Three-dimensional Ultrasonography in the Diagnosis of Müllerian Duct Anomalies

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Abstract

Aims: We studied the effectiveness of three-dimensional (3D) ultrasonography in the diagnosis of uterine malformations.

Methods: 175 patients with clinical or ultrasonographic suspicion of uterine malformation were studied between November 2004 and June 2008. In all women we measured uterine volume for processing and later reconstruction of 3D images. Cases in which no anomaly was detected with the 3D technique were excluded from study. A thorough physical genital examination with speculum was done before or after ultrasonography, except in three women with an imperforate hymen. Uterine malformations were recorded in detail, and the findings were catalogued according to the American Fertility Society (AFS) classification. In 32 women magnetic resonance (MR) imaging was also used, and agreement between the two techniques was calculated with the kappa index.

Results: The 175 müllerian anomalies we analyzed were diagnosed as agenesis (1 case), unicornuate uterus (1 genuine, 1 communicating), didelphys uterus (4), bicornuate uterus (22), septate uterus (80, 8 with two cervices) and arcuate uterus (68). For 1 unicornuate, 3 bicornuate, 25 septate (4 with two cervices) and 3 arcuate uteri we performed MR imaging. Diagnostic correlation between 3D ultrasonography and MR imaging was obtained in all cases according to the AFS classification (kappa = 100%); concordance was also seen for descriptions of associated uterine malformations except for two cases: 1 bicornuate uterus with the additional presence of a cervical septum as detected by MR imaging, which was not found on hysteroscopy for resection, and 1 septate uterus that appeared to have two cervices on 3D ultrasonography in a patient in whom physical examination was not possible, and in whom MR imaging showed a complete septum with hypointense signals (kappa = 93.45%; 95% confidence interval 80.75-100%).

Discussion: Owing to its ability to clearly render contours of anatomical structures, 3D ultrasonography provides detailed images of uterine malformations and yields very similar results to those obtained with MR imaging. For an accurate comparison of the two techniques, ultrasonography should be accompanied by gynecologic physical exploration, since the two methods yield equivalent results for the relation between the uterine cavity and the fundus. MR imaging is especially useful to evaluate the cervix and vagina.

INTRODUCTION

The uterus and probably the upper part of the vagina (controversy over this point not withstanding)[1] are derived from the paramesonephric or Müllerian ducts, after which anomalies in these structures are named. The Müllerian ducts start to differentiate to form the uterus in female embryos during the sixth week of gestation (until this time they are identical in male and female embryos), and descend in parallel and externally to the mesonephric ducts to drain into the urogenital sinus. Medially they cross the Wolffian or mesonephric ducts ventrally, and fuse along the midline to form the uterine primordium. The septum is subsequently reabsorbed in a craniocaudal direction, or according to an alternative hypothesis—fusion takes place bidirectionally simultaneously from the center toward both ends, with later resorption.[2] This process accounts for certain anomalies that are not explained by the classic theory of uterine development.

Uterine anomalies make up a heterogeneous group of congenital malformations that can arise due to lack of development of the Müllerian ducts, incomplete fusion, or alterations in septum resorption. It should be noted that any combination of malformations can arise, and pure forms of different entities cannot always be distinguished.

The prevalence of uterine anomalies is difficult to establish. It is estimated that in the general population the prevalence of uterine malformations is 0.4%, with different authors reporting rates that range from 0.1 to 3%,[3,4] whereas a prevalence of 4% has been described among infertile women, although not all authors distinguished between this group and the general population.[5] Among patients with recurrent miscarriages the rates vary from 3 to 38%.[6-10] This disparity among different publications reflects the use of different diagnostic techniques, nonhomogeneous population samples, and differences in the

clinical entities of uterine malformation considered by different authors. Symptoms vary from asymptomatic to serious gynecological (obstructive hematocolpos, hematometra) or obstetric problems in up to 25% of all cases, compared to 10% in the general population (recurrent miscarriage, placental insufficiency, incompetent cervix, etc.).[11] The most frequent anomalies in asymptomatic women and patients with recurrent first trimester miscarriages are arcuate and subseptate uterus. There are no differences in the size of the indentation between the two groups (except for nullipara), but in the recurrent miscarriage group, the uterine cavities are smaller than in healthy women regardless of parity.[12] Arcuate uterus tends to be associated with second trimester miscarriage, whereas first trimester miscarriage is more frequent in women with subseptate uterus.[13-15] Other anomalies are often present, most of them are urologic in nature given the parallel embryologic origin of the two organ systems.[2]

Uterine malformations tend to be sporadic; however multiple factors can be involved in their origin. This situation has been described in the etiology of septate uterus in the absence of the Bcl2 gene.[16] Some malformations appear in different chromosomal syndromes, although most women tend to have a normal karyotype and it is still unknown whether vertical inheritance is involved. Viral infections, teratogenic medicines (mainly diethylstilbestrol, DES) and other causes also seem to be related to the etiology of these malformations.[11,17, 18]

Many classification systems have been applied to uterine malformations. The most widely accepted is the American Fertility Society (AFS) system published in 1998, based not only on embryologic factors but also on prognosis, clinical features and treatment.[19] Although the AFS system is not perfect, it provides a useful categorization of the anomalies into seven groups (Fig. 1).

Role of Three-dimensional Ultrasonography in the Diagnosis of Uterine Malformations

Several techniques are available to evaluate uterine malformations. For studies of the uterine cavity, hysteroscopy and hysterosalpingography are especially useful. On the other hand, laparotomy and laparoscopy are helpful for examinations of the uterine fundus. However, only two methods allow both structures to be studied simultaneously (a requirement for diagnosis): magnetic resonance (MR) imaging and three-dimensional ultrasonography (3D US).

The introduction of 3D US in the field of uterine malformations was an important innovation because this noninvasive, reproducible, low-cost technique is well tolerated and makes highly precise diagnoses possible. In 1995 Jurkovik et al. studied the efficacy of two-dimensional (2D) and 3D US compared to hysterosalpingography (HSG). Their results showed that 3D US was more effective for the diagnosis of arcuate uterus, and had a high positive predictive value (PPV)
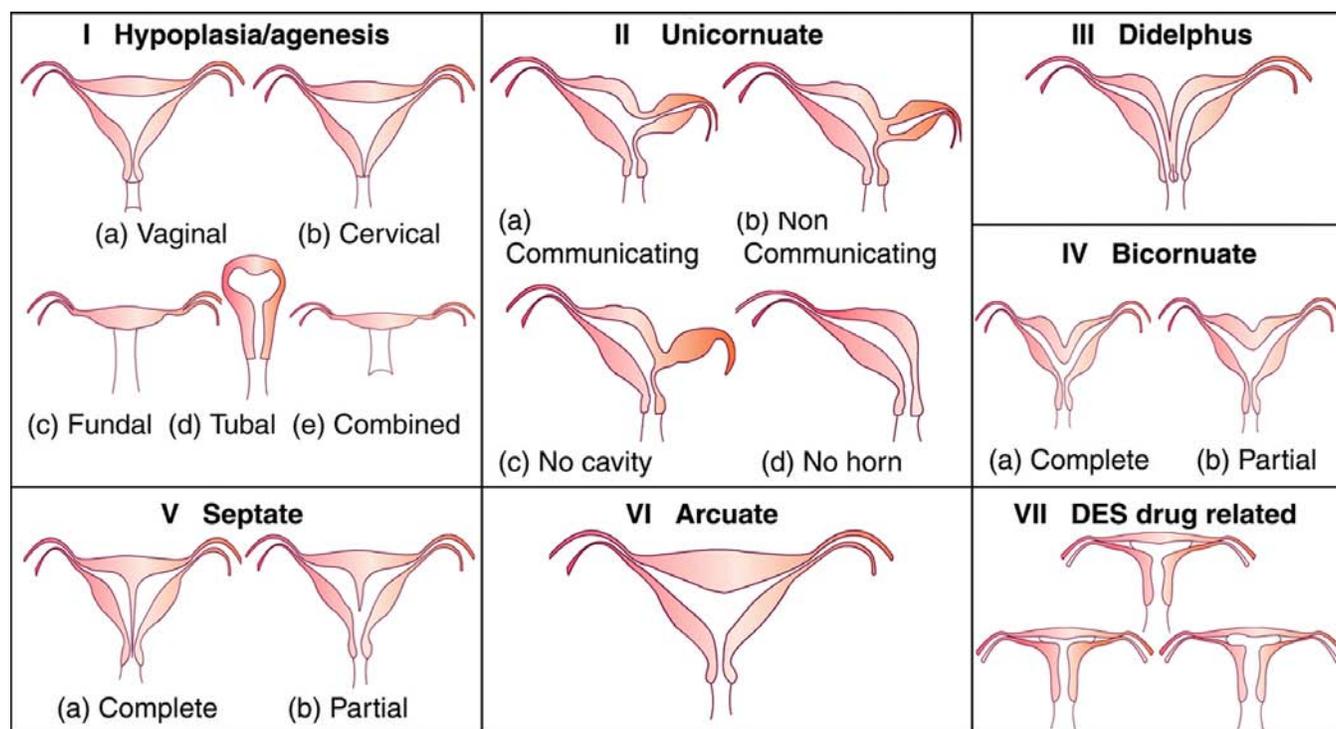

Fig. 1: American fertility society classification of uterine malformations[19]

for major anomalies, especially for distinguishing bicornuate from subseptate uterus.[20] More recent work by Raga et al.[21] found 91.6% agreement between 3D US and HSG when evaluating the fundus, and 100% efficacy with regard to examinations of the uterine cavity when 3D US was compared to laparoscopy. Wu et al.[22] correlated the technique (also using HSG and 2D US) with laparoscopy or hysteroscopy, and found 92% efficacy for the diagnosis of septate uterus and 100% efficacy for bicornuate uterus. In 2007, Mohamed et al. published a study that compared 3D US versus laparoscopy and hysteroscopy. They achieved a sensitivity of 97%, a specificity of 96%, a PPV of 92%, and a negative predictive value (NPV) of 99%.[23] In 2001, Salim et al demonstrated the reproducibility of 3D US for the diagnosis of uterine malformations, and modified the AFS classification according to ultrasonographic parameters.[24] These authors noted that 3D US was worthwhile as a screening method, since it improved reproductive outcome.[15] The same conclusion was reached by Kupesic and Kurjak based on the importance of septostomy. These authors studied large series of cases, the largest of which included 3850 patients from a tertiary infertility clinic where 894 had a uterine malformation, and detected 689 septate uteri.[25,26]

Magnetic resonance imaging was considered the gold standard for the diagnosis of müllerian duct anomalies, and multiple studies documented its efficacy.[27-30] However, 3D US can be considered a useful alternative to this technique, because in addition to its lower cost and the better tolerance by patients, it provides images of very similar quality that are almost superimposable with MR images for diagnostic purposes.[31] Studies in progress to compare these two methods have validated 3D US by documenting a high correlation between the findings obtained with the two techniques. However, a good patient history and thorough gynecologic physical examination are a necessary complement to MR imaging.

Ultrasonographic Diagnosis of Müllerian Duct Anomalies

How can a uterine malformation be diagnosed by ultrasonography? Usually the woman will have clinical symptoms or a suggestive physical exploration (vaginal partitions, two cervices, etc.) and follow-up will be needed for the diagnosis. Occasionally a malformation might be noticed during routine ultrasonography. In most uterine anomalies, 2D US will reveal two uterine cavities but little additional information on which to base a diagnosis. This is generally the case for nonextreme entities such as arcuate, septate and bicornuate uterus, and it is basically these forms that need to be distinguished in order to indicate suitable treatment.

Three dimensional US is suitable to study the relationship between the cavity and fundus, and almost always allows a correct diagnosis of nonextreme entities. The addition of the coronal plane (which cannot be acquired with conventional or 2D US) is the key enhancement that makes it possible to visualize these anomalies. Uterine volume needs to be measured for processing and later reconstruction into 3D images (rendering or reconstruction is part of the post-acquisition work required for diagnosis). By combining different planes the anomaly becomes available for study not only in the coronal plane (the most informative), but also in sagittal and axial sections (depending on the planes chosen for image capture), as with MR imaging. The data are not observer-dependent (any operator can use the acquired volumes) or exploration time-dependent (postacquisition rendering can be done later). The volumes obtained can be sent anywhere in the world to be processed and studied by any specialist with the required software.

Although one of the uses of 3D US is to evaluate morphology, this technique also makes it possible to measure distances of interest in the coronal plane[24] (or any other plane) and to calculate cavity volumes [e.g. with Virtual Organ Computer-aided Analysis™ (VOCAL)] (Fig. 2). This information can be used to obtain a reproductive prognosis, and to obtain informative images of blood supply.[32,33]

Figure 3 illustrates the shape of a normal uterus reconstructed with 3D US. This picture will serve as a reference to facilitate interpretation of the images used here to illustrate different entities of the AFS classification.

Class I: Agenesis or hypoplasia

This group accounts for 5 to 10% of all uterine malformations. As seen in Figure 1, the most frequent type corresponds to the Rokitansky-Kuster-Hauser syndrome, characterized by vaginal and uterine agenesis in 90% of cases. Three-dimensional US does not appear to be the most appropriate method for detecting agenesis or hypoplasia, since the diagnosis can be made by physical examination and conventional 2D US.
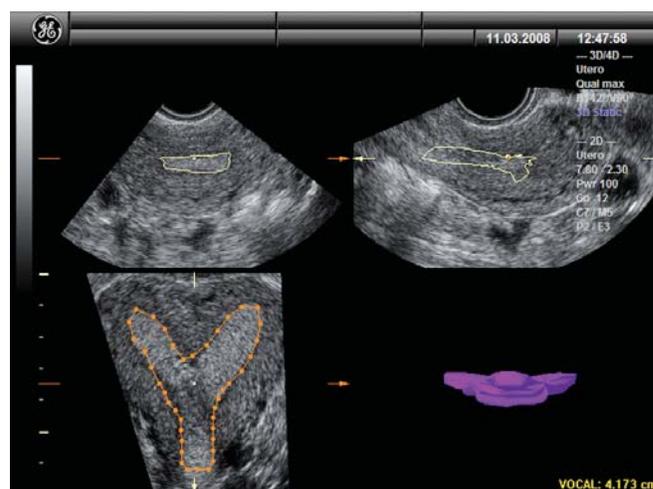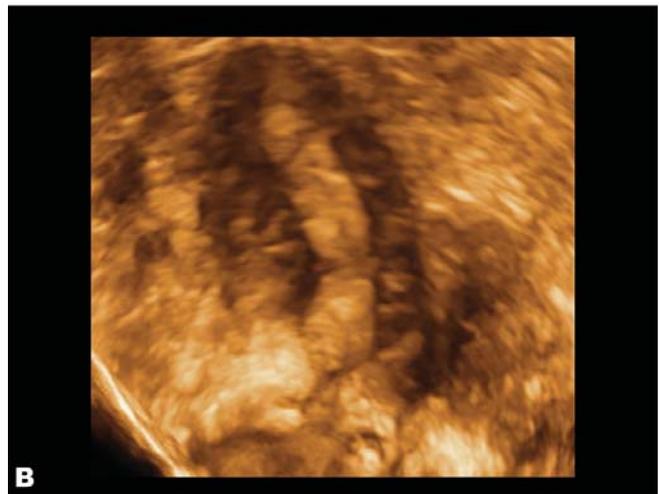

Fig. 2: Virtual organ computer-aided analysis showing the volume of the uterine cavity in a septate uterus
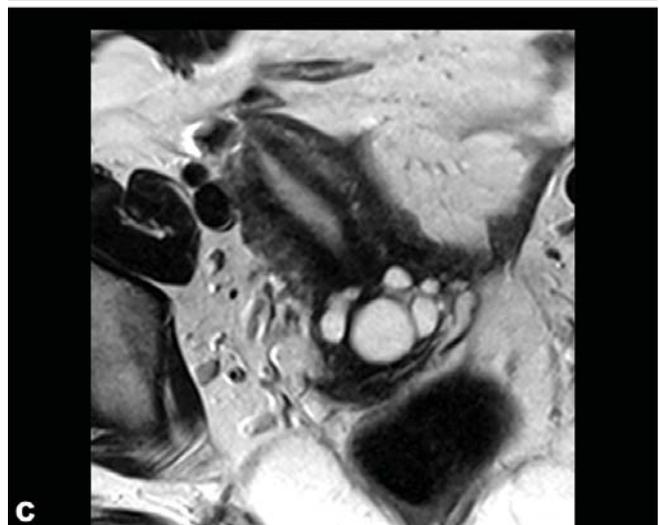
Fig. 3: Normal uterus in 3D US

Class II: Unicornuate Uterus

This anomaly results from poor or absent development of the paramesonephric ducts, and accounts for 20% of all uterine malformations. Figure 1 shows the subgroups of unicornuate uterus. (Figs 4A to C) depicts a unicornuate uterus seen with 2D US (note the single cavity, which is difficult to establish with this technique), 3D US (in the coronal plane the cavity does not appear triangular), and MR imaging.

Class III: Didelphys Uterus

This malformation, which comprises 5% of all uterine anomalies, is caused by complete nonfusion of the müllerian ducts, and is characterized by two completely separate hemiuteri with two uterine bodies and two cervices with no connection between the cervical cavities. The hemiuteri are tenuously connected via an isthmus in the serosal layer. In some cases one of the hemiuteri may be obstructed (blind hemivagina due to combined alteration of the urogenital sinus), resulting in hematocolpos or hematometra with acute clinical symptoms during menarche similar to those produced by a unicornuate noncommunicating uterus. It is not uncommon to find associated renal homolateral agenesis.[34] A precise diagnosis can be accomplished with physical examination (which discloses vaginal septae) and later exploration with 2D US. Studies with 3D US can be costly, since the two horns are generally separated by a considerable distance and may therefore appear in different planes, making image acquisition and rendering difficult (Fig. 5).

Class IV: Bicornuate Uterus

When müllerian duct fusion is incomplete, a bicornuate uterus results. The two hemiuteri are linked through a variable area in
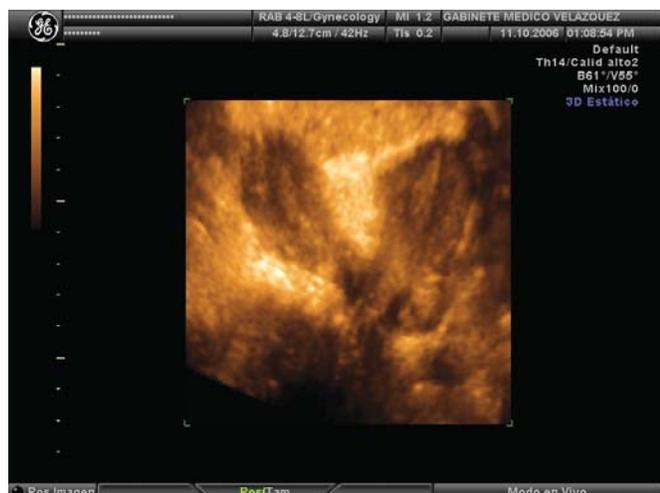

Figs 4A to C: Genuine unicornuate uterus in 2D US (A) 3D US (B) and MR imaging (C)

Fig. 5: Didelphys uterus in 3D US

Fig. 6: Bicornuate uterus in 3D US. A line drawn from horn to horn transects the fundus

the lower portion of the organ depending on the severity of the anomaly, and there is usually only one cervix although two cervices can be present. Bicornate uterus accounts for 10% of all uterine malformations.

Symmetry of the two hemiuteri is one of its main characteristics of this anomaly, and is what distinguishes it from communicating unicornuate uterus. In contrast to arcuate and septate uterus, a central cleft is present in the serosa of the fundus.

The clinical features related to this class of anomaly are mainly obstetric and tend to be less marked that in septate uterus. Treatment should be based on the severity of the clinical features, hence the importance of a correct diagnosis to distinguish between the two entities (given that sometimes, in view of its poor prognosis, treatment should begin promptly for septate uterus). Troiano and McCarthy proposed a practical formula to distinguish between septate and bicornuate uterus.[35] If a line drawn from horn to horn crosses or is less than 5 mm from the fundus, bicornuate uterus should be diagnosed. In contrast, if the line is further from the fundus, septate uterus should be diagnosed regardless of the appearance of the fundus (i.e. convex, flat, or with a slight indentation). Figure 6 shows a 3D US image illustrating bicornuate uterus. In this type of anomaly the horns are usually more than 4 cm apart, although this feature should not be used as an ultrasonographic criterion since it is simply an indicator used in HSG to distinguish between types of anomalies.

Class V: Septate Uterus

This anomaly originates from incomplete septum resorption resulting in an intermediate wall between the müllerian ducts;

as a result the uterine cavity is either partially (subseptate) or completely divided into two, but has a normal external morphology. Septate uterus is the most frequent malformation (55%), and the subseptate form is particularly frequent. This anomaly does not include arcuate uterus, since this should be considered a minor anomaly or a variation from normal. From an obstetric point of view, septate uterus has a poor prognosis since it is related with a high percentage of fetal loss and placental insufficiency.[35]

Figures 7A and B shows a subseptate uterus visualized with 3D US and MR imaging. Figure 8 depicts a septate uterus with two cervices, an uncommon malformation first described in 1994 by Brumsted and McBean, and explained by Müller's bidirectional theory of duct fusion.[36] Figures 9A and B shows another case of septate uterus visualized with 3D US and MR imaging.

The complex malformation illustrated in Figure 10 consists of a bicornuate uterus with a septum dividing the two cavities. This malformation can also be explained by Müller's theory of bidirectional fusion.

Class VI: Arcuate Uterus

Like the septate uterus, the arcuate uterus is considered a separate anomaly in terms of prognosis and treatment. Its external morphology is normal, and the uterine cavity shows only a mild indentation rather than an actual septum. The depth of the indentation is not well-established. Syed and colleagues[37] proposed a cutoff length no greater than 1.5 cm, but other authors such as Salim et al.[24] considered the angle of the indentation (e.g. obtuse arcuate, acute subseptate) to be a more important feature (Fig. 11).

Figs 7A and B: Subseptate uterus in 3D US (A) and MR imaging (B)
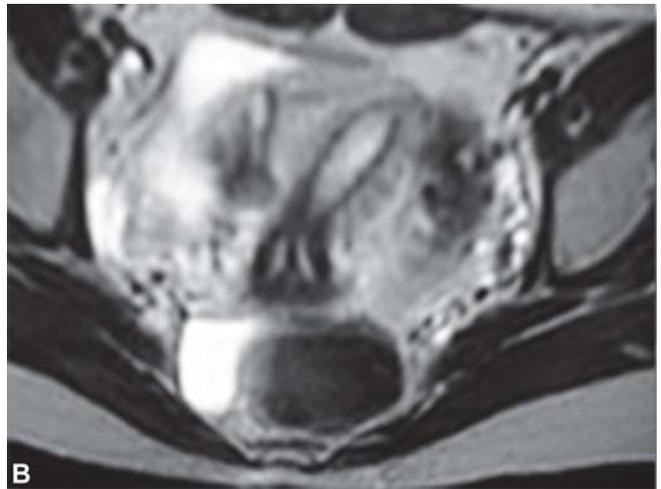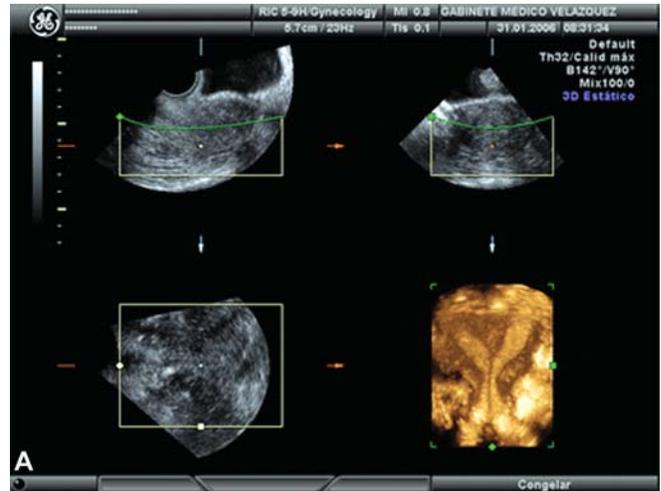
Figs 9A and B: Septate uterus with two cervices in 3D US (A) and MR imaging (B)

Fig. 8: Septate uterus with two cervices

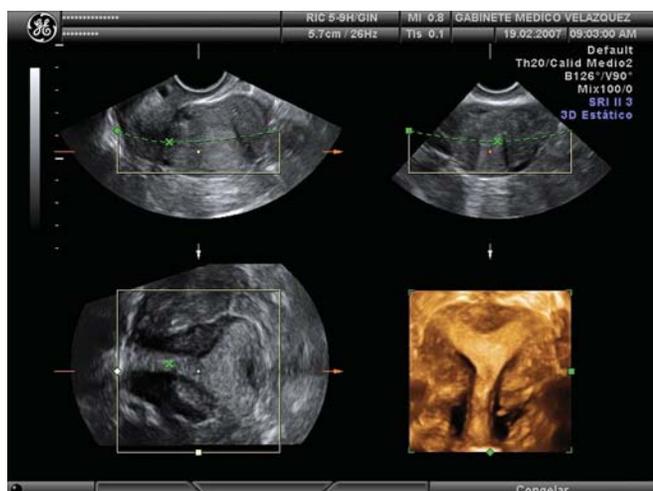**Fig. 10:** Bicornuate uterus with complete septum

Fig. 11: Arcuate uterus in 3D US

Class VII: Iatrogenic Uterus (DES)

This type of malformation has become less common in recent decades, since it was attributed to DES, which has not been used for gestational complications for many years.[38] The most substantial change is the typical T-shape of the uterine cavity. (Fig. 12) illustrates a uterus with this alteration as visualized with 3D US (courtesy of Dr Pascual, Instituto Universitario Dexeus, Barcelona, Spain).

PATIENTS AND METHODS

We studied 175 patients with clinical or ultrasonographic suspicion of uterine malformation between November 2004 and June 2008. Uterine volume was measured in all women for later processing and reconstruction of 3D images. Images were scanned with two General Electric Voluson Expert systems
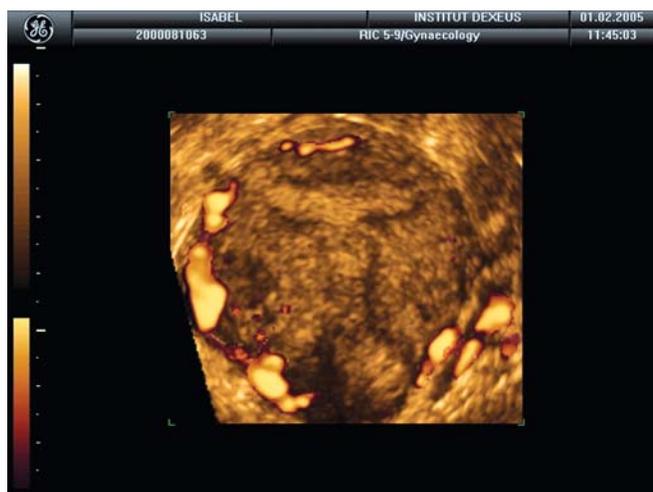

Fig. 12: Diethylstilbestrol-exposed uterus in 3D US

operated by a total of six observers. Volumes were captured with a volumetric vaginal transducer at 3.7-9.3 MHz. Images were acquired over a wide range of settings from medium to maximum, at an angle of 90º, adjusting the size of the region of interest in the midsagittal plane of the uterus to included the entire organ in the image. A transverse plane was also used for anomalies of the major transverse diameter (didelphys uterus, wide septate uterus, certain bicornuate malformations with a large separation between horns, and one communicating unicornuate uterus) to be able to capture both horns and establish the relationships between the cavity and fundus during 3D image reconstruction.

Rendering or reconstruction of all captured images was done with surface and light gradient modes. Sector planes were used for the diagnosis in three cases. If no anomaly was seen, the woman was not included in the present analysis. A thorough genital physical exploration with speculum was done before or after US except in three women with an imperforate hymen. The findings were catalogued according to the AFS classification, and the associated uterine malformation were recorded in detail. In the 32 patients for whom complete physical and US explorations were feasible, MR imaging was also done. These cases did not differ significantly from the general population of cases in terms of types of anomalies or other patient characteristics. All MR images were obtained by the same physician with a General Electric 0.2 tesla or a Siemens Avanto 1.5 tesla system, according to the usual sequence, with enhanced T2-weighted coronal planes (used because of their importance for the diagnosis). The kappa index was calculated to determine agreement between the two diagnostic techniques for uterine malformations. Additional findings were also analyzed in detail.

RESULTS

Of the 175 müllerian duct anomalies we analyzed, the diagnoses were 1 agenesis, 2 unicornuate uterus (1 genuine, 1 communicating), 4 didelphys uterus, 22 bicornuate uterus, 80 septate uterus (8 with two cervices) and 68 arcuate uterus. Magnetic resonance imaging was also done in 1 woman with unicornuate uterus, 3 with bicornuate uterus, 25 with septate uterus (4 with two cervices) and 3 with arcuate uterus. The 3D US and MR findings agreed in all cases regarding the relation between the uterine cavity and the fundus, so the results for AFS classification based on 3D US were consistent (kappa = 100%).

However, in two patients we noted discrepancies in the cervix. In one woman with bicornuate uterus, MR imaging showed the presence of a septum along the cervical canal, and in another woman a septum considered bicollis with 3D US was diagnosed with MR imaging as a complete septum producing a hypointense signal in the cervical canal. The first discrepancy resulted in a false positive finding with MR imaging,

revealed as such during hysteroscopy for resection. During hysteroscopy a fold was observed on the anterior cervical wall, which was probably responsible for the false septum image obtained with MR imaging. In the second case, divergence of the cervical canals in the coronal plane of 3D US led to the diagnosis of a double cervix. Physical examination was not possible because the patient had an imperforate hymen, so rectal US was used. Magnetic resonance imaging showed a wide septum dividing the whole uterus up to the external cervical os; the signals were compatible with fibrous tissue and differed from the myometrium signals that would have produced if a double cervix had actually been present.

Even considering these two cases of discrepant findings, concordance between the two techniques was high (kappa = 93.45%; 95% confidence interval 80.75%-100%).

DISCUSSION

Although 3D US is helpful as a complement to 2D US on multiple occasions on the field of gynecology, it is only indispensable for the diagnosis of uterine malformations, therefore suspected malformations are the only absolute indication for this technique. When a uterine malformation is suspected, our suggested protocol indicates initially 3D US, always accompanied by complete gynecologic exploration. For complex or doubtful cases, MR imaging should also be used. Surgery should be reserved exclusively for malformations that would benefit from this treatment.

Images produced by 3D US and MR imaging are nearly equivalent (see Figs 1 to 12). The relation between the fundus and uterine cavity can be well established with either ultrasonographic reconstructions in the coronal plane or with coronal sequences obtained by MR imaging. Hence the success of the combination of 3D US and MR imaging lies in the coronal sections, which are difficult to acquire with 2D US. In terms of diagnostic efficacy, neither technique is better than the other, and in our hands concordance based on classification of the anomalies according to the AFS system was complete. Differences may arise, however, in studies of the lower part of the uterus. Magnetic resonance distinguishes clearly between different tissues, and this is especially advantageous for studies of the cervix and vagina, which should not be overlooked during conventional ultrasonography. To analyze the cervix with ultrasonography, the transducer needs to be withdrawn slightly to visualize the cervical canal and myometrium. Sometimes this can disclose cervical cancer, which will unfortunately be in an advanced stage since early diagnosis with imaging techniques is not possible.

Excellent 3D images can be obtained from good 2D US images, and the combination of the two techniques is useful to evaluate the existence of one or two cervices, or of a septum in the cervical canal. The presence of two (generally wide) canals

that diverge in the lower region suggest a double cervix rather than a septate cervix, but although the ultrasonographic impression is almost always correct, only verification by speculoscopy can confirm the diagnosis. On the basis of differences in MR imaging signal intensity, radiologists can discriminate accurately between a septum (even if myometrium is present in its upper portion) and the cervical myometrium. Not unusually, MR imaging reports will describe vaginal septa that can be distinguished by their different signal intensities compared to the walls of the vagina. Gynecologists, however, cannot distinguish the latter with either of the techniques available for them (2D US or 3D US), and given the high incidence of association between these and other uterine malformations, is vital to use speculoscopy and manual vaginal exploration to search for septa. If the procedure is done as described, the efficacy of the two techniques would be equivalent, hence 3D US would thus be a better option than MR imaging because the former offers advantages such as lower cost and better tolerance by patients. A further advantage of 3D US is its simplicity during gynecologic examinations in the setting of everyday practice.

Although the cost of 3D US is substantial, this factor is offset by its good tolerance. Patients reported fear of the contrast medium, claustrophobia, and the duration of procedure as the main disadvantages of MR imaging. In the present study we encountered resistance to MR imaging and often needed to reassure women that contrast was not necessary, and use an open MR imaging system. As a result we were only able to use both techniques for a small sample, limited mainly to anomalies that did not pose a risk to the woman's reproductive goals and thus did not require more "aggressive" diagnostic techniques.

One of the most useful applications of 3D US is in differentiating between arcuate, septate and bicornuate uterus. Alcázar and colleagues, among others, reached the same conclusion and also noted its lower efficacy in diagnosing didelphys uterus.[39] Two-dimensional images sometimes do not reveal differences between markedly arcuate, subseptate or partial bicornuate uterus. The prognosis for these malformation varies substantially, hence the importance of a correct diagnosis for appropriate treatment. A number of publications advocate systematic septostomy based upon the improved reproductive outcome in a considerable percentage of patients. Among these publications, the work by Kupesic and colleagues merits particular attention, especially their larger study in which the authors advocate the efficacy of 3D US as a screening method for infertile patients, due to the high prevalence of septate uterus and the effectiveness of septostomy in the population they studied.[26,40] Other authors such as Tekes and colleagues[41] suggested that the finding of a septate uterus was not necessarily an indication for surgical treatment, which should be reserved for women in whom the diagnosis might interfere with obstetric

outcomes. We believe resection of large septa, which generally have a substantial myometrial component, could cause serious uterine scarring which could lead in turn to placenta accreta. On the other hand, septate uteri tend to have larger cavities, and in our experience are associated with fewer reproductive problems than narrow uteri (possibly because of the better blood supply). In our experience the prognosis and most suitable treatment for women with these anomalies can be determined with 3D US.

At our center hysteroscopic septostomy is practiced in women with antecedents of two or more miscarriages, with good results. The decision to use surgical correction for any uterine malformation is based on clinical criteria. We emphasize that our population of patients was not a preselected population, and that most studies that recommend systematic septostomy involved infertile women or women with a history of recurrent miscarriages. Some authors such as Tomazevic and colleagues favor surgical intervention for the correction of even arcuate uterus, but this may be because their definition of this anomaly is closer to that of subseptate uterus, i.e. with a septum from 1.3 to 1.5 cm long, for which resection could improve the reproductive prognosis.[42] Generally speaking, the management of to this type of anomaly is usually conservative. Authors such as Golan and colleagues maintain that the only surgery indicated for these cases is cervical cerclage, although this will not prevent first trimester miscarriages.[43]

We believe the most suitable approach to diagnosing a uterine malformation should take into account the clinical features and the patient's reproductive goals. We have used 3D US to diagnose and plan the most appropriate treatment, with good results.

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REFERENCES

1. Acien P, Acien M. Malformations of the Female Genital Tract and Embryological Bases. Curr Wom Health Rev 2007;3:248-88.
2. Muller P, Musset R, Netter A, Solal R, Vinourd JR, Gillet JY. Etat du haut appareil urinaire chez les porteuses de malformations uterines: etude de 133 observations. Presse Med 1967;75:1331-36.
3. Byrne J, Nussbaum–Blask A, Taylor WS, et al. Prevalence of mullerian duct anomalies detected at ultrasound. Am J Med Genet 2000;94:9-12.
4. March CM. Müllerian anomalies. Fertility news 24/1. Endocr Fert Forum 1990;13:1.
5. Acien P. Incidence of müllerian defects in fertile and infertile women. Hum Reprod 1997;12:1372-76.
6. Stampe Sorensen S. Estimated prevalence of mullerian duct anomalies. Acta Obstet Gynecol Scand 1988;67:441-45.
7. Stray-Pedersen B, Stray-Pedersen S. Etiologic factors and subsequent reproductive performance in 195 couples with a prior history of habitual abortion. Am J Obstet Gynecol 1984;148: 140-46.
8. Raga F, Bauset C, Remohí J, Bonilla-Musoles F, Simón C, Pellicer A. Reproductive impact of congenital mullerian anomalies. Hum Reprod 1997;12:2277-81.
9. Makino T, Hara T, Oka C, Toyoshima K, Sugi T, Iwasaki K, Umeuchi M, Iizuka R. Survey of 1120 japanese women with a history of recurrent spontaneous abortions. Eur J Obstet Gynecol Reprod Biol 1992;44:123-30.
10. Clifford K, Rai R, Watson H, Reagan L. An informative protocol for the investigation of recurrent miscarriage: Preliminary experience of 500 consecutive cases. Hum Reprod 1994; 9:1328-32.
11. Golan A, Langer R, Bukovsky I, Caspi E. Congenital anomalies of the mullerian system. Fertl Steril 1989;51:747-55.
12. Salim R, Regan B, Woelfer B, Backos M, Jurkovic D. A comparative study of the morphology of congenital uterine anomalies in women with and without a history of recurrent first trimester miscarriage. Hum Reprod 2003;18:162-66.
13. Tulandi T, Arronet GH, McInnes RA. Arcuate and bicornuate uterine anomalies and infertility. Fertil Steril 1980;34:362-64.
14. Acien P. Reproductive performance of women with congenital uterine anomalies. Hum Reprod 1993;8:122-26.
15. Woelfer B, Salim R, Banerjee S, Elson J, Regan L, Jurkovic D. Reproductive outcomes in women with congenital uterine anomalies detected by three-dimensional ultrasound screening. Obstet Gynecol 2001;98:1099-1103.
16. Lee DM, Osathanondh R, Yeh J. Localization of Bcl-2 in the human fetal mullerian tract. Fertil Steril 1998;70:135-40.
17. Edwards JA, Gale RP. Camptobrachydactyly: A new autosomal dominant trait with two probable homozigotes. Am J Hum Genet 1972;24:464-74.
18. Sarto GE, Simpson JL. Abnormalities of the mullerian and wolffian duct systems. Birth Defects Orig Artic Ser 1978;14: 37-54.
19. The American Fertility Society. Classifications of adnexal adhesions, distal tubal obstruction, tubal occlusion secondary to tubal ligation, tubal pregnancies, mullerian anomalies and intrauterine adhesions. Fertil Steril 1988;49:944-55.
20. Jurkovic D, Geipel A, Gruboeck K, Jauniaux E, Natucci M, Campbell S. Three-dimensional ultrasound for de assessment of uterine anatomy and detection of congenital anomalies: A comparison with histerosalpingography and two-dimensional sonography. Ultrasound Obstet Gynecol 1995;5:233-37.
21. Raga F, Bonilla-Mussoles F, Blanes J, Osborne NG. Congenital mullerian anomalies: Diagnostic accuracy of three-dimensional ultrasound. Fertil Steril 1996;65:523-28.
22. Wu MH, Hsu CC, Huang KE. Detection of congenital müllerian duct anomalies using three-dimensional ultrasound. J Clin Ultrasound 1997;25:487-92.
23. Mohamed M, Momtaz MD, Alaa N, Ebrashy MD, Ayman A, Marzouk MD. Three-dimensional ultrasonography in the evaluation of the uterine cavity. Middle East Fertil Soc J 2007; 12:41-46.
24. Salim R, Woelfer B, Backos M, Regan L, Jurkovik D. Reproducibility of three-dimensional ultrasound diagnosis of congenital uterine anomalies. Ultrasound Obstet Gynecol 2003; 21:578-82.
25. Kupesic S, Kurjak A. Septate uterus: Detection and prediction of obstetrical complications by different forms of ultrasonography. J Ultrasound Med 1998;17:631-33.

26. Kupesic S, Kurjak A, Skenderovic S, Bjloes D. Screening for uterine abnormalities by three-dimensional ultrasound improves perinatal outcome. J Perinat Med 2002;30:9-17.

27. Fedele L, Dorta M, Brioschi D, Massari C, Candiani GB. Magnetic resonance evaluation of double uteri. Obstet Gynecol 1989;74:844-47.

28. Carrington BM, Hricak H, Nuruddin RN, Secaf E, Laros RK Jr, Hill EC. Müllerian duct anomalies: MR imaging evaluation. Radiology 1990;176:715-20.

29. Pellerito JS, McCarthy SM, Doyle MB, Glickman MG, DeCherney AH. Diagnosis of uterine anomalies: Relative accuracy of MR imaging, endovaginal sonography and histerosalpingography. Radiology 1992;795-800.

30. Fischetti SG, Politi G, Lomeo E, Garozzo G. Magnetic resonance in the evaluation of mullerian duct anomalies. Radiol Med 1995; 89:105-11.

31. Deutch TD, Abuhamad AZ. The Role of 3-Dimensional Ultrasonography and Magnetic Resonance Imaging in the Diagnosis of Mullerian Duct Anomalies: A Review of the Literature. J Ultrasound Med 2008;27(3):413-23.

32. Raine-Fenning N, Fleischer AC. Clarifying the role of three-dimensional transvaginal sonography in reproductive medicine: An evidence-based appraisal. Exp Clin Assist Reprod 2005; 2:10.

33. Timor-Tritsch IE, Monteagudo A, Tsymbal T, Strok I. Three-dimensional inversion rendering: a new sonographic technique and its use in gynecology. J Ultrasound Med 2005;24:681-88.

34. Madureira A, Mariz C, Bernardes J, Ramos I. Case 94: Uterus Didelphys with Obstructing Hemivaginal Septum and Ipsilateral Renal Agenesis. Radiology 2006;239:602-06.

35. Troiano R, McCarthy S. Müllerian duct anomalies: Imaging and clinical issues. Radiology 2004;233:19-34.

36. Mc Bean JH, Brumsted JR. Septate uterus with cervical duplication: a rare malformation. Fertil Steril 1994;62:415-17.

37. Syed I, Hussain H, Weadock W, Ellis J. Uterus, Mullerian Duct Abnormalities. eMedicine. Article Last Updated: Oct 3, 2007.

38. Goldberg JM, Falcone T. Effect of diethylstilbestrol on reproductive function. Fertile Steril 1999;72:1-7.

39. Alcázar JL. Three-dimensional ultrasound in gynecology: current status and future perspectives. Curr Wom Health Rev 2005;1: 1-14.

40. Kupesic S. Clinical implications of sonographic detection of uterine anomalies for reproductive outcome. Ultrasound Obstet Gynecol 2001;18:387-400.

41. Tekes A, Macura K. Ultrasound and MR imaging correlation of uterine anomaly. J Wom Imag 2004;6:91-93.

42. Tomazevic T, Ban-Frangez H, Ribic-Pucelj M, Premru-Srsen T, Verdenik I. Small uterine septum is an important risk variable for preterm birth. Eur J Obstet Gynecol Reprod Biol 2007;135: 154-57.

43. Golan A, Langer R, Wexler S, Segev E, Niv D, David M. Cervical cerclage—its role in the pregnant anomalous uterus. Int J Fertil 1990;35:164-70.