

Evaluation of the Success of Hysteroscopic Uterine Septum Resection

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Abstract

Objectives: The aim is to use three-dimensional transvaginal ultrasonography (3-D TVUS) to evaluate the success of hysteroscopic metroplasty for the uterine septum and to compare the pregnancy outcomes.

Materials and Methods: Thirty-eight patients with uterine septum who had hysteroscopic uterine septum resection were recruited. Preoperative 3-D TVUS measurements of the septal apex to the uterine fundus (s1), septal apex to internal os distance (s2), and intercornual distance (s3) were compared with the postoperative values. The pregnancies of the patients were followed up for a year postoperative period.

Results: Out of the 38 patients, thirty-five had partial uterine septum (class U2a), while 3 patients had complete uterine septum (class U2b). Eighteen (47.36%) of the patients who underwent uterine septum resection achieved pregnancy, and thirteen of these pregnancies were (72.2%) term pregnancies, and all term pregnancies resulted in a live birth. Natural conception was achieved in 77.7% (14 of 18) of the patients. Term pregnancy occurred in 68.7% (11 of 16) of the patients with a partial septum and in 66.6% (2 of 3) of the patients with a complete uterine septum. A comparison of the 3-D TVUS measurements of the uterus pre- and postoperatively showed a decrease in s1 and an increase in s2 ($P < 0.05$). The uterine cavity length of pregnant patients was found to be higher than nonpregnant patients ($P < 0.05$).

Conclusion: Reproductive results of hysteroscopic metroplasty were favorable in achieving live and term birth. three-dimensional TVUS can be preferred as a noninvasive effective method in objective evaluation of the success of the hysteroscopic surgery.

Keywords: Hysterosalpingography, hysteroscopy, three-dimensional ultrasonography, uterine anomalies, uterine septum

INTRODUCTION

Müllerian anomalies are seen in 2%–4% of fertile women and 3% of infertile population. Complete or partial uterine septums constitute 22% of Müllerian anomalies.^[1] Congenital uterine anomalies are often asymptomatic; however, some of the Müllerian duct anomalies are diagnosed during the routine investigation of women with infertility or adverse pregnancy outcomes such as recurrent pregnancy loss (RPL), preterm labor, and intrauterine growth restriction.^[2-4] Although the exact incidence is not known, uterine septum is reported to be one of the most common congenital uterine malformations

as it accounts for approximately 80%–90% of all uterine malformations in some reported series.^[1,5]

Decreased vascularity, higher fiber content, and uncoordinated muscular activity of the fibromuscular septal tissue besides the relatively decreased response of the endometrium covering the septum are blamed for the deteriorated reproductive outcome observed in some of these patients.^[6]

Three-dimensional transvaginal ultrasonography (3-D TVUS) can also be used to monitor the changes in the cavity after

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hysteroscopic septum resection and evaluate the operation's success in the correction of the uterine anomaly. In this way, the need for a conventional and invasive method such as hysterosalpingography (HSG) or second-look hysteroscopy will not be required for evaluating the success of the primary surgery.

The aim of the presented series is to compare the reproductive results before and after hysteroscopic metroplasty and to objectively evaluate the surgical success with measurements of the 3D TVUS.

MATERIALS AND METHODS

This retrospective study was conducted at Ministry of Health EZH Women's Health Training and Research Hospital between January 2019 and September 2020.

Selection of the patients

The patients who were diagnosed to have a complete or partial uterine septum by HSG or diagnostic hysteroscopy during infertility and/or poor reproductive outcome investigation and underwent hysteroscopic metroplasty between January 2019 and November 2019 were recruited to this retrospective study. Pregnancy results of the patients were followed up until September 2020. The study protocol was approved by the Research and Educational Board of Ministry of Health EZH Research and Training Hospital (April 20, 2021, Decide No: 06). As a hospital policy, written informed consent was obtained from each patient before every procedure that gave permission to the use of the personal medical data anonymously for future medical studies. The presented study conforms to the Enhancing the Quality and Transparency Of health Research network guidelines.

Among the patients who underwent hysteroscopic surgery for uterine septum in our clinic between 2019-2020, patients under age 40 years with patent tubes, spontaneous ovulation were included in the study. Anovulation (D-21 progesterone < 4 ng/ml), diminished ovarian reserve (anti-Müllerian hormone [AMH] <1.1 ng/ml), presence of tubal blockage, systemic diseases such as diabetes mellitus, thyroid disease, renal or liver disease, acquired or congenital thrombophilia or having previous surgery for uterine anomaly and having a partner with male infertility according to WHO 2021 6th edition criteria were the excluded.^[7] Cases with other etiologic factors that may lead to infertility or RPL other than uterine septum (vaginal anomalies, gynecological pathologies such as fibroids, polyps, tubal pathologies, or ovarian cysts) were also excluded from the study.

Demographic characteristics and obstetric history of the patients who had infertility work-up including sperm analysis of the partner, day-3 Follicle Stimulating Hormone (FSH),

Day-21 Progesterone (P) and Anti-Müllerian Hormone (AMH) and thyroid hormone tests and hysterosalpingography and met the inclusion criteria were recorded.

Pelvic examination and speculum examination findings of the patients were recorded in order to detect the presence of accompanying anomalies such as vaginal septum. All patients were evaluated by the same team using 3-D TVUS (Samsung H570A, 5-6 MHz endovaginal probe manufactured by Samsung Medison Co., LTD in Seoul, Korea) during the early follicular phase after routine gynecological examination and uterine anomalies were classified according to the European Society of Human Reproduction and Embryology (ESHRE), and European Society for Gynaecological Endoscopy (ESGE) consensus on the classification 2013,^[8] and r-American Society for Reproductive Medicine (r-ASRM) 2021.^[9]

As shown in Figure 1, the distance from the uterine fundus to the apex of the septum (s1), the lower end of the septum apex to the internal cervical os (s2), and the distance between the uterine horns—intercornual distance (s3) were measured with 3D TVUS.^[10-14]

Surgical procedure

Hysteroscopic resection was performed from the internal cervical os to the septum apex under regional or general anesthesia during the early follicular phase of the cycle when the endometrium is thin. Resectoscopic division of uterine septum was performed with knife-electrode using monopolar energy after providing adequate distension of the cavity with %1.5 glycine (Bioflex %1.5 glycine irrigation solution, Osel Pharmaceuticals Industry, and Trade Corporation Turkey) with a distention pressure of 150 mm Hg. An incision was made in the longitudinal axis with a knife electrode with monopolar resectoscope from the beginning of the uterine septum until the cornual areas were seen. All the procedures were carried out with a resectoscope (Karl Storz, Germany) hysteroscopically without a concomitant laparoscopy or ultrasonography. An anti-adhesion barrier was not applied in any patient after hysteroscopic septum resection.

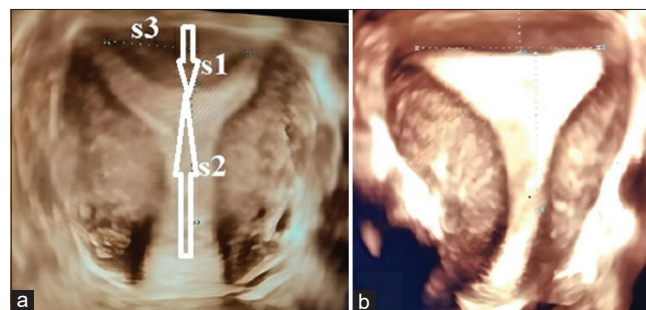


Figure 1: Three-dimensional ultrasound image of the same patient before (a) and after (b) hysteroscopic uterine septum resection
s1: Distance between septal apex and uterine fundal serosa, **s2:** Distance between septal apex and internal cervical os, **s3:** Intercornual distance

Postoperative period

All patients were routinely used cyclic estrogen + progesterone (Cycloprogynova; 2 mg estradiol valerate + norgestrel 0.5 mg, Bayer, Germany) drugs after the surgery, and three dimensions (s1, s2, s3) of the uterus were measured by performing 3D TVUS again in the follicular phase on the third day of the postoperative second menstrual cycle; [Figure. 1].

The patients were followed up for 1 year after the procedure and reproductive results were recorded. All of the patients' preoperative and postoperative 3D TVUS measurements were recorded, and the change of the measurements (preoperative measurements-postoperative measurements: (▲s1, ▲s2, ▲s3) were compared for pregnant and nonpregnant women.

Statistical method

The reproductive results after the hysteroscopic metroplasty, and difference between pre-postoperative measurements was statistically evaluated. Statistical analyses were performed using IBM SPSS 26.0 software (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY, USA: IBM Corp). Since there was no reference article similar to our study, power analysis could not be performed before the study, but when the results of 38 patients in our study were evaluated retrospectively with the G-Power 3.1.9.4 (Franz Faul, Universitat Kiel, Germany) program, the effect size was 0.86, $\alpha=0.05$, power $(1-\beta)$ = it was found to be 0.80.

The difference between the preoperative and postoperative dimensions measured by 3D ultrasound (3-D USG) (▲s1, ▲s2, and ▲s3) was compared and paired *t*-test was applied for comparison. Independent *t*-test was used for parametric parameters. $P < 0.05$ was considered statistically significant. The reproductive outcome was given as a percentage.

RESULTS

Forty-four patients who underwent hysteroscopic septum resection who met the inclusion criteria were included in the study, and 6 patients without postoperative follow-up were excluded from the study. Remaining thirty-eight patients who underwent metroplasty for uterine septum were evaluated. The mean age of the 38 patients recruited to the study was 26 ± 5.3 (range = 19–40) years. Demographic characteristics were as follows: gravida 1.2 ± 0.44 (R = 0–4), parity 0.8 ± 1.24 (R = 0–2), number of spontaneous abortion 2.1 ± 1.16 (R = 1–4), and number of living children 1 ± 0.63 (R = 0–2). The mean of the duration of infertility was 45 ± 43.44 months. The mean of the body mass index was 27.14 ± 5.09 kg/m².

Thirty-five (92.1%) patients had partial uterine septum, and 3 patients had complete uterine septum. Twenty-nine (73.6%)

patients had primary infertility and the remaining nine (23.6%) patients had RPL history. Out of the 38 women, eighteen (47.36%) achieved pregnancy. Out of the 18 pregnancies achieved, 13 (72.2%) were term pregnancies and resulted in a live birth. Term pregnancy was achieved in two (66.6%, 2 of 3) of the patients with the complete uterine septum after the natural conception. Pregnancy was achieved in 16 (45.7%) of 35 patients with partial septum. Of these, 11 (68.7%) ended in term and live birth [Table 1]. Pregnancy of 25% ($n=4$, 4 of 16) patients in the partial uterine septum group was achieved by assisted reproductive techniques (ART). Two (50%, 2 of 4) of these resulted in live birth. In the other two cases, intrauterine fetal loss occurred in the second trimester. Of the remaining 75% ($n=12$) pregnancies in the partial uterine septum group achieved after the natural conception, and 75% ($n=9$, 9 of 12) of them resulted in term and live birth.

Overall, 18 pregnancies were recorded during the first postoperative year after hysteroscopic metroplasty. While 9 (50%) pregnancies occurred in patients with RPL, the remaining 9 (50%) pregnancies were obtained from primary infertile patients [Table 2]. Six (66.6%) of the nine patients with RPL had term pregnancy, one had biochemical pregnancy, and two had second trimester intrauterine fetal loss. The term pregnancy rate was 77.7% ($n = 7$) in primary infertile patients [Table 2].

The patients did not develop any intraoperative or postoperative complication and were discharged uneventfully. Comparison of the pre- and postoperative 3-D TVUS measurements of the uterus showed a statistically significant decrease in s1 (16.15 ± 4.18 mm, $P=0.00$ vs. 8.23 ± 2.27 mm, $P=0.00$), and increase in s2 (19.65 ± 3.84 mm, $P=0.00$ vs. 26.65 ± 5.09 mm, $P=0.00$); however, the change in the intercornual distance (s3) was not statistically significant (19.34 ± 3.64 mm, $P=0.584$ vs. 19.42 ± 3.78 mm, $P=0.584$) [Table 3]. The change in s1, s2, and s3 in women who achieved pregnancy (Group 1) were compared with the difference in s1, s2, and s3 measurements of the women who failed to get pregnant (Group 2) [Table 4]. The change in s1 and s2 were statistically more significant in women who achieved pregnancy, while the change in s3 was not statistically significantly different between the 2 groups [Group 1 vs. Group 2; ▲s1 $P=0.007$, ▲s2 $P=0.015$, ▲s3 $P=0.219$, Table 4]. This results support the positive effect of maximum cavity length created in uterine septum resection on pregnancy outcomes, and the uterine cavity measurements evaluated objectively by 3D TVUS.

DISCUSSION

In the literature, reproductive results of the hysteroscopic metroplasty for uterine septum have been evaluated in many

Table 1: Pregnancy outcomes after hysteroscopic resection of the uterine septum in cases with complete and partial uterine septum

	Complete septum (Class U2 b) (n=3; 7.8%), n (%)	Partial septum (Class U2 a) (n=35; 92.2%), n (%)	Total (n=38), n (%)
Pregnancy (+)*	2 (66.6)	16 (45.7)	18 (47.3)
Pregnancy (-)	1 (33.4)	19 (54.3)	20 (52.7)
Term pregnancy*	2 (100% 2 of 2)	11 (68.7% 11 of 16)	13 (72.2% 13 of 18)

*Percentages were used for data frequencies. All 3 patients with complete uterine septum presented with recurrent pregnancy loss. Pregnancy (+) : pregnancy achieved, Pregnancy (-): pregnancy cannot be achieved

Table 2: Obstetric outcomes of patients with recurrent pregnancy loss and primary infertility after hysteroscopic septum resection

	Patients with recurrent pregnancy loss, n (%)	Patients with primary infertile, n (%)	Total, n (%)
Term-live birth	6 (66.6)	7 (77.7)	13 (72.2)
Ectopic pregnancy	0	1 (11.1)	1 (5.5)
Intrauterine fetal loss	2 (22.2)*	0	2 (11.1)
Biochemical pregnancy	1 (11.1)	1 (11.1)	2 (11.1)
Total	9 (100)	9 (100)	18 (100)

*One of the two intrauterine fetal losses was 24 gestational weeks and the other one was 27 gestational weeks

Table 3: Comparison of pre- and post-operative uterine dimensions measured by 3-dimensional transvaginal ultrasonography

	Mean±SD		P
	Preoperative	Postoperative	
s1 (mm)	16.15±4.18	8.23±2.27	0.000*
s2 (mm)	19.65±3.84	26.65±5.09	0.000*
s3 (mm)	19.34±3.64	19.42±3.78	0.584

*P<0.05 statistically significant. Paired *t*-test was applied. s1: Distance between apex of the uterine septum and uterine fundal serosa (mm), s2: Distance between apex of the uterine septum and internal cervical os (mm), s3: Intercornual distance (mm). SD: Standard deviation

Table 4: Comparison of the changes in uterine dimensions measured by TVUS (s1, s2, and s3) in women who achieved pregnancy with women who failed to get pregnant after hysteroscopic septum resection

	Mean±SD		P
	Pregnant patients Group 1 (n=18)	Nonpregnant patients Group 2 (n=20)	
▲s1 (mm)	9.83±4.96	6.20±2.56	0.007*
▲s2 (mm)	8.50±4.20	5.65±2.0	0.015*
▲s3 (mm)	0.50±0.51	0.30±0.47	0.219

*P<0.05 statistically significant. Independent *t*-test was applied. ▲s1: Preoperative – postoperative distance between apex of the uterine septum and uterine fundal serosa (mm), ▲s2: Preoperative – postoperative distance between apex of the uterine septum and internal cervical os (mm), ▲s3: Preoperative – postoperative: Intercornual distance (mm). SD: Standard deviation

studies, but there is no clear consensus on the diagnostic criteria and the possible benefits of uterine septum resection in infertile women or women with recurrent pregnancy loss. Three-D USG is a noninvasive method that can visualize the

endometrial cavity, uterine contours, and the relationship between the cavity with the external serosal surface of the fundus. In this study, reproductive outcomes of patients who underwent hysteroscopic metroplasty due to uterine septum were found successful in the native fecundation and live births, and using 3-D TVUS is the usable, noninvasive technic to evaluate the successful of the hysteroscopic metroplasty.

Hysteroscopy has been considered the first-line treatment for the treatment of uterine septum since the early 1970s.^[15] Hysteroscopic resection might be unsuccessful in achieving optimal resection when a residual septum > 1 cm is detected.^[16,17] Pre- and postoperative HSG can be used for the evaluation of the success of hysteroscopic septum resection and detecting the presence of residual septum, but the disadvantages of HSG outweigh the advantages of a repeated HSG in these patients.^[18] Second-look hysteroscopy can also be used for evaluation of the cavity after hysteroscopic septum resection, but it still is surgical intervention. In our study, postoperative HSG was not applied to the patients since our patients were routinely evaluated in the postoperative period with 3-D TVUS.

It has been reported that there is a high agreement between the use of laparoscopy-guided 3-D TVUS and/or hysteroscopy in the diagnosis of congenital anomalies.^[19] When 3-D TVUS is combined with saline infusion, it has been reported that there is high accuracy in identifying and classifying Mullerian anomalies according to the r-ASRM and ESHRE/ESGE classification.^[20] In our study, all of the patients were evaluated preoperatively and postoperatively by 3-D TVUS, so there was no need for simultaneous laparoscopy and a second-look hysteroscopy.

Jurkovic *et al.*^[21] compared 3-D TVUS with HSG and two-dimensional TVUSG in the diagnosis of uterine

anomalies and stated that 3-D TVUS was useful in differentiation between subseptate and bicornuate uteri. Magnetic resonance imaging (MRI) is a successful technique too, it allows identification of the internal and external contour of the uterus, and demonstration of the female genitourinary system anatomy, but routine usage of MRI isn't cost effective to use all of the patients.^[12] In the presented study, we did not necessary to perform an MRI none of the patients for visualization the external uterine contour.

The impact of hysteroscopic septum resection on infertility and pregnancy-related complications is still debatable.^[22] In a recent study, 278 women who underwent *in vitro* fertilization and embryo transfer for primary infertility with the complete and partial septate uterus, the miscarriage rate was found to be statistically significantly lower in the group who had hysteroscopic uterine septum resection when compared to the expectant management group.^[23] However, the live birth rates, obstetric and neonatal outcomes were similar. In our study, 47.8% ($n = 18$) of the patients were pregnant after hysteroscopic septum resection. Thirteen of them (72.2%) ended up with term and live birth. In the group of the complete uterine septum, live birth rate was 100% (2 of 2), and in the group of the partial septum, live birth rate was 75% (9 of 12).

There is a case of bone metaplasia of the endometrium, which is seen as a cause of infertility after repeated curettage in the literature, and spontaneous pregnancy was achieved after successful hysteroscopic resection.^[24]

Some authors indicate that the risk of preterm birth is significantly reduced after hysteroscopic metroplasty.^[25,26] When the reproductive results (preoperative, postoperative) of the patients who underwent metroplasty due to the septum were compared, the postoperative pregnancy and live birth rates were found to be significantly higher.^[27] In the presented study, all live births resulted as term and live births too, but in our patients, natural conception rate was higher than the ART cycles, 77.7% (14 of 18).

Similarly, a recent meta-analysis involving 7 studies demonstrated a lower miscarriage rate in the hysteroscopic septum resection group compared to the expectant management group, but clinical pregnancy, live, and preterm rates were similar.^[28] In addition, in patients with RPL, the rate of term pregnancy after surgery was found to be quite successful with 66%.

Hysteroscopic metroplasty is frequently used in women with uterine septum or dysmorphic uterus in order to improve fertility and/or reproductive outcome and ultrasonographic evaluation is important for the evaluation of these patients.^[28,29] The relationship between hysteroscopic surgery and future obstetric complications is also questioned.^[29,30] In a large case control study, the incidence of placentation anomalies were

compared in 746 women who had hysteroscopic surgery for uterine septum with 540 control patients. In first singleton pregnancies no association was found between hysteroscopic septum resection and placentation anomalies.^[29,30]

The studies on the impact of hysteroscopic septum resection on fertility demonstrate high heterogeneity of the patients' group, because there were remarkable discrepancies in the definition of the classification systems of uterine anomalies, and clinicians used different hysteroscopic surgery techniques and energy modalities for uterine anomalies.

High-quality randomized controlled studies with a higher number of patients evaluated and classified uniformly are required for a better understanding of the impact of hysteroscopic septum resection on subfertility and reproductive outcome.

The limitations of the study are the restricted number of patients recruited and the reproductive outcome is not compared with patients who did not receive surgical intervention. Although 3-D TVUS enables measurement of the uterine dimensions, intrauterine adhesions cannot be diagnosed by this method and saline infusion sonography or a repeat hysteroscopy might be required to rule out the presence of intrauterine adhesions.

CONCLUSION

The study aims to compare the change in uterine dimensions measured by 3D TVUS after hysteroscopic uterine septum resection and its impact on reproductive outcome in infertile women and women with RPL. Within 1 year after the procedure, the live birth rate was 72% (13/18) and 77.7% (14 of 18) achieved pregnancy through natural conception. 3-D TVUS measurements showed that the distance from the uterine fundus to the apex of the septum (s1) decreased and s2; the distance between the lower end of the septum apex and the internal cervical os (s2) increased after hysteroscopic metroplasty resulting with a long vertical dimension of the uterine cavity. The improvement in these 2 dimensions was more significant in women who achieved pregnancy. 3D TVUS measurements before and after surgery are an effective noninvasive method that demonstrates the changes in the dimensions of the uterine cavity. However, prospective studies with larger number of the patients are required in order to make a strong recommendation.

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Conflicts of interest

There are no conflicts of interest.

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