Full length article

A cohort study comparing the severity and outcome of intrauterine adhesiolysis for Asherman syndrome after first- or second-trimester termination of pregnancy

Ru Zhu[a,b], Lu Gan[a], Sha Wang[a], Hua Duan[a,*]

[a] Department of Minimally Invasive Gynecology, Beijing Obstetrics and Gynecology Hospital, Capital Medical University, No. 17 Qihelou Street, Dong Cheng District, Beijing, 100006, China
[b] Department of Obstetrics and Gynecology, Anqing Hospital Affiliated to Medical University of Anhui, Anqing, 246003, China

A B S T R A C T

Objective: To compare the clinical characteristics of Asherman syndrome and the outcomes of hysteroscopic adhesiolysis in women after first or second-trimester termination of pregnancy (TOP).
Methods: This was a retrospective descriptive analysis of patients with moderate-to-severe intrauterine adhesiolysis (IUAs) after TOP and treated by hysteroscopic adhesiolysis and followed by "second-look" hysteroscopy 3 months later at The Beijing Obstetrics and Gynecology Hospital (China) between January 2013 and March 2016. The American Fertility Society (AFS) scoring system was used to evaluate the intrauterine adhesions.
Results: A total of 236 patients with 180 first-trimester TOP and 56 s-trimester TOP patients were included. The severe adhesion and amenorrhea rates during the second-trimester group (69.6% and 39.3%, respectively) were significantly higher than those in the first-trimester group (36.7% and 7.2%, respectively). AFS score reduction in the second-trimester group (6.2 ± 2.8) was significantly lower than in the first-trimester group (6.5 ± 2.5). The pregnancy rates in the second-trimester group (21.4%) were significantly lower than that in the first-trimester group (43.3%). The pregnancy rate of severe intrauterine adhesions in second-trimester TOP (10.3%) was significantly lower than in first-trimester TOP (40.9%).
Conclusion: These findings suggested that second trimester TOP was associated with more severe intrauterine adhesion and a worse prognosis after hysteroscopic adhesiolysis in women with Asherman syndrome when compared to first-trimester TOP.

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Introduction

Intrauterine adhesions (IUAs) or Asherman syndrome is characterized by partial or complete adhesions of the uterine cavity and/or the cervical canal. IUAs manifest as amenorrhea, hypomenorrhea, pelvic pain, infertility, recurrent miscarriage or obstetric complications [1]. Trauma to the endometrial zona basalis, which typically occurs after intrauterine surgery, especially after dilation and curettage related to pregnancy, is the main cause of IUAs [2,3]. Intrauterine examination or surgery is often performed after second-trimester termination of pregnancy (TOP), as it may cause long-term complications, including IUAs

[4–6]. Nevertheless, there are no studies that reported the incidence of IUAs after second-trimester TOP and associated treatment outcomes after IUAs.

The prognosis of IUAs is closely related to the degree of adhesions [7]. With the increasing number of elderly pregnant women and the development of prenatal screening technology, more fetal malformations are diagnosed during the second trimester [8,9]. So, many of these patients choose a second-trimester abortion, but most of these patients will desire a normal pregnancy thereafter. Therefore, it is important to study the degree of IUAs and its impact on the outcome of treatment in these patients.

The occurrence of early complications including postpartum hemorrhage, pregnancy residue, uterine perforation, infection, and health risks after second-trimester TOP are more severe than those after first-trimester TOP [10,11]. We hypothesized that the degree of intrauterine adhesions after TOP during the

* Corresponding author.
  E-mail addresses: zhuru19790202@163.com (R. Zhu), gl19880508@163.com
(L. Gan), wangsha1020@163.com (S. Wang), duanhuasci@163.com (H. Duan).

second trimester would be more severe, and therefore the prognosis following hysteroscopic adhesiolysis would be worse than those patients who undergo first-trimester TOP. Hence, we retrospectively compared the degree of IUAs and the outcome of hysteroscopic adhesiolysis between patients who underwent first-trimester TOP and those who underwent second-trimester TOP.

Materials and methods

Patients

This study was performed at the Minimally Invasive Gynecologic Center of the Beijing Obstetrics and Gynecology Hospital affiliated to the Capital Medical University, Beijing, China. This is a tertiary hysteroscopic center that performs an average of 150 intrauterine adhesiolysis procedures for Asherman syndrome each year for over the last 4 years. Women who underwent hysteroscopic adhesiolysis from January 2013 to March 2016 were included in this study. The data for this study were obtained from the electronic medical records database; only hospitalized patients with moderate to severe intrauterine adhesions were included in the study. Patients with mild intrauterine adhesions were treated at the outpatient department and were not included in the database, nor in the current study due to lack of detailed electronic medical information. All patients underwent curettage after TOP. Institutional review board approval was obtained for data collection.

All participants met the following inclusion criteria: [1] <40 years of age; [2]; moderate or severe IUAs [American Fertility Society (AFS) score ≥ 5] [3]; IUAs after TOP during the first or second trimester; and [4] patients had fertility requirement. The exclusion criteria were as follows [1]: no follow-up hysteroscopy evaluation for 3 months after IUAs; and [2] previous hysteroscopic adhesiolysis; or [3] premature ovarian failure.

Classification of IUAs

The extent and severity of IUAs were measured according to the AFS scoring system (1988 version) [12]. Scores of 1–4, 5–8, and 9–12 were considered as mild, moderate, and severe adhesions, respectively.

Surgical procedure

Hysteroscopic adhesiolysis was performed by experienced senior surgeons using a bipolar electrode needle or loop. The coagulating and cutting power were set at 160 W and 320 W, respectively. The distention medium used was 0.9% saline. The extent of uterine cavity involvement and types of adhesions were visualized and evaluated. Similar techniques were used in all the cases. The surfaces involved in the adhesions were separated with a needle electrode, then the remaining endometrium was separated and protected, and the scar tissue excision was performed using the loop electrode until resumption of normal uterine cavity morphology was observed (revealing the bilateral uterine horn with or without tubal ostium). All procedures were performed under ultrasonographic and laparoscopic guidance. Because of the fertility intent, it allowed monitoring of the early occurrence of perforation and other complications, as well as abdominal exploration for other causes of infertility eventually.

Postoperative treatments

At the end of the procedure, an adhesion barrier was selected for insertion into the uterine cavity. Either an intrauterine balloon (filled with 3–5 ml water) was inserted and then was removed after 5–7 days, or a heart-shaped copper intrauterine device (removed 3 months later during the follow-up hysteroscopy). Hormonal therapy is routinely used at our center after hysteroscopic adhesiolysis and an intrauterine device is used during this period.

Hormone therapy was started on day 2 after the operation and consisted of estradiol valerate 4 mg/d for 21 days, and dydrogesterone of 20 mg/d was added for estrogen therapy in the last 10 days. This was followed by no hormone therapy for a period of 7 days. The hormone therapy regimen was then repeated for an additional 2 months. The use of estrogen in combination with dydrogesterone helps to achieve periodic menstruation in the postoperative patients.

The reduction of AFS score after hysteroscopic adhesiolysis was the primary efficacy outcome. A follow-up hysteroscopy was performed 3 months after the initial operation during the early proliferative phase of the menstrual cycle. If adhesions recur, a repeated hysteroscopic adhesiolysis was performed after the follow-up hysteroscopy. If adhesions did not recur, subjects were instructed to resume their efforts to conceive. The menstrual pattern was also recorded; the increased or normal volume was defined as an improvement, while unchanged or reduced volume was defined as no improvement.

Follow-up

Follow-up evaluations were conducted in the hospital outpatient department or by telephone call. Menstrual patterns, pregnancy outcomes, and obstetric complications were documented.

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 22.0 (IBM Corp, Armonk, NY, USA). Student's t test was used to compare normally distributed data between the two groups. Mann-Whitney U test was used to compare the non-normally distributed data. Chi-square test was used to compare the discrete variables between the two groups. A P value of <0.05 was considered to be statistically significant.

Results

In total, 236 patients were included in the final analysis, with 180 in the first-trimester TOP group and 56 in the second-trimester TOP group. A flowchart depicting the patient selection was presented in Fig. 1. No significant differences were observed between the two groups in age, number of pregnancies, number of curettage procedures, or use of postoperative adhesion barriers (Table 1). No serious complications including uterine perforation or air embolism occurred.

The clinical features of IUAs after TOP are shown in Table 2. The rates of amenorrhea and severe adhesions during the second-trimester TOP group (39.3% and 69.6%, respectively) were significantly (P < .05) higher than during the first-trimester TOP group (7.2% and 36.7%, respectively).

The reduction of AFS score was significantly lower in the second-trimester TOP group (6.2 ± 2.8), (P < .05) compared to the first-trimester TOP group (6.5 ± 2.5) (Table 3). The rate of adhesion recurrence in the second-trimester TOP group (62.5%) was significantly (P < .05) higher than in the first-trimester TOP group (31.5%). The improved rate of menstruation in the second-trimester TOP group (71.4%) was significantly (P < .05) lower compared to the first-trimester TOP group (87.2%).
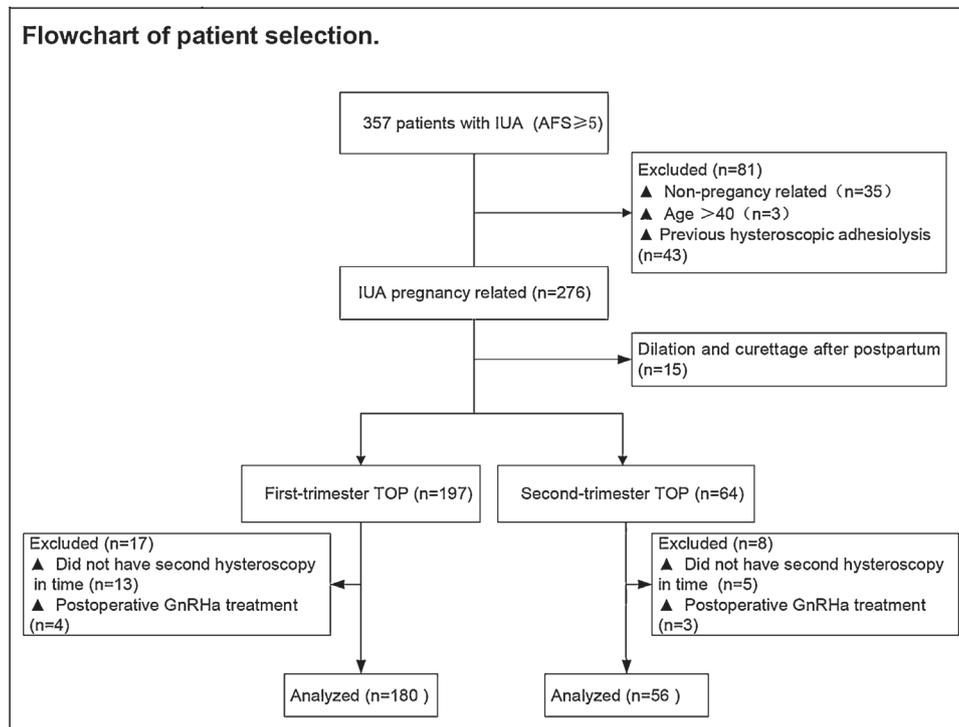
Flowchart of patient selection.

357 patients with IUA (AFS≥5)

Excluded (n=81)
▲ Non-pregnancy related（n=35）
▲ Age ＞40（n=3）
▲ Previous hysteroscopic adhesiolysis (n=43)

IUA pregnancy related (n=276)

Dilation and curettage after postpartum (n=15)

First-trimester TOP (n=197)   Second-trimester TOP (n=64)

Excluded (n=17)
▲ Did not have second hysteroscopy in time (n=13)
▲ Postoperative GnRHa treatment (n=4)

Excluded (n=8)
▲ Did not have second hysteroscopy in time (n=5)
▲ Postoperative GnRHa treatment (n=3)

Analyzed (n=180)   Analyzed (n=56)

Fig. 1. Flowchart of patient selection.

The average follow-up time was 24.6 ± 3.4 months (15–39 months). The reproductive outcomes in the two groups are summarized in Table 4. The rates of conception and term births in the second-trimester TOP group (21.4% and 58.3%, respectively) were significantly ($P < .05$) lower than in the first-trimester TOP group (43.3% and 71.8%, respectively). The premature birth rate in the second-trimester TOP group (25%) was significantly ($P < .05$) higher than in the first-trimester TOP group (1.3%). In the early and mid-term groups, there were 102 and 44 cases who were not pregnant. There was no pregnancy in patients with amenorrhea.

In subgroup analysis, subjects with moderate or severe adhesions before surgery were separately analyzed. The rate of adhesion recurrence in the moderate groups first-trimester TOP was 18.4%, and second-trimester TOP was 47.1%, showing statistically significant difference ($P < 0.05$). The improved menstruation in the severe groups second-trimester TOP was 69.2%, and first-trimester TOP 86.4%, showing significant differences ($P < .05$). The pregnancy rate in the severe groups second-trimester TOP was 10.3%, and first-trimester TOP was 40.9%, which was statistically significant ($P < .05$).

Discussion

In this study, the clinical features and treatment outcomes of IUAs were compared between first-trimester and second-trimester TOP patients. Our data confirmed that the IUAs were more severe after second-trimester TOP than after first-trimester TOP. The prognosis of IUAs caused by second-trimester TOP was worse than after first-trimester TOP, Subgroup analysis also confirmed this result.

Intrauterine procedures performed due to pregnancy damage of endometrial zona basalis potentially resulted in uterine adhesions [13]. During pregnancy, the endometrial zona basalis is loose and rich in blood vessels. Repeated and deep scratching can damage the endometrial zona basalis, while the endometrium repairs this damage. When the pregnancy is suddenly stopped, the sex hormone levels and the hormone receptor expression were rapidly declined, thus decreasing the angiogenesis and the oxygen supply, increasing the adhesion factor exudation, delaying the endometrial repair, and the occurrence of uterine cavity adhesions [14,15].

Table 1
Baseline characteristics of subjects with Asherman syndrome in the first- and second-trimester groups.

Variable	1st trimester (n = 180)	2nd trimester (n = 56)	P value
Age (years)[a]	31.4 ± 4.8	30.6 ± 0.5	NS
Gravidity[b]	2 (1–3)	3 (2–3)	NS
Gestational age (weeks)[b]	8 (7.25-9)	20 (18-22)	< .05
Median number of curettage procedures	2 (1–3)	2 (2–3)	NS
Use of adhesion barriers[c]			
Copper intrauterine device	98 (54.4)	30 (53.6)	NS
Intrauterine balloon	82 (45.6)	26 (46.4)	NS

Note: NS = not statistically significant; 1st trimester = first-trimester termination of pregnancy; 2nd trimester = second-trimester termination of pregnancy.
[a] Mean ± SD, *t* test.
[b] Median (95% confidence interval), Mann-Whitney *U* test.
[c] Number (percentage), χ^2 test.

Table 2
Preoperative clinical features in the first- and second-trimester termination of pregnancy groups.

Variable	1st trimester (n = 180)	2nd trimester (n = 56)	P value
Menstrual pattern[a]			< .05
Amenorrhea	13 (7.2)	22 (39.3)	
Hypermenorrhea	167 (92.8)	34 (60.7)	
Degree of adhesion[a]			< .05
Severe	66 (36.7)	39 (69.6)	
Moderate	114 (63.3)	17 (30.4)	
Preoperative adhesion score[b]	8 (7-10)	10 (10-12)	< .05

Note: 1st trimester = first-trimester termination of pregnancy; 2nd trimester = second-trimester termination of pregnancy.
[a] Number (percentage), χ^2 test.
[b] Median (95% confidence interval), Mann-Whitney U test.

To the best of our knowledge, there were very few studies that compared the incidence of IUAs after TOP and the outcome after hysteroscopic adhesiolysis [5]. Hooker and colleagues found that 21.2% of patients had IUAs after termination of first-trimester pregnancy [16]. Kajanoja and coworkers reported that the incidence of IUAs was 16.2% during the second trimester [4]. These studies did not evaluate the degree of IUAs and pregnancy outcomes. The present study demonstrated the differences in the degree of IUAs after TOP between the first two trimesters, and the higher rate of severe adhesions and amenorrhea after TOP in the second trimester than in the first trimester. After second-trimester TOP, the pregnancy rate was only 21.4%, and no pregnancy occurred in patients with amenorrhea. The pregnancy rate was significantly lower than that in the first-trimester TOP patients (43.3%). These rates are lower than those reported in the previous studies [2,17]. We hypothesized that TOP in the second trimester caused more serious damage to the endometrial zona basalis, and the treatment prognosis remained worse than that for the first-trimester TOP. Based on the related research, the following factors may play vital roles in the worse prognosis observed after TOP in the second trimester. Firstly, the second-trimester TOP patients have an increased gestational age, decreased uterine sensitivity and contraction, bleed more easily, undergo repeated uterine curettages and have a fragile endometrial zona basalis and uterine vasculature due to uterine procedures [18]. Secondly, during the second trimester, the placenta is relatively large, and the operation time is relatively long. A uterus with a large volume and multiple pregnancies will have an increased risk of IUA formation [19]. Thirdly, after the delivery of the placenta in the second trimester of

Table 3
Median reduction of AFS score, adhesion recurrence and menstruation improvement in the two groups.

Variable	1st trimester (n = 180)	2nd trimester (n = 56)	P value
Median reduction of AFS score[a]			
All	6.5 ± 2.5	6.2 ± 2.8	< .05
Severe IUAs	7.5 ± 2.8	6.4 ± 3.0	NS
Moderate IUAs	5.9 ± 2.2	5.7 ± 2.3	NS
Adhesion recurrence[b]			
All	57 (31.5)	35 (62.5)	< .05
Severe IUAs	36 (54.5)	27 (69.2)	NS
Moderate IUAs	21 (18.4)	8 (47.1)	< .05
Menstruation improvement[b]			
All	157 (87.2)	40 (71.4)	< .05
Severe IUAs	57 (86.4)	27 (69.2)	< .05
Moderate IUAs	100 (87.7)	13 (76.5)	NS

Note: 1st trimester = first-trimester termination of pregnancy; 2nd trimester = second-trimester termination of pregnancy. NS = not statistically significant; All = severe and moderate IUAs.
[a] Mean ± SD, t test.
[b] Number (percentage), χ^2 test.

Table 4
Reproductive outcomes in the first- and second-trimester groups.

Variable	1st trimester (n = 180)	2nd trimester (n = 56)	P value
Pregnancy[a]			
All	78 (43.3)	12 (21.4)	< .05
Severe IUAs	27 (40.9)	4 (10.3)	< .05
Moderate IUAs	51 (44.7)	8 (47.1)	NS
Term birth[a]	56 (71.8)	7 (58.3)	< .05
Premature birth[b]	1 (1.3)	3 (25.0)	< .05
Ongoing pregnancy	6 (7.7)	0 (0.0)	NS
Pregnancy loss	12 (15.4)	2 (16.7)	NS
Ectopic pregnancy	3 (3.8)	0 (0.0)	NS

Note: NS = not statistically significant; 1st trimester = first-trimester termination of pregnancy; 2nd trimester = second-trimester termination of pregnancy, All = severe and moderate IUAs.
[a] Number (percentage), χ^2 test.
[b] Number (percentage), corrected χ^2 test.

pregnancy, estrogens that support the endometrial repair after damage were decrease rapidly [13,20].

Due to high morbidity after TOP in the second trimester, clinicians should attempt to avoid TOP during the second trimester and provide services for early diagnosis and TOP to reduce the complications [21]. Secondly, they should select an appropriate mode of termination after evaluating the advantages and disadvantages of each method [7,22]. We advocate dilation and curettage after good cervical preparation in the second trimester to reduce the incidence of retained products of conception. Thirdly, when incomplete abortion occurs or products of conception were retained, non-invasive treatment should be considered to avoid unnecessary surgery and minimize the damage to the endometrium [16,22]. Finally, after pregnancy termination, preventive measures should be taken to promote the endometrium repair by estrogen and progestin supplementation following curettage [23]. Pregnancy after separation of IUAs is considered as high-risk and seriously threatens the reproductive health of the patients [2,13,24]. Our study found that the rate of preterm birth after termination at mid-pregnancy was significantly higher than that after early pregnancy termination. After termination of a mid-trimester pregnancy, a deformed cervical canal and/or a wide cervical internal orifice leads to incompetence of the cervix [4], which may in turn increase the incidence of preterm birth. Several treatment strategies should be used to prevent preterm birth and monitor patients during pregnancy.

In this study, there were no pregnancies in patients with amenorrhea after hysteroscopic adhesiolysis. We assume that the basal layer of the endometrium was severely damaged, thus preventing the uterine cavity wound to be covered by the normal function of the endometrium. These patients should be fully evaluated before the operation and carefully selected for the operation. Subgroup analysis showed that there was no significant difference in AFS score between moderate and severe intrauterine adhesions, and there was no significant difference in recurrence rate of severe intrauterine adhesions. We assumed that the sample size was insufficient and the proportion of moderate and severe intrauterine adhesions between the two groups was different. We plan to expand the sample size in our future research.

In our center, after hysteroscopic adhesiolysis, patients are comprehensively treated to prevent the recurrence of IUAs and promote endometrial growth. The IUAs are evaluated before and after the operation by the AFS score. All patients included in this study were followed-up with hysteroscopy 3 months after hysteroscopic adhesiolysis. Considering the degree of intrauterine adhesions as the primary factor that influences the postoperative efficacy, a subgroup analysis was performed according to the degree of intrauterine adhesions, followed by stratification of the patients with different degrees of adhesions.

Mechanical instruments are usually used when adhesiolysis is performed, as the use of energy may damage the endometrium and the zona basalis, leading to adhesions. The use of energy may also influence the rate of recurrent adhesion, which was quite high in the current study and also had the potential to affect reproductive outcomes. Therefore, we also used mechanical instruments.

The main limitation of this study was the retrospective nature. Future prospective studies are necessary to validate our data. Patients underwent curettage after first- or second-trimester TOP, and some of them were operated after failure of drug-induced termination. Unfortunately, because of the retrospective nature of our study and as some patients were referred at our center from other hospitals, the data about the drugs used to terminate pregnancy were unreliable. Oral antibiotics without any uniform drug or dose were routinely administered after surgery as per each physician's experience and preferences. Another possible limitation is that we included only patients with moderate to severe adhesions as mild adhesions does not require surgery. Future studies, preferably multicenter trials with increased sample size, including patients with mild adhesions, should be conducted to correct these biases.

There are serious challenges in the treatment of IUAs. Although there are many clinical methods for the prevention of adhesions after intrauterine procedures, the effects are not satisfactory. There are fewer studies and reliable methods for the prevention of primary IUAs. The main reason for the failure of IUAs prevention (using intrauterine devices or estrogens) is due to severe injury caused to the endometrial basal layer, which cannot be regenerated consequently. Hence, prevention is more important than treatment, and studies that examine on how to prevent primary IUAs should be investigated in future. Most importantly, how to avoid TOP should be investigated. If TOP is necessary, it should be conducted during the early stage of pregnancy. Complete dilatation and curettage operation can reduce the residues of pregnancy. For residual pregnancy, hysteroscopic removal of pregnancy, rather than blindly curettage, can be expected [16,21]. Nevertheless, the present study was lacked on how to prevent IUAs and should be investigated in future studies.

In conclusion, severe IUAs resulting from second-trimester TOP are more common. The outcomes after hysteroscopic adhesiolysis are worse in patients with second-trimester TOP than first-trimester TOP, especially in those with severe IUAs. Therefore, optional second-trimester TOP should be avoided.

Author contributions

Zhu Ru: Project development, Conduct, Data Collection, Manuscript writing.

Duan Hua: Project development, Perform the analysis with constructive discussions.

Gan Lu: Data collection, Manuscript writing.

Wang Sha: Data collection, Manuscript writing.

Conflict of interest

The authors have no conflicts of interest.

Acknowledgments

References

[1] Yu D, Wong YM, Cheong Y, Xia E, Li TC. Asherman syndrome-one century later. Fertil Steril 2008;89:759–79, doi:http://dx.doi.org/10.1016/j.fertnstert.2008.02.096.

[2] Xiao S, Wan Y, Xue M, Zeng X, Xiao F, Xu D, et al. Etiology, treatment, and reproductive prognosis of women with moderate-to-severe intrauterine adhesions. Int J Gynecol Obstet 2014;125:121–4, doi:http://dx.doi.org/10.1016/j.ijgo.2013.10.026.

[3] Wallach EE, Schenker JG, Margalioth EJ. Intrauterine adhesions: an updated appraisal. Fertil Steril 1982;37:593–610, doi:http://dx.doi.org/10.1016/S0015-0282(16)46268-0.

[4] Kajanoja P, Aantaa K. Radiographic findings in cervix uteri after prostaglandin abortion induction. Acta Obstet Gynecol Scand 1983;62:253–6.

[5] Hanstede MMF, Van Der Meij E, Goedemans L, Emanuel MH. Results of centralized Asherman surgery, 2003-2013. Fertil Steril 2015;104:, doi:http://dx.doi.org/10.1016/j.fertnstert.2015.08.039 1561–1568.e1.

[6] Hanstede M, Emanuel MH. Reproductive outcomes of 10 years Asherman's surgery. J Minim Invasive Gynecol 2019;22:S14, doi:http://dx.doi.org/10.1016/j.jmig.2015.08.045 n.d..

[7] Hooker AB, Aydin H, Brölmann HAM, Huirne JAF. Long-term complications and reproductive outcome after the management of retained products of conception: a systematic review. Fertil Steril 2016;105:, doi:http://dx.doi.org/10.1016/j.fertnstert.2015.09.021 156–164.e2.

[8] Lyus R, Robson S, Parsons J, Fisher J, Cameron M. Second trimester abortion for fetal abnormality. BMJ 2013;347:f4165, doi:http://dx.doi.org/10.1136/bmj.f4165.

[9] Duan Y, Li Y, Xue Q. Serological prenatal screening and diagnosis for down syndrome. Clin Exp Obstet Gynecol 2014;41:572–4, doi:http://dx.doi.org/10.12891/ceog16472014.

[10] Cabrera Y, Fernandez-Guisasola J, Lobo P, et al. Comparison of sublingual versus vaginal misoprostol for second-trimester pregnancy termination: a meta-analysis. Aust New Zeal J Obstet Gynaecol 2011;51:158–65, doi:http://dx.doi.org/10.1111/j.1479-828X.2010.01264.x.

[11] Bartlett LA, Zane SB, Berg CJ. Risk factors for legal induced abortion-related mortality in the United States. Obstet Gynecol 2004;104:636, doi:http://dx.doi.org/10.1097/01.AOG.0000137733.29798.4e.

[12] The American Fertility Society classifications of adnexal adhesions, distal tubal occlusion, tubal occlusion secondary to tubal ligation, tubal pregnancies, müllerian anomalies and intrauterine adhesions. Fertil Steril 1988;49:944–55, doi:http://dx.doi.org/10.1016/S0015-0282(16)59942-7.

[13] Yu D, Li T-C, Xia E, Huang X, Liu Y, Peng X. Factors affecting reproductive outcome of hysteroscopic adhesiolysis for Asherman's syndrome. Fertil Steril 2008;89:715–22, doi:http://dx.doi.org/10.1016/j.fertnstert.2007.03.070.

[14] Evans-Hoeker EA, Young SL. Endometrial receptivity and intrauterine adhesive disease. Semin Reprod Med 2014;32:392–401, doi:http://dx.doi.org/10.1055/s-0034-1376358.

[15] Sher G, Fisch JD. Effect of vaginal sildenafil on the outcome of in vitro fertilization (IVF) after multiple IVF failures attributed to poor endometrial development. Fertil Steril 2002;78:1073–6, doi:http://dx.doi.org/10.1016/S0015-0282(02)03375-7.

[16] Hooker A, Fraenk D, Brölmann H, Huirne J. Prevalence of intrauterine adhesions after termination of pregnancy: a systematic review. Eur J Contracept Reprod Heal Care 2016;21:329–35, doi:http://dx.doi.org/10.1080/13625187.2016.1199795.

[17] Myers EM, Hurst BS. Comprehensive management of severe Asherman syndrome and amenorrhea. Fertil Steril 2012;97:160–4, doi:http://dx.doi.org/10.1016/j.fertnstert.2011.10.036.

[18] Frick AC, Drey E, Diedrich JT, Steinauer JE. Effect of prior cesarean delivery on risk of second-trimester surgical abortion complications. Obstet Gynecol 2010;115:760–4, doi:http://dx.doi.org/10.1097/AOG.0b013e3181d43f42.

[19] Gilman AR, Dewar KM, Rhone SA, Fluker MR. Intrauterine adhesions following miscarriage: look and learn. J Obstet Gynaecol Canada 2016;38:453–7, doi:http://dx.doi.org/10.1016/j.jogc.2016.03.003.

[20] Buttram VC, Turati G. Uterine synechiae: variations in severity and some conditions which may be conducive to severe adhesions. Obstet Gynecol Surv 1979;34:292–3, doi:http://dx.doi.org/10.1097/00006254-197904000-00012.

[21] American College of Obstetrics and Gynecology. Practice bulletin no 135: second-trimester abortion. Obs Gynecol 2013;121:1394–406, doi:http://dx.doi.org/10.1097/01.AOG.0000431056.79334.cc.

[22] Harpham M, Abbott J. Use of a hysteroscopic morcellator to resect miscarriage in a woman with recurrent Asherman's syndrome. J Minim Invasive Gynecol 2014;21:1118–20, doi:http://dx.doi.org/10.1016/j.jmig.2014.05.006.

[23] Farhi J, Bar-Hava I, Homburg R, Dicker D, Ben-Rafael Z. Induced regeneration of endometrium following curettage for abortion: a comparative study. Hum Reprod 1993;8:1143–4.

[24] Roy KK, Baruah J, Sharma JB, Kumar S, Kachawa G, Singh N. Reproductive outcome following hysteroscopic adhesiolysis in patients with infertility due to Asherman's syndrome. Arch Gynecol Obstet 2010;281:355–61, doi:http://dx.doi.org/10.1007/s00404-009-1117-x.