

Infertility Following Retained Products of Conception: Does the Timing of Surgical Intervention Matter?

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ABSTRACT: **Background:** Despite the large volume of evidence on the management of retained products of conception (RPOC), there are virtually no data regarding the optimal time frame of surgical intervention in case of RPOC.

Objectives: To examine whether the time interval between spontaneous vaginal delivery or pregnancy termination and the uterine evacuation due to pathologically confirmed RPOC influences the reproductive outcome.

Methods: We retrospectively reviewed all the records of women who were admitted to our department due to pathologically confirmed RPOC following either spontaneous vaginal delivery or pregnancy termination between January 2000 and December 2010. Based on the median time from delivery or pregnancy termination until the operative intervention in the study group, patients were stratified into two groups: early intervention (< 3 weeks) and late intervention (> 3 weeks). Reproductive outcomes were compared between the two study groups.

Results: Reproductive outcomes were analyzed in 172 patients with pathologically confirmed RPOC. Of them, 95 (55.2%) were included in the early intervention group and 77 (44.8%) in the late intervention group. There were no significant differences in the conception rate, mean time to conception, and the occurrence rate of a new infertility problem in women with early surgical intervention compared to those with late surgical intervention ($P > 0.05$). Furthermore, there was no significant difference between the groups in pregnancy outcomes following RPOC.

Conclusions: Early surgical intervention in women with pathologically confirmed RPOC following spontaneous vaginal delivery or pregnancy termination yields the same reproductive outcomes as late surgical intervention.

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KEY WORDS: retained products of conception (RPOC), infertility, residua, curettage, hysteroscopy

This syndrome is manifested clinically by menstrual abnormalities, infertility and recurrent pregnancy loss, and predisposes to severe obstetric complications in future pregnancies, such as placenta accreta, preterm delivery, ectopic pregnancy and intrauterine growth restriction (IUGR) [4].

Traditionally, management of RPOC has been dilation and evacuation (D&E) and it remains a common procedure [5]. In 1997, Goldenberg et al. [6] reported on the use of hysteroscopy for the treatment of RPOC, which allows highly selective removal limited to the RPOC without affecting the adjacent endometrium [6]. Further studies have subsequently shown relatively low rates of postoperative adhesions using the operative hysteroscopy technique to treat RPOC after delivery and abortion [7–9]. However, operative hysteroscopy may be problematic in the immediate postpartum period due to heavy vaginal bleeding and the large size of the uterus. It has been suggested that hysteroscopic selective resection of the retained products of conception should be considered in patients with secondary (delayed) postpartum bleeding [10].

RPOC may have devastating fertility consequences when severe IUA develop [4]. Our group recently found that hysteroscopic removal of RPOC is associated with improved reproductive outcomes as compared to D&E [11]. We also found that the RPOC-associated infertility is primarily related to the presence of trophoblastic tissue rather than the surgical intervention in the gravid uterus [12], and pathologically confirmed RPOC leads to the same reproductive outcomes following spontaneous vaginal delivery and first-trimester pregnancy termination [13].

Despite the large volume of evidence on the management of RPOC, there are virtually no data regarding the optimal time frame of surgical intervention in case of RPOC. Therefore, this study aimed to examine whether the time interval from spontaneous vaginal delivery or termination of pregnancy to the uterine evacuation based on suspicion of RPOC influenced the reproductive outcomes of women with pathologically confirmed RPOC.

PATIENTS AND METHODS

A computerized retrospective search was conducted to identify women admitted to our department due to suspected RPOC

The diagnosis of retained products of conception (RPOC) is crucial because the possible sequelae may be serious [1]. Among the short-term complications of RPOC are bleeding and infections, while the long-term complications include formation of intrauterine adhesions (IUA) and Asherman syndrome [2,3].

following either spontaneous vaginal delivery or termination of pregnancy between 1 January 2000 and 31 December 2010. Data on demographic characteristics, operative findings, surgical procedure and pathologic diagnoses were retrieved from the medical records. Approval for the study was obtained from the Institutional Research Board.

The same skilled surgeons performed both the immediate and elective cases and decided whether to perform D&E or hysteroscopy. Traditionally, management of RPOC has been dilatation and evacuation. Hysteroscopic resection of RPOC is an alternative to non-selective blind curettage and allows highly selective removal that is limited to the RPOC without affecting the adjacent endometrium. Recently, hysteroscopic removal of RPOC was implemented in our department as the gold standard for treatment in cases of suspected RPOC. However, patients who are hemodynamically unstable or septic underwent prompt D&E. Hysteroscopy was favored in elective cases.

All women underwent uterine evacuation, either by D&E or hysteroscopy due to suspicion of RPOC. The extracted material obtained was sent for histological examination. The final diagnosis of RPOC was based on the presence of retained trophoblastic tissue, as confirmed by histological examination.

Based on the median time from delivery or pregnancy termination until the operative intervention in the study group,

patients were stratified into two groups: early intervention defined as operative intervention < 3 weeks, and late intervention defined as ≥ 3 weeks after the vaginal delivery or termination of pregnancy due to suspicious RPOC.

Patients with suspicion of RPOC based on history, physical examination and/or Doppler ultrasound imaging studies are managed as soon as possible. However, surgical intervention may be deferred and electively performed in asymptomatic women with suspected RPOC, in contrast to symptomatic women in whom the surgical intervention is performed earlier.

The fertility of participants was assessed by a review of their medical records and by telephone interviews. After obtaining verbal consent to participate in the study, details regarding fertility, infertility treatment (including ovulation induction and in vitro fertilization), and infertility workup were acquired telephonically.

Descriptive parameters are expressed as mean \pm SD. Frequencies are given as percentages. Statistical analysis was performed using the Student *t*-test, the χ^2 test, Fisher's exact test, and the Mantel-Haenszel test. Calculations were performed using SPSS software (Version 17, Chicago, IL, USA) by the Tel Aviv University statistical laboratory; *P* values of < 0.05 were considered statistically significant.

Table 1. Characteristics of the study group

	Early intervention (n=95)	Late intervention (n=77)	<i>P</i> value
Age (years, mean \pm SD)	30.7 \pm 6.2	30.2 \pm 6	0.94
Smoking (%)	36	31.1	0.102
Mode of conception preceding residua (%)			
Spontaneous	93.7	87	0.87
Assisted reproductive technologies	6.3	13	
Obstetric history			
Gravidity (n, mean \pm SD)	3.01 \pm 2.3	2.35 \pm 1.3	0.029
Parity (n, mean \pm SD)	1.66 \pm 1.7	1.4 \pm 0.95	0.7
Previous cesarean section (%)			
0	86.3	85.9	0.745
1	6.8	10.9	
2 and more	6.8	3.1	
Previous first-trimester missed abortion (%)			
0	69.5	75.3	0.545
1	20	15.6	
2 and more	10.5	9.1	
Previous second-trimester missed abortion (%)			
0	95.8	97.4	0.683
1	4.2	1.3	
2 and more	0	1.3	
Previous first-trimester induced abortion (%)			
0	56.8	66.2	0.45
1	33.7	26	
2 and more	9.7	7.8	
Previous second-trimester induced abortion (%)			
0	96.8	93.5	0.68
1	3.2	6.5	

RESULTS

Between January 2000 and December 2010, 368 women were admitted to our department due to suspected RPOC after either spontaneous vaginal delivery or termination of pregnancy. In 244 patients (66.3%) the diagnosis of RPOC was confirmed by histological examination. Reproductive outcomes were analyzed in 172 patients (70.5%) after excluding patients who did not wish to participate in the study and cases that were lost to follow-up. Of them, 83 (48.3%) were admitted after spontaneous vaginal delivery and 89 (51.7%) following D&C. Ninety-five (55.2%) were included in the early intervention group and 77 (44.8%) in the late intervention group.

There were no differences in demographic data, parity, obstetric history or mode of conception preceding the RPOC between the two study groups [Table 1]. The mean gravidity of women in the early surgical intervention group was significantly higher compared to the late surgical intervention (3.01 \pm 2.3 vs. 2.35 \pm 1.3 respectively, *P* = 0.029) [Table 1].

Regarding the clinical symptoms at admission, there were no significant differences in the rates of abdominal pain and bleeding between women in the early intervention and those in the late intervention group [Table 2]. However, a presenting sign of fever was more prevalent in women with early surgical intervention compared to women with late surgical intervention (21.1% vs. 7.8% respectively, *P* < 0.001) [Table 2].

Finally, concerning the treatment modality, more women with early surgical intervention underwent D&E as compared

Table 2. Comparison of clinical presentation and mode of treatment between women with early versus late surgical intervention due to pathologically confirmed retained products of conception

	Early intervention (n=95)	Late intervention (n=77)	P value
Clinical symptoms (%)			
Bleeding	69.5	79.2	0.811
Abdominal pain	21.1	14.3	0.83
Fever	21.1	7.8	0.018
Mode of treatment (%)			
Hysteroscopy	30.5	66.2	< 0.001
Dilatation & evacuation	69.5	33.8	

to late surgical intervention (69.5% vs. 30.5%, $P < 0.001$), whereas more women with late surgical intervention underwent hysteroscopy as compared to early surgical intervention (66.2% vs. 33.8%, $P < 0.001$).

The reproductive and pregnancy outcomes of the study group are presented in Table 3. There were no significant differences in the rate of women who desired pregnancy, the conception rate, mean time to conception, and the occurrence rate of a new infertility problem in women with early surgical intervention compared to those with late surgical intervention ($P > 0.05$). There were no significant differences between the groups in the pregnancy outcomes following RPOC [Table 3]. A logistic regression analysis that controlled for the surgical procedure type found no significant differences in both reproductive and pregnancy outcomes between the two study groups.

DISCUSSION

The diagnosis of RPOC is based on different clinical symptoms and signs as well as on sonographic assessment. The combination of clinical and Doppler sonographic evaluations before a decision to proceed with surgical intervention in cases of suspected RPOC was found to decrease the rate of unnecessary invasive procedures [1]. Since RPOC occurs in reproductive-age women who may desire future pregnancies, the most important long-term complication of this condition is infertility, which is mostly related to the formation of IUA following treatment. This study focuses on the impact of the timing of uterine cavity evacuation in women with pathologically confirmed RPOC following spontaneous vaginal delivery or D&E on their future fertility. To the best of our knowledge, this is the first study to address this issue.

The main findings of the present study were similar reproductive outcomes between early and late surgical intervention in women with pathologically confirmed RPOC, namely, no significant differences in the conception rate, mean time to subsequent pregnancy, and the occurrence rate of a new infertility problem. Also, there were no significant differences between the study groups in the subsequent pregnancy outcomes following RPOC.

Table 3. Comparison of reproductive and pregnancy outcomes between women with early versus late surgical intervention due to pathologically confirmed retained products of conception

	Early intervention (n=95)	Late intervention (n=77)	P value
Reproductive outcome following residua			
Desired pregnancy (%)	56.8	51.9	0.156
Conceived (%)	53.7	50	0.34
Time to conception (months, mean ± SD)	11 ± 14.1	8.1 ± 10.3	0.82
New infertility problem (%)	21.1	21.3	0.7
Pregnancy outcome following residua			
Delivery (%)	85.3	84.9	0.35
Abortion (%)	14.7	15.1	0.18
Placental complications (%)	13.8	4.4	0.55
Birth weight (g, mean ± SD)	2901.1 ± 818.7	3005.2 ± 524.4	0.81
Birth week (mean ± SD)	36.8 ± 1.4	37.6 ± 3.6	

Another question to be determined is the primary surgical intervention: D&E or hysteroscopy. A meta-analysis by Smorgick et al. [14] examined the evidence regarding the use of hysteroscopy for treatment of RPOC and concluded that hysteroscopy appears to have low complication rates, low rates of IUA, and high rates of subsequent pregnancies [14]. This is in agreement with our published data; accordingly, hysteroscopic removal of pathologically confirmed RPOC is associated with a shorter mean time to further conception and a lower rate of occurrence of newly diagnosed infertility problems than with blind dilation and curettage [11].

It is well known that failure to remove all placental tissue following birth, or incomplete evacuation of the products of conception during D&C, may manifest clinically with fever. In the current study we found that a presenting sign of systemic fever was more prevalent in the early intervention group as compared with the late intervention group (22.1% vs. 7.9% respectively, $P = 0.012$) [Table 1]. These findings could be explained by the fact that in contrast to vaginal bleeding or abdominal pain, systemic fever appearing in the early period after delivery or pregnancy termination increases the likelihood of a request for a medical examination and hence early diagnosis and treatment.

RPOC are common clinical complications that may carry a heavy medico-legal burden. When fertility problems develop secondary to intrauterine adhesions, legal action may be quick to follow. Malpractice claims regarding IUA and their consequences have become more common in recent years [15]. The problem when dealing with legal cases of RPOC is that there is no real “standard of care.” It is not clear which approach is better: immediate or delayed surgical intervention [15].

We are aware of the limitations of the present study, being retrospective and that the statistical analysis was conducted after a telephone interview which may be associated with recall bias. As there are no data in the literature concerning this important issue, further studies are needed to confirm these results.

In conclusion, the present study shows that early surgical intervention in women with pathologically confirmed RPOC

following spontaneous vaginal delivery or pregnancy termination yields the same reproductive outcome as late surgical intervention.

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