiofrequency Ablation and Bipolar Cord Coagulation. Gynecol Obstet Invest 2016;81(6):552-558. 12. Ratha C, Kaul A. An Analysis of Pregnancy Outcome in Dichorionic and Monochorionic Twins Given Special Antenatal and Intranatal Care: A Four-Year Survey. The Journal of Obstetrics and Gynecology of India 2014;64(4):255-259. 13. Bebbington MW, Danzer E, Moldenhauer J, et al. Radiofrequency ablation vs bipolar umbilical cord coagulation in the management of complicated monochorionic pregnancies. Ultrasound Obstet Gynecol 2012;40(3):319-24. 14. Roman A, Papanna R, Johnson A, et al. Selective reduction in complicated monochorionic pregnancies: radiofrequency ablation vs. bipolar cord coagulation. Ultrasound Obstet Gynecol 2010;36(1):37-41. 15. Chang Y. Fetoscopic guide laser therapy for twin–twin transfusion syndrome. Gynecology and Minimally Invasive Therapy 2013;2(1):8-12. 16. Townsend R, D'Antonio F, Sileo FG, et al. Perinatal outcome of monochorionic twin pregnancy complicated by selective fetal growth restriction according to management: systematic review and meta-analysis. Ultrasound Obstet Gynecol 2019;53(1):36-46. 17. Ozawa K, Sugibayashi R, Wada S, et al. EP21.24: Long-term outcomes in monochorionic twins complicated by amniotic fluid discordance adjoining Twin-twin transfusion syndrome treated by laser surgery. Ultrasound Obstet Gynecol 2016;48 Suppl 1:363. 18. Sauvanaud C, Equy V, Faure C, et al. [Transvaginal sonographic cervical length and prediction of preterm delivery in twin pregnancies with preterm labor]. J Gynecol Obstet Biol Reprod (Paris) 2013;42(5):488-92. 19. De Zoysa MY, Chon AH, Korst LM, et al. Membrane Separation and Perinatal Outcomes after Laser Treatment for Twin-Twin Transfusion Syndrome. Fetal Diagnosis and Therapy 2019:1-8. 20. Patel RM. Short- and Long-Term Outcomes for Extremely Preterm Infants. Am J

Perinatol 2016;33(3):318-28. 21. Sasaki Y, Ishikawa K, Yokoi A, et al. Short- and Long-Term Outcomes of Extremely Preterm Infants in Japan According to Outborn/Inborn Birth Status. Pediatr Crit Care Med 2019;20(10):963-969. 22. Dadhwal V, Sharma AK, Deka D, et al. Selective fetal reduction in monochorionic twins: Preliminary experience. J Turk Ger Gynecol Assoc 2019;20(2):79-83. 23. Zhang ZT, Yang T, Liu CX, et al. Treatment of twin reversed arterial perfusion sequence with radiofrequency ablation and expectant management: A single center study in China. Eur J Obstet Gynecol Reprod Biol 2018;225:9-12.

Hosted file

table1.docx available at https://authorea.com/users/307757/articles/438727-radio-frequency-ablation-in-complicated-monochorionic-multiple-pregnancy-prediction-of-perinatal-outcome-and-comparison-of-two-different-needle-insert-angles

Hosted file

table2.docx available at https://authorea.com/users/307757/articles/438727-radio-frequency-ablation-in-complicated-monochorionic-multiple-pregnancy-prediction-of-perinatal-outcome-and-comparison-of-two-different-needle-insert-angles

Hosted file

table 3.doc available at https://authorea.com/users/307757/articles/438727-radio-frequency-ablation-in-complicated-monochorionic-multiple-pregnancy-prediction-of-perinatal-outcome-and-comparison-of-two-different-needle-insert-angles

Hosted file

\begin{CJK}{UTF8}{gbsn}\end{CJK}\selectlanguage{english}4.doc available at https://authorea.com/users/307757/articles/438727-radio-frequency-ablation-in-complicated-monochorionic-multiple-pregnancy-prediction-of-perinatal-outcome-and-comparison-of-two-different-needle-insert-angles

Hosted file

\begin{CJK}{UTF8}{gbsn}\end{CJK}\selectlanguage{english}5.doc available at https://authorea.com/users/307757/articles/438727-radio-frequency-ablation-in-complicated-monochorionic-multiple-pregnancy-prediction-of-perinatal-outcome-and-comparison-of-two-different-needle-insert-angles

Hosted file

\begin{CJK}{UTF8}{gbsn}\end{CJK}\selectlanguage{english}6.doc available at https://authorea.com/users/307757/articles/438727-radio-frequency-ablation-in-complicated-monochorionic-multiple-pregnancy-prediction-of-perinatal-outcome-and-comparison-of-two-different-needle-insert-angles

Hosted file

figure1.docx available at https://authorea.com/users/307757/articles/438727-radio-frequency-ablation-in-complicated-monochorionic-multiple-pregnancy-prediction-of-perinatal-outcome-and-comparison-of-two-different-needle-insert-angles

Hosted file

\begin{CJK}{UTF8}{gbsn}\end{CJK}\selectlanguage{english}2.doc available at https://authorea.com/users/307757/articles/438727-radio-frequency-ablation-in-complicated-monochorionic-multiple-pregnancy-prediction-of-perinatal-outcome-and-comparison-of-two-different-needle-insert-angles