

# The Association between Placenta Implantation at Prior Myomectomy Locations and Perinatal Outcomes in Pregnant Women Who Previously Underwent One-Step Hysteroscopic Myomectomy

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## Abstract

**Objectives:** There are no data describing the correlation between placenta implantation at prior myomectomy locations and perinatal outcomes in pregnant women after transcervical resection myomectomy (TCR-M). The aim of the study is to investigate the correlations between placenta implantation at prior myomectomy locations and perinatal outcomes in pregnant women who had previously undergone TCR-M.

**Materials and Methods:** This was a retrospective, single-center study. We reviewed the records of 34 pregnant women who had previously undergone TCR-M for submucosal myoma and perinatal care in our hospital between January 2012 and January 2019. We examined surgical and pregnancy outcomes and evaluated correlations between placenta implantation at prior myomectomy locations and perinatal outcomes in women who delivered after 22 gestational weeks ( $n = 24$ ).

**Results:** Median maternal age at conception was 38 years (range, 28–44) and median duration between TCR-M and conception was 1.4 years (range, 0.3–5.8). There were 24 deliveries after 22 gestational weeks and 10 pregnancy losses. Among these 24 deliveries, the median gestational age at delivery was 39 weeks (range, 34–41); median birthweight, 3025 g (range, 2092–4012); and median blood loss at delivery, 573 g (range, 100–3000). There were no cases of placenta accreta and uterine rupture. Placenta implantation at a prior myomectomy location was detected in 14/24 women using transabdominal ultrasonography. Median blood loss was significantly higher in the implantation than in the nonimplantation group ( $P < 0.01$ ).

**Conclusion:** Our one-step TCR-M is useful for women with submucosal myoma. However, we suggest that clinicians should review and check the association between prior myomectomy locations and placenta implantation.

**Keywords:** Abnormal placentation, hysteroscopy, myoma, pregnancy, ultrasound

## INTRODUCTION

Myomas are often detected in childbearing women, and 5%–10% of infertile women are affected by submucosal myomas.<sup>[1]</sup> Myomectomy has been performed in women with submucosal myomas for both sterility and hypermenorrhea.

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Hysteroscopic myomectomy is a minimally invasive surgery, and some women have conceived after hysteroscopic

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transcervical myomectomy (TCR-M). The associations between number, localization or diameter of myomas, and pregnancy outcomes were evaluated in a previous report.<sup>[2]</sup> In addition, placenta accreta or increta and uterine rupture in pregnant women who previously underwent TCR-M was reported in previous case reports.<sup>[3-5]</sup>

In our hospital, TCR-M is performed by one-step hysteroscopic dissection as open myomectomy, as described previously. Since our method can preserve more endometrium, lessen injury to the uterine muscle layer, and completely remove the submucosal myoma,<sup>[6]</sup> we hypothesized that pregnant women who had previously undergone our one-step TCR-M would have good perinatal outcomes. In women with severe endometrial injury, there is an increased frequency of abnormal placentation.<sup>[7]</sup> Due to the increased incidence of abnormal placentation in pregnant women who previously underwent myomectomy, Milazzo *et al.* suggested that the substitution of muscle tissue with collagen repair tissue carried a high risk of placenta accreta.<sup>[2]</sup> However, there are no data describing the correlation between placenta implantation at prior myomectomy locations and perinatal outcomes in pregnant women who previously underwent TCR-M.

With this background, we investigated perinatal outcomes after one-step TCR-M in our hospital. In addition, we examined whether placenta implantation at prior myomectomy locations affected perinatal outcomes in pregnant women who had previously undergone our one-step TCR-M.

## MATERIALS AND METHODS

We retrospectively reviewed records of 34 pregnant women who had previously undergone hysteroscopic one-step myomectomy for submucosal myoma and perinatal care at our hospital between January 2012 and January 2019. We have described our hysteroscopic one-step myomectomy in a previous report.<sup>[6]</sup> We excluded women who underwent other hysteroscopic surgeries (e.g., polypectomy, intrauterine synechiotomy, plastic surgery of uterine malformation, and other types) and pregnant women who underwent perinatal care and delivery in other hospitals.

First, we examined the surgical and pregnancy outcomes of 34 women who conceived after TCR-M in our hospital. Second, we examined whether placenta implantation at prior myomectomy locations affected perinatal outcomes after TCR-M in women who delivered after 22 weeks gestation. Women with placenta implantation at prior myomectomy locations were included in the implantation group, while women whose placentas were not implanted at prior myomectomy locations were included in the nonimplantation group. Gestational age was confirmed in the first trimester by crown-rump length measurements. Perinatal management

for pregnancy-related symptoms (e.g., premature labor, rupture of the membrane, or hypertensive disorders) was conducted at the discretion of their own obstetrician, based on the clinical recommendations by the Japan Society of Obstetrics and Gynecology.<sup>[8]</sup> Using the Japanese standard sex- and parity-specific birth weight percentile curves, a birth weight  $\geq 90^{\text{th}}$  percentile was defined as large for gestational age (LGA), and a birth weight  $< 10^{\text{th}}$  percentile was designated as small for gestational age (SGA).<sup>[9]</sup> We examined the placental position using transabdominal ultrasound at 20, 28, and 34 gestational weeks and at full term with the help of the sonographers or medical doctors. Clinical information, hysteroscopic surgical findings, and sonographic findings were acquired from medical records in our hospital.

Data are presented as median (range) or number (percentage), as appropriate. Group differences were evaluated using the Mann–Whitney U-test for continuous data and the Chi-square test for categorical data. Statistical analyses were performed using R software (version 3.3.1; <https://cran.r-project.org/bin/macosx/>).  $P < 0.05$  was considered to indicate statistical significance.

This study was approved by the Institutional Review Board and Research Ethics Committee of our hospital on June 12, 2018 (reference number: 2018-4). The informed consent was waived by IRB.

## RESULTS

### Surgical characteristics and pregnancy outcomes of 34 women who conceived after hysteroscopic myomectomy

Surgical characteristics and pregnancy outcomes of the 34 women in this study are shown in Table 1; 26 had hypermenorrhea (74%), 18 had sterility (53%), and 3 had dysmenorrhea (9%). The median hemoglobin before operation was 11.9 g/dl (range, 6.5–13.9). The median operative time was 22 min (range: 4–65), the median number of samples was one (range: 1–10), and the median weight of samples was 8 g (range: 0.5–45). Regarding the histological type, 32 women had leiomyoma (94%), one had adenomyoma (3%), and one had atypical polypoid adenomyoma (3%). There was no massive vaginal bleeding during or after the operation. The median maternal age at conception was 38 years (range, 28–44) and median duration between TCR-M and conception was 1.4 years (range, 0.3–5.8). Of 34 pregnancies, seven were conceived by *in vitro* fertilization-embryo transfer (IVF-ET, 21%). There were 24 deliveries after 22 gestational weeks and 10 pregnancy losses (nine in the first trimester, one in the second trimester). Among the 24 pregnancies with delivery after 22 gestational weeks, the median gestational age at delivery was 39 weeks (range, 34–41), median birth weight was 3025 g (range, 2092–4012), and median blood loss at

**Table 1: Surgical characteristics and pregnancy outcomes of 34 women who conceived after hysteroscopic myomectomy (n=34)**

Symptom before operation	
Hypermenorrhea	26 (74)
Sterility	18 (53)
Dysmenorrhea	3 (9)
None	1 (3)
Hemoglobin before operation (g/dl)	11.9 (6.5-13.9)
Operative time (min)	22 (4-65)
Number of samples	1 (1-10)
Weight of samples (g)	8 (0.5-45)
Histological type	
Leiomyoma	32 (94)
Adenomyoma	1 (3)
Atypical polypoid adenomyoma	1 (3)
Maternal age at conception (years)	38 (28-44)
Duration from hysteroscopic myomectomy to conception (years)	1.4 (0.3-5.8)
Method of conception	
Spontaneous conception	27 (79)
IVF-ET	7 (21)
Pregnancy loss	
First trimester	9 (26)
Second trimester	1 (3)
Delivery after 22 gestational weeks	24 (71)

Data: Median (range) or *n* (%). IVF-ET: *In vitro* fertilization-embryo transfer

delivery was 573 g (range, 100–3000). The maximum blood loss of 3000 g was recorded in a lady who developed placental abruption. Among these 24 pregnancies, seven pregnant women had over 1000 g blood loss at delivery; six had atonic hemorrhages and one had abruptio placentae. Five of the seven cases who had more than 1000 g blood loss belonged to the implantation group. There were no cases of placenta accreta in this study.

### Effect of placenta implantation at prior myomectomy locations on perinatal outcomes in pregnant women who had previously undergone hysteroscopic myomectomy

The comparison of perinatal outcomes between pregnancies with placenta implantation at prior myomectomy locations and those without implantation at prior myomectomy locations is shown in Table 2. Of 24 pregnancies, placenta implantation at prior myomectomy locations was detected in 14 using transabdominal ultrasonography. There were no notable group differences in maternal age at delivery, maternal pregravid body mass index, gestational age at delivery, birth weight, rate of IVF-ET, perinatal complications, SGA, LGA, or mode of delivery. However, in the implantation group, the median blood loss was significantly higher than in the nonimplantation group ( $P < 0.01$ ).

## DISCUSSION

Overall, our results showed that the pregnant women who had previously undergone one-step TCR-M did not develop placenta accreta and uterine rupture. However, when we analyzed the correlations between placenta implantation at prior myomectomy locations and perinatal outcomes, the median blood loss was significantly higher in the implantation group than in the nonimplantation group.

In our study, there were no cases of placenta accreta in pregnant women who had previously undergone one-step TCR-M. In a previous case report of pregnancy after TCR-M, a 48-year-old woman had placenta increta after conception by oocyte donation.<sup>[3]</sup> The other case of placenta accreta after TCR-M was complicated with placenta previa.<sup>[4]</sup> As myomectomy (i.e., abdominal or laparoscopic) damages the endometrial layer and leads to abnormal placentation with invasion of the myometrium in the resection site, the risk of adherent placenta may increase in pregnant women who previously underwent TCR-M.<sup>[7,10]</sup> However, prior reports of the risk of placenta accreta in pregnant women who previously underwent TCR-M included cases with other risks for abnormal placentation (e.g., old age, infertility treatment, or placenta previa). Therefore, abnormal placentation may not have occurred in patients in our study because the patients had no other risks for abnormal placentation. Moreover, uterine rupture in pregnancy was not detected in our study. In our procedure of one-step TCR-M, transabdominal ultrasound is used during operation to avoid the risk of uterine rupture. Since our one-step TCR-M involves cutting the capsule of the myoma next to the muscular layer of the uterus, it has the advantage of preserving more endometrium, lessening injury to the uterine muscle layer, and removing the submucosal myoma completely, the uterine muscle layer could be repaired perfectly. When the women conceived after our TCR-M, the placenta could not infiltrate the uterine muscle layer, which could not then become thinner. Therefore, our TCR-M might inhibit the development of adherent placenta and uterine rupture in pregnancy. Our data suggest that our one-step TCR-M might be a more effective technique than other TCR-M techniques, both for curative effect and for good perinatal outcomes.

In the present study, when we analyzed the correlations between placenta implantation at prior myomectomy locations and perinatal outcomes, the median blood loss in implantation group was significantly higher than in nonimplantation group. Of 14 patients in the implantation group, one developed placental abruption and had massive postpartum hemorrhage (3000 g). Therefore, the median blood loss in the implantation group was significantly higher than in the nonimplantation group. The location of

**Table 2: Obstetrics outcomes in 24 pregnancies after 22 gestational weeks**

	Implantation (n=14)	Nonimplantation (n=10)	P
Maternal age at delivery (years)	36 (28-41)	38 (31-44)	0.10*
Maternal pregravid BMI (kg/m <sup>2</sup> )	21 (17-39)	20 (17-28)	0.97*
Underweight	2 (14)	2 (20)	1 <sup>†</sup>
Normal	11 (79)	5 (50)	0.20 <sup>†</sup>
Overweight/obese	1 (7)	3 (30)	0.27 <sup>†</sup>
IVF-ET	3 (21)	3 (30)	0.67 <sup>†</sup>
Perinatal complication			
Anemia during pregnancy	3 (21)	3 (30)	0.67 <sup>†</sup>
Placenta accreta	0 (0)	0 (0)	-
Postpartum hemorrhage	4 (29)	2 (20)	1 <sup>†</sup>
Placental previa	0 (0)	0 (0)	-
Placental abruption	1 (7)	0 (0)	1 <sup>†</sup>
Gestational diabetes	1 (7)	1 (10)	1 <sup>†</sup>
Hypertensive disorder in pregnancy	1 (7)	1 (10)	1 <sup>†</sup>
Preterm premature rupture of membranes	0 (0)	0 (0)	1 <sup>†</sup>
Prolonged labor	0 (0)	0 (0)	1 <sup>†</sup>
Gestational weeks at delivery (weeks)	40 (34-41)	38 (36-41)	0.17*
Preterm delivery	1 (7)	1 (10)	1 <sup>†</sup>
Birth weight (g)	3053 (2092-4015)	3018 (2185-3865)	0.82*
Small-for gestational age	1 (7)	2 (20)	0.55 <sup>†</sup>
Large-for gestational age	4 (29)	4 (40)	0.67 <sup>†</sup>
Mode of delivery			
Vaginal delivery	7 (50)	4 (40)	0.70 <sup>†</sup>
Vacuum delivery	2 (14)	1 (10)	1 <sup>†</sup>
Cesarean section	5 (36)	5 (50)	0.68 <sup>†</sup>
Blood loss at delivery	635 (110-3000)	487 (100-1438)	<0.01*

Date: Median (range) or n (%). \*Mann-Whitney U-test, <sup>†</sup>Chi-square test. BMI: Body mass index, IVF-ET: *In vitro* fertilization-embryo transfer

myoma before myomectomy is reportedly associated with placental abruption.<sup>[11]</sup> Furthermore, placental abruption developed in some pregnant women who previously underwent laparoscopic myomectomy, but not in those who previously underwent TCR-M.<sup>[12-14]</sup> It was unclear why placental abruption occurred in our case and whether placental abruption was correlated with placenta implantation at prior myomectomy locations. One possible explanation for higher blood loss in the implantation group compared to the nonimplantation group may be related to the development of placental adhesions when placenta forms at the prior myomectomy locations. These adhesions may cause the placenta to deliver easily, resulting in greater blood loss than expected.

In our study, of 24 women, two delivered preterm birth (<37 gestational weeks, 8%). One woman developed onset of labor in breech presentation at 36 weeks gestational age in the nonimplantation group, and the other woman developed nonreassuring fetal status at 34 gestational weeks in the implantation group. Litta *et al.* reported that of 68 pregnant women who previously underwent TCR-M, 26 delivered during the preterm period (38%); fundus fibroids were associated with preterm birth, but not with development of placenta accreta.<sup>[15]</sup> As perinatal complications were not

described in the previous report, the reason for preterm birth was unclear. However, since there were few perinatal complications in our patients, the incidence of preterm birth might have been lower than that in other reports.

There were several limitations to this study. First, during the period from January 2011 to May 2018, 1749 women with leiomyoma underwent TCR-M in our hospital. Our hospital is a referral institution; thus, women who could not undergo TCR-M in other institutions were referred to our facilities, and the majority of patients returned to their original institutions after TCR-M. As a result, we were only able to analyze perinatal outcomes for pregnant women who underwent perinatal care in our hospital. Furthermore, in these patients, we could not evaluate either the myometrial damage caused by TCR-M or the myometrial thickness by using ultrasound prior to pregnancy. Second, since we evaluated the placental position using transabdominal ultrasound, it was unclear whether the resected myoma and placenta were entirely at the same location. Therefore, it was difficult to evaluate the accuracy of ultrasound in this study. Third, this was a single institutional study and the sample size was small. However, all TCR-M procedures were performed by the same physician. Therefore, we are confident that surgical quality was maintained among all of the patients who underwent TCR-M in our hospital.

While this study included some limitations, to the best of our knowledge, it is the first to evaluate detailed perinatal outcomes in pregnant women who previously underwent TCR-M; in particular, it is the first to evaluate the correlations between placenta implantation at prior myomectomy locations and perinatal outcomes in pregnant women who previously underwent one-step TCR-M. Recently, birthing age has been increasing in Japanese women; in the future, there is likely to be an increased number of women with myoma who are recommended to undergo TCR-M. Therefore, we believe that this study is clinically important.

## CONCLUSION

Our one-step TCR-M is a useful procedure for women with submucosal myoma for both menstrual problems and perinatal outcomes. We strongly recommend that clinicians should review the surgical video of TCR-M, and based on the myomectomy locations, consider the possibility of postpartum hemorrhage due to placental abruption, especially in cases of implantation. However, we will need larger sample sizes to investigate the correlation between risk of placental abruption and placenta implantation at prior myomectomy locations in pregnant women who had previously undergone our one-step TCR-M.

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## Conflicts of interest

There are no conflicts of interest.

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