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7

Surgical management of congenital uterine anomalies (including indications and surgical techniques)

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A B S T R A C T

The prevalence of congenital uterine anomalies (CUA) is reported to be 4.3–6.7% in the general population, 3.4%–8% in the infertile population, and 12.6–18.2% of those with recurrent miscarriages. They are the result of abnormal formation, differentiation, and fusion of the Müllerian or paramesonephric ducts during fetal life. To date, various classification systems have been proposed for the categorization of CUA, but the recently introduced ESHRE/ESGE classification seems to be a new, clear, and systematic categorization, which could be the basis for clinicians to rely on when they refer to CUA and their clinical impact either generally or concerning pregnancy outcomes. CUA are apparently related to an impaired reproductive outcome, while their exact clinical impact as well as the effectiveness of their treatment remain considered controversial. Surgery is indicated in women presenting with symptoms related to specific uterine anomalies, especially in those with fertility problems. In this review, indications, surgical techniques for the repair of CUA according to their classification, and fertility and pregnancy outcomes before and after surgery will be thoroughly reviewed.

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Introduction

Embryology

Normal development of the female reproductive tract is based on the proper formation, differentiation, and fusion of the Müllerian or paramesonephric ducts. These ducts are initially formed as an invagination of the coelomic epithelium, and because of the lack of anti-Müllerian hormone (AMH) secretion in genetic female embryos (46,XX), they normally develop into the oviducts, the uterus, and the upper 2/3-part of the vagina [1–3]. It is not yet plainly comprehended what outlines the development of the uniform paramesonephric duct into the separate genital tract organs. It is thought that molecular mechanisms play a crucial role [4]. These molecules are encoded by specific genes; hence, the development of the female genital tract seems to have a genetic basis. Hormonal factors, especially sex steroids, may also be well involved in this developmental process [5,6].

Generally, during the 6th week of gestation, formation and canalization of the paramesonephric or Müllerian ducts occur followed by fusion of the caudal parts of the Müllerian ducts (7th–9th week of gestation) and absorption of the midline septum and formation of cavity (9th–13th week of gestation). Formation of the vagina is due to the fusion of the cavity coming from the Müllerian duct to that from the sinovaginal bulb. Sinovaginal bulb progresses the cephalad and fuses with the cavity coming from the caudal part of the Müllerian ducts to form the vaginal lumen [7,8].

Congenital anomalies of the female genital tract are the result of four major developmental defects during fetal life: (i) failure of one or both Müllerian ducts to form results in hemi-uterus (unicornuate) without rudimentary cavity or aplastic uterus, respectively. Aplastic uterus is the most severe Müllerian defect. Cervical and vaginal aplasia frequently co-exist, and this is known as Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome or Müllerian aplasia (MA); (ii) failure of the ducts to canalize results in hemi-uterus with rudimentary cavity; (iii) failure of or abnormal fusion of the ducts results in bicorporeal (bicornuate) uterus; (iv) failure of re-absorption of the midline uterine septum results in septate uterus. Dysmorphic appearance of the uterus can be attributed to abnormal formation of the ducts as a result of impaired segmental identity after drug exposure [7–10].

Classification

To systematize medical knowledge and facilitate clinicians' communication, classifications are necessary. To date, various classification systems have been proposed for congenital uterine anomalies (CUA). Among them, the AFS system [9] has been widely used, and until recently, it was the most accepted categorization of the anomalies. However, it is a reality that this system is associated with very serious disadvantages and the most important of them is that there are reported anomalies that could not be classified. Furthermore, obstructive anomalies are not clearly represented in the AFS system, and last but not least, the definitions of the system categories are not clear, thereby raising serious problems in the precise diagnosis and clinical significance of different classes [11]. Other classifications proposed are the embryological-clinical classification and the VCUAM system [12–14]. Nevertheless, they have difficulty in interpretation and in everyday application, and therefore, they have not been widely accepted by the medical community.

The European Society of Human Reproduction and Embryology (ESHRE) and European Society for Gynaecological Endoscopy (ESGE) together have recently published the new ESHRE/ESGE classification system of female genital tract congenital anomalies [10,15]. There are five main classes in the ESHRE/ESGE system on the basis of this classification of uterine anomalies: Class I is the dysmorphic uterus (including T-shaped and infantilis uteri), class II is the septate uterus (absorption defects/arcuate deleted), class III is the bicorporeal uterus (fusion defects including former didelphys and bicornuate uteri of AFS classification), class IV is the hemi of unicorporeal uterus (formation defect/former unicornuate uterus of AFS classification), and class V is the aplastic uterus (formation defect including only cases of uterine aplasia). Furthermore, normal uterus is categorized as class 0, and potentially unclassified cases could be categorized as class 6. Uterine, cervical, and vaginal anomalies were classified in autonomous categories.

This classification system introduced a new, clear, and systematic categorization, which could be the basis for clinicians to rely on when they refer to congenital uterine anomalies (CUA) and their clinical impact either generally or concerning pregnancy outcomes. In an attempt to emphasize the necessity of the system in clinical practice and the objective classification based on strict anatomical terms, a consensus has been published by the ESHRE and ESGE [16,17].

CUA are apparently related to an impaired reproductive outcome, while their exact clinical impact as well as the effectiveness of their treatment remain considered controversial. This justifies our effort to thoroughly review the indications for surgery, surgical techniques for the repair of CUA according to their classification, and fertility and pregnancy outcomes before and after surgical correction.

Prevalence of congenital uterine malformations

Malformations of the female genital tract are common but not always identified. CUA are the most frequent ones [18–21]. Probably, in addition to hysterosalpingography (HSG), the increasing and everyday use of high-accuracy imaging techniques such as 3D ultrasound (3D US), magnetic resonance imaging (MRI) and the application of minimally invasive surgical procedures (hysteroscopy and laparoscopy) resulted in a more accurate diagnosis and in an observed increase in their prevalence.

There are still difficulties to reveal the exact prevalence of CUA because of the heterogeneity in patient's selection criteria and the use of different methods for their diagnosis in the relevant studies. An important issue is the lack of an accurate and universal classification system, and therefore systematic grouping of the malformations is not always possible. The above-mentioned factors explain the subjectivity in the final verdict of the malformation and therefore justify the notable difference in the reported incidence between the studies.

Uterus, hosting the developing embryo, plays a detrimental role for implantation and evolution of pregnancy. To investigate the reproductive potential of women presenting with uterine abnormalities, scientists evaluated potential differences in the prevalence of CUA in general and infertile populations as well as in patients with recurrent pregnancy losses. This idea of indirectly concluding about the prevalence came up from the observation that in patients with conception problems or recurrent pregnancy losses, the CUA percentages were higher.

In an initial review by Grimbizis et al. [22], the prevalence of uterine anomalies has been found to be ~4% in the general population, ~4% in patients with infertility, and ~12% in patients with recurrent pregnancy losses. This review has limitations such as the retrospective design of the studies included, and the fact that the diagnostic method used in different studies included was not the same and of low accuracy.

To overcome this important limitation, Saravelos et al. [23] categorized the diagnostic methods as those with high and low diagnostic accuracy; reviewing the high diagnostic accuracy studies, they reported a prevalence of CUA of 6.7% (95% CI, 6.0–7.4) in the general/fertile population, 7.3% (95% CI, 6.7–7.9) in the infertile population, and 16.7% (95% CI, 14.8–18.6) in patients with recurrent miscarriages. It seems that the prevalence in the infertile population is similar to that of the general/fertile population; arcuate uterus was the commonest anomaly with a prevalence of 12.2% in women with recurrent pregnancy losses. However, in the infertile population, there seems to be a higher prevalence of septate uterus suggesting a possible involvement of this malformation in the poor obstetrical outcome. The prevalence of septate uterus was found to be ~2% in the general population, 3.5% in the infertile population, and 5% in recurrent aborters [23].

In a forthcoming review, including studies using optimal diagnostic tests for identification of uterine anatomy, Chan et al. [24] reported an overall incidence of congenital malformations of 5.5% (95% CI, 3.5–8.5) in an unselected population and 8.0% (95% CI 5.3–12.0) in infertile women. Statistically higher occurrence of congenital anomalies was present in women with a history of miscarriage (13.3%; 95% CI, 8.9–20) and in those with miscarriage in association with infertility (24.5%; 95% CI, 18.3–32.8). Uterine anomalies excluding arcuate uterus were present in 3.2% of the general population, 5.8% of infertile patients, and 9.3% of patients with recurrent pregnancy losses.

Furthermore, examining the different types of anomalies, the prevalence of septate uterus was found to be 2.3% (95% CI, 1.8–2.9) in the unselected population, 3.0%; (95% CI, 1.3–6.7) in infertile patients, 5.3% (95% CI, 1.7–16.8) in women with miscarriage, and 15.4% in those with a history of miscarriage and

infertility (15.4%; 95% CI, 12.5–19.0) [24]. The prevalence of bicornuate uterus was low in the unselected population (0.4%; 95% CI, 0.2–0.6), but considerably high in women with infertility (1.1%; 95% CI, 0.6–2.0), women with miscarriage (2.1%; 95% CI, 1.4–3.0), and cases presenting with a history of miscarriage and infertility (4.7%; 95% CI, 2.9–7.6) [24]. Unicornuate uterus was present in 0.1% (95% CI, 0.1–0.3) of the unselected population, 0.5% of women with a history of miscarriage (95% CI, 0.3–1.1), 0.5% (95% CI, 0.3–0.8) of women with infertility, and 3.1% of women with miscarriage and infertility (95% CI, 2–4.7) [24]. Didelphys uterus was found in 0.3% (95% CI, 0.1–0.6) of the unselected population.

Clinical impact of congenital anomalies: fertility and pregnancy outcome

Although data from prevalence of congenital anomalies in the general and selected population are useful, safe conclusions on the reproductive and clinical consequences of CUA and the need for their treatment could be drawn from a critical review of relevant preferentially comparative studies.

Uterine malformations seem to be associated with an impaired pregnancy outcome. Grimbizis et al. [22] reviewed the impact of congenital anomalies and reported an impaired evolution of pregnancy with a mean 44.1% abortion rate, 22.3% preterm delivery rate, and 32.9% term delivery rate in pregnant patients with septate uterus. Their conclusion on the effect of septate uterus on pregnancy outcome was in agreement with the results of others [25,26], but there were no data on the role of this malformation in women's fertility [22,27]. They further reported a mean 37.1% miscarriage rate, 16.4% preterm delivery rate, 45.3% term delivery, and 55.1% live birth rate in women with unicornuate uterus. The same group analyzed the impact of untreated bicornuate uterus and found that, in this group of pregnant women, mean miscarriage rate was 36.0%, mean preterm delivery rate 23.0%, mean term delivery rate 40.6%, and mean live birth rate 55.2%.

Reichman et al. [28] reported that in women with unicornuate uterus, 24.3% of pregnancies ended in first-trimester miscarriages and 9.7% in second-trimester miscarriages. Preterm delivery rate was 20.1%, and term delivery rate was 44%. Intrauterine fetal death was reported in as high as 10.5% of the patients, resulting in only 49.6% live birth rate.

Saravelos et al. [29] examined the clinical outcome of different types of CUA. Analyzing 881 pregnancies, they found that the presence of septate or bicornuate uterus significantly increased second-trimester miscarriages compared with that in controls (13.2% and 13.8% vs. 1.0%; $P < 0.001$ and $P < 0.05$, respectively). Moreover, live birth rates are also reduced in the same groups of CUA (9.4%, $P < 0.001$, and 13.8%, $P < 0.05$, respectively). Interestingly, in this study, women with an arcuate, septate, or bicornuate uterus had reduced rates of biochemical pregnancy losses compared with those in controls (9.5%, 11.1%, and 11.1% vs. 30.4%; $P < 0.01$, $P < 0.01$, and $P < 0.05$, respectively). The authors' conclusion was that pregnancies of women with RM and CUA usually represent a clinical problem not in the implantation period but at a more advanced gestational period.

Prior et al. [30] conducted a prospective observational study to examine the outcome of assisted reproduction in patients with CUA as compared to normal controls. Comparing women with arcuate uterus to normal controls, they observed similar clinical pregnancy (43.2% vs. 43.7%, $P = 0.78$) and live birth (36.7% vs. 37.2%, $P = 0.91$) rates. On the contrary, patients with more profound anatomical distortion (septate, bicornuate, didelphys, and unicornuate uteri) had significantly decreased clinical pregnancy (28.8% vs. 43.7%, $P = 0.048$) and live birth (22.2% vs. 37.2%, $p = 0.042$) rates. Preterm birth before 37 weeks of gestation was also increased in women with uterine anomalies compared to that in controls (22% vs. 14%, respectively; $P = 0.03$) [30].

In a systematic review evaluating the association between different types of CUA and reproductive outcome, Chan et al. [31] showed that arcuate uteri were associated with increased rates of second-trimester miscarriage (RR: 2.39; 95% CI, 1.33–4.27, $P = 0.003$) and fetal malpresentation at delivery (RR: 2.53; 95% CI, 1.54–4.18; $P < 0.001$). Septate or subseptate uterus were associated with significantly lower clinical pregnancy rates (RR: 0.86; 95% CI, 0.77–0.96; $P = 0.009$), as well as increased rates of first-trimester miscarriage (RR: 2.89; 95% CI; 2.02–4.14; $P < 0.001$), preterm birth (RR: 2.14; 95% CI, 1.48–3.11; $P < 0.001$), and fetal malpresentation at birth (RR: 6.24; 95% CI, 4.05–9.62; $P < 0.001$) [30]. Increased preterm birth (RR: 2.97; 95% CI, 2.08–4.23; $P < 0.001$) and fetal malpresentation (RR: 3.87; 95% CI, 2.42–6.18; $P < 0.001$) rates were also found in women with unicornuate, bicornuate, and didelphys uteri [31].

In a recent meta-analysis, Venetis et al. [32] found that in women with CUA, the probability of conception, in natural and ART cycles, is decreased by ~15% (RR: 0.86, 95% CI: 0.74–1.00). The likelihood of miscarriage during the first and second trimesters of pregnancy was high in patients with CUA (RR: 1.68, 95% CI: 1.31–2.17). Miscarriages in the first trimester were particularly evident with the presence of septate or bicornuate uterus, whereas in the second trimester, the detrimental effect of the presence of CUA is evident in all uterine malformations (arcuate, didelphys, septate, bicornuate, and unicornuate uteri). Furthermore [32], obstetrical outcome was adversely affected in patients with CUA: preterm (<37 weeks) (RR: 2.21, 95% CI: 1.59–3.08) and premature delivery (<34 weeks) (RR: 3.81, 95% CI: 1.48–9.83) rates were found to be notably increased for all types of CUA individually and combined. The negative effect of uterine malformations on the obstetrical outcome is also evident in the statistically significant difference of fetal malpresentation at delivery (RR: 4.75, 95% CI: 3.29–6.84) and perinatal mortality rates (RR: 2.43; 95% CI 1.34–4.42) [32].

Additionally, the authors found significantly more low-birth-weight newborns (<2500 g) (RR: 1.93; 95% CI: 1.50–2.49) in patients with CUA. More specifically, intrauterine growth retardation was statistically significant only in women with septate (RR 2.54, 95% CI 1.04–6.23), bicornuate (RR 2.80, 95% CI 1.06–7.34), and didelphys (RR 4.94, 95% CI 2.20–11.09) uteri. Placental abruption (RR: 2.47, 95% CI: 1.28–4.77) was also significantly increased in women with CUA as compared to that in those with a normal uterus [32]. Reproductive and obstetrical outcomes are affected in the presence of a dysmorphic uterus [33,34].

Apart from the impaired reproductive potential, women with c CUA associated with cervical and/or vaginal anomalies could present a variety of symptoms and health problems. Thus, cyclic pelvic pain and dysmenorrhea are the main complaints in obstructive types of anomalies such as unicorporeal uterus with rudimentary cavity and aplastic uterus with rudimentary cavity (Class U4a and Class U5a in ESHRE/ESGE classification, respectively). In noncommunicating horns, hematocavity and endometriosis are frequent findings [35–38]. Urinary tract anomalies are common in these women [35,36]. Pregnancy in the rudimentary horn of a unicorporeal uterus is a rare clinical complication. It is potentially life threatening, as rupture of the pregnant horn occurs, generally, in the second trimester of pregnancy [39].

Reproductive outcome after surgery – current indications for surgical treatment

Despite the limitations in the majority of the existing studies (retrospective design, inappropriate enrollment of patients, etc.), it appears that CUA have an adverse effect on reproductive outcome. Thus, their surgical treatment seems to be a logical option, especially for symptomatic patients. However, its application is dependent on its efficacy to reverse the reproductive consequences of CUA [22,40].

Two systematic reviews examined the reproductive outcome mainly in symptomatic patients before and after hysteroscopic septum incision (22, 41). Grimbizis et al. [22] reported a significant decrease in miscarriage rates from 86.4% before to 16.4% after and an increase in term delivery rates from 3.4% before to 76.2% after surgical correction. Although it could be argued that this result is attributed to a "tendency to return to the mean," the pregnancy outcome after surgical repair was even better from the observed pregnancy rates of unselected populations with CUA [22,29,31], indicating a positive effect of surgery. Homer et al. [41] also reported a drop in the miscarriage rate from 88% before to 14% after and an increase in the live birth rate from 3% before to 80% after surgery. Furthermore, Nouri et al. [42] reviewed the achievement of pregnancy in infertile women after septum incision: they reported ~60% pregnancy rate and ~45% live birth rate.

Mollo et al. [43] studied prospectively the conception rates in infertile women with unexplained infertility only and in infertile patients with unexplained infertility and septum who underwent septum incision. Conception (38.6% vs. 20.4%, $p = 0.016$) and live birth rates (34.1% vs. 18.9%, $p < 0.05$) rates were significantly higher in women with uterine septum after treatment than in those with a normal uterus. This supports the notion that septum adversely affects fecundity, and surgical treatment has a positive effect [43].

Gergolet et al. [44] prospectively compared the reproductive outcome in patients with small (group A) and large (group B) septa who underwent metroplasty. Miscarriage rates dropped from 94.9% to 82.1% in groups A and B, respectively, before treatment to 11.1% and 14.0%, respectively, after treatment.

Delivery rates were 2.6% and 15.7%, respectively, before operation and 88.9% and 84.2%, respectively, after surgery. It seems, therefore, that the length of the septum does not play a role in reproductive outcome, either before or after hysteroscopic metroplasty. Similar findings were also reported by Paradisi et al. [45] in women with small (<2.5 cm) large partial uterine septum (>2.5 cm) and by Tomazevic et al. [46], who stated that the clinical behavior of women with small septa is not different from that of women with large septa.

Venetis et al. [32], in their systematic review of comparative studies, examined the value of hysteroscopic septotomy in reproduction. After hysteroscopic treatment, they found an evident reduction in the probability of spontaneous miscarriage (RR: 0.37, 95% CI 0.25–0.55). Although not still statistically significant, septotomy seems to have the same optimistic effect on premature labor (RR: 0.66, 95% CI 0.29–1.49). On the contrary, they failed to find any difference in the probability of pregnancy achievement after surgery (RR: 1.14, 95% CI 0.79–1.65) [32]. However, the majority of the limited evidence included in this meta-analysis is based on retrospective studies with potential bias, and there is still need for sufficiently powered randomized controlled trials [32].

In the presence of a T-shaped configuration, an increased risk of infertility is reported along with compromised pregnancy outcomes such as miscarriage, ectopic pregnancies, and premature deliveries. Indications for surgical repair of T-shaped uterus is repeated miscarriage, preterm deliveries, long-term infertility, implantation failures, or an upcoming IVF treatment [33,47,48].

It is important to highlight the promising results in terms of reproductive outcome. There are two large studies that retrospectively evaluated the postoperative outcome after surgery for T-shaped uterus. Fernandez et al. [33] reported (49.5%) pregnancy rates after the hysteroscopic metroplasty with a mean time until the first conception of 10.5 months. Sixty-three percent of these women were DES-exposed. Miscarriage rate was 36.8% and 8 pregnant women delivered before 30 weeks of gestation. Among those with secondary infertility, the first trimester miscarriage rate decreased from 78.2% to 26.9% ($p < 0.05$) and the live birth rate increased up to 73% after the reconstructive surgery [33].

Meier et al. [48], in a pool of 100 women without DES-exposure, reported 57% of pregnancy rates, with the median time to the first pregnancy of 4 months (intermediate analysis). Miscarriage rate was 16%, and no ectopic pregnancy was reported, while 36 deliveries were at term [48].

Concluding, if we disregard the fact that the above results are based on retrospective studies, it is obvious that surgical enlargement of the endometrial cavity ameliorates the reproductive outcomes.

On the basis of the best currently available evidence, it seems that surgical treatment is indicated in women presenting with symptoms related to specific uterine anomalies. Therefore, women with a dysmorphic (class U1 in ESHRE/ESGE Classification), septate (class U2 in ESHRE/ESGE Classification), or bicorporeal septate (class U3 in ESHRE/ESGE Classification) uterus presenting with infertility or poor pregnancy outcome are candidates for surgical repair of the deformity. Furthermore, women with rudimentary uterine horn having functional endometrium (classes U4 and U5 in ESHRE/ESGE Classification) are also candidates for surgical removal of the rudimentary cavitated horn because of the presence of symptoms and complications.

Rudimentary horns with cavity (ESHRE/ESGE class U4a/U5a) have robust indications for surgical treatment because of symptoms and signs such as amenorrhea, severe dysmenorrhea, hematometra, retrograde menstruation, increased risk of endometriosis, and, rarely, ectopic pregnancy. The therapeutic objectives should always be pain relief and preservation of sexual and reproductive function, if possible [36,38,49].

Surgical techniques for the management of congenital uterine anomalies

Class U1a (ESHRE/ESGE classification): Dysmorphic (T-shaped) uterus

Dysmorphic T-shaped uterus is characterized by a narrow cavity due to the thickened lateral uterine walls [10,16]. The primary objective of the surgeon is to restore the normal triangular anatomy of the uterine cavity through incisions in the lateral walls of the dysmorphic uterus and, if necessary, in the fundus. Hysteroscopic scissors, monopolar or bipolar resectoscope, mini-hysteroscopes with 5 Fr needles, or micro-scissors could be used for the enlargement of the endometrial cavity by making successive incisions along an initial incision line from each tubal ostium to the isthmus uteri. Fundal

incision should be made if there is a coexisting fundal indentation. Avoidance of blind cervical dilatation and vaginoscopic approach is suggested to reduce the risk of unnecessary trauma or uterine perforations [33,48]. Potential complications are intrauterine adhesions, cervical insufficiency, and abnormal placentation in a future pregnancy. To prevent adhesions, an antiadhesion gel barrier is suggested to be inserted into the endometrial cavity [48].

Class U2 (ESHRE/ESGE classification): Septate uterus

Septum resection is a feasible procedure and can be easily performed by hysteroscopy. During the procedure, the tubal ostia are the surgical landmarks for proper orientation. Under clear vision of the cavity and its deformity, the septum is resected starting from the distal (outer) part of the septum. The incision of the septum is made equidistantly from the anterior and the posterior uterine wall and the procedure is completed when good visualization of a restored triangular cavity occurs, with free movement of the hysteroscope between the two ostia and exposure of the muscle fibers of the fundus.

Occasionally, a cervical septum (class U2C1) or a double cervix (class U2C2) might also be present. Incision of a coexisting cervical septum might be performed, although there are still some concerns about a potential cervical weakness after surgery [50–52]. On the other hand, in cases of a double cervix and complete septate uterus, unification of the cavity should only be performed from the level of isthmus up to the fundus; repair of the cervical deformity should be avoided because it is too traumatic for the cervix and it is associated with cervical insufficiency in a subsequent pregnancy. Unification of the cavity at the level of isthmus could be done blindly with hysteroscopic scissors after proper mapping with 3D ultrasound.

Traditionally, the instrument used for hysteroscopic metroplasty is the resectoscope. After cervical dilatation the procedure is based on the activation of an electrode (monopolar or bipolar). The cutting electrode more widely used is the 90°-angled electrode. When monopolar energy is used, the distention medium is nonionic low-viscosity fluid (sorbitol, dextran, and glycine). When surgery is prolonged, there is a risk of fluid overload complications [53]. When bipolar energy is used, the distention medium of the cavity is isotonic saline solution, and therefore, the risk of complications due to intravasation is low.

Simple operative hysteroscopes are also universally used for septum incision. Through the 5 Fr operative channel, hysteroscopic cold scissors or energy modalities can be introduced to perform the procedure. Septum consists mainly of fibrotic tissue with minimal vascularization. Hence, mechanical incision by scissors is simple and safe. Bipolar needle electrodes or NdYag laser fiber, despite their cost, has also been used as alternative hysteroscopic modalities for septum incision [54–56]. All hysteroscopic uterine septum resection procedures should be performed in the early proliferative phase of the cycle, and they are considered as day case or even office procedures.

Class U3 (ESHRE/ESGE classification): Bicorporeal uterus

One of the most common CUA is bicorporeal uterus (class U3), defined as any uterus having an abnormal fundus external indentation due to a paramesonephric duct fusion defect; complete bicorporeal uterus could be combined with the presence of double cervix (former AFS didelphys uterus). The necessity of surgical repair of this specific anomaly is currently highly debatable and generally not indicated because it is too traumatic for the uterus, and there are serious concerns about future fecundity and uterine integrity in a subsequent pregnancy, although an improvement of pregnancy outcome was reported by groups performing the procedure [57–59].

Historically, Strassman metroplasty by laparotomy was the gold standard for surgical correction of bicorporeal uterus [57]. The procedure involves a single longitudinal incision from one cornua to the other up to the endometrial cavity with the goal to unify the two endometrial cavities of an otherwise divided uterus. Then, eversion of each horn is made, and a single layer of interrupted figure-of-eight sutures is placed transversely to form a single uterine cavity beginning from the posterior and continuing with the anterior wall.

Recently, laparoscopic unification of bicorporeal uterus with normal (class U3bC0) or double cervix (class U3bC2) has been also reported [60], but it is technically quite challenging, and only very

experienced surgeons should perform it [60,61]. Laparoscopic subtotal hysterectomy in a woman with U3bC2 uterus for gynecological reasons (menorrhagia) has been recently reported as well [62]. The surgical steps of the procedure were similar to those of laparoscopic subtotal hysterectomy performed in morphologically normal uteri [63].

Counseling pregnant women with bicornuate uterus, either surgically repaired or not, about the necessity of a cesarean section is crucial because the risk of uterine rupture is increased [64]. Cervical cerclage might be considered because cervical incompetence is an issue in patients with bicorporeal uterus [65].

In cases of bicorporeal uterus with unilateral cervical aplasia (class U3bC3), removal of the obstructed hemi-uterus is indicated to relieve from obstructing symptoms and avoid a pregnancy in the obstructed part of the uterus. In these cases, the obstructed hemi-uterus might act as a rudimentary horn and has therefore similar clinical manifestation [66]. Restoration of utero-vagina continuity of the obstructed hemi-uterus might also be considered as an alternative either by laparoscopically assisted cervicoplasty in cases of cervical atresia or by isthmo-vagina anastomosis [66]. In these types of malformation, the risk of complications such as ectopic pregnancy should be addressed to the patients before surgical management.

Patients with bicorporeal uterus, double cervix, and longitudinal obstructing vaginal septum (class U3bC2V2) should be submitted to surgery by cutting or resecting the vaginal septum [66].

Finally, patients with a bicorporeal septate uterus (class U3) should be treated hysteroscopically by incising the septate part of the indentation. Improved reproductive outcome was reported post-operatively, and dysmenorrhea also remarkably improved [67,68]. In these cases, the surgeon must be very careful with the depth of incision. The risk of perforation is higher, and only the septate element should be incised. Correct preoperative diagnosis and mapping is essential to be used as a guide, and the concomitant use of ultrasonographic guidance is an option.

Classes U4a and U5a (ESHRE/ESGE classification): Rudimentary horns with cavity

According to the recently introduced ESHRE/ESGE Classification, class U4a entails cases with unicorporeal (hemi-) uterus with a rudimentary horn having cavity, and class U5a involves cases presenting with uterine aplasia with uni- or bilateral rudimentary cavity [10,16]. There are two anatomical variations concerning the attachment of the rudimentary horn to the unicorporeal uterus: either by a band of tissue or firmly [49].

Surgical excision of the rudimentary horn is the preferred treatment. This can be performed by laparotomy, but currently, laparoscopic removal is the usual practice [36,69]. Case series of successful laparoscopic rudimentary horn excision were reported by Theodoridis et al. [36] and Fedele et al. [70]. They reported that the ipsilateral fallopian tube should be removed to prevent ectopic tubal pregnancy [36,39,70,71].

The surgeon performing the procedure must pay special attention to avoid damage of the remaining unicorporeal uterus, especially in cases of broad attachment between the unicorporeal body and the rudimentary horn. Scissors, electrosurgery ultracision energy, and endoscopic staplers have been reported as tools to remove the rudimentary horn, while the simultaneous use of hysteroscopy to separate the two horns is also described [36,72,73]. The excised rudimentary horns can be removed through an enlargement of the suprapubic trocar site, by colpotomy, or using mechanical morcellation [36,49,74].

In the unlikely event of sperm migration through the peritoneal cavity, pregnancy in the rudimentary horn is possible. This rare situation may lead to other more serious complications such as rupture mainly during the second trimester and severe intraperitoneal bleeding with high maternal mortality rates. When a diagnosis of horn pregnancy is made, immediate surgical excision of the rudimentary horn and ipsilateral fallopian tube is the gold standard by either laparotomy or laparoscopy [39,71].

Regarding class U5a, prophylactic excision of the cavitated horn is still a subject of open debate. It is certain that excision is the preferred management if the patient is symptomatic with cyclic pelvic pain and/or hematocavity. The above-stated surgical steps apply here as well. An alternative aspect that should be mentioned in cases of patients with MRKH syndrome who have rudimentary functional uterine horns is the neovagina creation and uterovaginal anastomosis [75].

Summary

Congenital uterine malformations are common but not always identified. They are responsible for a variety of symptoms and health problems depending on the anatomical defect of the uterus and/or cervix. Amenorrhea, cyclical abdominal pain, retrograde menstruation and endometriosis, ectopic pregnancy in the noncommunicating horn, frustration and depression of young adolescent patients, and poor reproductive outcome are the main problems encountered. Various classification systems have been proposed for CUA, but the recently published new ESHRE/ESGE Classification seems to be a new clear and systematic categorization that could be the basis for the clinicians to rely on when they refer to CUA and their clinical impact either generally or concerning pregnancy outcomes. HSG, transabdominal (TAS) or transvaginal (TVS) 2D sonography, sonohysterography (SHG), 3D Ultrasound, MRI, hysteroscopy, and laparoscopy are the methods used to properly diagnose and classify a specific anomaly. Different techniques are described for the surgical management of dysmorphic, septate, and bicorporeal uteri, as well as noncommunicating rudimentary uterine horn with functional endometrium. Uterus, hosting the developing embryo, plays a detrimental role in implantation and evolution of pregnancy. It seems that surgical repair of uterine deformities is associated with an improvement in the achievement and evolution of pregnancy. Further investigation is required to establish unanimous guidelines for the individualized and suitable invasive or not management of CUA.

Practice points

- The new ESHRE/ESGE Classification, which has been recently published, seems to be a new, clear, and systematic categorization of CUA.
- Fertility and pregnancy outcomes are the main objective for each patient of reproductive age.
- CUA are apparently related to an impaired reproductive outcome, while their exact clinical impact, as well as the effectiveness of their treatment, is still considered controversial.
- Further large prospective studies are necessary to evaluate the role of surgical correction of uterine septum in fertility and pregnancy outcome.

Research agenda

- Most of the reviews performed to date were based on retrospective studies, and this is an important limitation.
- Many issues are still open for discussion among scientists, and prospective studies should be performed for a more reliable evaluation of outcomes of the proposed surgical techniques.
- Working on the basis for the development of unanimous well-accepted guidelines for the proper surgical management should be the main goal for all physicians involved in the field of these rare entities.

Conflicts of interest

The authors have no conflicts of interest.

References

[1] Guerrier D, Mouchel T, Pasquier L, Pellerin I. The Mayer-Rokitansky-Küster-Hauser syndrome (congenital absence of uterus and vagina) – phenotypic manifestations and genetic approaches. J Negat Results Biomed 2006;5:1.
[2] Okada A, Sato T, Ohta Y, Iguchi T. Sex steroid hormone receptors in the developing female reproductive tract of laboratory rodents. J Toxicol Sci 2005;30:75–89.
[3] Simpson JL. Genetics of the female reproductive ducts. Am J Med Genet 1999;89:224–439.
[4] MacLaughlin DT, Teixeira J, Donahoe PK. Perspective: reproductive tract development – new discoveries and future directions. Endocrinology 2001;142:2167–72.
[5] Akbas GE, Song J, Taylor HS. A HOXA10 estrogen response element (ERE) is differentially regulated by 17 beta-estradiol and diethylstilbestrol (DES). J Mol Biol 2004;340:1013–23.

[6] Ma L, Benson GV, Lim H, Dey SK, Maas RL. Abdominal B (AbdB) Hoxa genes: regulation in adult uterus by estrogen and progesterone and repression in müllerian duct by the synthetic estrogen diethylstilbestrol (DES). Dev Biol 1998;197:141–54.
[7] Moore KL, Persaud TVN, Torchia MG. The urogenital system. In before we are born: essentials of Embryology and birth defects. seventh ed. Philadelphia, PA: Saunders/Elsevier; 2008. p. 162–89.
[8] Acien P. Embryological observations on the female genital tract. Hum Reprod 1992;7:437–45.
[9] American Fertility Society. The American Fertility Society classification of adnexal adhesions, distal tubal occlusion, tubal occlusion secondary to tubal ligation, tubal pregnancies, Müllerian anomalies and intrauterine adhesions. Fertil Steril 1998;49:944–55.
[10] Grimbizis GF, Gordts S, Di Spiezio Sardo A, Brucker S, De Angelis C, Gergolet M. The ESHRE/ESGE consensus on the classification of female genital tract congenital anomalies. Hum Reprod 2013;28:2032–44.
[11] Grimbizis GF, Campo R. Congenital malformations of the female genital tract: the need for a new classification system. Fertil Steril 2010;94:401–7.
[12] Acien P, Acien M, Sanchez-Ferrer M. Complex malformations of the female genital tract: new types and revision of classification. Hum Reprod 2004;19:2377–84.
[13] Acien P, Acien MI. The history of female genital tract malformation classifications and proposal of an updated system. Hum Reprod Update 2011;17:693–705.
[14] Oppelt P, Renner SP, Brucker S, Strissel PL, Strick R, Oppelt PG, et al. The VCUAM (vagina cervix uterus adnex associated malformation) classification: a new classification for genital malformations. Fertil Steril 2005;84:1493–7.
[15] Grimbizis GF, Gordts G, Di Spiezio SA, Brucker S, De Angelis C, Gergolet M, et al. The ESHRE/ESGE consensus on the classification of female genital tract congenital malformations. Gynecol Surg 2013;10:199–212.
[16] Grimbizis GF, Di Spiezio Sardo A, Saravelos SH, Gordts S, Exacoustos C, Van Schoubroeck D, et al. The Thessaloniki ESHRE/ESGE consensus on diagnosis of female genital anomalies. Hum Reprod 2016;31:2–7.
[17] Grimbizis GF, Di Spiezio Sardo A, Saravelos SH, Gordts S, Exacoustos C, Van Schoubroeck D, et al. The Thessaloniki ESHRE/ESGE consensus on diagnosis of female genital anomalies. Gynecol Surg 2016;13:1–16.
[18] Byrne J, Nussbaum-Blask A, Taylor WS, Rubin A, Hill M, O'Donnell R, et al. Prevalence of Mullerian duct anomalies detected at ultrasound. Am J Med Genet 2000;94(1):9–12.
[19] Acien P. Incidence of Mullerian defects in fertile and infertile women. Hum Reprod 1997;12(7):1372–6.
[20] Tulandi T, Arronet GH, McInnes RA. Arcuate and bicornuate uterine anomalies and infertility. Fertil Steril 1980;34(4):362–4.
[21] Wu MH, Hsu CC, Huang KE. Detection of congenital mullerian duct anomalies using three-dimen- sional ultrasound. J Clin Ultrasound 1997;25(9):487–92.
[22] Grimbizis GF, Camus M, Tarlatzis BC, Bontis JN, Devroey P. Clinical implications of uterine malformations and hysteroscopic treatment results. Hum Reprod Update 2001;7:161–4.
[23] Saravelos SH, Cocksedge KA, Li T-C. Prevalence and diagnosis of congenital uterine anomalies in women with reproductive failure: a critical appraisal. Hum Reprod Update 2008;14:415–9.
[24] Chan YY, Jayaprakasan K, Zamora J, Thornton JG, Raine-Fenning N, Coomarasamy A. The prevalence of congenital uterine anomalies in unselected and high-risk populations: a systematic review. Hum Reprod Update 2011;17:761–71.
[25] Raga F, Bauset C, Remohi J, Bonilla-Musoles F, Simon C, Pellicer A. Reproductive impact of congenital Müllerian anomalies. Hum Reprod 1997;vol. 12:2277–81.
[26] Kupesic S. Clinical implications of sonographic detection of uterine anomalies for reproductive outcome. Ultrasound Obstet Gynecol 2001;18:387–400.
[27] Taylor E, Gomel V. The uterus and fertility. Fertil Steril 2008;89:1–16.
[28] Reichman D, Laufer MR, Robinson BK. Pregnancy outcome in unicornuate uteri: a review. Fertil Steril 2009;91(5):1886–94.
[29] Saravelos SH, Cocksedge KA, Li TC. The pattern of pregnancy loss in women with congenital uterine anomalies and recurrent miscarriage. Reprod Biomed Online 2010 Mar;20(3):416–22.
[30] Prior M, Richardson A, Asif S, Polanski L, Parris-Larkin M, Chandler J, et al. Outcome of assisted reproduction in women with congenital uterine anomalies: a prospective observational study. Ultrasound Obstet Gynecol 2018;51:110–7.
[31] Chan YY, Jayarpakasan K, Tan A, Thornton JG, Coomarasamy A, Raine-Fenning NJ. Reproductive outcomes in women with congenital uterine anomalies: a systematic review. Ultrasound Obstet Gynecol 2011;38:371–82.
[32] Venetis C, Papadopoulos S, Campo R, Gordts S, Tarlatzis BC, Grimbizis GF. Clinical implications of congenital uterine anomalies: a meta-analysis of comparative studies. RBM Online 2014;26:665–83.
[33] Fernandez H, Garbin O, Castaigne V, Gervaise A, Levaillant JM. Surgical approach to and reproductive out come after surgical correction of a T-shaped uterus. Hum Reprod 2011;26(7):1730–4.
[34] Barranger E, Gervaise A, Doumerc S, Fernandez H. Reproductive performance after hysteroscopic metroplasty in the hypoplastic uterus: a study of 29 cases. BJOG 2002;109(12):1331–4.
[35] Heinonen PK. Unicornuate uterus and rudimentary horn. Fertil Steril 1997;68:224–30.
[36] Theodoridis TD, Saravelos H, Chatzigeorgiou KN, Zepiridis L, Grimbizis GF, Vavilis D, et al. Laparoscopic management of unicornuate uterus with non-communicating rudimentary horn (three cases). Reprod Biomed Online 2006;12:126–8.
[37] Fedele L, Bianchi S, Di Nola G, Franchi D, Candiani GB. Endometriosis and non-obstructive mullerian anomalies. Obstet Gynecol 1992;79:515–7.
[38] Jayasinghe Y, Rane A, Stalewski H, Grover S. The presentation and early diagnosis of the rudimentary uterine horn. Obstet Gynecol 2005;105(6):1456–67.
[39] Daskalakis G, Pilalis A, Lykeridou K, Antsaklis A. Rupture of noncommunicating rudimentary uterine horn pregnancy. Obstet Gynecol 2002;100:1108–10.
[40] Doridot V, Gervaise A, Taylor S, Frydman R, Fernandez H. Obstetric out come after endoscopic transection of the uterine septum. J Am Assoc Gynecol Laparoscopists 2003;10(2):271–5.
[41] Homer HA, Li TC, Cooke ID. The septate uterus: a review of management and reproductive outcome. Fertil Steril 2000;73(1):1–14.
[42] Nouri K, Ott J, Huber JC, Fischer EM, Stogbauer L, Tempfer CB. Reproductive outcome after hysteroscopic septoplasty in patients with septate uterus. A retrospective cohort study and systematic review of the literature. Reprod Biol Endocrinol 2010;8:52.

[43] Mollo A, De Franciscis P, Colacurci N, Cobellis L, Perino A, Venezia R, et al. Hysteroscopic resection of the septum improves the pregnancy rate of women with unexplained infertility: a prospective controlled trial. Fertil Steril 2009;91(6):2628–31.
[44] Gergolet M, Campo R, Verdenik I, Suster NK, Gordts S, Gianaroli L. No clinical relevance of the height of fundal indentation in subseptate or arcuate uterus: a prospective study. Reprod Biomed Online 2012;24:576–82.
[45] Paradisi R, Barzanti R, Natali F, Guerrini M, Battaglia C, Seracchioli R, et al. Hysteroscopic metro- plasty: reproductive outcome in relation to septum size. Arch Gynecol Obstet 2014;289(3):671–6.
[46] Tomazevic T, Ban-Frangez H, Virant-Klun I, Verdenik I, Pozlep B, Vrtacnik-Bokal E. Septate, subseptate and arcuate uterus decrease pregnancy and live birth rates in IVF/ICSI. Reprod Biomed Online 2010;21:700–5.
[47] Garbin O, Ohl J, Bettahar-Lebugle K, Dellenbach P. Hysteroscopic metroplasty in diethylstilboestrol exposed and hypoplastic uterus: a report on 24 cases. Hum Reprod 1998;13:2751–5.
[48] Meier R, De Bruyn C, Mestdagh G, Dhont N, Ombelet W, Campo R. Reproductive outcomes after hysteroscopic management of dysmorphic uterus: report of 100 cases. Selected abstract ESGE 23rd annual congress, Brussels. 2014.
[49] Falcone T, Gidwani G, Paraiso M, Beverly C, Goldberg J. Anatomical variation in the rudimentary horns of a unicornuate uterus: implications for laparoscopic surgery. Hum Reprod 1997;12(2):263–5.
[50] Pavone ME, King JA, Vlahos N. Septate uterus with cer- vical duplication and a longitudinal vaginal septum: a müllerian anomaly without a classification. Fertil Steril 2006;85(2):494. e9–10.
[51] Saygili-Yilmaz ES, Erman-Akar M, Bayar D, Yuksel B, Yilmaz Z. Septate uterus with a double cervix and longi- tudinal vaginal septum. J Reprod Med 2004;49(10):833–6. PubMed PMID: 15568409.
[52] Celik NY, Mulayim B. A mullerian anomaly "without classification": septate uterus with double cervix and longitudinal vaginal septum. Taiwan J Obstet Gynecol 2012;51(4):649–50.
[53] Vercellini P, Rossi R, Pagnoni B, Fedele L. Hypervolemic pulmonary edema and severe coagulopathy after intrauterine dextran instillation. Obstet Gynecol 1992;79(5 Pt 2):838–9.
[54] Colacurci N, De Franciscis P, Mollo A, Litta P, Perino A, Cobellis L. Small-diameter hysteroscopy with Versapoint versus resectoscopy with a unipolar knife for the treatment of septate uterus: a prospective random- ized study. J Minim Invasive Gynecol 2007;14(5):622–7.
[55] 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 Pt 1):87–90.
[56] Fedele L, Arcaini L, Parazzini F, Vercellini P, Di Nola G. Reproductive prognosis after hysteroscopic metro- plasty in 102 women: life-table analysis. Fertil Steril 1993;59(4):768–72.
[57] Strassman EO. Fertility and unification of double uterus. Fertil Steril 1966;17:165–76.
[58] Lolis DE, Paschopoulos M, Makrydimas G, Zikopoulos K, Sotiriadis A, Paraskevaidis E. Reproductive outcome after Strassman metroplasty in women with a bicornuate uterus. J Reprod Med 2005;50(5):297–301.
[59] Papp Z, Mezei G, Gávai M, Hupuczi P, Urbancsek J. Reproductive performance after transabdominal metroplasty: a review of 157 consecutive cases. J Reprod Med 2006;51(7):544–52.
[60] Sinha R, Mahajan C, Hegde A, Shukla A. Laparoscopic metroplasty for bicornuate uterus. J Minim Invasive Gynecol 2006; 13(1):70–3.
[61] Alborzi S, Asadi N, Zolghardri J, Alborzi S, Alborzi M. Laparoscopic metroplasty in bicornuate and didelphic uteri. Fertil Steril 2009;92:352–5.
[62] Erian J, Lee C, Watkinson S, Alsheikh Ali A, Chaudhari L, Hill N. Laparoscopic subtotal hysterectomy in a case of uterine didelphys. Arch Gynecol Obstet 2012;285:139–41.
[63] Erian J, El-Toukhy T, Chandakas S, Theodoridis T, Hill N. One hundred cases of laparoscopic subtotal hysterectomy using the PK and lap-loop systems. J Minim Invasive Surg 2005;12:365–9.
[64] Reichman DE, Laufer MR. Congenital uterine anomalies affecting reproduction. Best Pract Res Clin Obstet Gynaecol 2010; 24(2):193–208.
[65] Golan A, Langer R, Wexler S, Seveg E, Niv D, David MP. Cervical cerclage – its role in the pregnant anomalous uterus. Int J Fertil 1990;35:164–70.
[66] Fedele L, Motta F, Frontino G, Restelli E, Bianchi S. Double uterus with obstructed hemivagina and ipsilateral renal agenesis: pelvic anatomic variants in 87 cases. Hum Reprod 2013;28(6):1580–3.
[67] El Saman AM, Nasr A, Tawfik RM, Saadeldeen HS. Müllerian duct anomalies: successful endoscopic management of a hybrid bicornuate/septate variety. J Pediatr Adolesc Gynecol 2011;24:e89–92.
[68] El Saman AM, Shahin AY, Nasr A, Tawfi k RM, Saadeldeen HS, Othman HR, et al. Hybrid septate uterus, coexistence of bicornuate and septate varieties: a genuine report. J Obstet Gynaecol Res 2012;38(11):1308–14.
[69] Canis M, Wattiez A, Pouly JL, Mage G, Manhes H, Bruhat MA. Laparoscopic management of unicornuate uterus with rudimentary horn and unilateral extensive endometriosis: case report. Hum Reprod 1990;5:819–20.
[70] Fedele L, Bianchi S, Zanconato G, Berlanda N, Bergamini V. Laparoscopic removal of the cavitated noncommunicating rudimentary uterine horn: surgical aspects in 10 cases. Fertil Steril 2005;83:432–6.
[71] Dulemba JF, Midgett WA, Freeman MVR. Laparoscopic management of a rudimentary horn pregnancy. J Am Assoc Gynecol Laparoscopists 1996;3:627–30.
[72] Mais V, Guerriero S, Ajossa S, Piras B, Melis GB. Endosonographic diagnosis, pre-operative treatment and laparoscopic removal with endoscopic stapler of a rudimentary horn in a woman with unicornuate uterus. Hum Reprod 1994;9: 1297–9.
[73] Nezhat F, Nezhat C, Bess O, Nezhat CH. Laparoscopic amputation of noncommunicating rudimentary horn after hysteroscopic diagnosis: a case study. Surg Laparosc Endosc 1994;4:155–6.
[74] Nakhal RS, Cutner AS, Hall-Craggs M, Creighton SM. Remnant functioning cervical tissue after laparoscopic removal of cavitated noncommunicating rudimentary uterine horn. J Minim Invasive Gynecol 2012;19(6):768–71.
[75] Grimbizis GF, Mikos T, Papanikolaou A, Theodoridis T, Tarlatzis BC. Successful isthmoneovagina anastomosis after Davydov's colpopoiesis in MRKH patients with functional rudimentary uterine horn. J Minim Invasive Gynecol 2015 Jan;22(1): 142–50.