When and how to perform surgical treatment for uterine septum? 
Quando e como realizar o tratamento cirúrgico do septo uterino?

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Abstract

Uterine septum is the most common uterine anomaly and is more prevalent in women with infertility and a history of recurrent miscarriage. There is no consensus on what the indications for treatment are, nor the specific surgical approach to be used. It is reasonable to consider incision of the septum in a patient with infertility, history of spontaneous abortion or adverse obstetric outcomes, but no solid published evidence supports surgical treatment in asymptomatic women. The decision on therapy must be shared with the patient, explaining the potential risks and benefits. The surgical technique must be chosen regarding the surgeon’s experience.

Keywords: Uterine septum; Hysteroscopy; Infertility; Metroplasty.

INTRODUCTION

Uterine anomalies were described for the first time by Cruveilhier and Von Rokitansky in the 1800s¹. They are collectively called Müllerian anomalies and there are several classification systems to describe them¹. Septate uterus is the most common uterine anomaly, accounting for 35% of all identified uterine anomalies².³. This pathology is believed to originate before the 20th embryonic week with failure in the absorption of Müllerian’s duct¹. As many defects are asymptomatic, its true prevalence is difficult to affirm and is probably underestimated, but it seems to be around 5.5% in the general population, rising to 8% in infertile women and 13.5% in those with a history of recurrent miscarriage¹.².

There is no universally accepted standard definition of septate uterus. But in general, it is defined as a uterus with an external contour without indentation and a division of its cavity at the fundal midline – the septum. According to the European Society of Human Reproduction and Embryology and the European Society for Gynecological Endoscopy (ESHRE-ESGE), the septate uterus (class U2) has an internal indentation exceeding 50% of the uterine wall thickness⁴. The American Society for Reproductive Medicine (ASRM) defines a uterine septum as an internal indentation of more than 1.5 cm deep and a central point at an acute angle (less than 90°)¹. According to the Congenital Uterine Malformation by Experts (CUME), the prevalence of septate uterus is overestimated by the ESHRE-ESGE definition and underestimated by the ASRM definition⁵. Thus, they proposed different cut-off values, namely indentation depth ≥ 10 mm, indentation angle < 140° and an indentation to wall thickness ratio > 110%². The spectrum of configurations varies if it divides the uterine cavity partly or completely¹.⁶. According to ESHRE-ESGE, a complete septate uterus (class U2b) has a uterine corpus deformity that fully divides the uterine cavity up to the level of the internal cervical orifice. On the other hand, and for the partial septate uterus (class U2a), the septum divides partly the cavity above the level of the internal cervical orifice¹.

Historically, for the diagnosis of Müllerian anomalies, direct visualization was necessary, and therefore the gold standard was laparoscopy and hysteroscopy¹.
Currently, because it is less invasive, the ASRM recommendation is to perform imaging studies combined with hysteroscopy\(^1\). According to the ThessalonikiESHRE/ESGE consensus, the ‘reference standard’ for diagnosis is 3D ultrasound, supplemented by magnetic resonance (MRI) and endoscopic evaluation for complex cases or in diagnostic dilemmas\(^2\). In addition to being a less expensive and non-invasive exam, 3D ultrasound has over 88% accuracy for diagnosing uterine septum when compared with direct visualization through hysteroscopy/laparoscopy\(^3\).

The existing data on medical implications of the septate uterus and the effects of its treatment are limited. Therefore, there is no consensus on what the indications for treatment are, nor the method to be used. Thus, the purpose of this study was to review the indications and techniques of surgical treatment of uterine septum.

**METHODS**

A research was carried out on PubMed using the keywords: “Uterine septum”; “Hysteroscopy”; “Infertility”; “Metroplasty”. Inclusion criteria were articles published in the last five years (2015–2020); papers written in Portuguese, English and Spanish; referring to indications for the treatment of uterine septum; and studies comparing the available surgical approaches and articles about associated treatments that can be used.

**INDICATIONS FOR UTERINE SEPTUM TREATMENT**

Uterine septum is often diagnosed during evaluation of infertility, and its incidence higher is in this population. However, there is a lack of solid evidence regarding its reproductive implications, so it is difficult to make firm recommendations for treatment.

The last Cochrane systematic review in this matter is consistent with the previous one, affirming that there is no consensus on the management of septate uterus in women with primary infertility\(^4\). This is due to the lack of randomized controlled trials (RCT) evaluating the impact of surgery on the improvement of live birth rates\(^5\). The same conclusion is affirmed by Rikken et al. 2020 in a cohort study with 257 women (20 recruited prospectively and the rest retrospectively). Moreover, the results of this study suggest that septum resection does not improved reproductive outcomes compared to expectant management\(^6\).

However, and according to ASRM, it is reasonable to consider septum incision in a patient with infertility, a history of spontaneous abortion or adverse obstetric outcomes. They also consider that may be reasonable to consider septum incision after counselling on the potential risks and benefits of the procedure in a patient without a history of infertility or miscarriage\(^1\).

On the other hand, the French College of Gynaecology and Obstetrics considers that surgical treatment should be proposed in symptomatic women, that is, with a history of recurrent spontaneous abortion, after excluding other causes, or with dysmenorrhoea refractory to medical treatment. However, surgical treatment in asymptomatic women or women with primary infertility is not recommended\(^7\).

Furthermore, ESHRE states that hysteroscopic septum resection should be evaluated in the context of surgical trials in women with recurrent pregnancy loss, despite its beneficial effects in decreasing miscarriage rates and improving live birth rates\(^8\).

This controversy arises because the pathophysiology behind poor reproductive outcomes in women with a septate uterus is unknown\(^9\). Earlier studies asserted that the septum is avascular and mainly consists of fibrous tissue, disturbing implantation\(^9,10\). More recent studies suggest that the septum consists of normal endometrium and myometrium and resembles the uterine wall\(^11\). So, it is unclear if restoring normal anatomy also restores normal function, and therefore improves fertility outcomes\(^9\).

On the other hand, infertility is multifactorial, so the fact that uterine septum is frequently diagnosed in this population, does not mean that it is the only aetologic factor. So, there is insufficient evidence to conclude that the uterine septum is associated with infertility\(^1\). However, hysteroscopic septum incision seems to be associated with better rates of clinical pregnancy in infertile women\(^1\).

Regarding obstetric outcomes, there is some evidence suggesting that it increases the risk of anomalous presentation, intrauterine growth restriction, placental abruption and perinatal mortality\(^1\). There is fair amount of evidence supporting its contribution to spontaneous abortion and preterm delivery\(^1\). Hysteroscopic septum incision is associated with a decrease in subsequent abortion rates and an increase in the rate of live births in women with a history of recurrent spontaneous abortion, as well as an increase in the rate...
of live births in women with a history infertility or miscarriage\textsuperscript{1,11,12}.  

Regarding septum characteristics, ASRM guidelines affirm that there is insufficient evidence to conclude that obstetric outcomes are different when comparing the size of the uterine septa defined by length or width\textsuperscript{1}. Subsequently, Wang et al. found that, after surgery, women with a complete uterine septum had a higher infertility rate and lower pregnancy rate than those with a large and small partial uterine septum, respectively\textsuperscript{13}.

**SURGICAL TECHNIQUE**

As concerns surgical technique, the ASRM guidelines affirm that there is insufficient evidence to recommend a specific method\textsuperscript{1}. Traditionally, uterine septum surgery was performed by a laparotomic hysterotomy, but since the introduction of hysteroscopic septum resection in 1970, the latter approach is considered first-line therapy\textsuperscript{2,3}.

Commonly, there are two types of hysteroscopic surgical interventions: incision and resection. Hysteroscopic metroplasty using the incision method is an easier and faster technique and is more appealing, mainly due to recent data that suggest that the septum consists of normal endometrium and myometrium\textsuperscript{14}. Additionally, Ono et al. concluded that uterine septum incision is not a risk factor for adverse obstetric outcomes, such as placenta previa, placenta accreta, placenta abruption, uterine rupture, or heavy haemorrhage\textsuperscript{15}.

Furthermore, various devices can be used for this surgery, including cold scissors, monopolar or bipolar electrode or laser. There are some studies that compared different devices according to post-surgical reproductive outcomes. Cararach et al. suggested that the use of scissors was associated with more pregnancies when compared with resectoscope, but it might be associated with a higher follow-up in that group. So, the authors conclude that operator experience is a major consideration in the selection of the technique\textsuperscript{16}. Candiian et al. compared the use of microscissors with argon laser and concluded that the former was preferable, as it is simpler, faster, more effective and less expensive\textsuperscript{17}. A prospective randomized study including 160 patients analyzed the hysteroscopic resection of the uterine septum using small-diameter hysteroscopy with bipolar electrode (Versapoint) and resectoscope with unipolar knife. Both were shown to be effective regarding reproductive outcomes, but utilization of Versapoint is associated with a shorter operating time and lower complication rate\textsuperscript{18}. Litta et al. also compared resectoscope with Versapoint for hysteroscopic septum surgery. Operative hysteroscopy with Versapoint is more advantageous as it does not require cervical dilation, avoiding complications related to surgery (uterine perforation and cervical lacerations) and reproductive outcomes (cervical incompetence). So, it could be used predominantly in patients with cervical canal stenosis or in nulligravida women\textsuperscript{19}.

The technique alone, therefore, does not seem to have an impact on reproductive outcome. Thus, complexity, cost, associated complications and surgeon's experience must be considered during surgical planning.

Associated techniques, such as laparoscopy or transabdominal ultrasound to confirm the uterine contour, decrease the risk of uterine perforation and the need for reintervention by evaluation of the complete removal of the septum and the presence of other abnormalities\textsuperscript{2,12}.

**PRE-OPERATIVE TREATMENT**

Preoperative preparation to thin the endometrium allows better viewing, so it should be done at the beginning of the cycle, in the early follicular phase. It could be manipulated with the use of continuous oestroprogestative contraceptive, a progestative pill, gonadotropin-releasing hormone (GnRH) agonists or danazol. However, ASRM defend that there is insufficient evidence regarding its use\textsuperscript{1,14}.

**POST-OPERATIVE CARE**

Regarding postoperative care, there is also insufficient evidence to recommend antibiotics and exogenous estrogens\textsuperscript{1}.

The effectiveness of anti-adhesion treatment following operative hysteroscopy in subfertility women remains uncertain, as the evidence is limited according to the Cochrane review, ASRM, Anti-adhesions in Gynaecology Expert Panel-group (ANGEL) and ESGE\textsuperscript{1,20,21}. Therefore, in order to advise those who may benefit from antiadhesin therapy, a necessary develop a universal intrauterine adhesions classification needs to be developed as well as a prognostic scoring system to identify high risk patients\textsuperscript{21}.
Some authors describe the postoperative evaluation of the results, through ultrasound and hysteroscopic examination performed 2 to 4 months after surgery\textsuperscript{1,14}.

**TIMING FOR PREGNANCY**

The ideal time between uterine septum surgery and attempting pregnancy has not been evaluated in randomized controlled studies. The hysteroscopic excision of uterine septum leaves an injured area within the endometrial cavity and the available evidence suggests that it heals 2 months after surgery, through coverage by healthy endometrium\textsuperscript{1,3,22}. Therefore, assisted reproductive treatment does not need to be delayed after the hysteroscopic procedure, as it does not impair the implantation rate or pregnancy rate\textsuperscript{3}. However, according to ASRM, there is insufficient evidence to advocate a specific length of time before a woman should conceive\textsuperscript{1}.

**ONGOING STUDIES**

As data from RCT is urgently needed, there are two ongoing trials, the results of which are highly anticipated\textsuperscript{2,8,23}. Both studies have the primary outcome and the patients’ allocation in common. Patients will be randomized either for hysteroscopic septum resection or expectant management. The primary outcome is live birth rate\textsuperscript{2,3}.

The Randomized Uterine Septum Transaction Trial (TRUST) is a Dutch multi-centre randomised controlled trial (NTR1676), that includes patients with septate uterus and story of recurrent miscarriage or subfertility\textsuperscript{23}. The other trial is the pilot randomized controlled trial of hysteroscopic septal section, an English pilot multi-centre randomized controlled trial (ISRCTN28960271), including women with a uterine septum, a history of miscarriage or preterm birth, or infertility\textsuperscript{2}.

**CONCLUSION**

In conclusion, it is reasonable to consider the septum incision in a patient with infertility, history of spontaneous abortion or adverse obstetric outcomes, but no solid published evidence supports surgical treatment in asymptomatic women. On the other hand, there is insufficient evidence to recommend a specific surgical approach. Thus, the therapeutic decision must be shared with the patient and the surgeons must choose the technique with which they are most familiar.

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