

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 anomalies^{2,3}. 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 miscarriage^{1,2}.

There is no universally accepted standard definition of septate uterus. But in general, it is defined as a ute-

rus with an external contour without indentation and a division of its cavity at the fundal midline – the septum. According to 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 $< 140^\circ$ and an indentation to wall thickness ratio $> 110\%$ ². The spectrum of configurations varies if it divides the uterine cavity partly or completely^{1,6}. 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 orifice⁴.

Historically, for the diagnosis of Müllerian anomalies, direct visualization was necessary, and therefore the gold standard was laparoscopy and hysteroscopy¹.

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Currently, because it is less invasive, the ASRM recommendation is to perform imaging studies combined with hysteroscopy¹. 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 dilemmas⁷. 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/laparoscopy¹.

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 infertility⁸. This is due to the lack of randomized controlled trials (RCT) evaluating the impact of surgery on the improvement of live birth rates⁸. 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 re-

section does not improved reproductive outcomes compared to expectant management⁹.

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 miscarriage¹.

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 recommended².

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 rates¹⁰.

This controversy arises because the pathophysiology behind poor reproductive outcomes in women with a septate uterus is unknown³. Earlier studies asserted that the septum is avascular and mainly consists of fibrous tissue, disturbing implantation^{1,8}. More recent studies suggest that the septum consists of normal endometrium and myometrium and resembles the uterine wall⁸. So, it is unclear if restoring normal anatomy also restores normal function, and therefore improves fertility outcomes⁸.

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 aetiologic factor. So, there is insufficient evidence to conclude that the uterine septum is associated with infertility¹. However, hysteroscopic septum incision seems to be associated with better rates of clinical pregnancy in infertile women¹.

Regarding obstetric outcomes, there is some evidence suggesting that it increases the risk of anomalous presentation, intrauterine growth restriction, placental abruption and perinatal mortality¹. There is fair amount of evidence supporting its contribution to spontaneous abortion and preterm delivery¹. 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^{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 width¹. 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, respectively¹³.

SURGICAL TECHNIQUE

As concerns surgical technique, the ASRM guidelines affirm that there is insufficient evidence to recommend a specific method¹. 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^{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 myometrium¹⁴. 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 haemorrhage¹⁵.

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 technique¹⁶. Candiani *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 expensive¹⁷. 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 Ver-

sapoint is associated with a shorter operating time and lower complication rate¹⁸. 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 women¹⁹.

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 trans-abdominal 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^{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 oestrogenic contraceptive, a progestative pill, gonadotropin-releasing hormone (GnRH) agonists or danazol. However, ASRM defend that there is insufficient evidence regarding its use^{1,14}.

POST-OPERATIVE CARE

Regarding postoperative care, there is also insufficient evidence to recommend antibiotics and exogenous estrogens¹.

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^{1,20,21}. Therefore, in order to advise those who may benefit from antiadhesion therapy, a necessary development is a universal intrauterine adhesions classification needs to be developed as well as a prognostic scoring system to identify high risk patients²¹.

Some authors describe the postoperative evaluation of the results, through ultrasound and hysteroscopic examination performed 2 to 4 months after surgery^{13,14}.

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^{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 rate³. However, according to ASRM, there is insufficient evidence to advocate a specific length of time before a woman should conceive¹.

ONGOING STUDIES

As data from RCT is urgently needed, there are two ongoing trials, the results of which are highly anticipated^{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^{2,23}.

The Randomized Uterine Septum Transection Trial (TRUST) is a Dutch multi-centre randomised controlled trial (NTR1676), that includes patients with septate uterus and story of recurrent miscarriage or subfertility²³. 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 infertility².

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 in-

sufficient 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.

REFERENCES

1. Pfeifer S, Butts S, Dumesic D, et al. Uterine septum: a guideline. *Fertil Steril*. 2016;106(3):530-540. doi:10.1016/j.fertnstert.2016.05.014
2. Corroenne R, Legendre G, May-Panloup P, et al. Surgical treatment of septate uterus in cases of primary infertility and before assisted reproductive technologies. *J Gynecol Obstet Hum Reprod*. 2018;47(9):413-418. doi:10.1016/j.jogoh.2018.08.005
3. Checa MA, Bellver J, Bosch E, et al. Hysteroscopic septum resection and reproductive medicine: A SWOT analysis. *Reprod Biomed Online*. 2018;37(6):709-715. doi:10.1016/j.rbmo.2018.09.013
4. Grimbizis GF, Gordts S, Di Spiezio Sardo A, et al. The ESHRE/ESGE consensus on the classification of female genital tract congenital anomalies. *Hum Reprod*. 2013;28(8):2032-2044. doi:10.1093/humrep/det098
5. Ludwin A, Martins WP, Nastri CO, et al. Congenital Uterine Malformation by Experts (CUME): better criteria for distinguishing between normal/arcuate and septate uterus? *Ultrasound Obstet Gynecol*. 2018;51(1):101-109. doi:10.1002/uog.18923
6. Knez J, Saridogan E, Van Den Bosch T, Mavrelou D, Ambler G, Jurkovic D. ESHRE/ESGE female genital tract anomalies classification system-the potential impact of discarding arcuate uterus on clinical practice. *Hum Reprod*. 2018;33(4):600-606. doi:10.1093/humrep/dey043
7. Grimbizis GF, Di Spiezio Sardo A, Saravelos SH, et al. The Thessaloniki ESHRE/ESGE consensus on diagnosis of female genital anomalies. *Hum Reprod*. 2016;31(1):2-7. doi:10.1093/humrep/dev264
8. Rikken JFW, Kowalik CR, Emanuel MH, et al. Septum resection for women of reproductive age with a septate uterus. *Cochrane Database Syst Rev*. 2017;2017(1). doi:10.1002/14651858.CD008576.pub4
9. Rikken JFW, Verhorstert KWJ, Emanuel MH, et al. Septum resection in women with a septate uterus: a cohort study. *Hum Reprod*. 2020;35(7):1578-1588. doi:10.1093/humrep/dez284
10. Bender Atik R, Christiansen OB, Elson J, et al. ESHRE guideline: recurrent pregnancy loss. *Hum Reprod Open*. 2018;2018(2):1-12. doi:10.1093/hropen/hoy004
11. Wang Z, An J, Su Y, et al. Reproductive outcome of a complete septate uterus after hysteroscopic metroplasty. *J Int Med Res*. 2019;030006051989383. doi:10.1177/0300060519893836
12. NICE. Hysteroscopic metroplasty of a uterine septum for primary infertility. 2015:1-7.
13. Wang X, Hou H, Yu Q. Fertility and pregnancy outcomes following hysteroscopic metroplasty of different sized uterine septa: A retrospective cohort study protocol. *Medicine (Baltimore)*. 2019;98(30):e16623. doi:10.1097/MD.000000000016623
14. Budden A, Abbott JA. The Diagnosis and Surgical Approach of Uterine Septa. *J Minim Invasive Gynecol*. 2018;25(2):209-217. doi:10.1016/j.jmig.2017.07.017
15. Ono S, Kuwabara Y, Matsuda S, et al. Is hysteroscopic

metroplasty using the incision method for septate uterus a risk factor for adverse obstetric outcomes? *J Obstet Gynaecol Res.* 2019;45(3):634-639. doi:10.1111/jog.13884

16. Cararach M, Penella J, Ubeda A, Labastida R. Hysteroscopic incision of the septate uterus: Scissors versus resectoscope. *Hum Reprod.* 1994;9(1):87-89. doi:10.1093/oxfordjournals.humrep.a138326

17. Candiani GB, Vercellini P, Fedele L, Garsia S, Brioschi D, Villa L. Argon laser versus microscissors for hysteroscopic incision of uterine septa. *Am J Obstet Gynecol.* 1991;164(1 PART 1):87-90. doi:10.1016/0002-9378(91)90632-2

18. Colacurci N, De Franciscis P, Mollo A, et al. Small-diameter hysteroscopy with Versapoint versus resectoscopy with a unipolar knife for the treatment of septate uterus: A prospective randomized study. *J Minim Invasive Gynecol.* 2007;14(5):622-627. doi:10.1016/j.jmig.2007.04.010

19. Litta P, Spiller E, Saccardi C, Ambrosini G, Caserta D, Cosmi E. Resectoscope or Versapoint for hysteroscopic metroplasty. *Int J Gynecol Obstet.* 2008;101(1):39-42. doi:10.1016/j.ijgo.2007.10.013

20. Bosteels J, Weyers S, Tm DH, et al. Anti-adhesion therapy following operative hysteroscopy for treatment of female subfertility

(Review). *Cochrane Database Syst Rev.* 2017. doi:10.1002/14651858.CD011110.pub3.Copyright

21. Torres-De La Roche L, Campo R, Devassy R, et al. Adhesions and Anti-Adhesion Systems Highlights. *Facts Views Vis Obgyn.* 2019;11(1):137-149.

22. Valle RF, Ekpo GE. Hysteroscopic Metroplasty for the Septate Uterus: Review and Meta-Analysis. *J Minim Invasive Gynecol.* 2013;20(1):22-42. doi:10.1016/j.jmig.2012.09.010

23. Rikken JFW, Kowalik CR, Emanuel MH, et al. The randomised uterine septum transection trial (TRUST): Design and protocol. *BMC Womens Health.* 2018;18(1):1-5. doi:10.1186/s12905-018-0637-6

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