



Surgical Treatment Options for Female Infertility

Kadın İnfertilitesi için Cerrahi Tedavi Seçenekleri

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ABSTRACT

Infertility, defined as failure to achieve pregnancy within 12 months of unprotected intercourse or therapeutic donor insemination in women younger than 35 years or within 6 months in women older than 35 years, affects up to 15% of couples. An infertility evaluation may be offered to any patient who by definition has infertility or is at high risk of infertility. Hysterosalpingography, hysterosalpingo-contrast sonography, saline infusion sonohysterography, hysteroscopy, laparoscopy, and bacteriological and endocrinological examinations that will be made after these studies aim to focus more on the causes of infertility. With the development of assisted reproductive technology, the need for major reproductive surgery, which may be necessary for the primary treatment of infertility, has decreased over the years. Surgical methods are mainly considered as laparoscopic and hysteroscopic techniques. However, laparotomy is also rarely required and may be needed in cases such as adhesions, mass lesions, unsuccessful surgeries, or emergency surgery. When a surgical treatment is planned for infertile patients who required surgery, it is very crucial that the procedure should be performed by experienced surgeons. In this review, pathologies that require surgery for infertility treatment and surgical methods that can be applied to infertile patients were discussed, rather than medical treatments.

Keywords: Infertility; laparoscopy; hysteroscopy.

ÖZ

İnfertilite 35 yaşın altındaki kadınlarda 12 ay veya 35 yaşın üstündeki kadınlarda 6 ay korunmasız cinsel ilişkiye veya terapötik donör inseminasyonuna rağmen gebe kalamama hali olarak tanımlanıp çiftlerin %15'ini etkileyen durumdur. Tanım gereği infertilitesi olan veya infertilite riski yüksek olan herhangi bir hastaya infertilite değerlendirmesi önerilebilir. Histerosalpingografi, histerosalpingo-kontrast sonografi, salin infüzyon sonohisterografi, histeroskopi, laparoskopisi ve bu çalışmalardan sonra yapılacak bakteriyolojik ve endokrinolojik incelemeler ile infertilite nedenlerine daha fazla odaklanılması amaçlanmaktadır. Yardımcı üreme teknolojisinin gelişmesiyle birlikte infertilitenin birincil tedavisi için gerekli olabilecek majör üreme cerrahisine olan ihtiyaç yıllar içinde azalmıştır. Cerrahi yöntemler temel olarak laparoskopik ve histeroskopik teknikler olarak kabul edilmektedir. Ancak laparotomi de nadiren de olsa gereklidir ve adezyonlar, kitle lezyonları, başarısız ameliyatlara veya acil ameliyat gibi durumlar söz konusu olduğunda ihtiyaç duyulabilir. Ameliyat gerektiren infertil hastalarda cerrahi bir tedavi planlanırken işlemin deneyimli cerrahlar tarafından yapılması çok önemlidir. Bu derlemede, medikal tedavilerden ziyade infertilite tedavisi için cerrahi gerektiren patolojiler ve infertil hastalarda uygulanabilecek olan cerrahi yöntemler tartışılmıştır.

Anahtar kelimeler: İnfertilite; laparoskopisi; histeroskopi.

INTRODUCTION

Infertility, defined as failure to achieve pregnancy within 12 months of unprotected intercourse in women younger than 35 years or within 6 months in women older than 35 years, affects up to 15% of couples (1). Women older than 35 years should receive an expedited evaluation and undergo treatment after 6 months of failed attempts to become pregnant or earlier if clinically indicated. In women older than 40 years, more immediate evaluation and treatment are warranted (1,2).

In the evaluation of etiologies, female factors are responsible for 45% of all infertility causes. Male factor is a cause of infertility in 40-50% of couples (3). With the development of assisted reproductive technology (ART), the need for major reproductive surgery, which may be necessary for the primary treatment of infertility, has decreased over the years. In addition to medical history and physical examination, pelvic evaluation is completed with a gynecological examination, pelvic ultrasonography (USG), and transvaginal ultrasonography (TVUSG). It is possible to detect pathologies such as polyps and leiomyomas in the cervical canal by TVUSG. Many of the congenital uterine anomalies also can be detected at this stage.

Hysteroscopy and saline infusion sonohysterography (SIS) for endometrial polyps, fibroids, or adhesions provide information about the cavity. Magnetic resonance imaging (MRI) may be required in a virgin patient, vaginal agenesis, and complex cases. Hysterosalpingography (HSG) is a radiological method in which both uterine cavity, tubal patency, and peritoneal spread can be evaluated. Although it is accepted that the cavity is also evaluated, it is not preferred for cavity evaluation. Because in cavity evaluation, hysteroscopy is considered as a superior method. 3D hysterosonography has been found to be as valuable and successful as hysteroscopy in terms of intrauterine evaluation (4).

Congenital uterine anomalies can be recognized by 2D and 3D TVUSG, HSG, MRI, and sonohysterography. MRI is an expensive, but also an effective method. The gold standard in the diagnosis of congenital uterine anomalies is hysteroscopy and 3D USG. The need for L/S or MRI can be eliminated owing to 3D USG. 3D USG also allows distinguishing the septum-bicornuate uterus more clearly. Diagnostic laparoscopy is very valuable when the anomaly cannot be evaluated clearly.

The requirement of reproductive surgery can be evaluated in three categories (Table 1).

In this review, we will focus on pathologies that require surgery for infertility treatment and surgical methods that can be applied, rather than medical treatments.

HYSTEROSCOPY

Hysteroscopy is a very valuable method in confirming the diagnosis of intracavitary lesions detected by other imaging methods in infertile patients. It is an invasive diagnostic method and allows treatment during the procedure. It is considered as the gold standard in the evaluation of the uterine cavity. The disadvantage of this method is that hysteroscopy cannot distinguish the septum and bicornuate uterus and cannot evaluate the uterine wall. Complementary laparoscopy may be required. It is considered to be the best diagnostic method for endometrial polyps, uterine synechiae, and submucous myomas, owing to the direct visualization of the uterine cavity. However, it is not considered as the first diagnostic evaluation in infertile women due to its high cost and not being an easily accessible method. It is considered as an advanced examination since it is not routinely used and does not need to be done on every patient.

Hysteroscopy is not a method that can be performed at any time of the cycle. It should be done in the early proliferative phase, in the 2-3 days immediately after menstruation; when the endometrium layer is the thinnest, in order to show organic pathologies or anatomical disorders and to get the maximum benefit from the treatment opportunity it provides. Distention media used in hysteroscopy are saline, glycine, sorbitol, and mannitol. The choice of medium is decided according to the incision technique to be made and the energy source to be used (4). It is possible to benefit from a laparoscopy and abdominal USG to be performed simultaneously during the cavity correcting hysteroscopic incision procedure for the uterine septum. Abdominal USG is of course more preferred because it is not invasive. The uterine contour can be seen more clearly thanks to laparoscopy and USG. In this way, the risk of uterine perforation is reduced and it can be ensured that the septum is completely removed (5).

The indications for hysteroscopy are very diverse. These are infertility, abnormal uterine bleeding, endometrial polyps, leiomyomas, chronic endometritis, intrauterine synechiae, isthmocele, Mullerian anomalies, cervical stenosis, cervical polyps, cervical insufficiency, and retention of the pregnancy material. Abnormal findings on

Table 1. The requirement for reproductive surgery

Conventional Treatments	Enhancements of Outcomes	Preservation of Fertility
Tuboplasty	Hydrosalpinx surgeries	Ovarian transposition
Neosalpingostomy	Salpingectomy	Ovarian transplantation
Fimbrioplasty	Proximal tubal occlusion	Ovarian tissue cryopreservation
Tubal anastomosis	Hysteroscopic tubal occlusion	
Excision of endometrioma		
Hysteroscopy	Hysteroscopy	
Polypectomy	Polypectomy	
Myomectomy	Myomectomy	
Metroplasty	Metroplasty	
Adhesiolysis	Adhesiolysis	

USG, HSG, or SIS also require this procedure. This procedure is contraindicated in the presence of active bleeding, pregnancy, acute pelvic infection, and uterine malignancy.

Hysteroscopy is basically done in two ways. Office hysteroscopy is for diagnostic purposes as mentioned above. It is also known as diagnostic hysteroscopy. In operative hysteroscopy, it is aimed to treat uterine pathologies.

Diagnostic hysteroscopy has the advantage that it can be performed in the office or in clinical conditions. It is performed in the early stages of the postmenstrual cycle without the use of a speculum and tenaculum. The patient and the doctor can decide before the procedure whether to give anesthesia or not. After vaginal observation, the cervical external orifice is found. The hysteroscope goes forward in by monitoring the cervical canal. After passing the cervical internal orifice, the uterine cavity is viewed panoramically. The close neighborhood of the uterine cavity to the cervix, the corpus level, and the walls of the cavity in the fundus region are observed on the right/left, anterior/posterior positions. Since this process is done immediately after menstruation, it will be easier to observe possible pathologies in the cavity such as myoma, polyp, and isthmocele. Later, both tubal ostia are observed on both sides of the inner surface of the fundus.

In operative hysteroscopy, entry into the cavity is performed after the speculum is inserted and the anterior lip of the cervix is grasped with the tenaculum. It is preferred more to be done under general anesthesia. Dilatation can be done with dilatation plugs in patients with cervical stenosis. As in office hysteroscopy, the hysteroscope goes forward into the cavity. Afterward, the planned surgical procedure is completed.

LAPAROSCOPY

Laparoscopy is the surgical method for both the diagnosis and treatment of infertile patients. It is often preferred for hydrosalpinx, endometriosis, endometrioma, leiomyomas, and intra-abdominal adhesions. A shorter hospital stay and faster recovery can be achieved with laparoscopy.

Chlamydia trachomatis, *Mycobacteria tuberculosis*, and other pelvic inflammatory disease (PID) agents also cause damage and adhesions in the tuba uterina. The clinical value of the *Chlamydia trachomatis* serological screening test has been shown to be limited (6).

Another important aspect of laparoscopy is the benefit it provides to patients with a history of pelvic surgery. Since synechiae developed after surgery also affect the tuba-ovarian function, it is important to open the synechiae in terms of infertility treatment. Although the synechiae of these patients tend to stick again after opening, they also provide benefits in terms of pelvic pain and dyspareunia. Since it is not possible to evaluate both the outer contour and the inner surface of the uterus together with laparoscopy. So hysteroscopy may be required as a complementary in the recognition of congenital uterine anomalies.

TUBAL CAUSES

It is important to have a complete, uninterrupted, and undamaged tubal anatomy and fimbrial tissue for the passage of both sperm, oocyte, and fertilized ovum in the

formation of a healthy pregnancy. Tubal diseases account for nearly one-third of female infertility. These diseases can involve the entire tuba, or they can only be seen proximal or distal region. Medical treatment of tubal diseases that cause infertility is not possible. Surgery is required for treatment.

The causes of tubal diseases are mostly salpingitis (7). Most tubal disease is caused by an episode of tubal infection, PID, or endometriosis, which are both very common problems. Sexually transmitted diseases such as gonorrhea, chlamydia or appendicitis, and bowel infection may also be the result of PID (8). Fimbrial adhesions and hydrosalpingial tubal damages due to salpingitis isthmica nodosa (SIN) (diverticulum of the fallopian tube), tubal or cornual polyps, ascending infections, and pelvic tuberculosis are frequently seen.

The use of laparoscopy in tubal diseases varies according to the type of tubal disease. Proximal tubal occlusion may be due to obstruction resulting from plugs of mucus and amorphous debris, to spasm of the uterotubal ostium, or to occlusion, which is a true anatomic blockage from fibrosis due to SIN, PID, or endometriosis (9). Tubal ligation or segmental salpingectomies that cause midtubal occlusion are counted as iatrogenic tubal factors. Tubal ligation is one of the most preferred contraceptive methods worldwide and also one of the causes of tubal damage. The demand for reopening the tubes is quite common due to the decision to have more children or the desire to have a child from a second spouse. Although few women seek reversal for the procedure. The prevalence of post-sterilization regret ranges from 20% to 30% and varies by the length of time since the procedure (10). In such a case, two ways to have a child are tubal anastomosis or in vitro fertilization (IVF). Although the general approach is to apply IVF treatment to these patients, tubal anastomosis may be preferred to IVF due to certain beliefs or concerns. The purpose of tubal anastomosis is to reapproximate and recanalize the 2 separated tubal segments. It is also important to prevent the formation of adhesions. Tubal patency should then be confirmed with HSG.

Factors determining success in tubal anastomosis technique are the age of the woman, the sterilization technique, the residual tubal length, and the time elapsed after sterilization. For example, the pregnancy rates of women aged 15-29 years, 30-33 years, and 34-49 years old after tubal anastomosis were 73%, 64%, and 46%, respectively (11). In terms of sterilization technique, it was shown that pregnancy success according to the method of sterilization was 16 of 24 in which Fallope-ring was used, 14 of 15 with cauterization, and 8 of 10 in patients in whom the Pomeroy technique was used (12). Anastomosis is mostly performed according to the length of the residual tuba segment mostly as isthmic-isthmic, isthmic-ampullary ones. Pregnancy rates after anastomosis were 75% in women with a residual tubal length of 4 cm or more, whereas it was only 19% in those with a shorter tube (13). Based on their findings, it is considered that laparoscopic sterilization reversal will be a better option in women younger than 37 years who have ≥ 4 cm of a residual tube. For others, IVF is better (14).

Anastomosis operation can be performed with laparoscopy, conventional microsurgery, or robot-assisted laparoscopy. Pregnancy results of laparoscopic tubal

anastomosis and conventional microsurgery techniques are similar (15). In the robot-assisted technique, success is similar to these two methods. Also, the duration of the surgery, costs, and the experience of the surgeon are important factors. While the short recovery time is an advantage, more studies are needed to evaluate whether the use of the robot in this procedure provides additional benefits. Ectopic pregnancy rates were found to be similar in laparoscopic tubal anastomosis and microsurgery techniques, 2.5%, and 2.8% (15). However, the laparoscopic method was also found to be more costly than mini-laparotomy (16). As a result, laparoscopic tubal anastomosis is less invasive and may be an alternative to laparotomy to reverse tubal sterilization. It is useful to know that tubal anastomoses created by the V-notes technique, as a new method, are also possible.

When we look at anastomosis, single suture, 2 suture, and 4 suture techniques are suitable, and both techniques can be done by both laparoscopic and laparoscopy-guided robotic methods. The single suture technique is performed at the 12 o'clock position from the serosal aspect of the tuba, and the 2 suture technique is performed at the 6 and 12 o'clock positions. The 4 suture technique is the classical anastomosis technique. In this technique, sutures are passed from the mucosa-muscular layer border at 3, 6, 9, 12 o'clock positions. Then the serosa layer is sutured continuously. It is possible to perform all three of these techniques with laparoscopic or laparoscopy-guided robotic techniques in experienced hands. Suture techniques include micro-suturing using 6-0/10-0 sutures. There is also a suture-free technique, in which tubal recanalization is provided with micro clips using tissue bonding technology.

Hydrosalpinx is the condition of tubal dilatation and distension due to occlusion of the distal tuba uterina for any reason. Almost 30% of tubal damages are hydrosalpinxes (17). The cause of this distention is mostly PID. If it occurs the progression of the sperm in the endometrium and tube, caught of the oocyte by the fimbrial ends, the progression of the oocyte in the tubes, the formation of fertilization in the ampulla, and the progression of the embryo towards the endometrium may be affected. Even if it reaches the endometrium, its implantation into the endometrial layer cannot occur because receptivity will be affected. In addition, if it is implanted, the possibility of abortion increases. These conditions may also occur due to endometrial local inflammatory factors. Hydrosalpinx is a reason for blocking pregnancy formation from occurring normally or failure in IVF treatments. Embryos to be transferred may be dragged out of the cavity due to the reflux of fluid in the fallopian tubes. As a result, in the presence of hydrosalpinx, the success of implantation, pregnancy, and live birth decreases, and the risks of abortion and ectopic pregnancy increase. With the removal of hydrosalpinxes, the chances of IVF success increase.

In addition to all these, histories of ectopic pregnancies that were treated without salpingectomy with drugs such as methotrexate, with surgical reasons such as salpingotomy or total or segmental salpingectomy due to the treatment of tubal ectopic pregnancies are also important reasons that should not be ignored.

Before IVF treatment in patients with hydrosalpinx, laparoscopic salpingectomy or proximal tubal occlusion

should be performed. Laparoscopic salpingoneostomy may also be an alternative method according to tubal score. The principle here is to preserve the integrity of the tuba and to make a distal tubal incision for the flow of the fluid in the tuba to the douglas instead of the endometrial cavity. For this procedure, the abdomen is entered with the laparoscopic technique, and scissors or electrocautery are used for the incision (18). An incision is made in an antimesenteric and avascular region of the distal tubal tip with a monopolar needle, scissors, or laser. Tubal mucosa is directly observed by entering with a thin hysteroscope. At this stage, apart from the laparoscopy equipment, a second telescope, additional light source, video camera, monitor, and irrigation are required for salpingoscopy. The tubal fimbriae are delicately grasped with laparoscopic tubal forceps. At this time, the hysteroscope is inserted through the 5 inch trocar and entered into the ampulla via fimbriae. The tubal mucosa is irrigated with saline and the ampulla area is observed for internal adhesion and damage to the tubal mucosa. The ostium is enlarged with fine forceps. In order to prevent the ostium from closing, the bulbous mucosa is everted and sutured to the serosa. Of course, for all these possibilities, the patient should not be old and the ovarian reserve should not be low. It would be more appropriate to perform salpingectomy or tubal blockage and apply IVF treatment for those with a tubal score of 3-4. An experienced surgeon is required in reconstructive tubal surgery. The patient should be informed that the risk of ectopic pregnancy is higher than that in the normal population.

Although it is preferred that salpingectomy to be laparoscopic, it can also be performed with open surgery technique. It is started from the closest border to the tuba by holding the fimbrial end. It is aimed to protect the ovarian vessels and not decreasing the reserve. Preferably scissors or bipolar energy powered ligasure are used. The tuba is removed from the closest place to the horn. The aim here is to reduce the risk of interstitial pregnancy. With salpingectomy, in which chronically infected tissue is excised, it is easier to reach the ovaries during oocyte collection for IVF. Risks such as abscess, torsion, and chronic pelvic pain are eliminated.

Proximal tubal occlusion is an alternative method to salpingectomy in patients with hydrosalpinx. The aim is to prevent the retrograde flow of tubal contents into the uterine cavity by creating a blockage in the cornual region between the tuba and the uterus. However, in patients with this blockage, fenestration to the distal tubal segment is required for fluid drainage in order to prevent a fluid increase in the tubal segment in between, and formation of cyst or abscess.

A proximal tubal occlusion is an option in excessive pelvic adhesions in cases where the pelvic anatomy is so distorted that the tuba cannot be released from the peritoneum, douglas, uterus, or ovaries; or in cases in which the ovarian reserve may be damaged during this procedure. Thus, ovarian blood flow is not impaired. It is less invasive than salpingectomy. In terms of implantation and pregnancy rates, is similar to salpingectomy, salpingostomy, and salpingoneostomy (19). Although it is theoretically possible to perform the blocking procedure hysteroscopically with the Essure method, the evidence for efficacy and safety is insufficient (20).

Tubal phimosis is the narrowing of the distal end of the fallopian tube which the tubal opening is still present. Fallopian tubes have a curled appearance. During laparoscopy, it is characteristic that the dyed fluid causes dilatation in the distal ampulla and gushes out from the narrow end (21). With laparoscopic tubal forceps, the tubal fimbriae is carefully grasped and lifted. A small incision is made from the antimesenteric side to the narrowed fimbrial end. The mucosa is everted to prevent reocclusion and closure of the ostium (22). This procedure in which phimosis is corrected is called laparoscopic fimbrioplasty. Fimbrial agglutination is the condition in which the adhesive brids of both tuba fimbrial ends are formed. It is mostly associated with serosal defects. In this case, it is unclear whether the fimbriae of the fallopian tubes can fully capture the ovum, and therefore their relationship with infertility. If seen, the brids can be cut (21). If these brids are cut, the fimbriae will also be opened.

UTERINE CAUSES

Uterine causes are not as common as tubal diseases. However, the uterus should be carefully evaluated. Because it can be one of the important causes of infertility that can be overlooked. When the fertilized ovum in the tuba reaches the uterine cavity, there should be no anatomical defect in the uterus, but an endometrium which ready for implantation is required for its receptivity. Acute or chronic endometritis, endometrial polyp, leiomyoma, congenital uterine pathologies, adenomyosis, Asherman syndrome, isthmocele, and previous uterine surgeries are uterine pathologies that may cause infertility. These pathologies are also important in terms of affecting the prognosis of pregnancies obtained by IVF. As a result, decreased endometrial receptivity or endometrial anatomical-mechanical disorders lie on the basis of uterine causes of infertility.

Mullerian anomalies cause infertility by preventing normal implantation, and are also a common cause of recurrent pregnancy loss. Among the different types of structural uterine anomalies, the septate uterus is the most common and associated with the poorest reproductive outcomes (23). The presence of a septum is also associated with poor obstetric outcomes such as malpresentation and preterm delivery (24). In the classification of anomalies, there are classifications of the European Society of Human Reproduction and Embryology-the European Society for Gynecological Endoscopy (ESHRE-ESGE), and the American Society for Reproductive Medicine (ASRM) (25). The issue of which anomalies will require treatment is still a discussion topic. Uterine septum, T-shaped uterus, and endometrial cavity presence types of uterine horns (endometriosis and due to adhesion risks) require treatment. Treatment for bicornuate uterus and uterus didelphis is controversial, but treatment may be required in cases of recurrent pregnancy loss.

It is recommended that uterine septums be treated in women who are infertile or have recurrent pregnancy loss (26). According to studies, pregnancy rate increases with septum incision; abortion and preterm birth rates decrease (27). The incision of the uterine septum is made under general anesthesia. It is important that the uterus is in the early proliferative phase so that the borders of the septum and how far it extends can be clearly determined. After

entering the cavity or cavities with the hysteroscope, tubal ostia are seen. From the lowest level of the septum, it would be cut with scissors at equal distances to the anterior and posterior walls and going forward to the fundus. The process is continued until the fundal vascular structures or the pink myometrium layer are seen.

In cases where the uterine septum reaches the external os of the cervix, if the septum in the cervix is opened, the risk of cervical insufficiency will increase in case of a subsequent pregnancy. For this reason, the septum section between the internal and external os of the cervix is preserved. For this, the internal os level is determined with the help of a balloon that is inflated through one of the two cervixes. The process of cutting the septum, which starts at the level of the internal os, is going through the fundus. As an alternative to scissors, monopolar cautery, bipolar cautery, or laser can also be preferred.

Further termination of the septum incision is primarily associated with the risk of perforation. In addition, a large amount of incision carries the risk of rupture during pregnancy and delivery. The use of electrosurgery also has the potential to create new adhesions. Although it is accepted that a period of 8 weeks may be sufficient for healing after the cavity is brought into the shape it should be, this period is still controversial in terms of conceiving (28). All women with congenital uterine anomalies and be treated should be screened for cervical insufficiency after the 18th week of gestation.

Residual septum requiring re-incision after treatment of the uterine septum has also been reported. Internal fundal recess should be evaluated for the necessity for re-incision. According to ASRM, it is sufficient for this indentation to be over 1 cm. According to ESHRE-ESGE re-incision can be done if the residual septum is more than 50% of myometrium thickness (29).

A T-shaped uterus is a congenital uterine malformation with a normal appearance from the outside but a T-shaped cavity according to the definition of ESHRE-ESGE. It can be seen as a congenital anomaly, or it can take a T shape later on due to intrauterine adhesions. This anomaly is characterized by stenosis of the uterine cavity, and the lateral myometrial layer may also be thick. The use of diethylstilbestrol in its etiology was defined many years ago.

2D and 3D TVUSG, HSG, sonohysterography, hysteroscopy, and MRI are used in the diagnosis of T-shaped uterine anomalies. Diagnostic laparoscopy may be useful in excluding other pathologies. MRI is also useful in adolescents and when there are complicated anomalies. HSG and hysteroscopy alone are insufficient since they cannot show the thickness of the uterine side walls. 3D TVUSG is the most valuable method in the demonstration, measurement, and diagnosis of this thickness. Thickness is best evaluated in the mid-luteal phase (21).

A woman with a T-shaped uterine anomaly may be asymptomatic. She may also become pregnant and have term delivery. However, in women with infertility, recurrent implantation failures and habitual abortions are evaluated by hysteroscopy in the early follicular phase. After entering the cavity with a hysteroscope, a normal uterine cavity appearance is obtained by cutting both lateral walls from the tubal ostia to the cervical isthmic region with monopolar or bipolar electrodes. It should be

noted that there may be a risk of cervical insufficiency if the incision extends into the cervical canal. The depth of the incision is planned at least 10 mm of myometrial wall thickness has remained.

The use of antibiotics, hormone therapy, and adhesion barriers in the postoperative period after hysteroscopic metroplasty is controversial (21). There may be paid attention to cervical insufficiency, synechiae, and if a uterine rupture occurred. Metroplasty is not an indication of a cesarean section, and vaginal delivery is not contraindicated in every woman who has had metroplasty. Endometrial polyps are pathologies that cause both infertility and excessive menstrual bleeding. Polyps vary in size, localization in the cavity, and whether their pedicles are thin or not. In terms of fertility, they may cause infertility by affecting embryo implantation and reducing uterine receptivity. It is clear that the removal of endometrial polyps in the cavity is associated with increased pregnancy rates (30,31). Localization may determine whether these polyps are the cause of infertility or not. For example, it is not clear whether very small polyps close to the tubal ostia cause infertility, but their removal is not recommended as they may cause postoperative stenosis and phimosis on or around the tubal os. Polyps are softer than fibroids. Some polyps may resemble pedunculated fibroids in appearance. Although the final decision will be made by pathological examination, it is essential for the infertile patient to be removed, even if there is a cavity-related myoma. In the presence of a polyp in the cavity, an observation is made in terms of the boundary line and vascularization by turning on the stem or base of the polyp. In the presence of significant vascularization, electrocoagulation is performed first. In terms of electrocoagulation preference, bipolar energy called the versa point can also be used. Thus, when the excision is made, precautions are taken in terms of bleeding, and the image is not distorted. Excision may be somewhat difficult in extremely mobile polyps. Dilated endometrial glands in the form of small white dots may also be exposed when the polyp is excised. After the stalks of the small polyps are cut from the place closest to the endometrium, the holder can be removed with forceps. If the polypoid mass is large, it can be taken out, but if it does not distort the image, it can remain inside to be removed at the end of the procedure. At the end of the resection, electrocoagulation can be performed at the base of the mass to prevent bleeding. One of the issues to be considered is to prevent the resectoscope from entering and exiting the uterine cavity too often. If the excised parts are more than one, they can be taken out of the cavity at the end of the procedure or intermittently. Thus, the risk of air embolism is not increased.

Leiomyomas are common benign smooth muscle tumors depending on their location in the uterus, the way they cause infertility and even their treatment may differ. Although not every fibroid is a cause of infertility. Pregnancy may be possible despite myoma. This is determined by the absence of submucosal or intracavitary component of the myoma, or the absence of pressure on the cavity despite being completely in the myometrium tissue.

It is clear that fibroids in the cavity and causing distortion in it, are associated with reduced pregnancy; but the effect

of intramural myomas that do not affect the cavity on pregnancy is controversial (32). Type 0 and Type I fibroids can be resected by hysteroscopy. An experienced surgeon and good surgical equipment are essential for resecting Type II fibroids with hysteroscopy. Myomectomies should be performed intermittently in order to prevent post-procedural adhesions in myomas located on the 2 opposite walls of the cavity. 2 months is considered sufficient for these procedures. Thus, hysteroscopic resection of submucous fibroids increases pregnancy and live birth rates (33).

Type 0 fibroids can usually be excised in one step. Dilated endometrial glands in the form of small white dots seen when the polyp is excised are not seen in the fibroid excision. A white, fibrous, non-bleeding tissue is exposed. If the resected parts cause deterioration in the field of view, they can be taken out with the resectoscope. But if they do not distort the image, they can remain inside to be removed at the end of the procedure. After making sure that the base and stem of the fibroid are completely removed, bleeding must be controlled. At the end of the resection, electrocoagulation can be performed with bipolar cautery at the base of the mass to prevent bleeding.

Hysteroscopic resection for Type I and II fibroids are the same in principle. The difficulty here is to remove the fibroid tissue from the uterus. The localization of the fibroid and how deep the myometrium extends also determine the difficulty of resection. Resection of myomas that narrow the internal os of the cervix too much, occupy a lot of space in the cavity, and are close to the tubal ostia will of course not be easy. Moreover, even if the cavity seems to have healed, not only the endometrial part of the fibroid but also the intramural part of the fibroid must be completely removed. And this procedure may be surgically difficult. As the size and depth of fibroids increase, this excision process becomes more difficult. The risk of intramural residue and uterine perforation increases. It is important to know how the endometrium, myometrium, endometrial polyps, and myoma tissues are seen during the procedure in order to be sure that the fibroid tissue is completely removed. In addition, myometrium is more fibrous and has the appearance of connective tissue. At the beginning of the excision of the fibroid, when the cleavage is entered between the myoma capsule and the myometrium, the blunt dissection will facilitate the separation of the myoma from the myometrium tissue. Here, the hydrodistension that occurs in the uterine cavity during the procedure will also contribute to this separation. Thanks to blunt dissection, the risks of perforation and bowel injury will be reduced. Performing operations accompanied by abdominal USG can also contribute. Residual myometrial thickness can be measured. In the presence of a deep-seated intramural fibroid, the procedure may be interrupted and the cavity may need to be evacuated. The procedure is facilitated when the endometrial cavity is re-entered with the resectoscope, as the residual myoma protrudes into the cavity with uterine contractions that occur after the cavity is emptied. With the same principle, the intrauterine pressure is changed rapidly and the intramural part of the fibroid is delivered into the cavity. Even drugs such as methylergonovine or oxytocin can be given to create uterine contraction (21). Different techniques have been

proposed for hysteroscopic surgeries of type II fibroids. These techniques are 2 intermittent surgical procedures, the enucleation technique (34), and Bettocchi's (office preparation of partially intramural myomas, OPPIuM) technique (35). The primary goal in all these techniques is easy removal of the fibroid. This convenience is achieved by extruding the fibroid into the cavity. A laparoscopic or abdominal approach may be required in Type II fibroids that cannot be removed by hysteroscopy, rarely.

The most important concern when resecting Type II fibroids with a hysteroscope is whether remaining myometrial tissue will create a risk of uterine perforation after myoma excision. For this, it is preferable to measure the distance between the pseudocapsule of the myoma and the uterine serosa by TVUSG in the preoperative period. This distance must be at least 4-5 mm. In addition, the appearance of bloodless and white tissue during the procedure is an important indicator for reaching the uterine serosa, and for taking precautions or terminating the procedure. Gonadotropin releasing hormone (GnRH) analogues can also be used prior to the excision of myomas. They make the operation easier by shrinking the fibroids. However, it is important to know that new fibroids may appear after the operation.

Bipolar cautery is preferred for hysteroscopic resection of myoma and saline is preferred for bipolar cautery. In healthy women, saline loss of up to 2500 cc can be tolerated. In case of further losses, the process should be terminated. A bipolar resectoscope is more suitable for Type II fibroids in difficult cases that are expected to take a long time. It is not appropriate to use saline solution in monopolar cautery planned cases. Nonionic forms are used for monopolar processes. If the nonionic distention medium is resorbed in large amounts, it may cause hypervolemia, hyponatremia, glycine toxicity, neurogenic coma, and even death. These risks increase in case of loss of 1000 ml for nonionic forms. Therefore, the process should be terminated in losses of 1000 ml or above.

It is controversial how the delivery method will be in pregnancy cases after the excision of myomas. However, cesarean section is preferred more in terms of rupture risk in Type I and Type II fibroids.

In intrauterine adhesions, menstrual abnormalities, infertility, and recurrent pregnancy loss are seen as a result of partial or complete obliteration of the cervical canal and uterine cavity. These adhesions are also described as Asherman's syndrome. Its frequency increases in cases of postpartum curettage, difficult removal of the placenta, or curettage due to the rest placenta. In the postpartum period, the endometrium is more vulnerable to damage. Delayed endometrial regeneration due to hypoestrogenism is accepted as the reason for this. In this case, as the endometrium is sensitive, the basal layer is more easily damaged and adhesion development becomes easier. In addition, more aggressive postpartum curettage contributes to this situation more. The developing granulation tissue also causes dense adhesions.

A history of any trauma to the endometrial cavity such as abortion, postpartum curettage, and placental adhesion anomalies is very valuable in diagnosis. Especially postpartum amenorrhea and hypomenorrhea should also be questioned. Hysteroscopy is the gold standard. 2D and 3D TVUSG, HSG, and SIS can be used. In these

examinations, endometrial irregularity, fibrosis, obliteration, differences in endometrial echogenicity, one or more linear echogenicities and abnormal shapes can be observed. Filling defects can be seen on HSG and SIS.

Besides being the gold standard in diagnosis, hysteroscopy is also very important in treatment. The aim of treatment is to restore the cavity, remove adhesions, regeneration of the impaired endometrium, integrity of the cavity, and continuity of the endometrium. Thus, menstrual irregularities and amenorrhea can be treated, as well as the implantation of the embryo to the endometrium and its progression to a healthy birth will be provided.

Hysteroscopy is performed under general anesthesia, preferably with a full bladder and abdominal USG guidance. After entering the cavity with the hysteroscope, avascular, simple, and thin adhesions are separated thanks to the pressure created in the cavity with saline. It is aimed to see bilateral tubal ostia and to observe the cavity integrity panoramically. The use of scissors is preferable to both monopolar and bipolar electrocoagulation. Because the use of electrosurgery has the potential to create new adhesions. In addition, endometrial damage is minimized with the use of scissors. Bipolar electrocoagulation is preferred if coagulation is required for bleeding that does not stop despite cutting with scissors.

One of the important complications is perforation. In the presence of advanced adhesion and obliterated cavity, hysteroscopy procedures should be performed by experienced surgeons. Preventing the recurrence of adhesions in the postoperative period is one of the important issues as well as complications. For this, some barriers are left in the cavity, and time is gained for the regeneration of the endometrium before new adhesions are formed. Even hormonal therapy containing estrogen is preferred by many surgeons to support this regeneration process. There is no standardization in hormonal therapy, duration, route of administration, and whether progesterone should be given together or not. Studies and evidence regarding the benefit and superiority of these postoperative treatments are not yet sufficient (21). Antibiotic treatment is also commonly preferred in the postoperative period.

Solid barriers such as foley catheters, intrauterine balloons, and intrauterine devices are preferred to reduce adhesion reformation. In addition, hyaluronic acid in gel form and combinations of carboxymethylcellulose and hyaluronic acid can also be used as semisolid barriers. Some surgeons also apply second look hysteroscopy within 2 months for control purposes. However, it should not be forgotten that approaches to prevent adhesions are also important rather than treating them. For example, in cases of abortion, hysteroscopic removal of residual pregnancy material instead of sharp curettage minimizes the damage to the endometrium (21).

Patients should be informed that pregnancy complications such as placenta accreta, increta, percreta, postpartum hysterectomy, and prematurity will increase in pregnancies after adhesiolysis. In addition, the follow-up and delivery of these pregnant women should be done in tertiary centers with experienced obstetricians (36).

Istmocele, also called diverticulum or niche, develops due to insufficient healing of the myometrium tissue on the

incision line of the uterus during a cesarean section. Isthmocele generates menstrual blood and mucus accumulate in the pouch. This blood and mucus can cause abscess formation, affecting sperm motility and causing infertility. In addition, cervical mucus also causes a chronic inflammatory environment.

The patient should be evaluated after menses for the diagnosis. It can be detected incidentally on TVUSG. TVUSG, SIS, HSG, and MRI help in diagnosis. Hysteroscopy is the gold standard in diagnosis.

Treatment should be done for symptomatic patients. For secondary infertility, hysteroscopy-guided isthmocele resection, vaginal repair, laparoscopic, laparotomic, or combined approaches may be appropriate. Hysteroscopy and laparoscopy are used together in combined approaches. In the hysteroscopic approach, fibrotic tissue in the endomyometrial area at the inferior and superior edges of the scar line is resected. The thinnest base of the defect is also coagulated with the roll ball electrode because this area contains ectatic vessels covered with thin mucous membranes. Thus, the niche formed here will be expanded a little and the accumulation of menstrual blood will be prevented.

The most important risk in the repair is uterine perforation and bladder injury during the procedure. This risk increases if the myometrial residual thickness is less than 3 mm. Therefore, in case of residual myometrial tissue thinner than 3 mm, the laparoscopic approach is preferred because of the risk of perforation of hysteroscopy. In the laparoscopic approach, fibrotic scar tissue and the isthmocele area are resected from the healthy myometrial tissue line. 2 layers are sutured with 2-0 vicryl. The peritoneum can also be sutured as the third layer. It has been shown that myometrial thickness increases with this technique (37).

In the combined hysteroscopy laparoscopy technique, the localization of the isthmocele is detected with a hysteroscope, and excision is made by laparoscopy from the line where the light transilluminates. With the vaginal approach, the scar tissue is cut and opened. The fibrotic scar is excised. The incision is sutured in 2 layers. In minilaparotomy, the scar defect is excised. The residual myometrium tissue is repaired by suturing again. In procedures where scar tissue is excised and sutured by making an incision, a hysteroscopy can be performed to check the adequacy of the repair.

In general, hysteroscopic resection can be performed on those who do not want pregnancy. Hysteroscopy is not recommended in patients with residual myometrial thickness <3 mm at the defect site, due to the risk of bladder injury and uterine rupture. Incision, excision, and multi-layered suture are preferred for those who want pregnancy. The chance of pregnancy with isthmocele repair in secondary infertile patients has been reported to be 40-80%. Surgical excision of the defect may increase fertility since endometriosis can also be seen in the excision material (37). Hysterectomy can also be performed in symptomatic women who do not intend to become pregnant.

OVARIAN CAUSES

Ovulatory causes are the most common factors related to female infertility (3). Ovarian causes are rare causes of

infertility that will require surgery. The most common cause of infertility due to anovulation is polycystic ovary syndrome (PCOS) (38). The ovulatory cause for which surgery may be most necessary is PCOS. Infertility treatment for women with PCOS includes lifestyle changes (diet, exercise, and changing habits), pharmacological treatments, surgical treatment (laparoscopic ovarian surgery), or IVF (39). Bariatric surgical treatment options are also on the agenda in the patient group where weight control cannot be achieved with diet and exercise.

The primary goal in patients with PCOS is monofollicular development. With the laparoscopic ovarian drilling (LOD) treatment method, monofollicular development can be achieved. Pregnancy can also be achieved without any additional treatment or follow-up. Concurrent LOD may also be appropriate in patients who have additional infertility factors and are currently scheduled for laparoscopy.

LOD may be advantageous in the group of patients who are difficult to follow up, who cannot be monitored for endocrine, who live far from the center, who have high luteinizing hormone (LH) values, and who are weak. Carbon dioxide, argon, or aluminum granite crystal laser, unipolar or bipolar electrocautery can be applied laparoscopically for the procedure. While a single ovary may be sufficient, both ovaries can be applied in the same session. There is no consensus on how many watts of energy will be used, how many holes will be drilled, and in how many seconds due to the risk of reducing the ovarian reserve for the procedure that can be applied to both ovaries in the same session. However, clinicians' preferences in this regard are accepted by using the watt X seconds X number formulation, not exceeding 600 watts. Accordingly, 4 or 5 holes, each of 30 watts, and drilling lasting 4 seconds are made.

CONCLUSION

Patient selection is important for laparoscopy and hysteroscopy procedures. Patients should be informed about the complications which can occur during the procedures and also during the pregnancy or giving birth if pregnancy happens. These operations must be done in tertiary centers by expert surgeons, preferably IVF specialists.

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REFERENCES

- American College of Obstetricians and Gynecologists Committee on Gynecologic Practice. Infertility workup for the women's health specialist: ACOG committee opinion, number 781. *Obstet Gynecol.* 2019;133(6):e377-84.
- American College of Obstetricians and Gynecologists Committee on Gynecologic Practice and Practice Committee. Female age-related fertility decline. Committee Opinion No. 589. *Fertil Steril.* 2014;101(3):633-4.
- Luciano AA, Peluso J, Koch EI, Maier D, Kuslis S, Davison E. Temporal relationship and reliability of the clinical, hormonal, and ultrasonographic indices of ovulation in infertile women. *Obstet Gynecol.* 1990;75(3 Pt 1):412-6.
- American College of Obstetricians and Gynecologists. ACOG technology assessment in obstetrics and gynecology, number 4, August 2005: hysteroscopy. *Obstet Gynecol.* 2005;106(2):439-42.
- Karande VC, Gleicher N. Resection of uterine septum using gynaecoradiological techniques. *Hum Reprod.* 1999;14(5):1226-9.
- Gardner DK, Weissman A, Howles CM, Shoham Z. Textbook of assisted reproductive techniques, 5th ed. volume 2: clinical perspectives. Boca Raton, FL: CRC Press; 2018.
- Honoré GM, Holden AE, Schenken RS. Pathophysiology and management of proximal tubal blockage. *Fertil Steril.* 1999;71(5):785-95.
- Yildizhan B, Durmusoglu F, Uygur M, Erenus M. A new technique for the diagnosis of fallopian tube patency by using hysteroscopy with ultrasound compared with hysterosalpingography in infertile women. *Arch Gynecol Obstet.* 2009;280(4):543-7.
- Practice Committee of the American Society for Reproductive Medicine. Committee opinion: role of tubal surgery in the era of assisted reproductive technology. *Fertil Steril.* 2012;97(3):539-45.
- Borrero SB, Reeves MF, Schwarz EB, Bost JE, Creinin MD, Ibrahim SA. Race, insurance status, and desire for tubal sterilization reversal. *Fertil Steril.* 2008;90(2):272-7.
- Trussell J, Guilbert E, Hedley A. Sterilization failure, sterilization reversal, and pregnancy after sterilization reversal in Quebec. *Obstet Gynecol.* 2003;101(4):677-84.
- Yoon TK, Sung HR, Cha SH, Lee CN, Cha KY. Fertility outcome after laparoscopic microsurgical tubal anastomosis. *Fertil Steril.* 1997;67(1):18-22.
- Rock JA, Guzick DS, Katz E, Zacur HA, King TM. Tubal anastomosis: pregnancy success following reversal of Falope ring or monopolar cautery sterilization. *Fertil Steril.* 1987;48(1):13-7.
- Boeckstaens A, Devroey P, Collins J, Tournaye H. Getting pregnant after tubal sterilization: surgical reversal or IVF? *Hum Reprod.* 2007;22(10):2660-4.
- Cha SH, Lee MH, Kim JH, Lee CN, Yoon TK, Cha KY. Fertility outcome after tubal anastomosis by laparoscopy and laparotomy. *J Am Assoc Gynecol Laparosc.* 2001;8(3):348-52.
- Hawkins J, Dube D, Kaplow M, Tulandi T. Cost analysis of tubal anastomosis by laparoscopy and by laparotomy. *J Am Assoc Gynecol Laparosc.* 2002;9(2):120-4.
- Harb H, Al-Rshoud F, Karunakaran B, Gallos ID, Coomarasamy A. Hydrosalpinx and pregnancy loss: a systematic review and meta-analysis. *Reprod Biomed Online.* 2019;38(3):427-41.
- Gomel V, Wang I. Laparoscopic surgery for infertility therapy. *Curr Opin Obstet Gynecol.* 1994;6(2):141-8.
- Kontoravdis A, Makrakis E, Pantos K, Botsis D, Deligeoroglou E, Creatas G. Proximal tubal occlusion and salpingectomy result in similar improvement in in vitro fertilization outcome in patients with hydrosalpinx. *Fertil Steril.* 2006;86(6):1642-9.
- Van Voorhis BJ, Mejia RB, Schlaff WD, Hurst BS. Is removal of hydrosalpinges prior to in vitro fertilization the standard of care? *Fertil Steril.* 2019;111(4):652-6.
- Şahin Y. İnfertilitede Başarıyı Artıran Endoskopik Girişimler. In: Fıçıcıoğlu C, editor. Üreme Endokrinolojisi, İnfertilite ve Yardımcı Üreme Teknikleri. İstanbul: Nobel; 2019. p.101-16. Turkish.
- Guan J, Watrelot A. Fallopian tube subtle pathology. *Best Pract Res Clin Obstet Gynaecol.* 2019;59:25-40.
- Homer HA, Li TC, Cooke ID. The septate uterus: a review of management and reproductive outcome. *Fertil Steril.* 2000;73(1):1-14.
- Valle RF, Ekpo GE. Hysteroscopic metroplasty for the septate uterus: review and meta-analysis. *J Minim Invasive Gynecol.* 2013;20(1):22-42. Erratum in: *J Minim Invasive Gynecol.* 2013;20(6):917-8.
- Ludwin A, Ludwin I. Comparison of the ESHRE-ESGE and ASRM classifications of Müllerian duct anomalies in everyday practice. *Hum Reprod.* 2015;30(3):569-80.
- Rikken JF, Kowalik CR, Emanuel MH, Mol BW, Van der Veen F, van Wely M, et al. Septum resection for women of reproductive age with a septate uterus. *Cochrane Database Syst Rev.* 2017;1(1):CD008576.
- Practice Committee of the American Society for Reproductive Medicine. Uterine septum: a guideline. *Fertil Steril.* 2016;106(3):530-40.
- Yang JH, Chen MJ, Chen CD, Chen SU, Ho HN, Yang YS. Optimal waiting period for subsequent fertility treatment after various hysteroscopic surgeries. *Fertil Steril.* 2013;99(7):2092-6.e3.
- Ludwin A, Ludwin I, Pityński K, Banas T, Jach R. Role of morphologic characteristics of the uterine septum in the prediction and prevention of abnormal healing outcomes after hysteroscopic metroplasty. *Hum Reprod.* 2014;29(7):1420-31.
- Stamatellos I, Apostolides A, Stamatopoulos P, Bontis J. Pregnancy rates after hysteroscopic polypectomy depending on the size or number of the polyps. *Arch Gynecol Obstet.* 2008;277(5):395-9.
- Shokeir TA, Shalan HM, El-Shafei MM. Significance of endometrial polyps detected hysteroscopically in eumenorrhic infertile women. *J Obstet Gynaecol Res.* 2004;30(2):84-9.
- Donnez J, Jadoul P. What are the implications of myomas on fertility? A need for a debate? *Hum Reprod.* 2002;17(6):1424-30.
- Pritts EA, Parker WH, Olive DL. Fibroids and infertility: an updated systematic review of the evidence. *Fertil Steril.* 2009;91(4):1215-23.
- Litta P, Vasile C, Merlin F, Pozzan C, Sacco G, Gravila P, et al. A new technique of hysteroscopic

- myomectomy with enucleation in toto. *J Am Assoc Gynecol Laparosc.* 2003;10(2):263-70.
35. Bettocchi S, Di Spiezio Sardo A, Ceci O, Nappi L, Guida M, Greco E, et al. A new hysteroscopic technique for the preparation of partially intramural myomas in office setting (OPPIUM technique): A pilot study. *J Minim Invasive Gynecol.* 2009;16(6):748-54.
36. Deans R, Vancaillie T, Ledger W, Liu J, Abbott JA. Live birth rate and obstetric complications following the hysteroscopic management of intrauterine adhesions including Asherman syndrome. *Hum Reprod.* 2018;33(10):1847-53.
37. Donnez O, Donnez J, Orellana R, Dolmans MM. Gynecological and obstetrical outcomes after laparoscopic repair of a cesarean scar defect in a series of 38 women. *Fertil Steril.* 2017;107(1):289-96.e2.
38. Homburg R. Management of infertility and prevention of ovarian hyperstimulation in women with polycystic ovary syndrome. *Best Pract Res Clin Obstet Gynaecol.* 2004;18(5):773-88.
39. Costello MF, Misso ML, Wong J, Hart R, Rombauts L, Melder A, et al. The treatment of infertility in polycystic ovary syndrome: a brief update. *Aust N Z J Obstet Gynaecol.* 2012;52(4):400-3.