

Does uterine septum resection improve IVF treatment success?

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ABSTRACT

Aim: Uterine septum is the most common type of congenital uterine malformation. The septum has also been suggested as a potential cause of infertility. The role of the septum in infertility and whether the septum can be resected is debatable. We aimed to reveal the results of assisted reproductive techniques in patients with septate uterus according to whether or not resection is performed.

Material and Method: 7790 patients were scanned retrospectively. 110 patients with the uterine septum and unexplained infertility were included in the study. Patients who underwent uterine septum resection were recorded. The clinical pregnancies of patients were compared according to whether or not resection was performed. In addition, patients with complete septum were evaluated according to whether or not resection was performed, and their clinical pregnancies were evaluated.

Results: It was revealed that 79 of the patients with uterine septum underwent septum resection operation. It was determined that 31 patients were not treated. Clinical pregnancy rates were found to be statistically significantly higher in the expectant management group ($p=0.02$). In addition, comparing the clinical pregnancy rates of the resection and expectant management groups in patients with a complete septum, no significant difference was found between the groups ($p=0.134$).

Conclusion: In our study, the success of treatment with assisted reproductive techniques did not change after septum resection. Although uterine septum resection is a simple and safe method, it has disadvantages such as the development of adhesions and rupture in the uterus. There is insufficient evidence to perform septum resection in patients with uterine septum prior to infertility treatment.

Keywords: Infertility, IVE, septum resection, uterine septum

INTRODUCTION

Uterine septum is the most common type and accounts for 35% of congenital uterine malformations (1). This situation can vary from a mild midline septum form (arcuate) to a complete septum. (2). Subfertility, pregnancy loss, preterm delivery, and fetal malpresentation may be more common in women with a septate uterus (3). The most common complication is miscarriage. Many studies have found that septum resection improves obstetric outcomes (4-6). Despite the potential benefits of hysteroscopic septum resection, a recent Cochrane review (7) concluded that there is no solid evidence supporting this procedure for women to improve reproductive outcomes due to the lack of published randomized controlled trials (RCTs) comparing hysteroscopic septum resection to expectant management. The main reason for septum resection is that the septum is structurally distinct from the uterine

wall. According to a recent review, the endometrial and myometrial tissue in the septum is similar to that in the normal uterine wall. The endometrial lining of the intrauterine septum exhibits lower or similar expression of HOXA genes and transcription factors and lower expression of VEGF receptors than does the endometrium of the uterine wall, according to the same study. (8).

Worldwide, hysteroscopic septum resection improves reproductive outcomes in women of reproductive age who have a septate uterus (7,9). However, the recommended resection treatment is based mainly on observational studies; well-designed prospective randomized controlled studies are unavailable. These studies also provide a low level of evidence. In a recent randomized controlled study with a small number of samples, septum resection was not

found to be statistically significant (10). The ASRM (2016) guideline recommends septum resection (11). ESHRE (2017) and RCOG (2011) guidelines state that resection should be repeated with other studies in patients with recurrent miscarriages. The uterine septum has also been suggested as a potential cause of infertility (12). Many studies have included uterine septums in the group of idiopathic infertility, so the role of the septum in infertility and whether the septum can be resected is debatable (13-16).

In our study, infertile patients with a septate uterus were filtered retrospectively in a single center. We aimed to reveal the results of assisted reproductive techniques in patients with septate uterus according to whether or not resection is performed.

MATERIAL AND METHOD

Study Design and Population

The study was initiated with the approval of the Gazi University Medical Faculty Clinical Researches Ethics Committee (Date: 01.06.2021, Decision No: 2021-666). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Between January 2000 and December 2021, data from 7790 patients were scanned retrospectively. A total of 196 patients with uterine septum were identified. Patients with infertility factors such as male factor, tubal pathologies, endometriosis, and PCOS were excluded. In addition, eight patients were excluded from the study because they did not complete their treatment. A total of 110 patients with the uterine septum and unexplained infertility were included in the study. The first cycles of each patient were evaluated.

The diagnosis of the uterine septum was made according to the AFS classification system by hysterosalpingography of the patients (16). Uterine septums were divided into two groups complete septum and partial septum. Patients who underwent uterine septum resection were recorded. It was learned from the notes in the file that it was a joint decision of the patient and the physician, depending on the conditions of the day, to whom resection and expectant management were performed. It was seen that the septum resection procedure was performed with the hysteroscopic resectoscope in the operating room.

Treatment Protocol

Age, gravida, duration of infertility, and BMI were examined in the database containing patient records (body mass index). Data were recorded. The patients' ovarian stimulation protocols were learned. Standardized ovarian stimulation protocols were started for the patients, and these protocols included GnRH antagonist,

long GnRH agonist, microdose flare-up protocols. These protocols were chosen based on the unique conditions of the patients. 225–300 IU of gonadotropins were used in the stimulation protocols. The patients' hormonal and ultrasonographic measurements were taken into consideration as the gonadotropin doses were adjusted. The Aloka SSD-1000 was used to measure each follicle using a 5 MHz transvaginal probe. Once at least two follicles had reached an average diameter of 18 mm, recombinant HCG (Ovitrelle; Serono) was injected to induce ovulation, and oocytes were retrieved 36 hours later while the patient was under general anesthesia. IVF/ICSI was used to fertilize mature oocytes. Three to five days after the oocyte retrieval, an embryo transfer (ET) under ultrasound guidance was carried out. From 12 days after ET until a pregnancy test was taken, patients received 200 mg of transvaginal micronized progesterone three times daily. Increased -hCG concentrations and sonographic evidence of an intrauterine gestational sac after ET were used to make the clinical diagnosis of pregnancy.

Outcome Measures

The clinical pregnancies of all patients were compared according to whether or not resection was performed. In addition, patients with complete septum were evaluated according to whether or not resection was performed, and their clinical pregnancies were evaluated.

Statistical Analysis

The Statistical Package for Social Sciences was used for all statistical analyses (SPSS, version 22.0, IBM, USA). The Kolmogorov-Smirnov test and other normality tests were applied to the analysis of normal distribution data. The Student's t-test was used to compare parametric data that were normally distributed. Mann-Whitney Data that did not exhibit a normal distribution were compared using the U test. The differences between categorical data were examined using the chi-square test or the Fischer's exact test. The presentation of continuous variables was as mean standard deviation. Categorical data were presented as a percentage and data with a non-D normal distribution were shown as the median. Statistical significance was accepted as $p < 0.05$.

RESULTS

Between January 2000 and December 2021, the uterine septum was detected in 196 of 7790 infertile patients who applied to our clinic, and the rate of patients with a uterine septum in the clinic was 2.5%. 110 of these patients had unexplained infertility and uterine septum. There were 17 secondary infertile patients and 93 primary infertile patients. Patients suffering from secondary infertility had previously had a single pregnancy. Four of the patients had living

children. Thirteen patients' pregnancies ended in abortion. There were 25 patients with a partial septum and 85 with a complete septum. It was revealed that 79 of the patients with uterine septum underwent septum resection operation. It was determined that 31 patients were not treated. When age, BMI, and infertility duration were compared between the resection and expectant management groups, there was no significant difference (**Table 1**).

Table 1. Comparison of demographic features between the resection and expectant management groups

	Septum resection group	Expectant management group	P value
Age (years) *	31.4±5.7	29.5±6.8	0.151
BMI*	26.6±5.2	26.5±4.9	0.932
Infertility duration (years) *	7.3±5.3	5.5±5.2	0.140

* Data are given as mean±SD, BMI: Body mass index, (p<0.05 was considered significant.)

Resection was performed in 10 patients (40%) out of 25 patients with the partial septum. Resection was performed in 69 (81%) of 85 patients with the complete septum. When the results of assisted reproductive therapy patients were examined, it was found that 35 of 110 patients had clinical pregnancies. In 75 patients, pregnancy was not detected.

It was found that 15 (48.4%) of the patients with 35 clinical pregnancies were in the non-resection group, while 20 (25.3%) were in the resection group. Clinical pregnancy rates were found to be statistically significantly higher in the expectant management group (p=0.02) (**Table 2**). In addition, patients with a complete septum were evaluated (n=85). Pregnancy rates of these patients were compared according to whether or not resection was performed. There were 27 patients with clinical pregnancies. Of these, 8 (50%) were in the non-resection group, while 19 (27.5%) were in the resection group. There was no statistically significant difference between the groups in terms of clinical pregnancy rates (p=0.134) (**Table 3**).

Table 2. Comparison of clinical pregnancy rates of resection and expectant management groups in the whole patient group

	Septum resection group	Expectant management group	P value
Clinical pregnancy positive	20 (25.3%)	15 (48.4%)	0.02
Clinical pregnancy negative	59 (74.7%)	16 (51.6)	

Table 3. Comparison of clinical pregnancy rates of resection and expectant management groups in the patients with complete septum

	Septum resection group	Expectant management group	P value
Clinical pregnancy positive	19 (27.5%)	8 (50%)	0.134
Clinical pregnancy negative	50 (72.5%)	8 (50%)	

DISCUSSION

In our clinic, the incidence of the uterine septum in the infertile population was found to be 2.5 percent. In the literature, the incidence is reported to vary between 1% and 15% (9). Especially in the infertile population, the prevalence of uterine septum in the literature varies between 5% and 25% (17). In this study, a statistically significant difference was found between clinical pregnancy outcomes, depending on whether or not septum resection was performed. This difference is that the clinical pregnancy rates were higher in the group that did not undergo treatment. Observational studies show that there is no significant change in clinical pregnancy rates after septum resection and support our results (18, 19) In the literature, there are not enough randomized controlled studies on this subject. A recent randomized controlled study also supports our results (10).

Previous studies have shown that there is a significant increase in viable pregnancy rates with septum resection (9,13). These studies are not randomized controlled trials. Therefore, the necessity of septum resection is presented with weak evidence.

In a recent review by Krishnan et al. (20), it was shown that there is a significant decrease in abortion rates with septum resection. However, this study found no substantial evidence to suggest that hysteroscopic resection improves live birth and clinical pregnancy rates and/or reduces preterm birth. Unlike previous reviews, patients with subfertility and poor obstetric outcomes are included in this review. And two recent studies are up to date (16,21).

In another recent meta-analysis showed that there was a significant decrease in abortions in the group that underwent hysteroscopic septum resection, and there was a significant decrease in the frequency of preterm birth and fetal malpresentation (22). Although many studies have shown that septum resection improves obstetric outcomes, most of them are retrospective studies (23,24).

A recent randomized controlled study by Rikken et al. (10) showed that there was no significant difference in pregnancy loss and preterm delivery rates between the group that underwent septum resection and the group that underwent expectant management.

In our study, it was observed that the success of treatment with assisted reproductive techniques did not change after septum resection. The biggest limitation of our study is that; follow-up of the cases resulting in clinical pregnancy was not performed. Therefore, our data on obstetric outcomes are insufficient. This study's retrospective design, which makes it challenging to access data and potentially biased records, is another drawback.

CONCLUSION

Although uterine septum resection is a simple and safe method, it has disadvantages such as the development of adhesions and rupture in the uterus, as well as being an invasive procedure (9). There is insufficient evidence to perform septum resection in patients with uterine septum before infertility treatment. Randomized controlled studies with large samples are needed.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was initiated with the approval of the Gazi University Medical Faculty Clinical Researches Ethics Committee (Date: 01.06.2021, Decision No: 2021-666).

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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