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Operative Hysteroscopy for Uterine Septum

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INTRODUCTION

This chapter presents a comprehensive review of the reproductive problems that could be associated with uterine septum. We believe that this topic has significant amount of controversy regarding its diagnosis and treatment due to the paucity of comprehensive evidence-based data on female congenital anomalies, in particular uterine septum. This resulted in the lack of a consensus on how the presence of a uterine septum might affect female reproduction. We will discuss the available data aiming at providing a balanced appraisal that can help the reproductive medicine specialists to better counsel patients about their reproductive potentials when a uterine septum is discovered.

Development

During the embryo development, the uterus forms from fusion of the paramesonephric ducts (Müllerian ducts), which join in the midline around the ''tenth'' week of gestation to form the unified body of the uterus. In the absence of Müllerian-inhibiting substance, the Müllerian ducts develop into the uterus and fallopian tubes (and possibly the upper part of the vagina) (1–4). It is interesting to note that the Müllerian ducts can develop into two distinct types of tissue: the smooth muscle tissue of the uterus and the fibrous tissue of the cervix (3). We believe this explains the various structural subtypes of uterine septum when it comes to different proportion of fibrous and muscle structure, that is, some uterine septa may contain more fibrous (cervical differentiation) component, while others contain more muscular (uterine differentiation) component. Such structural disparity might have implications on the mechanism of reproductive failure associated with uterine septum, as we will explain later.

A uterine septum results when there is incomplete resorption of the adjacent walls of the two Müllerian ducts. The resulting fibromuscular structure can range from a slight midline septum in the fundus of the uterus to complete midline division of the endometrial cavity. Even segmental septa can exist, resulting in partial communications of a partitioned uterus (4). Apoptosis has recently been proposed as the mechanism by which the fused portions of the two Müllerian tubes normally regress. Bcl-2, a protein involved with regulating apoptosis, was found to be absent from the septa of four uteri using a monoclonal antibody for Bcl-2 and immunohistochemical analysis. The absence of Bcl-2 may result in failure of resorption of the septum (5).

Reports of cases of complete vaginal septum associated with different degrees of uterine septum ranging from complete uterine septum with cervical duplication (6) to incomplete septum (subseptate uterus) (7, 8) challenged the classic theory of unidirectional (caudal to cranial) Müllerian development. We recently operated on a patient who had a complete longitudinal vaginal septum, but completely normal uterine cavity with no septum or bicornuate uterus (unpublished data). Therefore, an alternative ''bi-directional'' theory was proposed, which suggested that fusion and resorption begin at the isthmus of the uterus and proceed simultaneously in both the cranial and caudal directions (9).

Epidemiology

Although uterine anomalies have been reported in 0.1–2 percent of all women, in 4 percent with infertility and in up to 15 percent of those with recurrent miscarriage, their true incidence is not known (9a, 9b). Pedro Acien suggested that the variability in the reported incidence of uterine anomalies is due to the fact that it depends on five variables: 1) the population studied; 2) the study design and physician interest and awareness to find or reject an uterine anomaly; 3) the diagnostic method used; 4) the classes included as congenital uterine anomalies in the different studies, for example, hypoplastic uterus, T-shaped anomalies, and arcuate uterus frequently not included; and 5) the criteria and diagnostic tools used to classify the different types of uterine malformation (9b).

In 1998, a meta-analysis study that included a Medline search and standard reference tracing has located forty-seven studies from fourteen countries regarding the prevalence and distribution of uterine anomalies. In a pooled sample of more than 50,000 women from all included studies, the author calculated a prevalence of uterine anomalies in the general population of about 1 in 200 women (0.5 percent). The distribution of those anomalies was 39 percent bicornuate, 34 percent septate, 11 percent didelphic, 7 percent arcuate, 5 percent unicornuate, and 4 percent the remaining types including hypoplastic/aplastic/solid and other forms (10).

Comparable prevalence rate has been reported in a prospective study (11). In a cohort of girls and women who were evaluated for reasons unrelated to the presence of uterine anomalies, Byrne et al. (11) used standard ultrasound examinations to establish the prevalence of Müllerian duct abnormalities. The authors did prospective ultrasound examinations for nonobstetric indications in 2,065 consecutive girls and

women (aged eight to ninety-three years). They found Müllerian anomalies in eight girls and women, that is, about 1 in 250 women (0.4 percent) with 95 percent confidence interval 1.67–7.62. The anomalies included bicornuate uterus, septate uterus, and double uterus.

Other investigators reported higher prevalence (12–16). Grimbizis et al. reported that in a review of five relatively recent studies (9b, 12–18) (between 1988 and 1997) and about 3,000 cases, the mean overall incidence of uterine malformation in the general population and/or the population of fertile women was 4.3 percent (18). In a report on more than 3,000 women that included family planning and contraception clients or patients undergoing infertility evaluation, Raga et al. (11) have found the frequency of uterine malformations in fertile patients (family planning and contraception clients) to be 3.8 percent, while the prevalence in infertile patients (with history of recurrent miscarriage or preterm delivery) was almost twice as high (6.3 percent), a difference that was statistically significant. The authors included various modalities for the diagnosis of Müllerian anomalies including HSG and/or surgery (laparoscopy/laparotomy). Both uterine septum (33.6 percent) and arcuate uterus (32.8 percent) were the most common malformations observed.

In a selected group of women undergoing hysteroscopy for abnormal uterine bleeding, Maneschi et al. (13) assessed the prevalence of uterine anomalies and compared the reproductive outcome in women with Müllerian anomalies to those in women with a normal uterine cavity. The authors found Müllerian anomalies in about 10 percent of women. Their findings were similar to those reported in studies dealing with the frequency of diagnosis of uterine anomalies in women undergoing tubal sterilization investigated by HSG, when septate and bicornuate and arcuate uteri were found in 1.9 and 3.6 percent and 11.5 percent, respectively, of women with no history of reproductive problems (14, 15).

Higher prevalence was also reported by other investigators who found that the overall prevalence of Müllerian defects was 5 percent among women with normal reproductive histories, 3 percent among infertile women, 5–10 percent among women with first-trimester recurrent miscarriages (excluding women with hypoplastic and arcuate uterus), and greater than 25 percent among women with late first-trimester/early second-trimester miscarriages and preterm labor (9b). Despite the discrepancy in the reported figures on the prevalence of Müllerian anomalies, almost all studies agreed upon the very high proportion of uterine septum anomaly among the other Müllerian anomalies. Uterine septum (complete or partial) has been the most common (34–48 percent) type of structural uterine anomaly (12, 17, 18). The significance of the uterine septum comes from the fact that it is the form of Müllerian anomaly that is believed to be associated with the poorest reproductive outcome including low fetal survival rates of 6–28 percent and high rates of spontaneous miscarriages (19).

Types

The classification of uterine anomalies divides the uterine septum into complete (septate) or partial (subseptate) groups, according to whether the septum approaches the internal os or not, respectively (20). The complete septum that divides both the uterine cavity and the endocervical canal may be associated with a longitudinal vaginal septum (1). However, the presence or absence of a longitudinal vaginal septum is not considered in the classification (20). Different classification systems were proposed for Müllerian anomalies with the early classification systems criticized for their confusion, incompleteness, or irrelevant details. In 1979, Buttram and Gibbons (20) introduced a classification system of Müllerian anomalies shown in Table 13.1. The American Fertility Society (currently known as the American Society for Reproductive Medicine or the ASRM) revised the Buttram and Gibbons's classification system of Müllerian anomalies (21) with the aim to make it an easy-to-use reporting system that would allow clinicians to classify patients better, so that data could be accumulated more readily concerning the incidence of fetal wastage and obstetric complications for these malformations (Box 13.1 and Figure 13.1).

Table 13.1: Buttram and Gibbons Classification of Mullerian Anomalies (20)

Uterine morphology	*Fundal contour*	*External contour*
Normal	Straight or convex	Uniformly convex or with indentation <10 mm
Arcuate	Concave fundal indentation with central point of indentation at obtuse angle	Uniformly convex or with indentation <10 mm
Subseptate	Presence of septum that does not extend to cervix, with central point of septum at an acute angle	Uniformly convex or with indentation <10 mm
Bicornuate	Two well-formed uterine cornua, with a convex fundal contour in each	Fundal indentation >10 mm dividing the two cornua

As shown in Drawing 13.1 and Figures 13.2–13.5, the uterine septum has three parts: *base* (where it attaches to the fundus), *body* of the septum that extends down from the fundus all the way toward the cervix (complete septum) as shown in Figure 13.5 or stops somewhere between the fundus and the cervix (subseptate or short septum) as shown in Figures 13.2 and 13.3, and *apex* of the septum (the cervical end of the septum).

In addition to the regular classification into long (complete) or short (incomplete) subtypes, as shown in Drawings 13.2 and 13.3, in our experience, we observed two different subtypes of the short uterine septum based on the width of the uterine septum and the symmetry between the two uterine cavities on either side of the septum: broad-based (sometimes has a broad apex too) and asymmetrical (unequal sided) septa as shown in Figure 13.5B (usually has a broad base too), in Drawings 13.4 and 13.5, respectively. We noticed those subtypes to be frequently encountered in infertile patients and in patients with poor reproductive outcomes including assisted reproductive technology (ART) failure, pregnancy loss (unpublished data). Another investigator using Three-dimensional (3D) ultrasonography (US) and saline sonogram with 3D US has

Box 13.1: American Fertility Society Classification of Congenital Uterine Anomalies (21)

1. Agenesis: vagina, cervix, uterine fundus, fallopian tube, or any combination thereof
2. Unicornuate uterus
   - – Connected
   - – Not connected
   - – Without a cavity
   - – Without a horn
3. Uterus didelphys (double uterus and cervix)
4. Bicornuate uterus (complete, partial, or arcuate)
5. Septate uterus
   - – Complete
   - – Partial
6. Arcuate
7. DES drug related, e.g., T-shaped uterus resulting from diethylstilbestrol exposure

observed similar subtypes of the short uterine septum, which he named ''wide-shallow septum'' and ''irregular septum.'' This author also reported a special type, which he called ''T-shaped-shallow septum.'' The latter type was also observed by our group using 3D US (unpublished data).

We believe that the diagnosis of those two subtypes of short septum (broad based and asymmetrical) may be missed or at least confused with the diagnosis of arcuate uterus. This is particularly true when only HSG is relied upon without further evaluation by ultrasonography, especially 3D US and hysteroscopy. This confusion could explain the controversy in the literature regarding the association of reproductive problems (pregnancy loss and preterm labor) and arcuate uterus, as will be discussed later.

Structure

The high rate of spontaneous abortion in patients with uterine septa has been related to a specific histological feature of the septum, in which there is less vascularity and inadequate endometrial development that results in abnormal placentation (22). It has also been claimed that during hysteroscopic excision of the septum when bleeding appears, the natural wall of the uterus (because of its increasing vascularity) has been reached and further excision is not needed (22, 23).

Classically, the uterine septum structure has been described as a ''fibroelastic'' tissue that has three main features: first, very little amount of muscle tissue (22, 23); second, mainly formed of fibroelastic tissue (24); and third, very scanty vasculature (avascular) (25, 26).

Interestingly, contrary to the classic description of the uterine septum Dabirashrafi et al. (27) reported opposite findings of significantly less connective tissue in the septum and higher amount of muscle tissue and vasculature when compared to posterior uterine muscle away from the septum. In a group of sixteen patients with uterine septum undergoing Tompkins technique abdominal metroplasty, the authors compared three biopsies obtained from the septum to a fourth biopsy obtained from the posterior uterine wall away from the septum. The three septum biopsies were obtained from the septum as follows: first biopsy obtained from the septum near the serosal layer (base, as shown in Drawing 13.1), second biopsy from the midpoint of the septum (body, as shown in Drawing 13.1), and third biopsy from the tip (apex, as shown in Drawing 13.1) of the septum. The authors examined thirteen characteristics in those specimens by calculating the mean ridit analysis and Bonferroni criteria for multiple comparisons in relation to three outcomes: first amount of connective tissues (four characteristics), second amount of muscles (four characteristics), and third amount of blood vessels (five characteristics) (27). The authors concluded that their findings challenged the classic theory about the cause of fetal wastage associated with uterine septum (avascularity of the septum). They proposed two other mechanisms for the increased pregnancy loss: first the poor decidualization and placentation due to reduced connective tissue and the second, the higher noncoordinated contractility in the uterine septum due to the higher amounts of interlacing muscle tissue (27). Kupesic and Kurjak using color and pulsed Doppler sonographic studies of the septal areas reported vascularity in 71 percent of patients. Therefore, this study suggests that uterine septum can be made of muscular tissue in some patients and primarily of fibroelastic tissue in others (28).

DIAGNOSIS

It is very important to distinguish between the bicornuate uterus and the septate uterus. This is crucially important because the bicornuate uterus is infrequently associated with reproductive problems, whereas the septate uterus is frequently associated with reproductive problems such as pregnancy failure that usually require further intervention (28). It is also important to differentiate between arcuate uterus and short incomplete septum and between complete septum with cervical duplication and longitudinal vaginal septum and uterus didelphys.

Imaging

Although surgery (hysteroscopy, alone or with laparoscopy) constitutes the gold standard for the diagnosis of uterine septum, various imaging tools including hysterosalpingography (HSG), ultrasonography, and magnetic resonance imaging (MRI) have great value in the diagnosis with high level of accuracy.

Hysterosalpingography

HSG provides *valuable* information about tubal patency in addition to *some* information about the uterine cavity. However, its usefulness is limited in identifying uterine anomalies including the uterine septum because it does not provide definitive information about the external contour of the uterus. Other imaging modalities including ultrasonography and MRI have been shown to be useful complementary tools in characterizing and delineating more clearly the exact nature of the Müllerian anomalies (30). This is particularly true for the distinction between the uterine septum and bicornuate uterus that cannot be

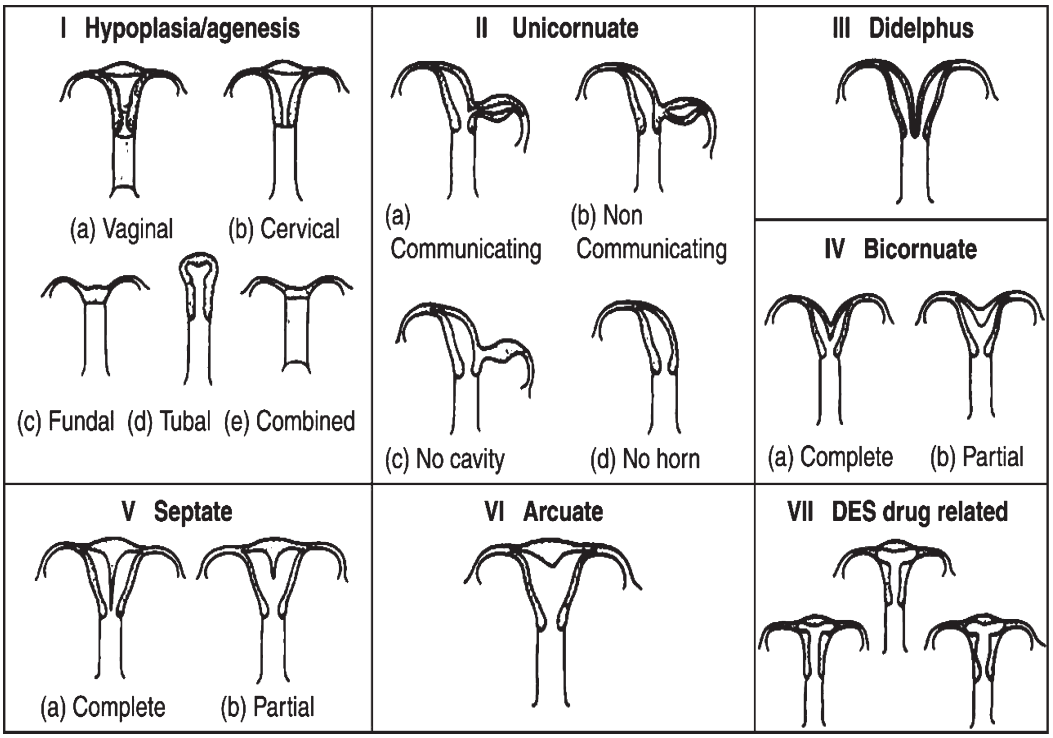


Figure 13.1. American Fertility Society (recently American Society for Reproductive Medicine) classification of congenital uterine anomalies (21).

made definitely by examination of a hysterogram (during HSG) because the image of the cavities may be exactly the same (28).

Ultrasonography

Ultrasonography has the advantages of minimal invasiveness, relatively low cost, and ease of performance. Although transabdominal two-dimensional (2D) US was the first ultrasound technique used for identifying uterine cavity disorders, transvaginal ultrasonography has become the modality of choice replacing the transabdominal approach. This is because of its ability to be closer to the uterus that allows better anatomical delineation, in addition to its higher resolution associated with high frequency of the ultrasound beam that provides images with better contrast and resolution (29).

Despite the advantages of the transvaginal 2D US, it has a fairly low sensitivity as a screening test of uterine anomalies (~70 percent) (31). In addition, sometimes the distinction between different types of anomalies is often impossible. Another problem is that a transverse or oblique transverse view of the uterus is not optimal in diagnosing uterine abnormalities, particularly when the uterine body has a retroverted position. Furthermore, ultrasound is operator dependent, and hard-copy images can be difficult for a third party to interpret (29).

SONOHYSTEROGRAPHY

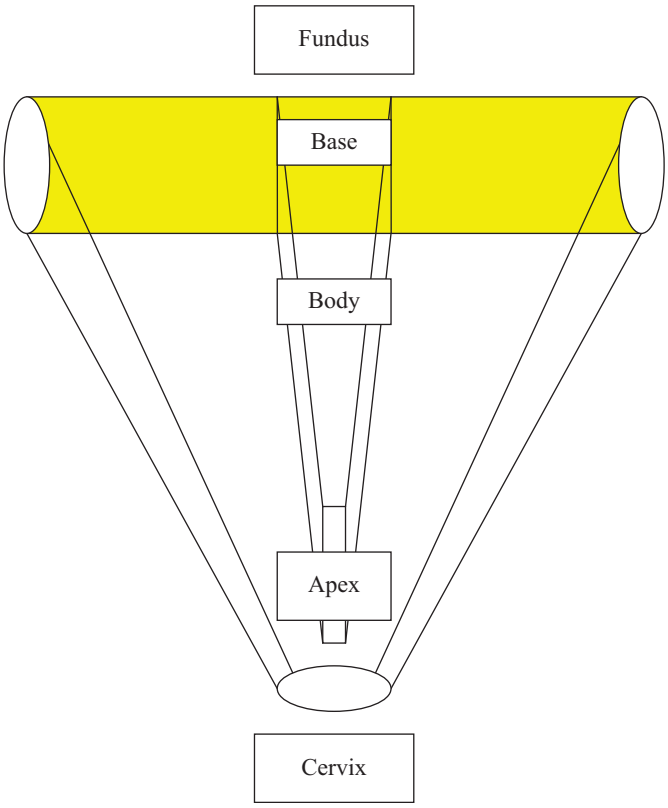
Optimal imaging of the endometrium and myometrium may require distension of the uterine cavity with saline to separate the walls of the uterus to make it clear to outline the endometrial contour and to detect endoluminal lesions, that is, lesions protruding into the uterine cavity or uterine septum. This procedure is frequently called sonohysterography (SHG) or saline infusion sonohysterography.

Preparing the patient for the SHG is more or less similar to HSG, that is, ensuring that the patient is not pregnant or there is any evidence of active pelvic infection or other less likely contraindications to the procedure such as allergy to the ultrasound contrast medium. In addition, conventional transvaginal ultrasound examination should be done before the SHG to assess the appearance of the uterus before fluid instillation into the uterine cavity and to determine the orientation of the uterus to facilitate insertion of a catheter into the cervical canal for instillation of the saline or the ultrasound contrast medium (29). Performing the procedure during the follicular phase has the advantages of avoiding the risk of disturbing an early pregnancy. It is preferable to use a balloon-bearing catheter to occlude the internal os to allow adequate distension of the uterine cavity (29). However, this has the disadvantages of being more uncomfortable to the patient and its shadow might obscure lesions present in the lower uterine segment or the cervical canal.

SHG is thought to have 100 percent sensitivity and specificity when compared with the gold standard, that is, surgery (32). Another study (33) found SHG having the same diagnostic accuracy as the gold standard for polypoid lesions and endometrial hyperplasia. The overall belief by the experts in the area of ultrasonography of uterine cavity disorders is that SHG or HSG are highly sensitive in the diagnosing of major uterine malformations; however, it is not sufficiently sensitive in the diagnosis of minor uterine abnormalities (29). A recent report suggests the use of a very small volume of viscous gel with impressive results (29a).

THREE-DIMENSIONAL ULTRASONOGRAPHY

Transvaginal 3D US is a noninvasive imaging technique with the ability to generate accurate images of the endometrial



Drawing 13.1. Shows the different parts of the uterine septum in relation to the uterine walls: base of the septum where it meets the fundus, body of the septum that extends down dividing the uterine cavity into two sides, and apex of the septum that is the lower most part of the septum.

cavity and of the external contour of the uterus (34, 35). A major advantage of the 3D US is the ability to obtain the coronal views of the uterus, which is usually not obtainable by the 2D US because of anatomical limitations (the vaginal probe has limited mobility within the confines of the vagina).

Figure 13.2. Hysterosalpingogram shows incomplete uterine septum. This type of uterine septum is much commoner than the complete one (septum that extends all the way down to the cervix).

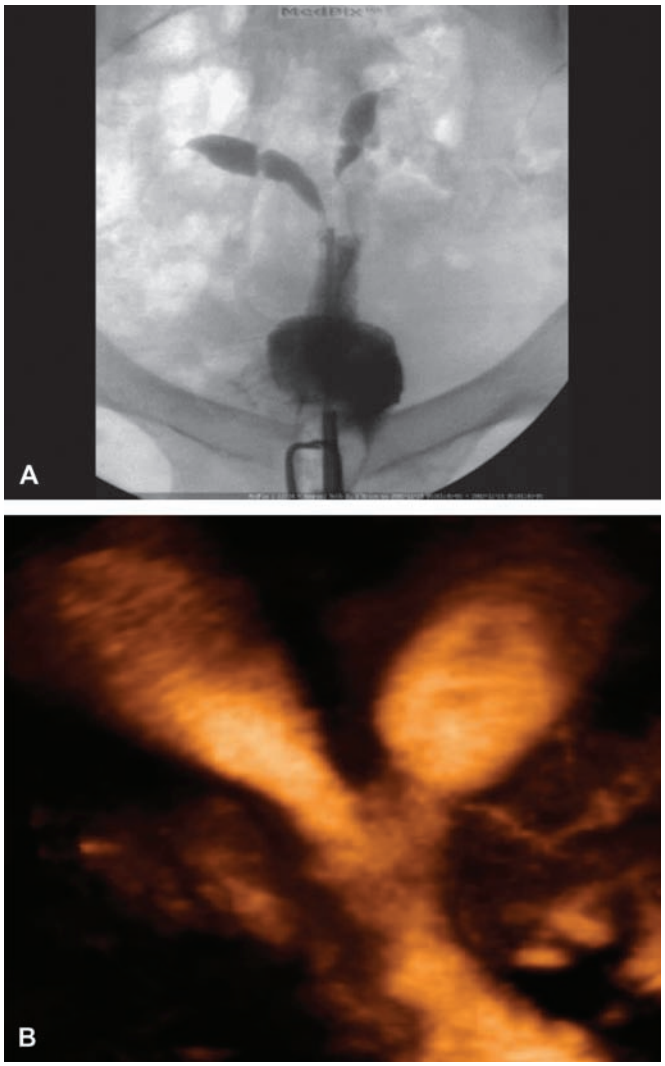


Figure 13.3. The figure shows two hysterosalpingograms of complete uterine septum (A) and bicornuate uterus (B). Notice the wider angle between the two sides of the uterine cavity in the hysterosalpingogram picture of the uterine septum. Such an angle is much smaller in case of the bicornuate uterus.

These coronal views show the relationship between the endometrium and the myometrium at the uterine fundus, delineate the entire cervical canal, and depict the corneal angles. This enables the operator to measure the depth of uterine septum and the distance between the apex of the septum and the internal os. In addition, the use of 3D US enables us to diagnose new types of uterine septum, for example, unequal sides (35a, 35b). Furthermore, 3D US can differentiate between arcuate uterus and a short incomplete septum. Another major advantage is that with 3D US, a volume of ultrasonographic data is rapidly stored and made available for later analysis. This is particularly helpful in case of SHG. The ability to store data would shorten the amount of time during which the uterine cavity must remain distended (36). Obviously, it is a major advantage of 3D US because all of the original ultrasonographic data are contained in the saved volume without loss of information, as might occur when only selected static images are available for interpretation, which is the case with 2D US (37). Even if the

Figure 13.4. Sonohysterogram showing uterine septum. A transverse section through transvaginal ultrasonography shows both sides of the uterine cavity distended with fluid injected through the procedure of sonohysterography. The two sides of the cavity are separated with the septum.

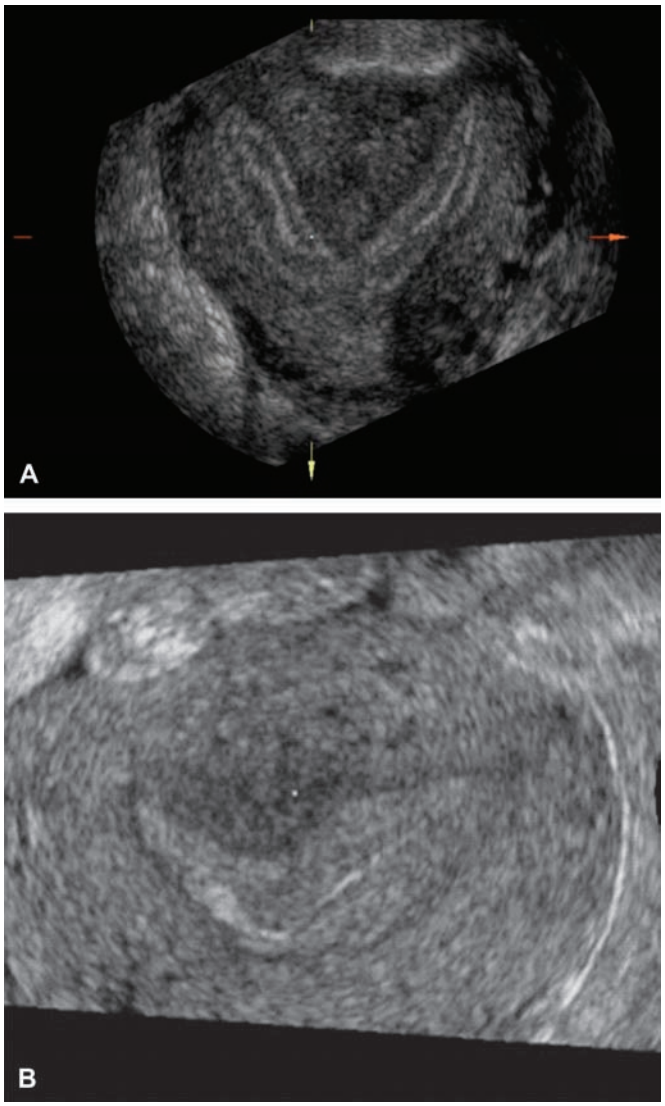


Figure 13.5. Three-dimensional transvaginal ultrasonography showing incomplete uterine septum (A), and the subtype of the incomplete uterine septum that we call as asymmetrical, incomplete uterine septum (B). Notice the advantages of this ultrasound technique in visualizing the dimensions of the septum, relationship to different parts of the uterine cavity, as well as the external contour of the uterus.

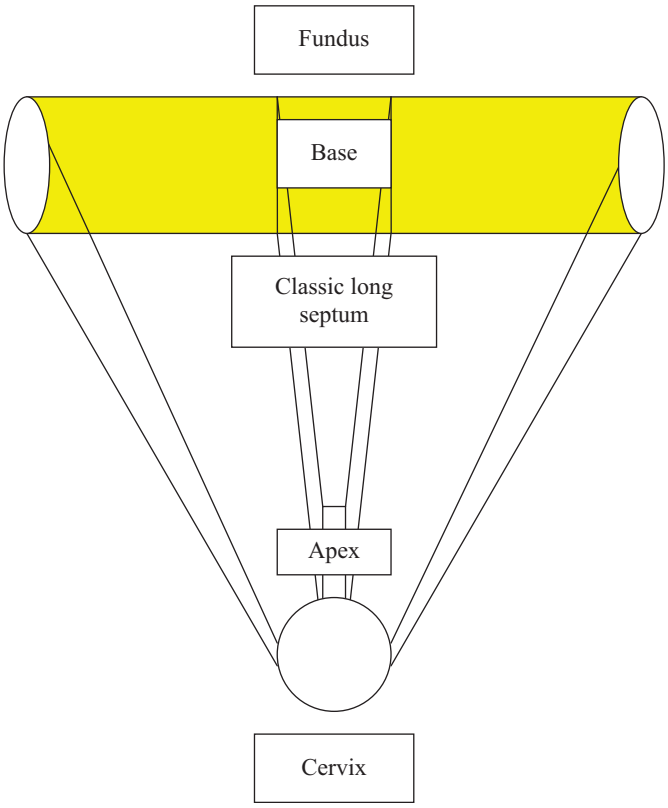
ultrasonographic procedure is videotaped, findings remain operator dependent, and any observation not clearly documented on the tape would be lost. The multiplanar capability of 3D US permits an unlimited number of scan planes to be obtained from the original data set, an advantage that would significantly reduce the operator-dependant bias. This data set is available for interactive review at any time after the patient has been discharged or before surgical intervention. Additional findings not initially detected during the real-time examination can be made by "scrolling" through the volume data. Clearly, this can be accomplished without inconveniencing the patient by prolonged or repeated vaginal scanning (37). Clearly, combining SHG with 3D US can add to the accuracy of both procedures (38).

A disadvantage of 3D US is the time required to learn to manipulate the 3D volume data, although this decreases with experience. Also, shadowing caused by the uterine fibroids, irregular endometrial lining, or thickened endometrial lining (as seen during the periovulatory period), as well as the decreased volume of the uterine cavity (in cases of intrauterine adhesions), are obvious limitations of 3D US (29).

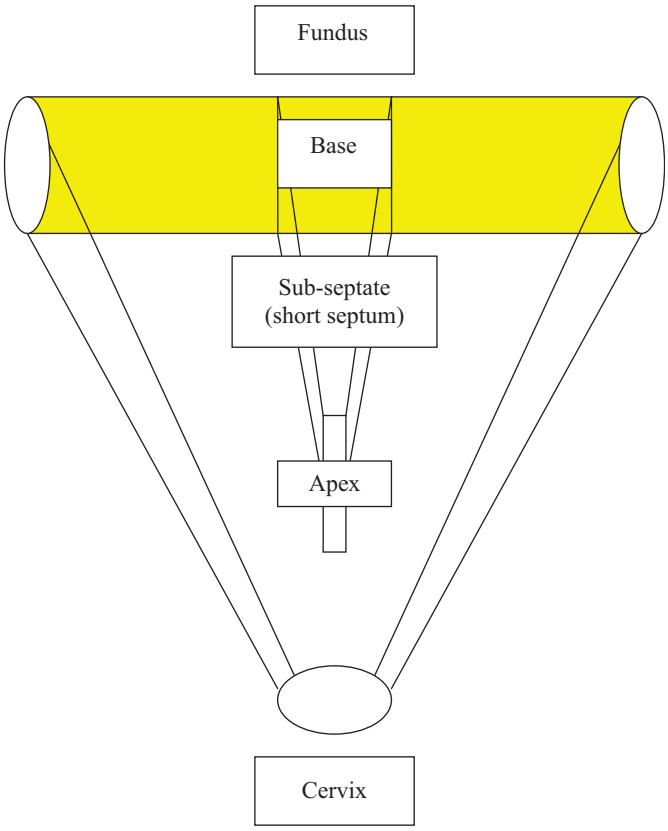
Three-dimensional US was reported to have a sensitivity and specificity of 100 percent in diagnosing arcuate uteri compared with 67 and 94 percent, respectively, for transvaginal 2D US. Interestingly, in diagnosing major Müllerian anomalies, while the sensitivity and specificity of transvaginal 3D US were both 100 percent compared with 100 percent sensitivity and 95 percent specificity for transvaginal 2D US, the positive predictive value was 100 percent for the 3D US but only 50 percent for 2D US (34). Because of the higher accuracy of the 3D US in diagnosing Müllerian disorders, higher prevalence (~6 percent) was reported when 3D US was applied for detecting those disorders (35).

DOPPLER ULTRASONOGRAPHY

Evaluating the septum vascularity by Doppler ultrasonography is believed to provide important information about its structure and the risk of reproductive problems. Kupesic and Kurjak (35c) attempted to evaluate the combined use of transvaginal 2D US, transvaginal color and pulsed Doppler ultrasonography, HSG, and transvaginal 3D US in the preoperative diagnosis of uterine septum in a group of 420 infertile patients undergoing operative hysteroscopy. Two hundred and seventy-eight patients had an intrauterine septum (66.2 percent of all patients) that was corrected surgically. In forty-three patients with a uterine septum, there was a history of repeated spontaneous miscarriage, and seventy-one had had one spontaneous miscarriage (fifty-six in the first trimester and fifteen in the second trimester). Each patient underwent transvaginal ultrasound and transvaginal color Doppler examination during the luteal phase of their cycle. Color and pulsed Doppler were superimposed to visualize intraseptal and myometrial vascularity in each patient. It is interesting that although the authors did not find correlation between septal length or the septal



Drawing 13.2. Shows the complete or long septum type (septate uterus). In this type of the uterine septum, the body of the septum extends all the way down from the fundus to the cervix, completely separating the uterine cavity into two sides.



Drawing 13.3. Shows the incomplete short type of the uterine septum (subseptate uterus). In this type, the apex of the septum stops somewhere below the fundus before reaching the cervix.

thickness, and occurrence of obstetric complications, they found the septal vascularity to correlate significantly with those complications. The authors extrapolated from those data that that this might reflect an increased amount of muscle in the septum, producing local uncoordinated myometrial contractility resulting in adverse obstetric outcomes (39).

Magnetic Resonance Imaging

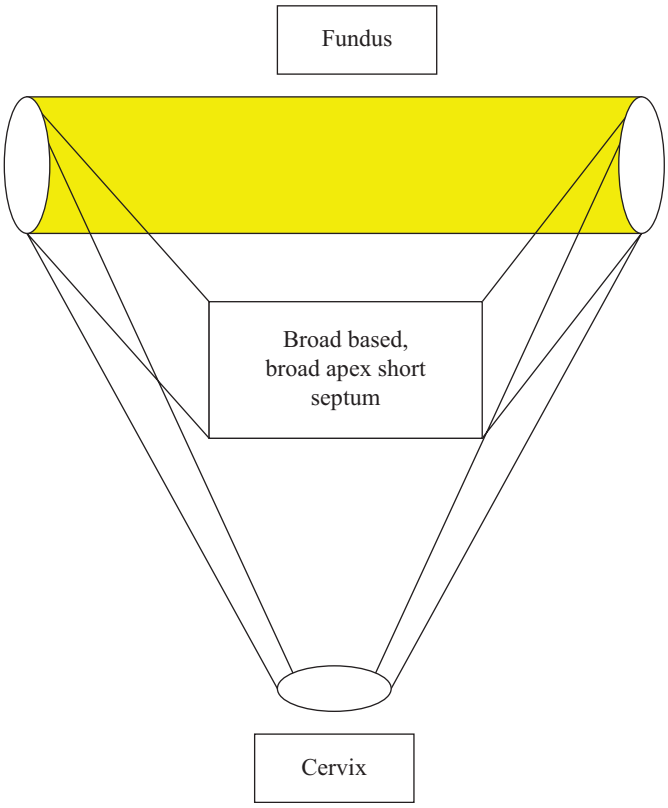
MRI can delineate both internal and external uterine architecture, which provides an interesting alternative diagnostic method for the evaluation of Müllerian tract anomalies. However, several disadvantages make it difficult to apply for routine practice including high cost, being not suitable for office practice, and, most important, the extreme high accuracy of the 3D US that can provide very comparable information to MRI while having the advantages of low cost, suitability for office practice, and even more information including Doppler examination of the vascularity. However, MRI is mandatory for differentiating between uterus didelphys and long, complete uterine septum with cervical duplication and a vertical vaginal septum.

Surgery

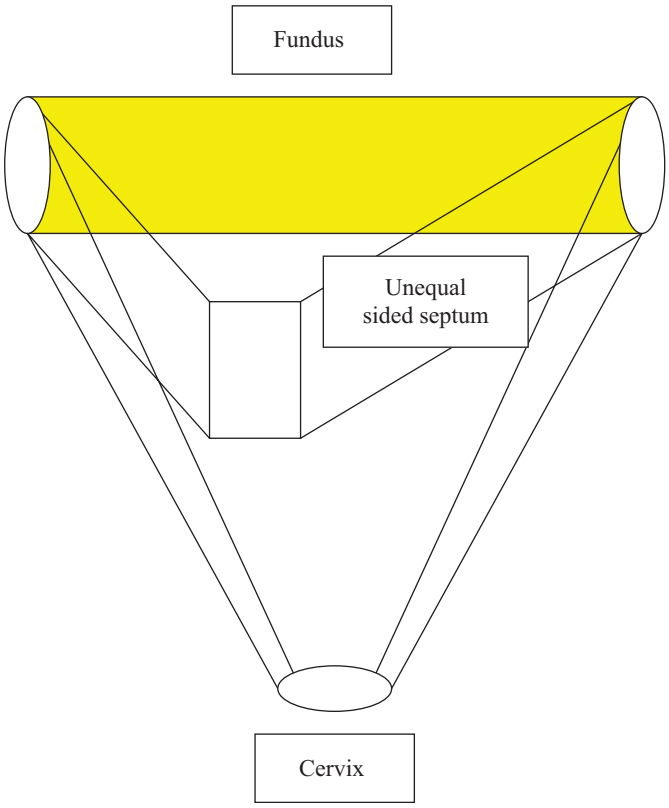
Hysteroscopy allows both direct visualization of the uterine cavity and operative intervention when uterine septa are encountered. However, as is the case with HSG, hysteroscopy cannot evaluate the external contour of the uterus. However, an advantage of hysteroscopy is the direct visualization of the endometrium and that it can be performed as an outpatient procedure, but one should be aware of the risk of surgical complications, for example, perforation, infection, and bleeding. Concurrent laparoscopy is essential for evaluation of the external contour of the uterus mainly to differentiate between uterine septum and bicornuate uterus, which cannot be surgically corrected through the hysteroscopic approach if even surgical correction is warranted. In addition, laparoscopy is helpful for assessing the extent of hysteroscopic resection of uterine septa and identifying and repair of uterine perforation promptly should it occur (29). Furthermore, laparoscopy should be mandatory if hysteroscopic metroplasty is performed in a patient with history of infertility to rule out endometriosis, pelvic adhesions, and subtle fimbrial pathology (39a). This is particularly the case in view of recent data suggesting an association between uterine septum and endometriosis (39b).

REPRODUCTIVE PROBLEMS ASSOCIATED WITH UTERINE SEPTUM

Congenital uterine anomalies vary in frequency and are usually estimated to be present in up to 5 percent in the general population, although less than half of those affected have clinical symptoms (2). Various clinical problems have been reported including pregnancy failure and other obstetric complications, for example, preterm labor and placental abruption. Other reproductive problems, especially infertility, have been suggested,



Drawing 13.4. Shows a subtype of the short septum. We call it broad-based short septum. In this type, the base of the septum is very broad, extending between almost the whole distance between the two tubal ostia. The base in this subtype is usually broad.



Drawing 13.5. Shows another subtype of the short septum (asymmetrical). In this type, the two sides of the uterine cavity are unequal. The apex of the septum is deviated more toward one side.

though not universally accepted. Other conditions, for example, endometriosis and urinary tract anomalies and even malignancy have been thought to be associated with congenital uterine malformation.

Pregnancy Loss and Obstetric Complications

Congenital uterine malformations, particularly uterine septum, have been associated with poor reproductive outcome including an increased risk of first- and second-trimester miscarriage, preterm delivery, placental abruption, intrauterine growth restriction, fetal distress, and fetal and maternal death (39–42). It is estimated that 36 percent of uterine malformations have an associated cervical insufficiency. Although congenital uterine malformations are associated with poor reproductive performance, each type may have a different impact on reproduction (23). Pregnancy loss in patients with uterine septa has been reported to be as high as 90 percent, after other causes for miscarriage have been excluded (23, 43, 44). During the first trimester of pregnancy, the risk of spontaneous miscarriage in patients with uterine septum has been reported between 28 and 45 percent, whereas the frequency of spontaneous miscarriage during the second trimester in these patients is approximately 5 percent (44, 45).

Buttram (46) reported a 67 percent miscarriage rate, 33 percent prematurity rate, and 28 percent live birth rate in patients with uterine septum. In a pooled cohort of pregnancies that were reported in thirteen studies, Kupesic calculated the incidence of pregnancy loss and preterm labor in a total of 1,304 pregnancies achieved in women with untreated uterine septum. She found an incidence of 81.9 and 9.6 percent for pregnancy loss and preterm labor, respectively (29). However, such figures should be carefully interpreted as those studies possibly excluded reports on women with uterine septum associated with normal reproductive outcome.

With the exception of the arcuate uterus, which some believe to have no adverse impact on reproductive outcome (although this is not universally accepted) (47, 48), it is interesting that an inverse relationship has been seen between the extent of the vertical Müllerian duct fusion defect and the risk of pregnancy loss (miscarriage). The less severe the vertical Müllerian duct fusion defect (the shorter the septum), the higher the spontaneous miscarriage rate (49). Therefore, the frequency of pregnancy loss was found to be highest, in descending order, in a partial uterine septum, followed by bicornuate uterus, followed by a complete uterine septum, and finally the didelphic uterus (50). Unfortunately, these conclusions are drawn from studies that suffered from having small numbers, no control population, and different diagnostic criteria for determining the Müllerian anomaly. However, recently with the introduction of 3D US, consistent and strict criteria can be used to define particular Müllerian anomalies (1). Recently, however, Kupesic and Kurjak (29) could not find such a correlation to exist between risk of pregnancy loss and length of the uterine septum or its thickness.

A prospective study looked, over a period of three years, at reproductive outcomes in 106 women with congenital uterine anomalies detected, *incidentally*, by 3D US screening. Compared to a matching control group that included 983 women with normal uterine cavity, confirmed sonographically, at the same period of follow-up, women with uterine cavity anomalies were found to have significantly more adverse obstetric outcomes (51). The authors found women with uterine septum (twenty-eight women) had a significantly higher proportion of first-trimester loss ($Z = 4.68$, $P < 0.01$) compared with women with a normal uterus. Interestingly, women with an "arcuate" uterus (seventy-two women) had a significantly greater proportion of second-trimester loss ($Z = 5.76$, $P < 0.01$) and preterm labor ($Z = 4.1$, $P < 0.01$) (51), opposite to what is believed to be the case in the reported literature (52, 53). It is worth mentioning here that there was no correlation between the depth of fundal indentation in the arcuate uteri and percentage of first-trimester miscarriages ($r = -0.18$, $P = 0.126$), second-trimester miscarriages ($r = 0.1$, $P = 0.398$), or preterm labor ($r = -0.63$, $P = 0.6$), while in women with a subseptate uterus, the first-trimester miscarriage rate appeared to "decrease" with "increasing" length of uterine septum. However, this finding did not reach statistical significance ($r = -0.46$, $P = 0.702$). Furthermore, there was no correlation between septum length and second-trimester miscarriage ($r = 0.211$, $P = 0.273$) or preterm labor ($r = 0.117$, $P = 0.298$) (51). Later, the same team examined the uterine cavity in 509 women with a history of unexplained recurrent miscarriage and 1,976 low-risk women for the presence of congenital uterine anomalies by 3D US. Although the authors found no significant difference in relative frequency of various anomalies or depth of fundal distortion between the two groups, in women with both arcuate and subseptate uteri, the "length" of the remaining uterine cavity was significantly "shorter" ($P < 0.01$) and the "distortion ratio" was significantly higher ($P < 0.01$) in the recurrent miscarriage (54).

Recently, Tomazevic et al. challenged the concept that arcuate uterus or small uterine septum does not compromise reproductive function (54a). This was an observational study that included 826 singleton deliveries to 730 women with history of hysteroscopic resection of uterine septum. They compared the perinatal outcome before and after hysteroscopic resection in two groups of women: women with a small uterine septum (Group A) and those with larger uterine septum (Group B) (54a). The preterm birth rate and the very preterm birth rate in Group A ($n = 420$) were 33.9 and 12.5 percent before and 7.2 and 3.1 percent after hysteroscopic resection, respectively ($P < 0.001$). Similarly, the preterm birth rate and the very preterm birth rate in Group B were 36.5 and 15.0 percent before and 8.0 and 2.9 percent after hysteroscopic resection, respectively ($P < 0.001$). They concluded that similar to a large uterine septum arcuate or small uterine septum is an important hysteroscopically preventable risk variable for preterm birth.

We believe, as supported by the above literature, that the type, extent, and shape of the uterine cavity are important determinants of the reproductive outcomes rather than the simple diagnosis of uterine cavity anomaly. It appears that the shorter and more distorted the uterine cavity (e.g., when the septum distorts that uterine cavity unequally), the more the likelihood of having adverse reproductive outcomes including pregnancy loss (early or mid-trimester), preterm labor, or even placental complications such as placental abruption.

Termination of Pregnancy

The presence of uterine abnormalities may increase both the failure and complications of the procedure including higher risk of uterine perforation and adhesion formation. This advocates the use of transvaginal ultrasonography during pregnancy termination in patients affected with a uterine anomaly (55).

Mechanism of Adverse Obstetric Outcomes in Association with Uterine Septum

Although no studies attempted to elucidate the underlying mechanisms why some women with uterine septa suffer from reproductive loss while others have normal pregnancies, several mechanisms have been suggested including increasing intrauterine pressure with relative cervical incompetence and a poor blood supply to the endometrium through the septum. Another suggested mechanism is the luteal defect associated with uterine septum that could be a result of the local vascular insufficiency and not a hormonal deficiency (56). Fedele in a small study of twelve pregnancies in eight patients suggested that miscarriage is related to septal implantation (56a).

However, according to the most widely accepted theory, the septum is thought to consist of fibroelastic tissue with inadequate vascularization and altered relations between myometrial and endometrial vessels. The poor response to estrogen of the endometrial mucosa covering the septum, including irregular differentiation and estrogenic maturation, is probably because of the scanty vascularization of the septal connective tissue (57, 58). As a result, implantation may be compromised and decidual and placental growth inadequate, resulting in early pregnancy loss and infertility. In addition, impaired fetal growth and placental abruption may occur as a result of an already poorly vascularized placenta and distorted uterine cavity, causing second- and third-trimester complications. Therefore, removing the septum may eliminate an unsuitable site for implantation, improve endometrial function, expand uterine capacity, and dramatically enhance reproductive outcome in selected patients.

Contrary to this classic concept, Dabirashrafi et al. (27) (as discussed earlier) found significantly less connective tissue, a greater proportion of muscle tissue, and more vessels in the septum. They, therefore, suggested that pregnancy wastage is caused by poor decidualization and placentation due to the reduced amounts of connective tissue, as well as by higher or uncoordinated contractility due to the increased muscle content (27). It also has been suggested that estrogen and progesterone receptor deficiency in the endometrium of malformed uteri may further increase abnormal uterine contractions that lead to fetal wastage (57, 58). Pellerito et al. (59) performed MRI of patients with a septate uterus and found a muscular septal component (differentiated from fibrous tissue by its higher signal intensity). This was confirmed by histological examination of biopsy specimens. Another investigator used MRI to assess the composition of the septa in twenty-nine patients and showed that all of them had myometrial tissue with histological confirmation in four of them (59a).

Infertility and ART Failure

The incidence of uterine defect in infertile women has been estimated to be approximately 3 percent, which is similar to

the prevalence of approximately 4 percent found in the general population and/or in fertile women (18). The incidence of uterine malformations in infertile women varies between 0.5 and 26 percent (16, 53, 59b–d). In a report by Hinckley and Amin on 1,000 routine office hysteroscopies in infertility patients undergoing IVF treatment, they reported that 0.5 percent of patients were found to have uterine septum (59b). Tulandi et al. also reported a low incidence of uterine anomalies in 2,240 infertile women (1.03 percent), with 78.3 percent having primary infertility (59c). However, other reports indicated that there might be a higher prevalence of uterine anomalies in infertility patient from 16 to 26 percent (16, 59d, e). Raga et al. in 1996 reported a prevalence of 26 percent in a rather small, selected group of patients (59e). Similar results (24 percent) were reported in a small study (59d). Interestingly, Raga et al. in 1997 published a much larger study on 1,024 women, but this time the prevalence was only 2.4 percent (53). However, Acien in 1997 reported an incidence of 16 percent in a large study of 1,200 infertile women. Our group reported recently similar results in a study on 1,011 infertile patients who underwent hysteroscopy and laparoscopy for diagnosis and treatment of infertility (59f). The overall incidence of uterine septum in all infertile patients studied was 17.6 percent, with 15 and 2.5 percent being short incomplete uterine septum and long incomplete uterine septum, respectively (59f). We believe that the variability in the reported incidence of uterine anomalies depends on similar variables as suggested by Acien on the incidence in general/fertile population especially the diagnostic methods used and physician interest and awareness to find or reject uterine anomaly (9b). This topic will remain controversial until a well-designed prospective multicenter study utilizing 3D US and/or hysteroscopy is completed.

Patients with secondary infertility usually have a history of spontaneous miscarriages, while patients with primary infertility have no such history. In those primary infertility patients, when uterine septum is detected, there is more controversy as regards whether to treat the uterine septum or not than with the secondary infertility group that has a poor reproductive history (29). Obviously, future studies would be difficult as resection of uterine septum is so simple and efficacy so dramatic that randomized trials would be ethically questionable (28).

Despite the paucity of data concerning the contribution of the uterine septum to infertility, hysteroscopic resection of uterine septum is recommended before initiation of treatment in women undergoing ART (60). In support for that, Kirsop et al. (61) reported improved results with ART after hysteroscopic treatment of uterine abnormalities among 144 women who had preclinical miscarriage after ART. Dicker et al. (62) found uterine abnormalities (mainly uterine septa) in 14 cases (9.7 percent) and surmised that an incomplete uterine septum may be an important factor predisposing to early pregnancy wastage. In addition, Syrop et al. (63) showed higher prevalence of uterine anomalies (18.2 percent) in patients with repeated ART failure.

Contrary to the above data supporting the recommendation to treat uterine anomalies, in particular short uterine septum in women before undergoing ART treatment, other investigators did not find the presence of uterine anomalies to reduce the chance of pregnancy after ART treatment (64, 65). However, those studies suffered from several methodological problems including small sample size and retrospective analysis (64), as well as mixing different types of uterine malformations and failure to control significant confounding factors that might affect the outcome of ART treatment.

Endometriosis

Endometriosis is a frequent reproductive disorder that is associated with pelvic pain and infertility. A correlation between retrograde menstruation and likelihood of endometriosis has been shown with a significantly higher prevalence of endometriosis in patients with Müllerian anomalies in comparison with women without such anomalies (controls) (66, 67). However, no difference between nonobstructive anomalies (e.g., uterine septum) and controls was found (68).

Most recently, higher incidence of endometriosis in patients with a uterine septum was reported in a retrospective study that included 120 patients with a uterine septum compared to a control group of 486 consecutive infertile patients with a normal hysteroscopy and laparoscopy. The authors found the incidence of endometriosis significantly higher in patients with uterine septum (25.8 versus 15.2 percent, $P = 0.006$) (69).

In addition, our own data suggest an association between uterine septum and endometriosis (39b).

Interestingly, uterine dysperistalsis was suggested to be the mechanical cause of endometriosis rather than retrograde menstruation (70). One could imagine that uterine anomalies irrespective of their obstructive or nonobstructive character could be associated with a disturbed uterine peristalsis as a risk factor of endometriosis (69). However, further studies are needed.

Urinary Problems

A small percentage of patients (usually less than 10 percent) with a ''symmetric'' malformation of the uterus have abnormalities of the urinary tract, usually congenital absence of a single kidney. For that reason, urological evaluation is recommended for patients with uterine anomalies uterus, particularly with the more severe uterine anomalies (28).

Polycystic Ovarian Syndrome

The association between polycystic ovary (PCO) appearance on ultrasound and uterine Müllerian anomalies was suggested when PCO was found in 29.9 percent of women with Müllerian anomalies (167 women) compared to a prevalence of 20.1 percent in a control group of 3,165 women with normal uterine cavity (a statistically significant difference) (71). Interestingly, when the Müllerian anomalies were further grouped according to the American Fertility Society classification (21), patients with septate uteri and bicornuate uteri malformations had a statistically higher prevalence of PCO than the controls. While the difference was much more significant with the septate uterus subgroup, it was insignificant in patients with unicornuate and didelphic uteri compared to controls (71).

Malignancy

It is believed that uterine malformations including uterine septum, with its different forms, do not predispose a patient to the development of a malignancy (72, 73).

MANAGEMENT OF UTERINE SEPTUM

Treatment of uterine septum has come full circle that started in 1919, with successful transcervical therapy (74, 75) that was replaced by abdominal approach (e.g., Jones and Tompkins procedures). This approach turned almost obsolete with the consensus now back to the transcervical approach (hysteroscopic metroplasty). Hysteroscopic resection is favored due to its simplicity compared with the abdominal metroplasty that is performed through a laparotomy (76). However, abdominal approach has been advised for extremely wide uterine septum, but transcervical approach can still be accomplished in most cases, although a second attempt might be necessary in certain instances to completely incise the septum (28).

Which Septum Needs Resection?

The answer to which septum needs resection depends on the reproductive history rather than the type of the septum itself, that is, hysteroscopic metroplasty is obviously recommended for patients with a history of recurrent pregnancy loss or bad obstetric history. However, it is important to evaluate patients with pregnancy loss who also have uterine septa, to rule out additional underlying etiologies (77).

Other reasonable indications include women with history of adverse obstetric outcomes including second-trimester losses, abnormal presentation, preterm deliveries, or antepartum hemorrhage when associated with a uterine septum. Again, it is important to reiterate it that it is the history of reproductive problems rather than the extent of the uterine septum that should determine the decision to resect it or not. Age is another consideration because older women may benefit from prompt treatment to optimize outcome. Choe and Baggish (78) suggested that the uterine septum should be corrected as early as possible, especially in patients older than thirty-five years of age, to increase fecundity.

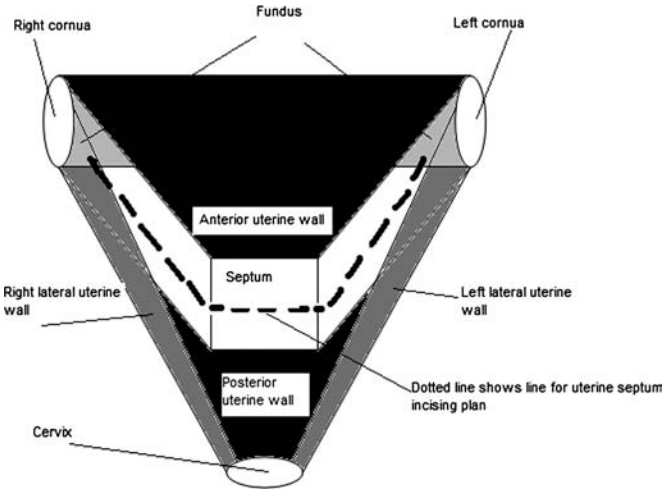
When a uterine septum is an incidental finding in a woman without a history of reproductive problems that are known to be associated with uterine septum, it is still a controversial issue whether prophylactic metroplasty should be done to prevent those complications. Limited data suggest that metroplasty is not indicated for treatment of infertility because primary infertility patients conceived after metroplasty at a similar rate as infertile counterparts without septa (79). In women with the incidental diagnosis of uterine cavity disorders at the time of abdominal or pelvic surgery performed for other reasons, successful pregnancy was achieved in the majority of patients with didelphys, bicornuate, and septate uteri with success rates of 93, 84, and 78 percent (80). Such findings support believes of other investigators that surgical corrections of all uterine defects are not indicated unless patients do poorly on a repetitive basis. In addition some investigators have reported better reproductive outcome among women with a septate uterus not subjected to surgical interventions (47, 82, 83) favoring the opinion that hysteroscopic incision of the uterine septum is not absolutely necessary in these patients, excluding those with recurrent miscarriage (83). However, the achieved pregnancies could simply reflect the draw of luck that the implanting embryo found its way at a place away from the defective endometrium, that is, away from the uterine septum (56a).

However, in our hands (unpublished data), we have extensive experience with a large number of cases (more than 300 cases) in which short uterine septum was diagnosed as an incidental finding during routine infertility workup (~50 percent with primary infertility). After diagnosis, patients with primary infertility were counseled regarding the two options of prophylactic metroplasty versus proceeding with infertility interventions (ovarian hyperstimulation with intrauterine insemination [COH + IUI] and ART when insemination is not successful) without surgical correction of the uterine septum. The majority of these patients opted to undergo hysteroscopic metroplasty. We observed an increased fecundity rate, excellent pregnancy rates after COH + IUI and ART, and good obstetric outcome (unpublished data). Interestingly in patients with secondary infertility, hysteroscopic metroplasty has reversed previous poor outcomes and the majority of those patients achieved full-term deliveries spontaneously or after receiving their infertility intervention following hysteroscopic metroplasty (unpublished data). These findings prompted us to believe and recommend in favor of routine resection of uterine septum (irrespective to its extent) before undergoing infertility interventions (ovarian stimulation with insemination or ART) or even when patients want to continue to try to achieve pregnancy spontaneously (79). Moreover, the simplicity of hysteroscopic treatment and low morbidity have argued for prophylactic hysteroscopic metroplasty particularly in women with unexplained infertility, before ART treatment, or even for removal of the septum at the time of diagnosis to increase fecundity and to prevent miscarriages and obstetric complications (81).

It is also interesting to mention that recently a large series of complete septate uterus with longitudinal vaginal septum has not been found to be associated with increased risk of primary infertility, and pregnancy was reported to progress successfully without surgical treatment. Those results do not support elective hysteroscopic incision of the septum in asymptomatic patients or before first pregnancy. However, that study suffered from several problems including being a descriptive study covering a very long period (almost four decades), which makes the comparison between surgically treated and untreated patients difficult. In addition, the study is associated with many limitations such as absence of a control group and thus no comparative analysis and changes in clinical strategies during the long period. However, that the particular malformation of a complete uterine and vaginal longitudinal septum is so rare and its hysteroscopic surgical correction requires more expertise make the data provided by the study still valuable information (73). Interestingly, we see the findings of this study support what has been previously reported regarding higher risk of reproductive problems with shorter uterine septum than longer ones as discussed earlier.

Other important variables can explain the controversy that some investigators did not find prophylactic resection of uterine septum to be necessary to improve reproductive performance include two major flaws: first those investigators failed to control for important variables that affect reproductive performance in particular age and presence of other infertility factors. Clearly, the presence of uterine septum is not an absolute reason for reproductive failure. It is one factor among several others, all determining reproductive performance, that is, achievement and maintenance of pregnancy until full term. The second, failure to control for the type and extent of the uterine septum. As we mentioned before, there seems to be an inverse relationship between the length

and extent of the uterine septum and reproductive failure (not university accepted). Worse outcomes were associated with shorter uterine septum than longer ones. Because it is usually easier to detect and diagnose more extensive (longer) uterine septum than shorter ones, this could have caused a selection bias in earlier studies. Those studies have included more women with longer uterine septum. Those women already have an overall much lower chance of poor reproductive outcome. So exposing them to surgical treatment or not would not be expected to make a significant difference (a huge sample size would be required to show statistical significance). In our experience, the longer the septum, the more vascular it was compared to the shorter septum. This observation was noticed during hysteroscopic metroplasty. This could explain why Dabirashrafi et al. (27) found higher amount of muscle tissue and vasculature in biopsies obtained from patients with uterine septum undergoing Tompkins procedure. Presumably, the majority of these patients had significant septum to warrant abdominal metroplasty.



Drawing 13.6. Shows the technique of hysteroscopic incision of the uterine septum. The hallmark of success of this procedure lies in incising the septum in the right plan, that is, the middle of the septum (as shown by the dotted line), avoiding too much digging into the anterior or the posterior wall of the uterus or into the fundus.

Preoperative Preparation

Timing of Surgery

It is advisable to perform surgery early during the follicular phase, or patients are preoperatively treated with a gonadotropin-releasing hormone analog, to eliminate the possibility of endometrium, diminishing clarity of view during surgery. We have fairly good experience with endometrial preparation with few weeks of combined oral contraceptives. It is interesting to mention here a novel approach for preparing the endometrial cavity before hysteroscopic metroplasty (and other forms of hysteroscopic surgeries) that benefit from achieving thin endometrium. This novel approach is using one of the new third-generation aromatase inhibitors, for example, anastrozole or letrozole. By shutting off estrogen production, the use of aromatase inhibitors for few days before hysteroscopic surgery is expected to result in a thin endometrium that will facilitate the performance of the surgery (84).

Preoperative Preparation

Preoperative antibiotics are often empirically given, despite the lack of strong evidence to support it (28). In our practice, we do not routinely administer any antibiotics either preoperatively or postoperatively.

Operative Technique

Before proceeding into the detailed description of the surgical management of uterine septum (septum resection), it is important to clarify the misnomer of the word ''resection.'' This is because surgical management of the uterine septum actually involves its ''incision'' and not ''resection.'' Some prefer the word ''lyse'' rather than ''resect'' to describe the surgical management of the uterine septum.

As explained earlier, uterine septum results from the incomplete fusion between the two Müllerian ducts. Anatomically, the two ducts are side to side. So the incomplete fusion results in the persistence of the wall between the two tubes (the uterine septum) that extends anteroposteriorly (sagittal axis). For that reason, the uterine septum extends between the ''anterior'' and ''posterior'' walls of the uterus. Hence, the septum should be incised transversely. Every effort should be taken to make the transverse incision equidistant between the anterior and posterior uterine wall up to the fundus, without entering the fundal myometrium. The septum should be transected systematically in the midline, avoiding drifting to the posterior or anterior wall.

There are three important tools to help marinating the systematic resection of the septum in the midline (as illustrated in Drawing 13.6): 1) following the symmetry of both uterine tubal openings, 2) observing the rich myometrial vascularization when cutting through the uterine wall, and 3) observing the uniform translucency of the hysteroscopic light laparoscopically.

When the junction between the septum and myometrium is reached, small arteries may be seen pulsating. If these are cut, they bleed upon division, indicating that the septum has been transected completely. With the symmetric visual view of the uterotubal junctions and the laparoscopic uniform translucency of the hysteroscopic light, the hysteroscopist can safely transect the uterine septum without danger of perforation (77).

At the completion of the procedure, the intrauterine pressure produced by the distending fluid may be lowered to less than 50 mmHg. This helps in identifying areas of bleeding. Usually, small bleeders stop on their own, but if the number of active arterial bleeders is significant, these can be individually coagulated with a pinpoint electrode (26, 85–87).

Scissors Versus Resectoscope

As explained earlier, observing fundal bleeding helps in determining the depth of the resection (how close into the uterine fundus). Observing such fundal bleeding suggests transition to the vascular myometrium from the avascular tissue of the septum. For that reason, some surgeons prefer using sharp scissors without applying energy (as in the case with resectoscope) to be able to determine the extent of fundal bleeding the depth of cutting through the base of the uterine septum. However, in the hands of experienced hysteroscopic surgeons, the problem of identifying the depth of the base of the uterine septum and where to stop does not seem to be a problem.

Surgeons favoring sharp scissors than the resectoscope believe that the scissors have the advantage of avoiding greater cervical dilation that is necessary for introduction of the resectoscope into the uterine cavity. Also, when uterine perforation occurs with the resectoscope, it is mandatory to explore potential thermal damage beyond the uterine wall, that is, bowel thermal injury. This is because electrical current can spread a few millimeters beyond the point of contact of the electrode.

Some surgeons tried flexible microscissors. However, they are difficult to direct due to their flexibility and can be tedious with a large septum. However, rigid microscissors mounted on the sheath do not allow resection of a wide septum. The recommended scissors are those semirigid ones. Beside the advantage of watching for fundal bleeding to determine the depth of incision into the base of the uterine septum, semirigid scissors are simple and usually able to resect at a variable distance from the tip of the hysteroscope.

The resectoscope has the advantage of coagulation-resection, which is most beneficial when dealing with a very broad septa. A special straight knife or a loop oriented forward can be used for this purpose, using the blended current for simultaneous cutting and coagulation. Care should be taken not to overcorrect the defect because bleeding may not be a warning sign of invading myometrium when blended current (cutting/coagulating) is used (77). It is important also to realize that the extent of thermal damage is usually few millimeters distal to the damage observed visually. Thermal damage beyond the base of the septum into the myometrium could at least, theoretically, increase the risk of uterine rupture during subsequent pregnancy.

Concomitant laparoscopy was suggested to confirm the diagnosis of the uterine septum and monitor the extent of the depth of incising the base of the uterine septum. Concomitant laparoscopy also allows visualization of the transilluminated uterus by the hysteroscope light. By decreasing the intra-abdominal lighting, the laparoscopist can advice the hysteroscopist when a unified uterine cavity is achieved. Intraoperative ultrasound monitoring is a possibility and needs to be explored clinically. This is specially the case when hysteroscopic metroplasty is performed without concomitant laparoscopy. The availability of the modern 3D US that can very accurately distinguish between different uterine anomalies, especially bicornuate uterus versus uterine septum and can precisely determine the extent of the uterine septum.

The uterine cavity may be distended with several different solutions. Obviously, when energy is used such as electric energy with the hysteroscope, an electrolyte-free solution is necessary. However, with the use of sharp scissors, simple, safer distension media (such as normal saline) can be adequate (1).

Technique of Resecting a Complete Uterine Septum

In patients in whom the uterine is complete, that is, extending from the fundus to the cervix, hysteroscopic resection is still a safe and effective procedure. It may be completed after placing a Foley catheter into one cavity while the other cavity is distended with the distension media through the hysteroscope (76). Incision of the septum should begin ''above'' the level of the internal cervical os, which can be assisted by creating a window at the level of the internal os with the help of an ancillary probe inserted from the opposite cervical canal and then be continued superiorly until the septum is completely incised until the level of the fundus. It is important to stress here that the lower portion of the septum that lies ''below'' the level of the internal cervical os has been suggested to be left without incising it (76). This is because it is believed that the cervical portion of the septum should be preserved to avoid disturbance of the internal os sphincter mechanism (88). However, conserving the cervical part of the complete septum is thought to increase the risk for cesarean section. In addition, it appears that the incidence of cervical incompetence after removal of the complete septum is rare (88a, b). Furthermore, a recent report suggested that resection of the cervical portion of the complete septum makes the procedure safer, easier, and less complicated than on preserving it, without impairment of reproductive outcome (88c).

Postoperative Care

After the procedure, uterine bleeding may be controlled using a Foley catheter to tamponade the cavity. It is important to ensure the patient's ability to void on her own before discharge home. Pain medications are usually administered in the form of mild analgesics. The use of strong analgesics is particularly important when a Foley catheter is left inside the uterine cavity. Some may insert an intrauterine device to prevent intrauterine adhesion formation (synechiae). However, other surgeons may opt to leave the uterine cavity empty. Hormonal therapy is often prescribed after the procedure to promote rapid epithelialization and decrease the risk of intrauterine synechiae. Estrogens are usually given in the form of conjugated estrogens and progesterone such as medroxyprogesterone acetate after estrogen course is completed. At the completion of hormonal treatment, after completing a withdrawal bleeding, SHG with 3D US is performed to assess the results of the hysteroscopic treatment by evaluating the uterine cavity. If the uterine cavity is satisfactory, the patient is allowed to conceive. Once pregnancy is achieved, consideration should be given to cervical cerclage versus careful monitoring of the cervical length with frequent transvaginal ultrasound. Attempts at pregnancy should be postponed for two months after surgery because postoperative hysteroscopy with biopsy has shown the uterine cavity to be normal at eight weeks after surgery (89).

Postoperative Ultrasonography

There have been some pathological studies showing that residual septa on the anterior and posterior walls, after septal incision, retract underneath the endometrium, and then the endometrium overgrows the area (29). Traditionally, most gynecologists are very conservative while performing hysteroscopic metroplasty for fear of uterine perforation or subsequent uterine rupture during pregnancy. Some noted that postoperative HSG always showed a residual septum (89a). Others found that the reproductive performance was not adversely affected by residual septum by up to one centimeter (89b). However, a recent report challenges that concept and suggests that women with a residual uterine septum have an increased chance of successful pregnancy with improved obstetric outcome after normalization of the uterine cavity (90).

OUTCOME OF SURGICAL EXCISION OF UTERINE SEPTUM

Grimbizis et al. (91) reported that all patients with recurrent miscarriage and normal fertility who were trying to become pregnant conceived spontaneously at least once after their

treatment. Daly et al. (92) have reported normal postoperative monthly fecundity rates. This confirms that the application of hysteroscopic metroplasty does not impair the fertility potential of women with a history of recurrent miscarriages.

Grimbizis et al. (91) found significant improvement in pregnancy outcomes following hysteroscopic resection of the uterine septum including a drop in the miscarriage rate to 25 percent and increase in term delivery rate to 63.7 percent (although 4.5 percent of the pregnancies were still ongoing at the time of their publication). Other investigators have also described a significant improvement in pregnancy outcome after hysteroscopic metroplasty. Postoperative miscarriage rates between 5 and 20 percent and live birth rates between 73 and 87 percent were reported (22, 23, 26, 78, 87, 93, 94). However, these reports had significant limitations including the retrospective design and absence of control groups (patients served as their own historical control in some). Interestingly, data are more impressive in women with uterine septum undergoing ART. While pregnancy rates achieved after ART treatment done before and after hysteroscopic resection of the septum were comparable, the improvement of pregnancy outcome was very impressive (29). In a review of the literature, an overall term delivery rate of about 50 percent in patients with untreated uterine malformations was achieved, while the term delivery rate after hysteroscopic treatment was about 75 percent. The rate of pregnancy wastage in the post-treatment group was 15 percent compared with 96.3 percent in the pre-treatment group. The authors concluded that hysteroscopic septum resection can be applied as a therapeutic procedure in symptomatic patients and also as a ''prophylactic'' procedure in asymptomatic patients in order to improve their chances of a successful delivery (91, 95).

Patients with a previous hysteroscopic metroplasty or complicated hysteroscopy should be aware of the potential risks for uterine rupture during pregnancy. In a recent review of the literature to identify predictors of uterine rupture following operative hysteroscopy, the authors found a history of uterine perforation and/or the use of electrosurgery increase this risk but was not considered an independent risk factor. The authors concluded that uncomplicated hysteroscopic surgery did not alter obstetrical outcome and that apart from favorable use of scissors for hysteroscopic metroplasty, no accurate method to prevent or detect impending ruptures in subsequent pregnancies was found (96). In another series, two cases of uterine rupture during the delivery of twin pregnancies after hysteroscopic metroplasty led the investigators to suggest cesarean section to be performed for multiple pregnancy (97). In our experience, we did not have any patients who experienced uterine rupture in a subsequent pregnancy following hysteroscopic resection of the uterine septum (98).

SUMMARY AND FUTURE RESEARCH

There is significant controversy concerning diagnosis and management of uterine septum. The technology of 3D US constitutes a major breakthrough in evaluating the uterine cavity. This is particularly true when the assessment is complemented by both color Doppler examination and distension of the uterine cavity with saline or ultrasound contrast medium (SHG).

There are enough data supporting the routine surgical excision of the uterine septa, irrespective of their types, in women with poor reproductive history, in particular, recurrent pregnancy loss. However, in asymptomatic patients, the prophylactic excision of incidentally discovered uterine septum in asymptomatic patient is still controversial. In women undergoing ART treatment, surgical excision of an incidentally discovered uterine septum is more universally accepted. In infertility patients, we believe that incidentally discovered uterine septum and even arcuate uterus should be corrected hysteroscopically prior to any infertility treatment to enhance reproductive outcome.

The hysteroscopic approach for surgical resection of uterine septum is a safe and effective approach (77, 98). While generally it is an operator preference whether to utilize ablative energy, for example, electrical diathermy or laser, or to utilize sharp scissors without energy, the outcome of treatment is comparable as regards complication and reproductive performance after surgery.

For women with incidentally discovered uterine septum, there is a need for randomized prospective trials comparing pregnancy rate and pregnancy outcome in a treated and an untreated group. In such studies, accurate diagnosis of the extent and structure of the uterine septum can provide extremely valuable information about which septum subtypes correlate significantly with the different reproductive outcomes.

KEY NOTES

- The reproductive implications associated with the presence of uterine septa are a matter of significant controversy in the literature.
- There is a consensus on a relationship between uterine septa and various reproductive problems. However, the nature and extent of this relationship is still a big dilemma.
- Significant part of this dilemma is due to variation in the literature as regards the methods of diagnosis, treatment, and follow-up of women with uterine septa.
- The technology of 3D US constitutes a major breakthrough in evaluating the uterine cavity disorders, including uterine septa.
- While there are enough data supporting the routine surgical excision of the uterine septa, irrespective of their types, in women with recurrent pregnancy loss, in asymptomatic patient, the prophylactic excision of incidentally discovered uterine septum is still controversial. However, before assisted reproduction, surgical excision of an incidentally discovered uterine septum is more universally accepted.
- In infertility patients, we believe that incidentally discovered uterine septum and even arcuate uterus should be corrected hysteroscopically prior to any infertility treatment to enhance reproductive outcome.
- While the hysteroscopic approach for surgical resection of uterine septum is a safe and effective approach, the choice of surgical technique (using sharp scissors or electrocautery) is an operator preference.
- For women with incidentally discovered uterine septum, there is a need for randomized prospective trials, comparing reproductive performance in a treated and an untreated group.

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