



## Original Article

## Comparisons between two methods of multifetal pregnancy reduction in women with a dichorionic triamniotic triplet pregnancy



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## ABSTRACT

**Objective:** To compare the different pregnancy outcomes of women with a reduced dichorionic triamniotic (DCTA) triplet managed with radiofrequency ablation (RFA) or potassium chloride (KCL).

**Materials and methods:** This was a retrospective cohort study. We studied 30 women of DCTA triplets managed with RFA as well as 85 managed with KCL. We compared the mean neonatal birthweight, median gestational age and perinatal mortality of two groups.

**Results:** The mean neonatal birthweight of children in RFA group was 2572.4 g (SD, 407.0), vs 2899.3 g (SD, 554.9) in KCL group ( $P < 0.001$ ). The rate of low birth weight infants was 23 (42.6%) vs. 16 (18.0%), respectively, ( $p < 0.005$ ). However, there was no statistically significant difference in the median gestational age of delivery, premature birth before 32&37 weeks' gestation, neonatal brain injury or successful pregnancy between two groups. (We define the successful pregnancy as the condition that at least one child survives for a specific woman, while the failed one as no child survives.)

**Conclusion:** What we took it for granted was that pregnancy outcomes in women with a reduced DCTA triplet managed with RFA was riskier than with KCL, however, we proved that it is not accurate. For women with a reduced DCTA triplet, managed with RFA is not much riskier than with KCL. What's more, most women have two children survived in RFA group, while in KCL group, only one child survives for most women. This result may change the management alternative for those women with DCTA triplet pregnancies who choose reduction, especially for women who desire to have two surviving and healthy fetuses.

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## Introduction

It is generally believed that the incidence of triplet and high-order multiple gestations has risen drastically in the last few decades owing to wide application of assisted reproductive

techniques (ART) and an increasing maternal age [1]. However, in the past few years, this number has decreased as a result of the limitation of the number of embryos transferred in women undergoing ART [2].

The triplet pregnancies consist of trichorionic triamniotic triplets and dichorionic triamniotic (DCTA) triplets. Compared with twin or singleton pregnancy, triplet pregnancy has an increased risk for both pregnant women and newborn [3]. Since a triplet pregnancy consists of a monochorionic (MC) twin and a singleton alongside, women with DCTA triplets not only have the risks of triplet pregnancies, but also have some unique complications of MC twin pair such as twin-to-twin transfusion syndrome (TTTS), selective intrauterine growth restriction (sIUGR), and twin reversed arterial perfusion sequence (TRAP sequence) and so on [4]. In addition, there are cases in which DCTA triplets with fetal malformations need reduction. Previous studies [5,6] showed that the

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median gestational age of women with DCTA triplets after reduction of one or both fetuses of MCDA component was significantly higher than women with ongoing DCTA triplets, and perinatal mortality was lower. However, how to choose the reduction method could attain better pregnancy outcomes remains a problem. So, we did this study to offer better guidance for women with DCTA triplets struggling on how to choose the reduction method.

In our hospital, two methods are presented for women with DCTA triplet pregnancies who desire to reduce one or two fetuses: 1) using RFA to reduce one twin in a MCDA pair in DCTA triplets; this method can coagulate one of the umbilical vessels attached to the twins who share placenta, so that one fetus of MCDA and the isolated DC triplet, that is to say, two fetuses can survive theoretically; 2) using KCL to reduce MC twin pair: KCL is likely to metastasize to the co-fetus who shares the placenta with the reduced fetus, as a result, injecting KCL into the heart of the fetus may well result in the death of MCDA twin pair in the DCTA triplets. Therefore, in most cases, only one fetus can be kept with this method theoretically. So, which fetal reduction method could attain better pregnancy outcomes? We compared the mean neonatal birthweight, median gestational age and perinatal mortality of the two groups.

## Methods

In this retrospective study, all DCTA triplets who chose radio-frequency ablation (RFA) or potassium chloride (KCL) method to reduce their fetuses in Obstetrics of Central District of Shandong Provincial Hospital from 2011 to 2018 were selected. In KCL group, 94 women were included, 9 of whom were out of touch and thus were excluded from this study. As a result, 85 women were suitable for the study. A total of 30 women were identified in RFA group, all of their pregnancy outcomes were successfully tracked, so all of them were suitable for the study. The baseline characteristics of these two groups are shown in Table 1.

### Chorionicity in multiple pregnancies

It is judged by the number of embryos and gestational sacs between 8 and 10 weeks of gestation. Between 10 and 14 weeks of pregnancy, chorionicity is determined by twin fetal peaks (lambda sign) or T signs. After 14 weeks of gestation, when the chorionicity is not clear, it is based on the sex of the fetus, the number of placenta, and the thickness of the membrane separation membrane [7,8].

### Analysis of the indications of fetal reduction

DCTA pregnancies with fetal loss/demise prior to reduction were excluded. Among all the thirty cases in RFA group, we did not find complications such as TTTS, sIUGR or other complicated complications of MCDA. They chose reduction just to reduce the number of fetuses or to avoid complications as mentioned before. As for KCL group, one case was found to have brain deformity in a fetus, another case was found to have lymphatic cyst in a fetus and the

remaining 83 cases did not find any complication as mentioned before.

### The choice of the reduction method

Firstly, we explained the possible benefits and risks of the three management alternatives (including expectant management) to the patients. Then, the patients chose one of the management method after understanding all the potential benefits and risks. Certainly, the cases in which patients opted for expectant management were excluded from the study.

### Operation process

The gestation age of receiving reduction for our patients in RFA group ranged from 14.7 to 26.3 weeks, while that of KCL group ranged from 11 to 21.1 weeks.

Antibiotics should be used to prevent infection after operation, and patients must rest in bed for 24 h. Then ultrasound examination was performed the day next to surgery to observe the status of the remaining fetuses, such as the fetal heart rate, fetal growth and condition of amniotic fluid and placenta. What's more, patients in RFA group should be observed the umbilical arterial blood flow and middle cerebral artery blood flow of the remaining fetuses by color Doppler ultrasonography, and evaluated whether the fetuses had intrauterine hypoxia.

Postoperative follow-up: two groups of pregnant women were advised to perform regular prenatal examination after operation and received follow-up until delivery. So, we could keep pace with the growth and development of the remaining fetuses, threatened abortion, premature delivery, pregnancy complications as well as the maternal and neonatal situations. Besides, the RFA group received MRI half a month later to evaluate the intracranial condition of the remaining fetuses and whether hypotensive brain injury occur.

We retrospectively collected data by reviewing maternal and neonatal medical records and the follow-up. Maternal and fetal characteristics composed of the mode of conception, gestational age, gestational age at reduction, primipara or not, ultrasound results including fetal measurements, chorionicity, and pregnancy outcomes.

### Statistical analysis

The results of the two groups were compared in terms of gestational age at delivery, delivery before 28 weeks, delivery before 32 weeks, and delivery before 37 weeks, neonatal birthweight, the number of the low& very low birth weight infants, and perinatal mortality. Perinatal mortality includes intrauterine death, death during childbirth, or death 7 days after delivery.

To analyze the gestational age at delivery of each group, we constructed the Kaplan–Meier curve. Since the gestational age at delivery was not normally distributed, we used Mann–Whitney U to compare the median between the groups. The birth weight of the newborn was normally distributed, therefore we used independent

**Table 1**  
Characteristics of pregnant women.

Characteristic	RFA group (n = 30)	KCL group (n = 85)	P-value
Maternal age	31.4 (4.7)	29.6 (4.2)	P = 0.052
Spontaneous conception	7 (23.3%)	32 (37.6%)	P = 0.155
Primipara	20 (66.6%)	60 (70.6%)	P = 0.688
Caesarean section	27 (90%)	51 (60%)	P = 0.005
For reducing number	30 (100%)	83 (97.7%)	P = 1.000
For fetal malformation	0	2 (2.2%)	P = 1.000

Data are presented as mean (SD) or number (percentage).

samples t-test to compare the average birth weight between the two groups. And Chi-Square test was used to compare the number of deliveries before 28, 32 and 37 weeks and the number of perinatal deaths in the two study groups.

What's more, we compared the number of perinatal deaths, the number of women who had all their children or no children survived, and the number of women who had a successful pregnancy.

We used SPSS 20 (SPSS Inc, Chicago, IL) for statistical analysis.

## Results

In this study, a total of 115 cases (85 cases in KCL group and 30 cases in RFA group) were finally identified. Then, we compared their pregnancy outcomes.

There were three operators for fetal reduction in KCL group, and only one operator in RTF group in our hospital. There was no significant difference in pregnancy outcomes of the cases operated by the three operators (data is not shown).

In our study, the median gestational age for women in RFA group was 37.1 weeks (interquartile range [IQR], 35.9–37.8 weeks), while in KCL group was 38.0 weeks ([IQR], 36.1–39.0 weeks,  $P > 0.05$ ). Neither of two groups had surviving infants delivered before 28 weeks. Among the RFA group, no one delivered before 32 weeks' gestation, compared to 4 [4.7%] in KCL group (0 vs 4/85 [4.7%], respectively) ( $P > 0.05$ ). And 9 women in RFA group delivered before 37 weeks' gestation vs 16 in KCL group (9/30[30%] vs 16/85[18.8%], respectively) ( $P > 0.05$ ) (Table 2(a)).

The mean neonatal birthweight of children in RFA group was 2572.4 g (SD, 407.0), and 2899.3 g (SD, 554.9) in KCL group ( $P < 0.001$ ). It was obvious that the neonatal birthweight of RFA group was smaller than that of KCL group. The number of low birth weight infants of RFA group was 23 (42.6%), while that of KCL group was 16 (18.0%) (RR, 3.39 [95% CI 1.58–7.27]). None of children in RFA group was very low birth weight infant, and that of KCL was 2 (2.2%), but there was no statistically significant difference between the two groups.

Among the RFA group, 2(6.7%) women had only one fetus survived, vs 63(71.4%) in the KCL group (RR 0.09 [95% CI 0.02–0.35]). And 26 (86.7%) in the RFA group had two fetuses survived, compared 13 (15.3%) in the KCL group (RR36.00 [95% CI 10.77–120.37]). There were a total of 28 (93.3%) women in the RFA group got pregnancy success (We define the successful pregnancy as the condition that at least one child survives for a specific woman, while the failed one as no child survives.), vs 76 (89.4%) in the KCL group (RR1.66 [95% CI 0.34–8.15]). And the number of cases ended in pregnancy failure in RFA group was 2 (6.7%), vs 9 (10.6%) in KCL group (RR 0.63 [95% CI 0.12–2.97]) (Table 2(b)).

## Discussion

Summarizing the above data, we can draw the following conclusions. (Since one twin in a MCDA pair in DCTA triplets was reduced in KCL group, we will compare the RFA group results with results of a reduced MCDA twin pregnancy).

1. We can see that the rate of RFA group was higher than KCL group in the aspect of pregnancy success (28 [93.3%] vs 76 [89.4%]), though there was no statistically significant difference between the two groups. And this result was different from the previous studies [5,19], which recommended women with DCTA triplets to reduce to a singleton pregnancy by reducing the MCDA pair.
2. Theoretically, because of MCDA component in DCTA triplets sharing the same placenta, when KCL is injected into the heart of one fetus, the co-twin is likely to die. As a result, this method can nearly only keep one single fetus alive. The following reasons may explain it: it may be caused by the KCL injection through the placental vascular shunt; it may also be due to acute hemodynamic changes inside the survivors' bodies, which may be related to blood loss in the vascular system of the dead fetus [9]. For women in our KCL group, we unexpectedly observed that 13 of 85 (15.3%) had two fetuses alive. (Owing to the later examination indicating that the remaining co-twin was not found abnormality temporarily, the parents chose to give up reduction once again.) And this number may be larger than what we generally believed. This is possibly because that the dosage of KCL precisely just causes one fetus dying (Absolutely, if there was a malformed fetus in DCTA triplets, the malformed one would be reduced), or in spite of sharing the same placenta, their mutual blood communication was very little or even not exist. We found out through follow-up that all these children were well-developed and healthy yet, having no complications such as brain damage.
3. For women in RFA group, it was found that women with a DCTA triplet pregnancy had a better pregnancy outcome compared with women with a MCDA twin pregnancy [10,11]. We thought that this was because, in previous reports, MCDA complications such as TTTS, sIUGR and TRAP sequence had occurred before reducing their fetus, but none of our 30 patients with a DCTA triplet pregnancy found any complications mentioned above when they were performed the reduction surgery. And the 30 patients received fetal reduction only aiming to reduce the number of fetuses or to avoid the complications mentioned above and therefore had a better pregnancy outcome.
4. Our first advantage in this research lie in the fact that numerous cases were available and from the same database. Secondly, there were one operator in RTF group and three in KCL group, and there was no significant difference in pregnancy outcome between the three operators, so the data is more reliable. What's

**Table 2a**  
Pregnancy outcomes.

Variable	RFA group (n = 30)	KCL group (n = 85)	P-value
Median gestational age, wks	37.1 (35.9–37.8)	38.0 (36.1–39.0)	$P = 0.070$
delivery <28 weeks	0	0	
Delivery 28–31 <sup>+6</sup> weeks	0	4 (4.7%)	$P = 0.571$
Delivery <32 weeks	0	4 (4.7%)	$P = 0.571$
Delivery 32–36 <sup>+6</sup> weeks	9 (30%)	12 (14.1%)	$P = 0.053$
Delivery <37 weeks	9 (30%)	16 (18.8%)	$P = 0.202$
Delivery ≥37 weeks	19 (63.3%)	60 (70.6%)	$P = 0.461$
Mean neonatal birthweight, g	2572.4 (407.0)	2899.3 (554.9)	$P < 0.001$
low birth weight infants (<2500 g)	23 (42.6%)	16 (18.0%)	$P = 0.001$
Very low birth weight infants (<1500 g)	0	2 (2.2%)	$P = 1.000$

Data are presented as median (IQR), number (percentage), or mean (SD).  
CI, confidence interval; IQR, interquartile range; RR, relative risk.

Table 2b

Surviving number	RFA group (30)	KCL group (85)	RR (95%CI)	P-value
1	2 (6.7%)	63 (74.1%)	0.09 (0.02–0.35)	P < 0.001
2	26 (86.7%)	13 (15.3%)	36.00 (10.77–120.37)	P < 0.001
at least 1	28 (93.3%)	76 (89.4%)	1.66 (0.34–8.15)	P = 0.790
0	2 (6.7%)	9 (10.6%)	0.63 (CI 0.12–2.97)	P = 0.790

Data are presented as number (percentage).

CI, confidence interval; IQR, interquartile range; RR, relative risk.

- more, baseline characteristics were nearly identical for two groups, so we could ignore selection bias.
- Among the survived children of two groups, no one was found obvious brain damage. According to previous research, after one twin in a MCDA pair dying, perinatal mortality and brain damage probability of the remaining fetus were up to 30% and 25% respectively [6]. After spontaneous intra-uterine fetal death (IUFD) of one fetus in MC twin, there is the risk of IUFD or brain damage to the remaining one [12–14]. Theoretically, this risk probably was lower after fetal reduction, but only three small studies confirmed it [15–17]. Another study reported that in a group of 45 patients with a MCDA twin pregnancy after managed with RFA reduction, one case was detected level-3 intracranial hemorrhage using fetal cranial ultrasound, and the systolic peak in cerebral artery was found to be abnormal within 4 cases [18]. Compared with this, we did not find any obvious brain damage within the survived children after reduction with RFA. This result is mainly due to the accurate position of the puncture by our operators, then the umbilical blood flow of the reduced fetus was quickly blocked so that the hot blood flow cannot enter co-fetus's blood. Also, insufficient cases or insufficiently long-term follow-up work may be responsible for the result.
  - In consideration of the fact that there are more normal twin or triplet pregnancy in secondary hospital or primary hospital, and the cases with pathological pregnancy were likely to be referred to our hospital, so, the data of women with an ongoing DCTA triplet pregnancy in our hospital, could not represent average level in China. As a result, there was no further comparison with the women with an ongoing DCTA triplet pregnancy, because we did not have a suitable control group for this experiment. However, according to previous studies, it can be seen that the pregnancy outcome of women with a reduced DCTA triplet pregnant was better than ongoing DCTA triplets [5,6].

We compared the pregnancy outcomes of two groups. Compared with reduction with KCL, the mean neonatal birthweight was smaller ( $P < 0.001$ ) and the ratio of low birth weight infants was higher ( $P < 0.005$ ) in RFA group. However, there was no statistically significant difference in the mean gestational weeks of delivery, the rate of preterm delivery before 32&37 weeks' gestation and the rate of very low birth weight infants, and so was it in terms of pregnancy success or pregnancy failure. What we took it for granted was that pregnancy outcomes in women with a reduced DCTA triplet managed with RFA was riskier than with KCL, however, we proved that it is not accurate. For women with a reduced DCTA triplet, managed with RFA is not much riskier than with KCL. What's more, most women have two surviving fetuses in RFA group, while in KCL group, only one fetus survives for most women. This result may change the management alternative for those women with DCTA triplet pregnancies who choose reduction, especially for women who desire to have two surviving and healthy fetuses.

### Conflicts of interest

The authors have no conflicts of interest to declare.

### Author contributions

Ai-Jun Zhou: Collecting cases, follow-up, analyzing cases, summary of information.

Lei Li: Designing the research, surgical implementation, collecting cases, analyzing cases.

Hong-Mei Wang: Clinical consultation, surgical implementation.

Yan-Yun Wang: Collecting cases, follow-up.

Li-Hang Zhong: Collecting cases.

Ting-Ting Dong: Collecting cases.

Xie-Tong Wang: Designing the research, clinical consultation, surgical implementation.

Hong-Yan Li: ultrasound diagnosis, ultrasound guidance, summary of information.

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