

Hysteroscopic resection of uterine septum improves reproductive performance in women with unexplained infertility

Selçuk AYAS, Ayşe GÜRBÜZ, Güray TUNA, Mehmet Akif SARGIN, Akif ALKAN, Sadiye EREN

Aim: To evaluate the reproductive outcome after hysteroscopic metroplasty in women with a septate uterus, with particular focus on patients suffering from unexplained infertility.

Materials and methods: Hysteroscopic septum resection was performed on 181 patients with uterine septa, including 98 patients with infertility and 83 patients with secondary infertility. Patients were placed into 1 of 3 groups: those with unexplained infertility, those who had experienced 1 miscarriage, and those who had experienced 2 or more miscarriages. All were analyzed retrospectively in terms of their reproductive outcome.

Results: After undergoing the hysteroscopic septum resection, 43 out of 98 primary infertility patients became pregnant (43.8%). This figure was lower than the pregnancy rates for patients who had experienced 1 miscarriage or 2 or more miscarriages, 70.2% and 82.6%, respectively ($P < 0.05$). In spontaneous pregnancies, the miscarriage rate for those who had experienced 1 previous miscarriage decreased from 88.1% (37/42) to 13.6% (3/22, $P < 0.001$); for those who had experienced 2 or more previous miscarriages, it decreased from 96.5% (168/174) to 17.1% (7/41, $P < 0.001$). The term delivery rate and live birth rate also rose significantly in all of the groups ($P < 0.05$). The rate of cesarean sections was 28 out of 107 births, or 26.1%.

Conclusion: The reproductive prognosis for patients with unexplained infertility can be improved significantly by performing hysteroscopic metroplasty. Vaginal delivery is a safe way of giving birth for these patients.

Key words: Uterine septum, infertility, hysteroscopic metroplasty

Uterin septumun histeroskopik rezeksiyonu açıklanamayan infertilitesi olan kadınlarda reproduktif sonuçları iyileştiriyor

Amaç: Uterin septumlu kadınlarda histeroskopik septum rezeksiyonunun reproduktif sonuçlarını açıklanamayan infertilite grubuna yoğunlaşarak irdelemektir.

Yöntem ve gereç: Doksansekiz primer infertil ve 83 sekonder infertil hastadan oluşan toplam 181 hastaya histeroskopik septum rezeksiyonu uygulandı. Hastaların reproduktif sonuçları retrospektif olarak açıklanamayan infertilitesi, 1 gebelik kaybı olan ve ≥ 2 gebelik kaybı olanlar olmak üzere 3 grupta incelendi.

Bulgular: Septum rezeksiyonu sonrası 43 primer infertil hasta gebe kalabildi (% 43,8, 43/98) ki bu gebelik hızı bir gebelik kaybı olan (% 70,2) veya ≥ 2 gebelik kaybı olan (% 82,6) gruplardakinden daha düşük olarak tespit edildi ($P < 0,05$). Bir gebelik kaybı olan ve ≥ 2 gebelik kaybı olan gruplarda spontan gebeliklerde gebelik kaybı sırası ile % 88,1'den (37/42) % 13,6'e (3/22, $P < 0,001$) ve % 96,5'den (168/174) % 17,1'e (7/41, $P < 0,001$) azaldığı bulundu. Benzer şekilde

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Department of Obstetrics and Gynecology, Zeynep Kamil Maternity and Pediatric Research and Training Hospital, İstanbul - TURKEY

Correspondence: Selçuk AYAS, İnönü Cad. Sinan Sok. No: 1/10 34734 İstanbul - TURKEY

E-mail: sayas55@hotmail.com

miadında doğum oranları ve canlı doğum oranları tüm gruplarda yükseldi ($P < 0,05$). Sezaryen oranı % 26,1 (28/107) olduğu izlendi.

Sonuç: Uterin septumlu açıklanamayan infertil kadınlarda reproduktif prognoz histeroskopik metroplasti ile iyileştirilebilir. Vajinal doğum bu hasta grubu için güvenli bir yöntemdir.

Anahtar sözcükler: Uterin septum, infertilite, histeroskopik metroplasti

Introduction

A uterine septum is the most common congenital anomaly of the female reproductive tract, with an incidence of 2%-3% in women. Patients with a septate uterus have a relatively high rate of spontaneous abortion (21%-27%) and preterm delivery (12%-33%), as well as a low term pregnancy rate (40%-43%) (1-3).

A uterine septum may result in first or second trimester fetal loss, preterm delivery, presentation anomalies, intrauterine growth restriction, and infertility. Septum resection is worth considering in women who can conceive to improve fecundity and to decrease the rates of miscarriage and preterm labor. However, controversies exist regarding the use of uterine septum resection in patients with unexplained infertility and previous miscarriage (4).

In the last 3 decades, doctors have shown that a septate uterus can be effectively treated without serious complications by operative hysteroscopy (5). The incision of the septum can be carried out by resectoscope, scissors, or laser, and none of these techniques seem to have any apparent advantage over the others (6-9). In addition, hysteroscopic metroplasty has been linked to shorter hospitalization time, a lower risk of pelvic adhesion, and reduced morbidity. The procedure also allows women to retain the option of subsequent vaginal delivery (10-11).

The aim of the present study was to share our experience in hysteroscopic septum resection and determine the reproductive benefits in 181 women with uterine septa, specifically focusing on those with unexplained infertility.

Material and methods

Study design

This study is a retrospective study.

Subjects

Our study, which took place between January 2005 and October 2009, examined 181 patients with septate uteri who underwent hysteroscopic metroplasty in the department of obstetrics and gynecology of Zeynep Kamil Maternity and Pediatric Research and Training Hospital. The approval of the relevant ethics committee was obtained.

Patient characteristics were obtained by chart review and reproductive results were recorded during a planned interview. All of the patients and their partners had complete infertility or recurrent miscarriages and underwent investigations with detailed history, clinical examination, and laboratory analysis. Potential causes such as diabetes, dysthyroidism, hypopituitarism, hyperprolactinemia, luteal insufficiency, and hyperandrogenism were analyzed in endocrinometabolic assessment records along with third-day follicle-stimulating hormone (FSH), luteinizing hormone (LH), and estradiol (E2) test results. Transvaginal ultrasounds (TVUSG), cervical smears, and sexually transmitted diseases records were obtained, as was a semen sample from the partner.

The initial diagnosis of septate uterus was confirmed by hysterosalpingography (HSG) for the 98 patients with unexplained infertility. Diagnostic hysteroscopy was performed in the 83 remaining women, all of whom had experienced 1 or more miscarriage during the first or second trimester, preterm labor with the indication of habitual miscarriage, suspicious transvaginal ultrasound, or referral to our clinic for further investigation. Patients who underwent diagnostic laparoscopy were included in the study. Patients who had other possible causes of infertility were excluded.

The metroplasty procedure was performed with a 26 French resectoscope (Karl Storz, Tuttlingen, Germany) with a cutting monopolar 90°-angle knife

electrode. The cutting current was set to 50-70 W. The uterine cavity was distended with 1.5% glycine at an inflow pressure of 70-100 mmHg. The inflow and outflow fluid volumes were measured to ensure that the differences never exceeded 1000 mL. In addition, the VersaPoint system (Gynecare VersaPoint with spring-type electrode; Ethicon, Somerville, NJ, USA) was used for 10 patients and a saline solution was used as the distention medium for this bipolar instrument. All operations were performed under general anesthesia. The septum was divided in an upward direction until both tubal ostia were equally visible. After division of the septum, uterine pressure was decreased and any bleeding points were electrodesiccated. Intrauterine prosthetic devices were not used postoperatively. The duration of the procedures was measured from the insertion of the resectoscope to the final extraction.

The patients were seen on the first postoperative day and returned for a follow up visit approximately 2 months later for an assessment of the surgical outcome. The diagnostic hysteroscopy procedure was offered to and performed on all of the patients in this study (n = 181). Patients that had not undergone a diagnostic hysteroscopy at the time of the first follow-up visit, 2 months after operation, received the offer again, and the procedure was scheduled during the planned interview. Patients that did not have information about the postoperative follow-ups (diagnostic hysteroscopy or hysterosalpingography) or did not agree to follow-up care were excluded from the study. After the hysteroscopic exam, those patients that were not able to conceive within 12 months were advised to apply to the Assisted Reproductive Technology Department. Information on both ART pregnancies and spontaneous pregnancies are given in Table 2, but only spontaneous pregnancies were included in the statistical analysis.

Statistical analysis was carried out with a statistical software program (Number Cruncher Statistical System (NCSS) 2007 and Power Analysis and Sample Size (PASS) 2008 Statistical Software; Utah, USA). Descriptive statistics (mean, standard deviation, frequency) were used to describe the features of the data. A chi-square test and Fisher's exact test were used to analyze the pregnancy outcomes (pregnancy, miscarriage, live birth, etc.) before and after

treatment as both a comparison between groups and an assessment of the procedure within each of the 3 groups. $P < 0.05$ was considered to be statistically significant.

Results

A total of 181 patients who underwent uterine septum resection were included in the study. The number of patients with unexplained infertility in the study group was 98. The other 83 women with more than 1 miscarriage constituted the control group, which was further divided into 2 groups, namely a group of those with 1 previous miscarriage and a group of those with 2 or more previous miscarriages. This was done because the management of these groups is controversial. The patients' mean age was 29.47 ± 5.84 years (range: 18-38). The operation time varied between 10 and 33 min with a mean duration of 18 ± 4.92 min. The distention fluid deficits were between 200 and 800 mL (mean: 319 ± 114). The mean infertility period was 4.0 ± 2.9 years. All septa were resected until both tubal ostia could be seen in a panoramic view of the uterine cavity. Repeated hysteroscopic septum resection was necessary in 9 patients with a residual uterine septum (≥ 1 cm) in the diagnostic hysteroscopic evaluation. Postoperative uterine synechiae were detected in 4 patients, and these patients were operated on once again in order to remove the synechiae. The operations were complicated by 3 uterine perforations, but close monitoring of vital signs and 24-72 h of hospitalization were enough and no further intervention was needed. The duration of hospitalization for patients who had complications was between 1 and 3 days (mean: 2.17 days). Those who had no complications were discharged from the hospital on the first postoperative day. These complications reflect the total group. The mean period of follow-up was 25.3 months (range: 6-56 months). The mean time required to get pregnant was 9.77 months (range: 2-42 months). Details about the pregnancies are given in Tables 1 and 2. The overall rate of cesarean sections was 28/104 (26%), including 13/21 (61.9%) preterm and 15/83 (18%) term births.

With regard to the data collected before the hysteroscopic metroplasty, the difference in the miscarriage rates among groups was found to be

Table 1. Reproductive outcomes of the patient groups before hysteroscopic metroplasty.

	Unexplained infertility (n = 98)		1 previous miscarriage (n = 37)		2 or more previous miscarriages (n = 46)		P-values
	n	%	n	%	n	%	
Before metroplasty	0						
Pregnancies	0	0	42		174		
Miscarriages	0	0	37	88.1	168	96.6	0.001**
Preterm deliveries	0	0	4	9.5	4	2.3	0.004**
Term deliveries	0	0	1	2.4	2	1.1	0.384
Live births	0	0	2	4.8	5	2.9	0.149

**P < 0.01

Table 2. Reproductive outcomes of the patient groups after hysteroscopic metroplasty.

	Unexplained infertility (n = 98)		1 previous miscarriage (n = 37)		2 or more previous miscarriages (n = 46)		P-values
	n	%	n	%	n	%	
Patients that conceived	43	43.9	26	70.3	38	82.6	0.001**
Pregnancies	51		28		44		
Spontaneously	36	70.5	22	78.5	41	93.1	-
After ART	15	29.5	6	21.5	3	6.9	
Live births	41	80.4	22	78.6	35	76.1 (79.5)	0.981
	n = 36 (spontaneously)		n = 22 (spontaneously)		n = 41 (spontaneously)		
Miscarriages	6	16.7	3	13.6	7	17.1	0.935
Preterm deliveries	8	22.2	5	22.7	5	12.2	0.430
Term deliveries	22	61.1	14	63.6	29	70.7	0.658

**P < 0.01

statistically significant (P < 0.001). This difference is mainly because of the unexplained infertility group. However, miscarriage rates between 1 previous miscarriage and 2 or more previous miscarriages were also statistically significant (P = 0.025; P < 0.05). The miscarriage rate in the group with 1 previous miscarriage was statistically lower than that of the group with 2 or more previous miscarriages.

Preterm rates among the groups were determined to be statistically significant (P < 0.01). Again, this difference is mainly due to the group with unexplained infertility. Preterm rates among those with 1 previous miscarriage and 2 or more previous miscarriages were also statistically significant (P = 0.026; P < 0.05). The miscarriage rate for the group with 1 previous miscarriage was statistically lower

than that of the group with 2 or more previous miscarriages. The rates of term delivery and live birth were not statistically different ($P > 0.05$) (Table 1).

Looking at the data collected after the septum resection, the pregnancy rate was statistically different in the unexplained infertility group when compared to those with 1 previous miscarriage and 2 or more previous miscarriages ($P < 0.001$). This means that more patients in the previous miscarriage groups were able to conceive after surgical intervention. However, pregnancy rates were not statistically different between the previous miscarriage groups ($P > 0.05$). The live birth rates did not show a statistically significant difference among the groups ($P > 0.05$). The percentages of live birth were 80.4%, 78.6%, and 79.5% in the groups for unexplained infertility, 1 previous miscarriage, and 2 or more previous miscarriages, respectively. The rates of miscarriages, preterm deliveries, and term deliveries in spontaneous pregnancies between groups were not found to be statistically different ($P > 0.05$) (Table 2).

Miscarriages rates were not statistically different among the 3 groups after resection ($P > 0.05$). However, when we individually compared the miscarriage rates in the 1 previous miscarriage group and the 2 or more previous miscarriages group before and after septum resection, the differences were statistically significant ($P < 0.05$). This reflects reproductive improvement in the groups.

In the unexplained infertility group, the miscarriage rate before treatment (0%) was statistically different from the rate determined after treatment (16.7%) ($P < 0.001$). The preterm delivery rate before treatment (0%) was also statistically different from that found after treatment (22.7%) ($P < 0.001$). Similarly, the preoperative term delivery rate for this group was statistically different from the term delivery rate after treatment (61.1%) ($P < 0.001$).

In the group that experienced 1 previous miscarriage, the miscarriage rate before treatment (88.1%) showed a statistically significant decrease after treatment (13.6%) ($P < 0.001$). Preterm deliveries before treatment (9.5%) also showed an increase after treatment (22.7%), but this was not found to be statistically significant ($P = 0.149$). The term delivery rate before treatment (2.4%) showed a statistically significant increase after treatment (63.6%) ($P < 0.001$).

In the group with 2 or more previous miscarriages, the miscarriage rate before treatment (96.6%) showed a statistically significant decrease after treatment (17.1%) ($P < 0.001$). The rate of preterm deliveries before treatment (2.3%) also showed a statistically significant increase after treatment (12.2%) ($P < 0.01$), as did the comparison of the term delivery rate before treatment (1.1%) with the term delivery rate after treatment (70.7%) ($P < 0.001$) (Table 2).

Discussion

Hysteroscopic repair has become the most popular method for the management of septate uteri. The advantages of this method include less morbidity, no abdominal or transmyometrial incisions, and a shorter time until the patient can return to normal activities. Because no abdominal incision is made in this method, possible infections and intraabdominal adhesions that may cause future fertility problems or pain are avoided. Pregnancy can also be planned sooner after the hysteroscopic approach than after abdominal procedures, and vaginal delivery remains a viable choice for these patients. Different techniques and instruments are used for septal incisions, such as microscissors, electroresectoscopes, or lasers. In our study, the VersaPoint system was used in 10 operations. No complications were recorded and no cervical dilatation was performed with this instrument. Additionally, the use of this device allowed for a shorter operation time (15.5 ± 4.97 min) and pregnancy was detected in 4 out of the 10 cases.

It has been demonstrated that the prevalence of a septate uterus is high in women with recurrent miscarriages. The prevalence of a septate uterus is also high in women with repeated pregnancy loss. Fortunately, in the literature, the overall miscarriage rate after hysteroscopic metroplasty shows a significant decrease (between 88% and 5.9%) for patients with a history of recurrent miscarriage (4). In our study, an initial miscarriage rate of 96.5% among 46 women with 2 or more previous miscarriages improved dramatically, to 15.9%.

Hysteroscopic metroplasty for septate uterus in women with unexplained infertility is a controversial issue because the role of septate uteri in infertility

has not been clearly established. The septum may have a role in implantation failure or early pregnancy development. There are several ideas about the underlying mechanism of the implantation failure or pregnancy loss. These include maturation defects of the endometrium covering the septum with a reduced number of glandular ostia, altered maturation of the cilia, altered proportions between muscular and fibroelastic connective tissue, or an abnormal vascularization in the histologic examination of uterine septa (12,13). Resection of the septum may restore the normal function of the endometrium. Although current evidence is not strong enough to justify surgical intervention in patients with unexplained infertility, the reported pregnancy rates for these patients in the self-control designed studies are between 29% and 71% (14-19). Thus far, only randomized controlled studies including patients with uterine septa and otherwise unexplained infertility and patients with unexplained infertility have shown improvement in fecundity. The improvements in the pregnancy and live birth rates were from 20.4% to 38.6% and from 34.1% to 18.9%, respectively (20). On the other hand, there are also studies that do not recommend septum resection in infertility patients (21,22). In their own retrospective study, Marcus et al. did not recommend metroplasty for patients without any prior pregnancy loss. Instead, their results showed comparable implantation and pregnancy rates in ART cycles for patients with septa and without septa (21). Our pregnancy rate among primary infertility patients was 43/98 (43.8%), which included 8 miscarriages, 24 term deliveries, and 9 preterm deliveries. These figures and the low intraoperative and postoperative complication rates of hysteroscopic septum resection are compatible with the information found in the literature and seem to encourage operating on patients with primary infertility and uterine septa.

The debate over the management of patients with a uterine septum and a single miscarriage also seems

to continue because the high rates of delivering a viable infant after a single miscarriage (80%-90%) may justify or deserve a more conservative approach (4). Still, patients who have experienced a miscarriage and are aware of the possibility of a diagnosis of septate uterus as a finding of transvaginal ultrasound or a diagnostic hysteroscopy may often direct the management plan. The possibility of a second miscarriage resulting from a known uterine septum makes them anxious and these patients may prefer surgical intervention. Furthermore, studies that support surgical intervention argue that up to one-fourth of all miscarriages are accompanied by a partial septate uterus, indicating that this may be an important predisposing factor (4,10,23,24). For the 37 patients in our study that had experienced 1 previous miscarriage, the miscarriage rate decreased from 88% to 14.2%, which was found to be statistically significant ($P < 0.05$). The increased term delivery rate (18 versus 1) after hysteroscopic metroplasty supports the use of surgical intervention after 1 miscarriage in women with septate uteri.

Out of 104 total deliveries, the rate of cesarean sections was 28/104 (26%), which is lower than other rates reported for the procedure (58%) and proves the reliability of vaginal delivery for these patients (19).

Factors such as the retrospective analysis and the absence of control groups limit the value of our study, but we are encouraged by our findings for pregnancy outcome. Our study is also notable for involving one of the largest numbers of patients in the literature.

In conclusion, hysteroscopic metroplasty significantly improves reproductive performance in patients with unexplained infertility and a septate uterus, although postoperative reproductive performance remains better in patients that were able to conceive previously. For these patients, the procedure should be highly considered as a corrective approach.

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