The early second-trimester multifetal pregnancy reduction improves pregnancy outcome

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DOI: 10.31083/j.ceog.2021.01.5519

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Submitted: February 05, 2020 Revised: August 31, 2020 Accepted: September 02, 2020 Published: February 15, 2021

Purpose: To evaluate pregnancy outcome of selective second-trimester multifetal pregnancy reduction (MFPR) compared with that of first-trimester MFPR, and control group which consists of women with ongoing primary twin pregnancies. Materials and Methods: This retrospective cohort study included all women with triplet pregnancies who underwent fetal reductions to twin pregnancies from January 2010 to December 2019 in Shandong Provincial Hospital. 154 MFPR were performed by intracardially injection of potassium chloride, 8 MFPR were performed by intracranially injection of potassium chloride. Reductions to monochorionic twins and reductions to one embryo were excluded. All procedures were performed at 12-24+6 wks gestation. The outcome of pregnancy in women with reduced triplets was compared with that of the control group. Results: We identified 162 women with reduced triplet pregnancies who underwent fetal reductions to twin pregnancies, and 160 women with ongoing primary twin pregnancies as the control group. There was a significant difference in the abortion rate between MFPR and control group. The abortion rate of the early second trimester MFPR group (at gestation 14-15+6 wks) (13.3%, 5/38) was not significantly different compared with that of the first trimester MFPR group (at gestation 12-13+6 wks) (8.3%, 8/96) or that of the control group (6.9%, 11/160). There were no significant differences in average gestation time at delivery, delivery rate in 28-34 wks, neonatal birth weight, gestational diabetes mellitus, or hypertensive disorder complicating pregnancy among the first trimester MFPR group, the early second trimester MFPR group, and the control group. Conclusion: In women with triplet pregnancy, fetal reduction in the early second trimester is an effective way to avoid delivery of abnormal fetuses, reduce complications during delivery, and improve neonatal quality.

Keywords
Multiple pregnancy, Multifetal pregnancy reduction

1. Introduction
Multiple births have steadily increased in recent years because of increased usage of assisted reproductive technologies in China and other countries [1–5]. Compared with women with singleton and twin pregnancies, those with triplets have significantly increased risks of maternal morbidity [6], which includes gestational diabetes [7], hypertensive disorders [8], Cesarean delivery [9, 10], excessive hemorrhage [11], and non-spontaneous heterotopic triplets [12]. To decrease the risks associated with triplet pregnancies, multifetal pregnancy reduction (MFPR) has been proposed [13, 14]. The most frequently used method is ultrasound-guided transabdominal injection of potassium chloride into the fetal heart in the chest cavity [15]. Our objective in the present study was to evaluate pregnancy outcomes after selective MFPR in the second trimester and to compare it with the those after first-trimester MFPR. Ongoing twin pregnancies were used as a control group.

2. Materials and methods
This retrospective study included all women with triplet pregnancies who underwent fetal reductions to twin pregnancies from January 2010 to December 2019 in Shandong Provincial Hospital, which lies in Shandong provincial peninsula in eastern China with a population of 98 million. 154 MFPR were performed transabdominally after local anesthetics by using a 20G needle to intracardially inject potassium chloride, 8 MFPR were performed to intracranially inject potassium chloride. Reductions to monochorionic twins and reductions to one embryo were excluded. All procedures were performed at 12-24+6 wks gestation. The reductions were carried out by highly skilled physicians with at least 5 year’s experience in multifetal reduction. The outcome of pregnancy in women with reduced triplets was compared with that of the control group which consists of women with ongoing twin pregnancies. All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of Reproductive Hospital, Shandong University (#202060).

3. Statistical analysis
Data are expressed as means ± standard deviation. Comparisons between groups were performed with Student’s t-test for parametric data. Homogeneity of sample variances was performed with the homogeneity test of variances and
Table 1. Comparison of abortion rate in MFPR and control (ongoing twin pregnancy) groups.

| Group       | Cases | Abortion |
|-------------|-------|----------|
|             | Cases | Percentage (%) |
| MFPR        | 162   | 23       | 14.2 |
| 12-13 wk    | 96    | 8        | 8.3  |
| 14-15 wk    | 35    | 5        | 13.3 |
| 16-24 wk    | 31    | 9        | 29.0% |
| Control     | 160   | 11       | 6.9  |

The abortion rates at 28-34 wks of gestation in the MFPR and control groups were 12.2% (17/139) and 10.7% (16/149), respectively. The abortion rates at 28-34 wks of gestation in the MFPR and control groups were 6.5% (9/139) and 7.4% (11/149), respectively. The abortion rate of the MFPR group (14.2%, 23/162) was significantly higher compared with that of the control twin group (6.9%, 11/160; \( \chi^2 = 4.570, P < 0.05 \)). The abortion rate of the late second trimester MFPR group (29.0%, 9/31) was significantly higher compared with that of the first trimester MFPR group (8.3%, 8/96; \( \chi^2 = 9.768, P < 0.01 \)) and that of the control group (6.9%, 11/160, \( \chi^2 = 15.140, P < 0.001 \)). The abortion rate of the early second trimester MFPR group (13.3%, 5/35) was not significantly different compared with that of the first semester MFPR group (8.3%, 8/96) or that of the control group (6.9%, 11/160) (Table 1).

The average gestation time at delivery of the MFPR group (36.8 ± 1.8 wks) was not significantly different compared with that of the control group (36.9 ± 1.4 wks) (\( t = -0.346, -0.163, -0.136; P > 0.05 \)). The incidences of high and low fetal weight in the MFPR group were not significantly different compared with those of the control group. The delivery rates at 28-34 wks of gestation in the MFPR and control groups were 6.5% (9/139) and 7.4% (11/149) respectively (\( \chi^2 = 0.010 \)). Incidences of asymmetric fetus growth were 12.2% (17/139) and 10.7% (16/149) respectively (\( \chi^2 = 0.057 \)); incidences of GDM were 2.9% (4/139) and 2.0% (3/149) respectively (\( \chi^2 = 0.662 \)); and incidences of HDCP were 11.5% (16/139) and 8.1% (12/149), respectively (\( \chi^2 = 0.013 \)); there were no statistically significant differences between the MFPR and control group for any of these variables (\( P > 0.05 \) for all) (Table 2).

## 5. Discussion

The hospital was the first in China to perform MFPR during the second trimester [15]. Since the first MFPR in the second trimester was performed in January 2002 [16], we have performed hundreds of MFPR by injection of potassium chloride into the fetal heart by now; the success rate is 90.04%, the abortion rate is 9.06%. The reason of abortion includes bleeding and infection after MFPR as well as natural abortion led by abnormal embryos.

We have also tried other methods, such as intracranial injection of potassium chloride and radiofrequency ablation, when frequent fetal movements, the awkward position of fetuses, poor thoracic display, and extremely small thorax because of fetal thoracic abnormality happened. We postponed MFPR to the second trimester. By contrast, most MFPR in China were performed during the first trimester [3]. During the first trimester, it was often difficult to confirm suspected fetal defects, and there were a higher fetal damage rate and a higher infection rate associated with transvaginal procedures.

In Ata et al’s study, it suggests that the obstetric outcomes of IVF triplets which spontaneously reduce to twins are similar to that of elective reduction to twins and pregnancies conceived as dichorionic twins. In our study, we try to find a better opportunity to reduce fetuses [17]. Our results suggest that MFPR in the early second trimester does not increase the risk of complications for pregnant women and newborn infants. The early second trimester MFPR is an effective way to reduce fetal defects associated with first trimester MFPR, as well as to avoid the birth of abnormal fetuses, reduce complications of pregnant women, and improve neonatal quality.

Of course, there are some limitations in our study, one of which is that we did not study the result of reducing the triplet pregnancies into singletons. In Haas et al’s study, it suggests that triplet pregnancies reduced to singletons rather than twins, result in better obstetric outcomes [18]. We will study the early second-trimester multifetal pregnancy reduction to singleton in the coming stage.

## Abbreviations

ART, assisted reproductive technologies; GDM, gestational diabetes mellitus; HDCP, hypertensive disorder complicating pregnancy; MFPR, multifetal pregnancy reduction.

## Author contributions

Yanhui Zhu designed the research study. Ting Han collected data. Jingjing Jiang performed statistics and wrote the method and results. Yanhui Zhu finished the left parts of writing and polished the whole paper. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

## Acknowledgment

I would like to express my gratitude to all those who helped me during the writing of this manuscript.

The authors thank Dr. Yan Sheng (Center for Reproductive Medicine, Cheeloo College of Medicine, Shandong University) for the critical reading of this manuscript.

Thank numerous individuals participated in this study.

Thanks to all the peer reviewers and editors for their opinions and suggestions.
Table 2. Comparison of pregnancy outcome and complications among MFPR and control groups.

| Groups          | Delivery after 28 wk gestation | Average gestation time before delivery (mean ± SD, wk) | Delivery at 28–34 wk | Birth weight (mean ± SD, g) | Asymmetric fetal growth | GDM    | HDCP   |
|-----------------|--------------------------------|-------------------------------------------------------|----------------------|-----------------------------|-------------------------|--------|--------|
|                 | Cases Percentage (%)          | A (mean ± SD, g)                                      | B (mean ± SD, g)     | Cases Percentage (%)        | Cases Percentage (%)    |        |        |
| MFPR            | 139                            | 36.8 ± 1.8                                           | 9                    | 6.5                         | 2729.2 ± 449.4          | 2411.5 ± 424.3          | 17     | 12.2   | 4      | 2.9    | 16     | 11.5   |
| 12–13 wk        | 88                             | 36.4 ± 1.9                                           | 8                    | 9.1                         | 2692.9 ± 445.8          | 2368.3 ± 401.9          | 9      | 10.2   | 2      | 2.2    | 10     | 11.4   |
| 14–15 wk        | 30                             | 37.7 ± 1.2                                           | 0                    | 0                           | 2849.0 ± 454.9          | 2534.1 ± 389.5          | 5      | 16.7   | 1      | 3.3    | 3      | 10     |
| 16–24 wk        | 22                             | 36.1 ± 1.8                                           | 1                    | 4.5                         | 2731.5 ± 521.1          | 2414.0 ± 491.4          | 3      | 13.6   | 1      | 4.5    | 3      | 13.6   |
| Control         | 149                            | 36.9 ± 1.4                                           | 11                   | 7.4                         | 2741.6 ± 406.5          | 2420.5 ± 475.8          | 16     | 10.7   | 3      | 2      | 12     | 8.1    |
| χ² value<sup>a</sup> | 4.57                           | −0.338                                               | 0.01                 | −0.158                      | −0.138                  | 0.057   | 0.662  | 0.013  |
| P value<sup>a</sup> | 0.033                          | 0.813                                                | 0.865                | 0.868                       | 0.885                   | 0.874   | 0.425  | 0.916  |
| χ² value<sup>b</sup> | 8.653                          | 1.281                                                | 2.693                | 1.31                        | 1.396                   | 1.652   | 0.418  | 0.298  |
| P value<sup>b</sup> | 0.011                          | 0.294                                                | 0.281                | 0.288                       | 0.276                   | 0.447   | 0.832  | 0.883  |
Conflict of interest
The authors declare no competing interests.

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