Clinical Analyses of 66 Cases of Mid-trimester Pregnancy Termination in Women with Prior Cesarean

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Abstract

Background: The rate of cesarean delivery has significantly increased in China in the last decade. Women with prior cesarean history tend to have a higher risk of uterine rupture during termination of the pregnancy in mid-trimester than those without such a history. The aim of our study was to evaluate the influences of the potential risk factors on uterine rupture in women with prior cesarean.

Methods: We conducted this retrospective study of women with prior cesarean section, who underwent mid-trimester pregnancy termination between January 2006 and December 2013 in Peking Union Medical College Hospital. The protocol was oral administration of mifepristone and misoprostol for the patients with the gestational ages below 16 weeks or intra-amniotic injection of ethacridine lactate (EL) for those with at least 16 weeks of gestational ages. The thickness of the lower uterine segment (LUS) was measured before the termination of pregnancy. Logistic regression was used to study the risk factors of uterine rupture.

Results: The total rate of successful abortion was 93.9% (62/66). Four patients failed in induction, and one of them received curettage, whereas the other three experienced uterine rupture (4.5%). The successful rates of abortion were 85.7% (30/35) for women treated with mifepristone-misoprostol and 86.1% (31/36) for those treated with EL. There was a significant difference in the mean LUS thickness between the uterine rupture group (3.0 ± 2.0 mm) and the nonrupture group (7.0 ± 3.0 mm) ($P < 0.05$). The LUS thickness of <3 mm was associated with uterine rupture during mid-trimester pregnancy termination in women with prior cesarean (odds ratio, 94.0; 95% confidence interval 4.2–2106.1) after adjusted maternal age, gestational age, interdelivery interval and prior cesarean section. Severe bleeding that required transfusion occurred in one case (1.5%).

Conclusions: Both the mifepristone-misoprostol and the EL regimens were effective and safe for the termination of mid-trimester pregnancy in women with prior cesarean. A thinner LUS is associated with a relatively high risk of uterine rupture.

Key words: Lower Uterine Segment Thickness; Mid-trimester Pregnancy Termination; Prior Cesarean; Uterine Rupture

INTRODUCTION

Concurrent with the development of prenatal diagnosis, the improvement of operational skills, and the expansion of the indications for cesarean section, the rate of cesarean delivery has significantly increased to 46.2% in China in the past decade.[1] Consequently, the population of women with prior cesarean who experienced pregnancy termination was also increased. However, women with a prior cesarean history tend to have a higher risk of uterine rupture during the termination of pregnancy in the mid- or third-trimester than those without such a history (0.28–4.80% vs. 0.04%).[2-6] Moreover, sonographic lower uterine segment (LUS) thickness is a strong predictor for uterine scar defect in women with prior cesarean section.[6] In this study, we sought to determine the characteristics of the mid-trimester pregnancy termination and evaluate the influences of several potential risk factors on uterine rupture in women with prior cesarean.

METHODS

A retrospective study was performed on the patients with a previous lower segment cesarean that underwent indicated mid-trimester pregnancy termination in Peking Union Medical College Hospital (PUMCH) from January 1, 2006 to December 31, 2013. All the terminations were performed between 13 and 27 weeks of gestation. The gestational age was estimated from the first date of the last menstrual period and an ultrasound scan during the first-trimester. The latter one was adopted if the discrepancy between the two methods exceeded 7 days. The following data were collected from each patient's record: Inpatient record, obstetric history, indications for pregnancy termination, interdelivery intervals, induction agents, delivery time since regular uterine contraction, complications and pregnancy outcomes.

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Sonographic examinations of all the patients were performed by one of two experienced physicians in PUMCH using the GE LOGIQ E9 ultrasound imaging system (GE Healthcare) and measurements of the parameters were routinely cross-checked prior to the termination of pregnancy. The full LUS is a two-layer structure that consists of an echogenic layer and a layer that is usually less echogenic. The thinnest region of LUS was identified and measured at least 3 times both transabdominally and transvaginally, and the lowest value of the LUS thickness was analyzed in this study.

In China, oral administration of mifepristone and misoprostol for the termination of pregnancy in weeks 10–16 and intra-amniotic injection of ethacridine lactate (EL; Rivanol®) for the termination of gestation after the 16th week are the standard procedures in clinical practice. Women in the mifepristone-misoprostol group received 200 mg of mifepristone, followed with 600 µg of misoprostol 36–48 h later. If necessary, 200 µg of vaginal misoprostol was given every 3 h for a maximum of 1800 µg daily. Women in the EL group received an intra-amniotic injection of 100 mg ethacridine, which is a dye with antiseptic properties. EL induces the production of endogenous prostaglandins and thromboxane, probably by provoking a chemical trauma to the fetal membranes and the deciduas, and thus promoting cervical priming and initiating of labor. All women were hospitalized for the termination procedure. Adverse events, uterine contractions, blood pressures, pulse rates and temperatures were recorded. Pelvic examination was performed every 3 h since uterine contraction began or otherwise medically indicated. The expulsed fetuses were carefully examined for their integrities and subsequently, curettage was performed for the patients. All the tissues passed out were submitted for histological assessment to ensure that the abortion was complete. The patients without any complications were discharged 24 h after abortion. Successful abortion was defined as the expulsion of the fetus, irrespective of whether evacuation was necessary because of incomplete termination. The patients, who had unsuccessful abortion after the initially allocated treatment, were received the same treatment again or an alternative treatment in the next week. Each patient was scheduled for a follow-up assessment in the clinic 6 weeks after the abortion with questionnaires on the duration of bleeding after abortion, recommencement of menstruation and complications after the abortion. A pelvic examination was also performed.

Statistical analyses were performed using SPSS version 19.0 software (SPSS Inc., Chicago, IL, USA). Student's t-test and Fisher's exact test were used to compare the differences between continuous data and categorical variables, respectively. Logistic regression was used to study the risk factors of uterine rupture. $P < 0.05$ was considered as statistically significant.

RESULTS

The study population consisted of 66 women with a prior lower segment cesarean who underwent mid-trimester pregnancy termination in PUMCH between the years 2006 and 2013. Thirty-three women received oral mifepristone-misoprostol, and 33 women received intra-amniotic injection of EL as the initial allocated treatment according to their pregnancy weeks.

The characteristics of the study subjects are compared in Table 1. The study group was comprised of three cases of uterine rupture (4.5%), while the remaining 63 women with an uncomplicated vaginal delivery comprised the control group. All the factors evaluated in both groups had no statistically significant difference except for the LUS thickness. In the uterine rupture group, the average maternal age was 33.0 ± 8.0 years and the average gestational age was 18.7 ± 3.1 weeks, comparing with 34.3 ± 4.0 years and 17.7 ± 3.6 weeks in the nonuterine rupture group ($P > 0.05$). Among the 66 patients studied, four had two previous cesarean sections (4/66, 6.1%), and three had received myomectomy (3/66, 4.5%). For the patients who had multiple uterine surgery histories, only one with two cesarean sections was in the uterine rupture group whereas all the others delivered without any complications. The mean interdelivery intervals were 19.0 ± 7.2 months and 49.2 ± 33.1 months in the uterine rupture group and the nonrupture group, respectively, but the difference between these two groups was not statistically significant ($P > 0.05$). One woman experienced uterine rupture was induced in mid-trimester using agents of mifepristone and misoprost and two women experienced uterine rupture was induced using agents other than mifepristone or misoprost. However, there was no significant difference in the induction agents used between the uterine rupture group and the nonrupture group ($P > 0.05$).

Table 1: Patient's characteristics in both groups

Items	Uterine rupture ($n = 3$)	Nonuterine rupture ($n = 63$)	P
Maternal age (years)	33.0 ± 8.0	34.3 ± 4.0	0.584
Gestational age (weeks)	18.7 ± 3.1	17.7 ± 3.6	0.635
Interdelivery interval (months)	19.0 ± 7.2	49.2 ± 33.1	0.122
Prior cesarean section (n (%))			
1	2 (3.0)	60 (91)	0.174
2	1 (1.5)	3 (4.5)	
Induction agent (n (%))			
Mifepristone-misoprostol	1 (1.5)	32 (48.5)	1.000
No nmifepristone-misoprostol	2 (3.0)	31 (47.0)	
Ethacridine	1 (1.5)	31 (47.0)	
Mifepristone and ethacridine	1 (1.5)	0 (0)	
Full LUS thickness (mm)	3.0 ± 2.0	7.0 ± 3.0	0.006

Values were presented as n (%) or mean ± SD. Maternal age, gestational age, interdelivery interval and full LUS thickness were compared with Student's t-test. Statistical analyses of categorical variables were performed using continuity-corrected Chi-square or Fisher's exact test. A $P < 0.05$ was considered statistically significant. Data were analyzed using commercially available software (SPSS version 19.0). SD: Standard deviation; LUS: Lower uterine segment.

In the nonrupture group, the average LUS thickness examined was 7.0 ± 3.0 mm, whereas the average LUS thickness in the uterus rupture group was 3.0 ± 2.0 mm. There was a significant difference in the LUS thickness between these two groups ($P < 0.05$). A LUS thickness of <3 mm was associated with uterine rupture during mid-trimester pregnancy termination in women with prior cesarean (odds ratio, 94.0; 95% confidence interval: 4.2–2106.1) after adjusted maternal age, gestational age, interdelivery interval and prior cesarean section.

The indications for pregnancy termination of all the patients are shown in Table 2. Twenty-two (33.3%) cases terminated pregnancy because of fetal deformity and 6 (9%) cases terminated pregnancy because of stillbirth. There were 21 (31.8%) patients who were not aware of their pregnancies in the first-trimester because of lactation (13/66, 19.7%), irregular bleeding, prolactinoma or polycystic ovary syndrome, and therefore, terminated pregnancy because of unintended pregnancy during mid-trimester. Fifteen (22.7%) cases had serious medical disorders, such as hypertensive disorders during pregnancy, systemic lupus erythematosus, rapid enlargement of uterine myoma, nephrotic syndrome, and diabetes, and were unable to carry on. Social factors like divorce occurred in 2 (3.0%) cases.

Uterine rupture occurred in 3 out of 66 women of the study group (4.5%). Among 63 patients in the nonuterine rupture group (control group), 59 (89.4%) had successful initial induction and virginal deliveries, whereas 4 (6.1%) failed

in initial induction, but finally managed virginal deliveries as well. A patient, who failed to deliver after initial induction with EL, delivered 5 days after an additional amniotic administration of 100 mg of EL. Another patient failed after EL administration and was treated with mifepristone-misoprostol administration for the termination of the pregnancy. Patient 3 had unsuccessful abortion after mifepristone-misoprostol administration, and the fetus was expelled after EL administration. Patient 4 had to receive curettage under ultrasonic monitoring in the 17th pregnancy week, following twice of induction with mifepristone and misoprostol in 2 weeks, plus 1 week of induction with intra-amniotic injection of EL. Therefore, the rates of successful abortion were 85.7% (30/35) of women treated with mifepristone-misoprostol administration and 86.1% (31/36) of those treated with EL. The overall rate in successful abortion was 93.9% (62/66). There was no trauma of the birth canal occurred in all the patients.

Uterine rupture occurred in three out of 66 women (4.5%). Table 3 summarizes the pertinent clinical data on each of the three patients who had uterine rupture and received emergency laparotomy without hysterectomy. Their abortion regimens were as followed: The first patient of 16 weeks received 50 mg of mifepristone, twice a day, for two days, followed with 1200 μg of misoprostol within the 3th day. Patient 2 of 22 weeks received 100 mg of EL given in amniotic fluid. Patient 3 of 18 weeks was administrated with 50 mg of mifepristone, twice a day, for two days, and intra-amniotic injection of 100 mg of EL at 9 a.m. on the second day. All three patients suffered persistent and progressive lower abdominal pain after treated in other hospital prior to transfer to the Emergency of PUMCH and received immediate surgical intervention. There were rupture and active bleeding in the uterine scar in the first two patients. But in patient three the uterine scar thickness was 0.5 cm without break, uterine left side wall ruptured long about 5 cm and the fetal limb stretched out of the uterus during the operation. The ruptured uteri were successfully sutured. Although patient two required transfusion of 12 units of packed red blood cells, all the patients had a smooth postoperative recovery and were discharged later in good conditions. The study group was comprised of three cases (4.5%) of uterine rupture. The remaining 63 women with an uncomplicated vaginal delivery comprised the control group. In the follow-up of 6 weeks after the abortion, all patients recovered well and pelvic examination was normal.

Table 2: Indications for pregnancy termination

Indication	Number	Percentage (%)
Fetal deformity	22	33.3
Fetal death	6	9.0
Maternal diseases	15	22.7
Hypertensive disorders during pregnancy	6	9.0
SLE	4	6.1
Rapid enlargement of uterine myoma	3	4.5
Diabetes	1	1.5
Hyperthyroidism	1	1.5
Unintended pregnancy	21	31.8
Lactation	13	19.7
Polycystic ovary syndrome	4	6.1
Menstrual disorder	3	4.5
Prolactinoma	1	1.5
Social factor (divorce)	2	3.0

SLE: Systemic lupus erythematosus.

Table 3: Clinical data of the patients with uterine rupture

Patient number	Maternal age (years)	Parity	Gestational age (weeks)	Prior cesarean	Initial induction agent	Interdelivery interval (months)	LUS thickness (cm)
1	41	1	16	1	Mifepristone-misoprostol	25	0.2
2	25	1	22	1	Ethacridine	11	0.1
3	33	2	18	2	Mifepristone-ethacridine	21	0.5

LUS: Lower uterine segment.

Discussion

There have been reports demonstrating that the misoprostol appears to greatly increase the risk of uterine rupture. Based on the information available up to date, it is not recommended to be used in the delivery for women with a previous cesarean.[7] Although several literatures revealed that both the intra-amniotic injection of EL and oral mifepristone-misoprostol regimens were safe during the termination of second-trimester pregnancy,[8-10] little is known about these regimens on the termination of mid-trimester pregnancy in women who had a history of cesarean. In our study, the successful abortion rates were 85.7% (30/35) for women treated with mifepristone-misoprostol administration and 86.1% (31/36) for those treated with EL. The overall rate of successful abortion was 93.9% (62/66). There was no significant difference in the induction agents between the uterine rupture group and the nonrupture group ($P > 0.05$). Both mifepristone-misoprostol and EL regimens were effective and safe for the termination of mid-trimester pregnancy in women with prior cesarean.

Sonographic LUS thickness is a strong predictor for uterine scar defect in women with prior cesarean.[10,11] Many studies have demonstrated that the full LUS thickness affected the safety of vaginal birth at term after a prior low transverse cesarean delivery.[11-14] Basic *et al.* showed that the median myometrial thickness at the level of the isthmus was 6.7 mm in women, who had undergone one cesarean section, and the cut-off value of the thickness of the scars, which indicated the possibility of vaginal birth after previous incision, was 3.5 mm.[15-17] However, whether the full LUS thickness affected mid-trimester pregnancy termination was not confirmed. By comparing the LUS thickness in women suffered uterine rupture with those who delivered smoothly, we defined that the full LUS thickness of less than 3.0 mm was an independent risk factor of uterine rupture during mid-trimester pregnancy termination in women with prior cesarean (odds ratio, 94.0; 95% confidence interval). In the nonrupture group, the LUS thickness ranged from 3 mm to 12 mm, regardless of the gestational age and the interdelivery intervals. By contrast, three patients with ruptured uteri had lower LUS, indicating that the defective scars were too weak to sustain uterine contraction while induction. This supports our assumption of a LUS thickness being associated with increased risk of uterine rupture in mid-trimester pregnancy termination complicated with prior cesarean. One of the patients, who had an unruptured scar of 5 mm in thickness, was found to have a left lateral uterine rupture of 5 cm in length during the emergency cesarean section. This suggested that the uterine rupture could also occur in some area other than the scar. Because of uncoordinated uterine contraction and unfavorable cervix, the uterus could rupture in the weakest area. There were also reports of uterine rupture during uterine curettage in induced labor in the second-trimester.[3] As a result, for women with previous cesarean section who undergo induced labor in the second-trimester, examinations of the LUS thickness and cervical motion tenderness are very important, as well as close monitoring during labor as it can detect tetanic contractions so to prevent severe complications, such as uterine rupture and hemorrhagic shock.

It has been demonstrated that interdelivery intervals were related to a high risk of uterine rupture during term labor.[17-19] In our study, the mean (±SD) interdelivery interval in the uterine rupture group (19.0 ± 7.2 months) was less than that of the nonrupture group (49.2 ± 33.1 months). However, the difference in the mean interdelivery interval between these two groups was not statistically significant ($P > 0.05$). Moreover, there was a report showing that interdelivery interval had no significant adjusted odds for failed TOLAC.[20]

In summary, our findings enhanced the counseling of women with a prior cesarean section undergoing a mid-trimester termination. A thinner LUS at 13–27 weeks of gestation is associated with a high risk of uterine rupture during mid-trimester termination. Therefore, measurement of the full LUS thickness in women with a prior cesarean before the termination of pregnancy at mid-trimester is essential and likely to reduce the risk of uterine rupture. Although we cannot define the cut-off value of LUS thickness precisely for prediction of uterine rupture as the case number was low, for women with a LUS thickness below 3 mm, intensive monitoring is strongly recommended and emergency cesarean, if necessary, is warranted. In order to evaluate the risk factors of uterine rupture more precisely, a very large case series is required, preferably using data collected nationally.

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