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THE INFLUENCE OF DIFFERENT METHODS OF HYSTEROSCOPIC METROPLASTY USING A BIPOLAR RESECTOSCOPE ON THE RESTORATION OF REPRODUCTIVE FUNCTION IN WOMEN WITH A SEPTATE UTERUS

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Abstract

Uterine septum is the most common congenital anomaly of the uterus, accounting for 35% of all diagnosed malformations. Data on the effectiveness of restoring reproductive function in women with a septate uterus after hysteroscopic metroplasty are contradictory, there are no data on the comparison of reproductive results after removal and dissection of the septum using a bipolar hysteroresectoscope. **The purpose of the study** was to assess the effectiveness of reproductive function recovery after dissection and removal of the uterine septum using a bipolar hysteroresectoscope. **Material and methods.** 78 patients of group B with uterine septum, reproductive failure, bipolar hysteroscopic metroplasty were under observation. Among the examined patients, 39 suffered from miscarriage and 39 suffered from infertility. 37 women of the BI group underwent hysteroscopic bipolar dissection of the uterine septum; 41 women of the BII group underwent hysteroscopic bipolar resection of the

septum. **Results and their discussion.** Within 2 years after metroplasty, pregnancy occurred in 86.49% of women in the BI group and in 100% of women in the BII group ($p>0.05$); the specific weight of miscarriages was 9.38% and 0.00%, respectively ($p>0.05$); childbirth - 58.88% and 70.97% ($p>0.05$); premature births – 17.65% and 6.45% ($p>0.05$); term deliveries - 38.24% and 64.52% ($p<0.04$, SD 0.34 [0.12-0.93]). In women with initial infertility, pregnancy occurred in 61.54% of women in the BI group ($n=13$) within 2 years after the operation, in 69.23% in the BII group ($n=13$) ($p>0.05$); the specific weight of miscarriages was 25.00% and 22.22%, respectively ($p>0.05$); childbirth - 75.00% and 77.78% ($p>0.05$); premature births – 12.50% and 11.00% ($p>0.05$); term deliveries - 62.50% and 66.67% ($p>0.05$). Analysis of recovery of reproductive function 2 years after surgery in women with initial miscarriage showed that 90.48% of women in the BI group became pregnant, 94.44% in the BII group ($p>0.05$); the specific weight of miscarriages was 31.58% and 11.76%, respectively ($p>0.05$); childbirth - 68.42% and 88.24% ($p>0.05$); premature births – 26.32% and 5.88% ($p>0.05$); term deliveries - 42.11% and 82.35% ($p<0.02$, SD 0.16 [0.03-0.73]).

Conclusions. The use of the technique of removal of the uterine septum during bipolar hysteroscopy compared to the technique of its dissection in women with a septate uterus and reproductive failure leads to a probable increase in the termination of pregnancy by term delivery both in the general group and in the group of patients with initial miscarriage.

Key words: septate uterus; bipolar hysteroscope; septum dissection; septum removal; reproductive failure; infertility; miscarriage; reproductive results.

Congenital uterine anomalies (CUAs) are estimated to affect 1% to 4% of the general fertile population, although the prevalence is reported to be significantly higher (8.5–12%) in patients with infertility and recurrent pregnancy loss. The uterine septum is the most common CUAs, accounting for 35% of all diagnosed malformations [6, 7].

Data on the effectiveness of restoring reproductive function in women with a septate uterus after hysteroscopic metroplasty are contradictory.

J. F. W. Rikken et al. (2021) [9] conducted the first multicenter randomized controlled trial (RCT) on this topic (TRUST—The Randomized Uterine Septum Trial). In this study, the authors found no significant difference in the live birth rate in patients who underwent septum resection compared with expectant management (31% vs. 15%, relative risk, 95% CI 0.47 to 1.65), thus putting questioning any rationale for supporting surgical treatment.

In a meta-analysis by M. Krishnan et al. (2021) [4] included 407 women with hysteroscopic resection of the septum and 252 with conservative treatment. Hysteroscopic

resection of the septum was associated with a lower rate of miscarriage (OR 0.25, 95% CI 0.07–0.88) compared with untreated women. No significant effect on live birth, clinical pregnancy rate, or preterm birth was observed. However, there were fewer presentations during labor in the treatment group (OR 0.22, 95% CI 0.06–0.73). The authors concluded that resection of the septum was associated with a lower rate of miscarriage compared with untreated women, and no significant effect on live birth, clinical pregnancy, or preterm birth was observed. Although interesting, this meta-analysis is incomplete, considering the low number of included papers (only seven) and the fact that all patients were evaluated together without distinguishing between infertile patients and patients with recurrent miscarriage. In addition, no meta-regression or subgroup analysis was performed, limiting the clinical applicability of the results.

A systematic review and meta-analysis by M. Carrera et al. (2022) [1], which compared reproductive outcomes between women who underwent hysteroscopic hysterectomy and those who received expectant management, confirmed that hysteroscopic metroplasty was effective in reducing the risk of miscarriage in patients with complete or partial hysterectomy. As a result of the systematic electronic search, 1076 studies were found; after removing duplicates, 688 titles and abstracts were selected, and 55 were assessed for eligibility. Eleven studies were included in the quantitative synthesis: one RCT and 10 observational studies, which included reproductive outcomes in 1589 patients with complete or partial endometriosis. The pooled OR for miscarriage was 0.45 (95% CI, 0.22-0.90). When the analysis was performed considering subgroups by septum type, the pooled OR in the complete septum subgroup was 0.16 (95% CI 0.03-0.78), OR 0.36 (95% CI 0.19-0.71) in the partial septum subgroup and 0.58 (95% CI 0.20-1.67) in these studies without differentiation of complete or partial septum. No significant differences were found between the two groups in terms of clinical pregnancy outcomes, full-term live births, or cesarean section risk. A significant decrease in the frequency of preterm birth was observed in patients who underwent partial resection of the septum (OR 0.30, 95% CI 0.11-0.79). The risk of fetal malpresentation was also significantly reduced (OR 0.32, 95% CI, 0.16-0.65). M. Carrera et al. conclude that the results of this meta-analysis support the effectiveness of hysteroscopic metroplasty in reducing the risk of miscarriage in patients with complete or partial endometriosis, although these data need to be confirmed by a well-designed RCT.

In a systematic review and meta-analysis published by Y. Jiang et al. (2022) [3], 5 cohort studies and 22 case series involving 1506 patients were included. In patients with hiatus and recurrent miscarriage, hysteroscopic hiatus resection was associated with an

increased live birth rate (OR 1.77; 95% CI 1.26–2.49), resulting in a postoperative live birth rate of 66% (95% CI 59-72), and resection of the septum was associated with a reduction in the rate of preterm birth (OR 0.15; 95% CI 0.04-0.53) and the rate of miscarriage (OR 0.36; 95% CI 0.20-0.66). In patients with endometriosis and primary infertility, hysteroscopic resection of the endometrium was associated with an increase in the frequency of live birth (OR 4.12; 95% CI 1.19-14.29) and clinical pregnancy (OR 2.28; 95% CI 1.04-4.98). The live birth rate after surgery was 37% (95% CI 30-44), and the miscarriage rate was reduced in patients with primary infertility (OR 0.19; 95% CI 0.06-0.56). The effectiveness of hysteroscopic resection of the septum in patients with secondary infertility was unclear. However, the postoperative live birth rate was 41% (95% CI 2-88). Y. Jiang et al. (2022) concluded that hysteroscopic resection of the septum was associated with increased live birth rates and decreased rates of miscarriage in patients with recurrent miscarriage or primary infertility, indicating that resection of the septum may improve reproductive outcomes in these patients. The efficacy of septum resection was unclear in patients with secondary infertility. These findings are limited by the quality of the included studies, which warrants further RCTs including only patients with recurrent miscarriage or primary infertility.

X. Wu et al (2022) [12] determined pregnancy-related outcomes, along with adverse obstetric outcomes after hysteroscopic resection, and whether women with hysteroscopic resection have the same outcomes as women with a normal uterus. 22 studies were included in this meta-analysis. The control groups of 14 studies were women who underwent treatment, and the control groups of the other 8 studies were patients with a normal uterine cavity. Hysteroscopic resection was associated with a higher rate of term delivery (OR 2.26, 95% CI 1.26-4.05) and a lower rate of spontaneous abortion (OR 0.50, 95% CI 0.27-0.93) and a lower frequency of incorrect presentation (OR 0.31, 95% CI 0.19-0.50). However, compared with the normal uterus group, the rates of preterm delivery, cesarean section, and postpartum hemorrhage did not return to normal after resection. The authors concluded that hysteroscopic resection can effectively reduce the risk of miscarriage and malpresentation of the uterus in patients with endometriosis, while increasing the rate of term delivery. Well-designed RCTs should confirm this meta-analysis.

Z. Lan (2023) [5] conducted a single-center retrospective study. The cases of women who underwent hysteroscopic resection of the septum were divided into three groups: group A was the group with recurrent miscarriages, group B had a history of pregnancy with no more than one spontaneous miscarriage, and group C was the group with primary infertility. Each patient was followed up by telephone for subsequent pregnancies, miscarriages, and live

births for at least 1 year. 176 surgical patients were included in this study. 42, 74 and 60 cases belong to groups A, B and B, respectively. The frequency of postoperative pregnancies in the three groups was 71.4%, 82.4% and 75.0%; live birth rates were 50.0%, 74.3% and 71.7%; and the frequency of spontaneous miscarriages was 21.4%, 17.6% and 13.3%. 62 patients had a complete uterine septum, 114 – a partial one. For patients with a complete uterine septum, the preoperative pregnancy rate was 54.84%, and after the operation, the pregnancy rate increased to 85.48%; at the same time, the frequency of preoperative and postoperative pregnancy in patients with partial uterine septum was close (from 71.9% to 72.8%). The authors summarized the study: after resection of the uterine septum, the frequency of pregnancy and the frequency of spontaneous miscarriages in patients with repeated miscarriages did not differ significantly from the other two groups, but the birth rate was significantly lower; patients with a complete uterine septum may benefit more from surgery; surgical indications should be carefully and rigorously evaluated.

The purpose of the study was to assess the effectiveness of reproductive function recovery after dissection and removal of the uterine septum using a bipolar hysteroscopic resectoscope.

Material and methods

The study was conducted at the clinical facilities of Odessa National Medical University in the period from 2018 to 2022. Ethical approval was obtained from the University Ethics Committee.

78 patients of group B with uterine septum, reproductive failure, bipolar hysteroscopic metroplasty were under observation. Among the examined patients, 39 suffered from miscarriage and 39 suffered from infertility. The study did not include women with combined factors of infertility. The uterine septum was identified as the leading factor in infertility in all the studied women. The fallopian tubes of all patients were patent. The men had normal parameters of the spermogram in accordance with the norms approved by the WHO [11].

In group B, 2 groups were distinguished: group BI - 37 women who underwent hysteroscopic bipolar dissection of the uterine septum; group BII – 41 women who will undergo hysteroscopic bipolar resection of the uterine septum.

All patients underwent a physical and gynecological examination. According to the ESHRE/ESGE classifications and the ASRM MAC2021 classification [2, 8, 10], a septate uterus was previously confirmed by transvaginal pelvic ultrasound or pelvic magnetic resonance imaging. The final diagnosis of uterine anomaly was established based on the results of gynecological examination, hysteroscopy and laparoscopy.

Hysteroscopic metroplasty was performed under the control of laparoscopy under general anesthesia. After dilation of the cervix with the help of Hegar dilators to No. 10.5 mm, a 9 mm bipolar hysteroresectoscope with a viewing angle of 30° (Tontarra Medizintechnik GmbH, Germany) was inserted into the cervical canal. A continuous flow of fluid was used to stretch the uterus. Physiological solution was used as a medium for stretching, and the stretching pressure was set at the level of 13–20 kPa (95–150 mm Hg).

Dissection/resection was started from the lower edge of the septum with the help of a bipolar electrode and was carried out perpendicular to the axis of the uterus along the midline in the cranial direction. They focused on the middle line in the horizontal plane of the septum, which minimizes the incision of the myometrium and preserves most of the superficial muscle fibers. Whether the metroplasty should be completed was judged by several parameters obtained by hysteroscopy, laparoscopy, or intraoperative ultrasound: visualization of a pink vascularized myometrium rather than a white avascular septum; the relationship between the resection area and the fallopian tubes; the proximity of the resection area to the serous septum of the uterus. Metroplasty was considered completed when the eyes of the fallopian tubes were visible without any formations that form a dividing line between them. After dissection of the septum, the uterine cavity increased, its shape normalized, but a tissue comb from the dissected parts of the septum was noted along the front and back walls. After removal of the septum, the uterine cavity looked normal during a panoramic examination, its bottom was easily visualized throughout, including between the eyes of the fallopian tubes, the front and back walls looked almost flat. In the presence of a complete septum, gentle resection of its cervical area was performed and preservation of the septum below the internal opening of the cervix in order to minimize the risk of isthmic-cervical insufficiency during the next pregnancy.

When resecting the septum using a coaxial bipolar electrode surgical system, vaporization or excision of the septum was performed. An incision was made with the help of steam or drying with a power of no more than 200 W, and the first of these options was used in the treatment of women suffering from infertility.

Patients were discharged on the day of surgery 4-5 hours after completion of metroplasty. Three months after metroplasty and if there are indications, it was recommended to plan a pregnancy naturally or, if necessary, with the help of DRT. All operated patients were under observation for a year.

In the postoperative period, a drug containing 2.0 mg of estradiol for 14 days, then 2.0 mg of estradiol and dydrogesterone for 14 days for three menstrual cycles was prescribed for

normal epithelization for 3 months; rectal suppositories with 15,000 IU streptokinase and 1,250 IU streptodornase for 3 days - 1 sup. three times a day, 3 days - 1 soup. 2 times a day, 3 days - 1 soup. 1 time a day. All patients were advised to use contraception for 3 months after the procedure.

Three months after surgery, a follow-up transvaginal pelvic ultrasound or pelvic MRI was performed using traditional procedures to assess the shape and size of the uterus. In the presence of intrauterine synechiae or residual septum of more than 1 cm, repeated hysteroscopy, synechiolysis or other incision/removal of residual septum was performed. Symptoms, operative complications, and reproductive outcomes of all patients were assessed in outpatient settings or by telephone during the follow-up period.

Statistical data processing was carried out using the "Microsoft Excel 2020" application program package (Microsoft Corporation, USA). Arithmetic mean (M), error of standard deviation (\pm SE) was evaluated. The probability coefficient p was calculated using the Student's t-test. Absolute frequency (n) and relative frequency (%) were determined for binomial signs. For intergroup comparisons, Pearson's χ^2 test was used, taking into account the degree of freedom (df). The critical level of significance for testing the null hypothesis was $p < 0.05$. Odds ratio (OR) and 95% confidence interval (CI) were calculated, which were presented as OR [95% CI].

Results and their discussion

The average age of patients in the BI group was 30.19 ± 0.30 years, in the BII group - 30.29 ± 0.34 years ($p > 0.05$).

According to anthropometric indicators, groups BI and BII probably did not differ: body weight - 57.51 ± 1.34 kg vs. 56.51 ± 1.21 kg, height - 1.65 ± 0.01 m vs. 1.64 ± 0.01 m, body mass index - 21.05 ± 0.44 kg/m² against 21.07 ± 0.46 kg/m².

The uterine septum in 13 (35.14%) women of the BI group was complete, in 24 (64.86%) patients - incomplete ($p > 0.05$), in the BII group - in 15 (36.59%) and 26 (63.41%) ($p > 0.05$). Among women with initial infertility in the BI group, the septum was complete in 6 (33.33%) and incomplete in 12 (66.67%) cases, in the BII group - in 9 (42.86%) and 12 (57.14%). Among women with early miscarriage in the BI group, the septum was complete in 7 (36.84%) and incomplete in 12 (63.16%) cases, in the BII group - in 6 (30.00%) and 14 (70, 00%).

According to the reproductive anamnesis of women, groups BI and BII did not statistically significantly differ (Table 1).

Table 1 – Reproductive anamnesis of women of the studied groups

Indicator	Group BI, n=37	Group BII,n=41
Infertility, n (%)	18 (48.65)	21 (51.22)
Primary infertility, n (%)	10 (55.56)	10 (47.62)
Secondary infertility, n (%)	8 (44.44)	11 (52.38)
Mean duration of infertility, M±SE, years	6.17±0.31	7.33±0.44
Presence of pregnancies, n (%)	27 (72.97)	31 (75.61)
Mean number of pregnancies, M±SE	1.65±0.21	1.66±0.19
Availability of artificial abortions, n (%)	4 (10.81)	6 (14.63)
Mean number of induced abortions, M±SE	0.22±0.10	0.22±0.09
Presence of miscarriages, n (%)	27 (72.97)	31 (75.61)
Mean number of miscarriages, M±SE	1.38±0.17	1.39±0.16
Presence of childbirth, n (%)	0 (0.00)	0 (0.00)
Presence of ectopic pregnancies, n (%)	2 (5.41)	2 (4.88)
Note. No statistically significant differences were found between the indicators of the BI and BII groups (p>0.05).		

When evaluating the operative indicators of performed hysteroscopic metroplasty, it was found that the average duration of surgery in the BI group compared to the BI group was 1.27 times shorter (p<0.01), intraoperative blood loss was 1.44 times shorter (p<0.01) (Table 2).

Table 2 – Operational indicators of hysteroscopic metroplasty in the studied groups

Indicator	Group BI, n=37	Group BII, n=41
Operation time, M±SE, min.	23.76±1.47 ^{bII}	30.19±0.52 ^{bI}
Intraoperative blood loss, M±SE, ml	14.03±1.43 ^{bII}	20.19±0.52 ^{bI}
Subfebrile after surgery, n (%)	2 (5.41)	1 (2.44)
Postoperative pain, n (%)	3 (8.11)	2 (4.88)
Intrauterine synechiae, n (%)	1 (2.70)	0 (0.00)
Residual septum over 1 cm, n (%)	1 (2.70)	0 (0.00)
Intraoperative bleeding, n (%)	0 (0.00)	0 (0.00)
Note. ^{bI, bII} - statistically significant difference with indicators of groups BI, BII (p<0.05).		

The frequency of postoperative complications in groups BI and BII did not have significant differences: subfebrile after surgery was registered in 5.41% and in 2.44% of patients, postoperative pain in 8.11% and in 4.88%, intrauterine synechiae in 2.70% and in 0.00%; residual septum over 1 cm – in 2.70% and in 0.00%. Bleeding during metroplasty did not occur in both groups.

Within 2 years after metroplasty, pregnancy occurred in 86.49% of women in the BI group, in 100% in the BII group ($p>0.05$); the specific weight of miscarriages was 9.38% and 0.00%, respectively ($p>0.05$); childbirth - 58.88% and 70.97% ($p>0.05$); premature births – 17.65% and 6.45% ($p>0.05$); term deliveries – 38.24% and 64.52% ($p<0.04$) (Table 3).

Table 3 – Indicators of restoration of reproductive function in the studied groups depending on the hysteroscopic metroplasty technique used within 2 years after the operation, n (%)

Indicator	Group BI, n=37	Group BII, n=41	OR [95% CI]	P=
Onset of pregnancy	33/37(89.19)	40/41 (97.56)	0.74 [0.21-2.64]	0.64
Onset of pregnancy in the natural cycle	26/37 (70.27)	29/41 (87.88)	0.75 [0.26-2.14]	0.59
Pregnancy in IVF cycles	6/11 (54.55)	4/4 (100.00)	0.89 [0.16-5.11]	0.90
Miscarriages	3/32 (9.38)	0/41 (0.00)	2.08 [0.56-7.74]	0.28
Childbirth	29/32(90.63)	33/41 (100.00)	0.52 [0.19-1.45]	0.21
Premature birth	3/32 (9.38)	2/41 (6.06)	2.74 [0.51-14.57]	0.24
Term delivery	26/32 (81.25)	31/41 (93.94)	0.34 [0.12-0.93]	0.04

An analysis of recovery of reproductive function was carried out depending on the type of reproductive disorders prior to surgical intervention.

In women with initial infertility, pregnancy occurred in 61.54% of women in the BI group and 69.23% in the BII group ($p>0.05$) within 2 years after the operation; the specific weight of miscarriages was 25.00% and 22.22%, respectively ($p>0.05$); childbirth - 75.00% and 77.78% ($p>0.05$); premature births – 12.50% and 11.00% ($p>0.05$); term deliveries – 62.50% and 66.67% ($p>0.05$) (Table 4).

Table 4 – Indicators of restoration of reproductive function among women with initial infertility depending on the hysteroscopic metroplasty technique used within 2 years after the operation, n (%)

Indicator	Group BI, n=37	Group BII, n=41	OR [95% CI]	P=
Onset of pregnancy	8/13 (61.54)	9/13 (69.23)	0.71 [0.14-3.61]	0.68
Miscarriages	2/8 (25.00)	2/9(22.22)	1.17 [0.12-10.99]	0.89
Childbirth	6/8 (75.00)	7/9 (77.78)	0.86 [0.09-8.07]	0.89
Premature birth	1/8 (12.50)	1/9 (11.11)	1.14 [0.06-21.87]	0.93
Term delivery	5/8 (62.50)	6/9 (66.67)	0.56 [0.06-4.76]	0.59

Analysis of recovery of reproductive function within 2 years after surgical intervention in women with initial miscarriage showed that 90.48% of women became pregnant in the BI group, 94.44% in the BII group ($p>0.05$); the specific weight of miscarriages was 31.58% and 11.76%, respectively ($p>0.05$); childbirth - 68.42% and 88.24% ($p>0.05$); premature births – 26.32% and 5.88% ($p>0.05$); term deliveries – 42.11% and 82.35% ($p<0.02$) (Table 5).

Table 5 – Indicators of recovery of reproductive function in women with initial miscarriage depending on the hysteroscopic metroplasty technique used within 2 years after the operation, n (%)

Indicator	Group BI, n=37	Group BII, n=41	OR [95% CI]	P=
Onset of pregnancy	19/21 (90.48)	17/18 (94.44)	0.56 [0.05-6.73]	0.65
Miscarriages	6/19 (31.58)	2/17 (11.76)	3.46 [0.59-20.21]	0.17
Childbirth	13/19 (68.42)	15/17 (88.24)	0.29 [0.05-1.69]	0.17
Premature birth	5/19 (26.32)	1/17 (5.88)	5.71 [0.59-54.96]	0.13
Term delivery	8/19 (42.11)	14/17 (82.35)	0.16 [0.03-0.73]	0.02

In the conducted study, for the first time, the influence of the metroplasty technique (dissection or resection) using a bipolar resectoscope was evaluated in women with initial infertility and miscarriage against the background of a septate uterus.

As can be seen from the table. 4, no statistically significant differences between any reproductive outcomes in women with initial infertility depending on the technique of metroplasty were found. Metroplasty led to improved reproductive outcomes in the group

with initial miscarriage: the specific weight of term births increased 1.96 times (OR 0.16 [0.03-0.73]).

The weakness of the conducted study was the small sample of examined women, therefore, it is necessary to conduct large RCTs clarifying the impact of metroplasty on fertility, especially in the cohort of infertile women.

Conclusions

The use of the technique of removal of the uterine septum during bipolar hysteroscopy compared to its dissection in women with a septate uterus and reproductive failure leads to a probable increase in the termination of pregnancy by term delivery both in the general group and in the group of patients with initial miscarriage.

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