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DIFFERENTIAL DIAGNOSIS OF THE UTERINE SEPTUM: PROBLEMS AND SOLUTIONS

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▪ The article presents literature data on the peculiarities of diagnosing different types of uterine abnormalities. The main topic of the publication is the role and effectiveness of three-dimensional ultrasound in the differential diagnosis of the uterine septum.

▪ **Keywords:** uterine septum; uterine malformation; three-dimensional ultrasound.

ДИФФЕРЕНЦИАЛЬНАЯ ДИАГНОСТИКА ПЕРЕГОРОДКИ МАТКИ: ПРОБЛЕМЫ И ПУТИ РЕШЕНИЯ

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▪ В статье представлены данные литературы об особенностях диагностики типов аномалий развития матки. Основная тема — роль и эффективность трехмерного ультразвукового исследования в дифференциальной диагностике перегородки полости матки.

▪ **Ключевые слова:** внутриматочная перегородка; аномалии развития матки; трехмерное ультразвуковое исследование.

Background

Uterine abnormalities may adversely affect women's reproductive function, leading to infertility, miscarriage, and ineffective *in vitro* fertilization protocols [1, 2]. Its incidence can reach up to 10% in the general population and 5%–25% among women with miscarriages. Among uterine abnormalities, uterine septum has the most adverse effect on reproductive function [3]. According to the European Society of Human Reproduction and Embryology (ESHRE), uterine septum was one of the ten most pressing problems associated with female and idiopathic infertility in 2019.

Despite the large number of studies on uterine abnormalities, many questions regarding the differential diagnoses of uterine septum remain controversial to date.

Prevalence and significance of uterine septum in the realization of the reproductive function

It is difficult to determine the true prevalence of uterine abnormalities, since many congenital uterine defects are not clinically evident. According to L. Fedele et al. (2006), uterine septum is the most common of all uterine malformations, occurring in approximately 1% of the fertile population [4] and accounting for approximately 55% of all abnormalities [5]. There are two different types of uterine septum: complete septum, in which the uterine shape is not altered and the cavity is divided by a septum extending from the uterine fundus to the internal or external orifice; and incomplete septum, in which the uterus is not altered and the cavity is divided by a septum at

the uterine fundus. The septum may be thin or have a wide base, and the hemicavities may differ from each other [6]. A concomitant urinary tract abnormality (predominantly unilateral renal agenesis and duplex kidneys) has been reported in 14% of patients with uterine septum [7].

Pregnancy with uterine abnormalities is associated with a high risk of obstetric complications, such as malpositioning, premature amniorrhea, uterine inertia, placental insufficiency, postpartum hemorrhage, intrauterine growth retardation, intrapartum fetal death, and premature delivery [8, 9]. Spontaneous miscarriages occur in 26%–94% of women with uterine septum [10].

The negative effect of uterine septum on the reproductive process can be probably due to impaired endometrial morphology, blastocyst implantation in the septum, and uncoordinated myometrial contractions [11].

The timely diagnosis and treatment of this pathology to improve the reproductive function is essential for practical healthcare. For example, the information obtained by two-dimensional (2D) ultrasound and hysteroscopy may not be sufficiently accurate, subsequently leading to laparoscopic surgery and an increase in the number of surgical interventions. Thus, according to L.V. Adamyan et al., the frequency of unjustified surgical interventions ranges from 24% to 34% [12].

Basic principles of uterine septum diagnosis

Currently, anatomical uterine defects can be diagnosed by hysterosalpingography, (2D) and three-dimensional (3D) pelvic ultrasounds, magnetic resonance imaging (MRI), hysteroscopy, and laparoscopy.

Historically, hysterosalpingography has been the most commonly used method for diagnosing uterine malformations. According to A. Ludwin et al. (2011), hysterosalpingography cannot reliably differentiate between a uterine septum and duplex uterus because of the inability to assess its external contours [5, 13]. Hysterosalpingography is now widely used in diagnosing an arcuate uterus, and other imaging techniques are not necessary to confirm this abnormality. The specificity of this technique for diagnosing uterine abnormalities ranges from 6% to 60% [10].

A revolutionary method for diagnosing uterine abnormalities in modern clinical practice has been the 2D ultrasound, which is the most accessible diagnostic technique. According to G.F. Grimbizis et al. (2016), the accuracy of this technique in diagnosing congenital uterine abnormalities is approximately 86.6%. However, it is difficult to identify the types of abnormalities with this technique since images obtained in longitudinal and transverse planes do not provide complete data on the state of the uterine fundus [14].

In cases of suspected uterine malformations, a 3D ultrasound can be performed, in which the external and internal uterine contours are displayed on a coronal plane. Due to improved imaging, it is possible to distinguish between the types of abnormalities [15].

Jurkovic et al. (1995) compared 3D ultrasound with hysterosalpingography and invasive techniques, such as hysteroscopy and laparoscopy, and the 3D accuracy was found to be 95% [16]. F. Raga et al. (1996) conducted a blinded controlled trial involving 42 infertile patients: 30 women with a normal uterine anatomy and 12 patients with uterine abnormalities. Hysterosalpingography, 3D ultrasound, and laparoscopy were performed on all subjects, and the accuracy of the 3D ultrasound was 91.6% [17].

A. Kougioumtsidou et al. conducted a blinded prospective trial (2012–2016) to assess and compare the effectiveness of 3D scanning and invasive diagnostic techniques (hysteroscopy and laparoscopy). A total of 62 women with uterine abnormalities detected by 3D ultrasound participated in the study. The uterine malformation was confirmed using an endoscope in 61 women, and the prevalence was 98.4%. The most frequently diagnosed abnormality was uterine septum [18].

Given the high diagnostic accuracy, Y.Y. Chan et al. recommended 3D ultrasound as the "gold standard" noninvasive technique for diagnosing uterine malformations [19, 20]. All of the above indicates that 3D ultrasound is a highly sensitive technique for diagnosing congenital uterine abnormalities and can be used as an accurate noninvasive diagnostic method to provide mass screening of the population in outpatient settings [16, 17, 21].

The American Fertility Society (AFS) and the ESHRE together with the European Society for

Gynecological Endoscopy (ESGE) proposed classification systems based on 3D ultrasound data for the differential diagnosis of uterine abnormalities.

The AFS proposed to assess parameters, such as Г, cavity indentation; Ш, uterine cavity width; and B, angle of cavity indentation (Figs. 1–4).

Uterine septum is diagnosed using the following indicators: Г ≥15 mm, angle B <90°, while uterus arcuate is diagnosed using the following indicators: D ≥10 mm, but <15 mm and angle B >90° [11].

The ESHRE, together with the ESGE, have proposed their own ultrasound criteria for diagnosing a uterine septum (Figure 5, Table) [2, 14, 22].

MRI plays an important role in diagnosing uterine abnormalities and has an accuracy rate of 85.5%. However, the disadvantage of this technique is its high cost and lower availability compared with 3D ultrasound [14]. There are several MRI contraindications, including claustrophobia, severe obesity, and the presence of implantable ferromagnetic medical devices.

The standard MRI is conducted with T1-weighted images and T2-weighted images. The T2-weighted images are used to diagnose uterine abnormalities [23].

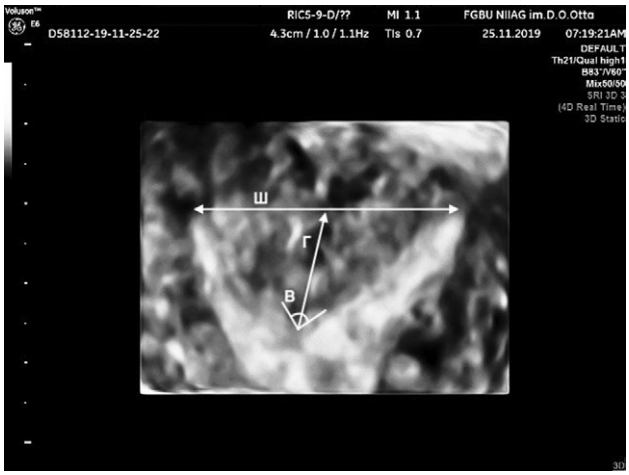

Fig. 1. 3D ultrasound reconstruction of the uterine cavity: subseptate uterus, where Ш, uterine cavity width; Г, cavity indentation; B, angle of cavity indentation (86°)

Рис. 1. Ультразвуковая 3D-реконструкция полости матки — внутриматочная перегородка: Ш — ширина полости матки; Г — глубина вдавления полости матки; угол В — угол вдавления полости (86°)

Compared to 3D ultrasound imaging, MRI has been shown to be more accurate in detecting a rudimentary uterine horn. The ability to assess anatomical zones and signal intensity from the endometrium allows to distinguish a non-functional rudimentary horn from a functional

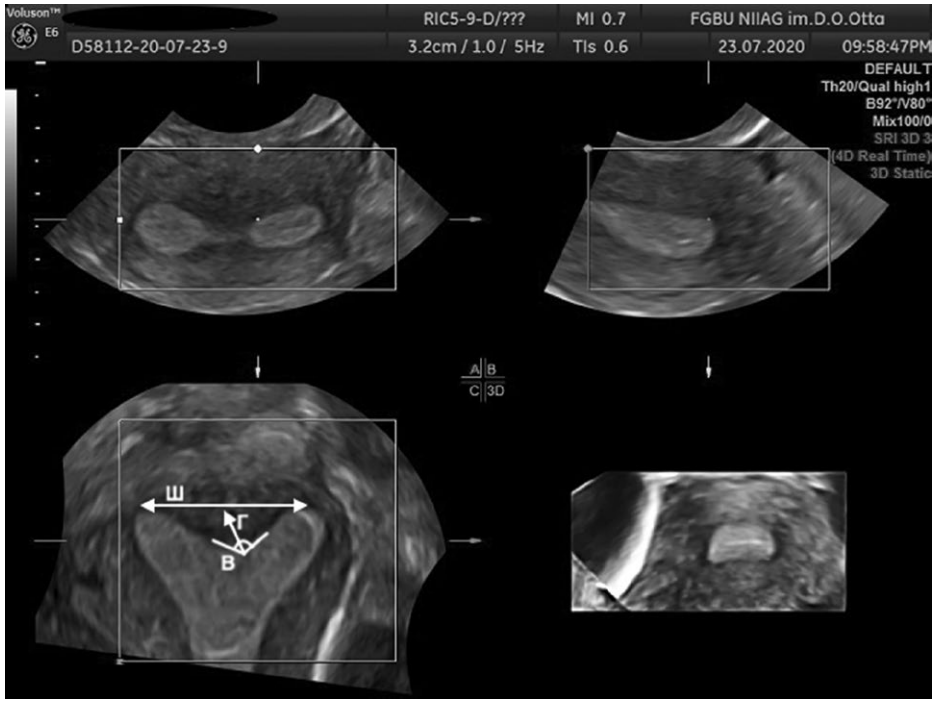

Fig. 2. 3D ultrasound reconstruction of the uterine cavity: arcuate uterus, where Ш, uterine cavity width; Г, cavity indentation; B, angle of cavity indentation (120°)

Рис. 2. Ультразвуковая 3D-реконструкция полости матки — седловидная матка: Ш — ширина полости матки; Г — глубина вдавления полости матки; угол В — угол вдавления полости (120°)

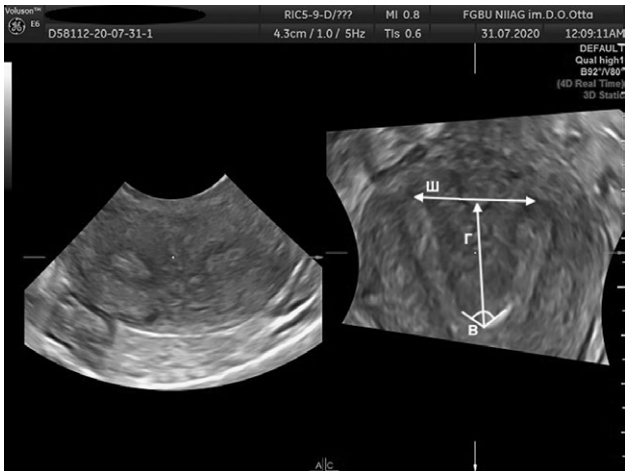

Fig. 3. 3D ultrasound reconstruction of the uterine cavity: bicornuate uterus, where Ш, uterine cavity width; Г, cavity indentation; B, angle of cavity indentation

Рис. 3. Ультразвуковая 3D-реконструкция полости матки — двурогая матка: Ш — ширина полости матки; Г — глубина вдавления полости матки; угол В — угол вдавления полости

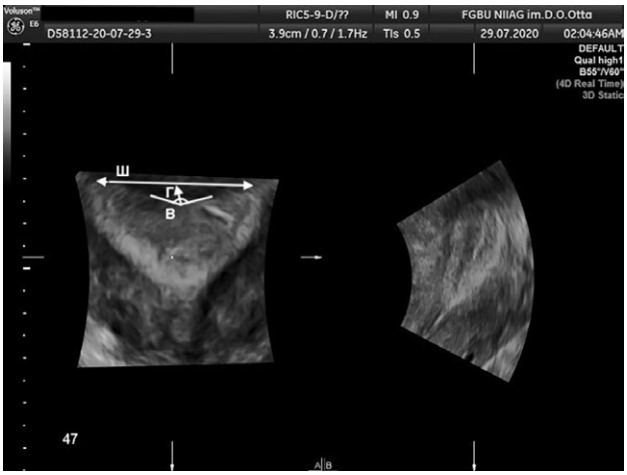

Fig. 4. 3D ultrasound reconstruction of the uterine cavity: normal uterus, where Ш, uterine cavity width; Г, cavity indentation; B, angle of cavity indentation

Рис. 4. Ультразвуковая 3D-реконструкция полости матки — нормальная анатомия матки: Ш — ширина полости матки; Г — глубина вдавления полости матки; угол В — угол вдавления полости

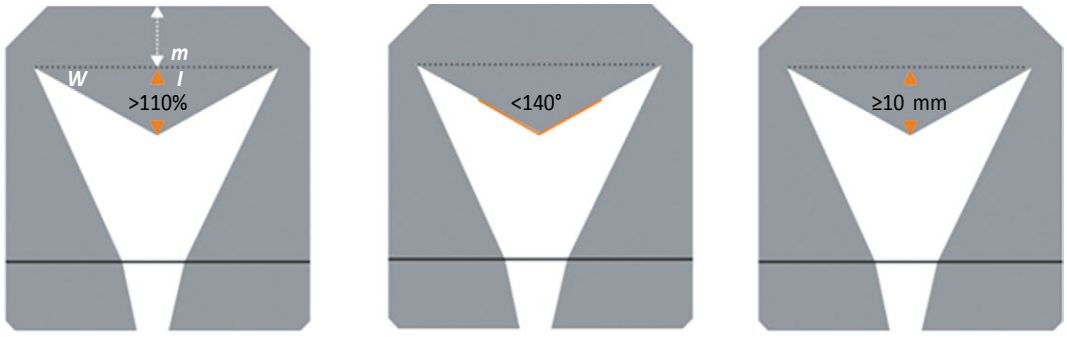

Fig. 5. Ultrasound criteria for the diagnosis of the uterine septum, where *m*, uterine wall thickness; *I*, cavity indentation; *I*/*m*, ratio of cavity indentation to uterine wall thickness; *W*, uterine cavity width; α, angle of cavity indentation

Рис. 5. Ультразвуковые критерии диагностики перегородки полости матки: *m* — стенка матки; *I* — глубина вдавления; *I*/*m* — отношение глубины вдавления к стенке матки; *W* — ширина полости матки; угол α — угол вдавления полости (ESHRE–ESGE, 2016)

non-communicating rudimentary horn using this technique [24, 25].

A few studies have described the role of dynamic contrast-enhanced MRI (DCE-MRI) in diagnosing uterine malformations. Until recently, this technique has been widely used in oncogynecology for studying cervical cancer, endometrial cancer, and ovarian tumors. DCE-MRI produces sequential images of the tissue volume before, during, and after the injection of the contrast agent injection. The plotted graphs allow to assess the vascular tissue density and blood flow velocity [26]. DCE-MRI enables a differentiated approach to the treatment choice for patients with a uterine septum. A decrease in the uterine septum blood flow >20% is an indication for its dissection. The sensitivity and specificity is 80.95% and 99.11%, respectively [27].

Hysteroscopy is a modern technique that allows both the direct visualization of the uterine cavity and a surgical intervention if it is necessary to remove the uterine septum. However, a disadvantage of the technique is its inability to assess the external uterine anatomy, which limits the differential diagnosis of the uterine septum and bicornuate uterus [28].

To date, there is no consensus on managing women with a uterine septum. R. Corroenne

et al. (2018) believe that the surgical correction of the uterine septum before the embryo transfer increases the frequency of embryo implantation, thereby improving the outcomes of *in vitro* fertilization programs [29].

Marcus et al. (1996) estimated pregnancy rates in women with infertility and congenital uterine malformations using assisted reproductive technologies. The retrospective analysis involved 24 patients (6 women with unicornuate uterus, 9 women with bicornuate uterus, 5 women with uterine septum, and 4 women with duplex uterus). This study showed worse outcomes in patients without the surgical correction of the uterine septum, with higher rates of spontaneous abortion and premature birth of 30% and 10%, respectively [30]. Tomaževič et al. (2010) studied the effectiveness of *in vitro* fertilization programs in patients with uterine septum in transferring 2,481 embryos. The fertility rates for women with complete and incomplete uterine septum were 2.7% and 2.8% preoperatively, respectively, and 15.6% and 18.6% postoperatively, respectively. Preoperative pregnancy and labor rates were lower compared with the control group, but after surgical malformation correction, the difference was statistically insignificant [31].

Paradisi et al. (2014) in a retrospective study involving 112 women with incomplete uterine septa of various sizes found that hysteroscopic metroplasty improved reproductive outcomes in patients with infertility and an incomplete uterine septum regardless of the septum size [32]. Homer et al. (2000) demonstrated a significant reduction in the spontaneous abortion rate from 88% to 5.9% after hysteroscopic metroplasty [33]. Similar findings have been reported by K. Zabak et al. (2001) [34].

Hysteroscopic septal resection is considered to improve natural conception rates for up to one year after the surgery [32, 34].

Hysteroscopic metroplasty can be performed using the following instruments: mechanical scissors; electrosurgery with specially designed electrodes mounted on the hysteroscope or resectoscope; bipolar electrodes; and fiber lasers, such as neodymium:YAG, argon laser, and mechanical morcellators.

The main aim of the procedure is to minimize trauma to both the endometrium and myometrium and to prevent the formation of uterine synechiae [35]. However, several authors believe that reproductive outcomes in women who underwent hysteroscopic metroplasty with scissors are better than those of women who underwent another method of malformation correction [36, 37].

Criteria for uterine septum diagnosis (ESHRE-ESGE, 2016)

Критерии определения внутриматочной перегородки (ESHRE–ESGE, 2016)

Indicators	Value
Cavity indentation (*I*)	≥10 mm
Ratio of cavity indentation to uterine wall thickness (*I*/*m*)	>110%
Cavity indentation angle (α)	<140°

It should be added that diagnostic laparoscopy is often performed together with hysteroscopy, providing a determination of the uterine configuration and accordingly, the extent of surgical treatment [28].

Conclusion

Despite numerous studies on uterine septum, current diagnostic methods are still widely debated. Increasingly, experts agree that in everyday practice, 3D ultrasound is the most effective, less expensive, and a promising technique for diagnosing uterine septum.

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