Three-dimensional Ultrasound in Evaluation of the Ovary

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Three-dimensional (3D) ultrasound is an easy, important and noninvasive method for the differential diagnosis of ovarian disease in the clinical practice of obstetrics and gynecology. With advances in ultrasonographic technology, the application of higher-frequency scanning probes can evaluate the ovary in the analysis of morphological anatomy and in volume measurement, and is highly reproducible. The potential of power Doppler ultrasound with vascular indices that can further depict and quantify the microcirculation of the ovary has been extensively explored. The aim of this review is to report the present status and the recent development of 3D ultrasonography in the evaluation of the ovary. In conclusion, 3D ultrasound examination may help us to investigate the functional and potential roles of ultrasonography in clinical practice concerned with the ovary. Furthermore, 3D ultrasound may provide more substantial assistance in the differential diagnosis of various physiological or pathological conditions of the ovary.

Introduction

Three-dimensional (3D) ultrasound is an easy and noninvasive method for the differential diagnosis of various physiological and pathological conditions of the ovary in the clinical practice of obstetrics and gynecology. With advances in 3D ultrasonographic technology, although 3D imaging is still at a relatively early stage, the application of
higher-frequency scanning probes can evaluate the ovary in the analysis of morphological anatomy and in volume measurement, and is highly reproducible [1,2]. The three dimensions improve spatial orientation and access multiplanar views, especially the coronal (reconstructed) plane, which can provide additional information that can depict lesions not easily diagnosed by two-dimensional (2D) ultrasound imaging. It can rotate and magnify the acquired stored volume for re-evaluation with reduced scanning time and without increasing patient discomfort. The 3D volume measurement of the ovary, follicles and stroma can be determined more precisely by outlining meticulously the region of interest. The potential of power Doppler ultrasound with vascular indices that can further depict and quantify the microcirculation of the ovary is extensively explored. Furthermore, some 3D software programs using the virtual organ computer-aided analysis (VOCAL) system have been developed but further work is needed to ensure a clinically relevant benefit. The aim of this review is to report the present status and the recent development of 3D ultrasonography in the evaluation of the ovary.

Parameters for evaluation of the ovary using 3D ultrasound

The length (one dimension) of the ovarian diameter, area (two dimensions) and volume (three dimensions) can be easily calculated; especially the rotatable perpendicular planes of the ovary using 3D ultrasound. The ovarian volumes are estimated using the trapezoid formula by 3D ultrasound that is compared with the ellipsoid formula (height × width × length × 0.523) by conventional 2D ultrasound scanning [3]. The most common indices of color Doppler examination followed B mode are pulsatility index (PI), resistance index (RI) and systole to diastole (S/D) ratio [4]. The calculation of RI and PI is based on the following formulas: $\text{RI} = (S - D)/S$ and $\text{PI} = (S - D)/\text{mean}$, where S is the peak systolic velocity, D is the end diastolic velocity and the mean is the averaged maximum velocity.

SonoAVC (Automatic Volume Calculation) is a software program that can identify and quantify ovarian hypoechoic regions within a 3D dataset and provide automatic estimation of their absolute dimensions, mean diameter and volume of fluid-filled areas of the ovary. Each different volume of cyst or follicle is color coded separately, SonoAVC can evaluate follicular development within the ovary [5].

Power Doppler ultrasound can provide information on the quantity of moving blood cells per volume, which will demonstrate the real vascularity of the ovary. Several indices for 3D power Doppler angiography have been proposed using the VOCAL system: MG (mean gray value), VI [vascularization index, an estimation of vessel density, determined by the formula: color voxels/(total voxels − background voxels)], FI [flow index, the average intensity of the flow, determined by the formula: weighted color voxels/(color voxels − border voxels)], and VFI [vascularization flow index, both flow and vessel intensity, determined by the formula: weighted color voxels/(total voxels − background voxels)] to examine and quantify the blood flow and vascularization of the ovarian stroma [2].

Recently, a new four-dimensional (4D) method for assessment of ovarian vascularization changes during the cardiac cycle using spatiotemporal image correlation-high definition flow (STIC-HDF) to overcome the influence of machine settings and attenuation is described [6]. Based on 1-cm³ spherical sampling, VI from the most vascularized part of the ovarian stroma in 3D volumes of the 4D STIC-HDF chain is calculated. The maximum $\text{VI(sys)}$ and minimum $\text{VI(diast)}$ values are assumed to represent two different moments of the cardiac cycle (systole and diastole), respectively. In addition, the mean VI for all chain volumes for one cardiac cycle is calculated. Based on these three VI values, three new indices including volumetric systolic/diastolic ratio ($\text{vS/D}$), volumetric resistance index (vRI) and volumetric pulsatility index (vPI) are calculated. These volumetric Doppler indices overcome the influence of angle of insonation and vessel diameter by application of ratios between values obtained within a cardiac cycle.

Ovary

Three perpendicular planes of bilateral ovaries are rotatable to obtain the largest dimensions after the digital data have been documented using 3D ultrasonography [3]. Stroma and volume determinations can be obtained more accurately by 3D images than by conventional 2D ultrasonography. 3D ultrasonography not only facilitates noninvasive retrospective evaluation and volume calculation but also shortens examination time without increasing patient discomfort.

The ovarian volume, number and volume of antral follicles, and ovarian power Doppler vascular indices can be assessed easily by 3D transvaginal grayscale and power Doppler ultrasound [7]. The right ovary is larger and contains more follicles than the left one in asymptomatic women aged 20–29 years with follicles 2–10 mm, on menstrual cycle day 4–8, using combined oral contraceptives. The differences between the right and left ovary are less obvious in women aged 30–39 years. Ovarian volume tends to be smaller in women aged 20–29 years than in those aged 30–39 years, but there are no clear differences. There is no statistical significance in the size of the largest follicle, total follicular volume and vascular indices between the age groups. The flow intensity in ovarian stroma decreases along with the aging process, using 3D power Doppler ultrasound [8]. The vascular indices, including VI, FI and VFI, all decrease significantly in the order of premenopause, perimenopause, and then postmenopause. However, this situation is reversed after 3 months of continuous—combined hormone replacement therapy [9]. All 3D power Doppler indices of ovarian stromal flow show a significant increase after treatment.

SonoAVC with 3D ultrasound examination can evaluate the different stages of follicular development within the ovary [5]. This 3D automated technique for the measurement of antral follicle number and size is significantly quicker than 2D ultrasound imaging [10]. However, fewer antral follicles are found when SonoAVC software program is used to analyze 3D ultrasound data.

The median VI, FI and VFI calculated using HDF are significantly higher when compared with conventional
power Doppler imaging in the endometrium of asymptomatic premenopausal women undergoing 3D transvaginal sonography [11]. When assessing ovarian vascularization with these 3D vascular indices using STIC-HDF throughout the cardiac cycle, the mean VI during systole is significantly higher than that during diastole, which means VI calculation is affected by the time in the cardiac cycle when the measurement is taken [6]. However, the mean FI values during systole and diastole remain constant in the normal nondominant ovary. When further assessing the new volumetric impedance indices of ovarian vascularization, using STIC-HDF technology is also reproducible [12].

Polycystic ovarian syndrome (PCOS)

PCOS is a common cause of ovarian dysfunction and anovulation in women of reproductive age. The ovaries of the patients with PCOS are larger in size, area and volume when compared with those of normal controls [3]. The Rotterdam ESHRE/ASRM-sponsored PCOS 2003 consensus workshop group define the ultrasound criteria of PCOS as the presence of at least 12 follicles in each ovary, which measure 2–9 mm in diameter, and/or increased ovarian volume (>10 mL) [13]. In our study, the mean ovarian volume using 3D transvaginal ultrasound was 11.3 ± 3.5 cm³ in PCOS patients (compared with 5.5 ± 1.4 cm³ in the control group), which is near the value of the revised Rotterdam consensus ultrasound diagnostic criteria for PCOS. Although polycystic ovary ultrasound appearance is not a prerequisite for the diagnosis of PCOS, ovarian stromal area/total area ratio is the most efficient diagnostic indicator for hyperandrogenism that is significantly correlated with androgen levels [14].

Our study further demonstrated increased VI, FI and VFI in the ovarian stromal Doppler signals in PCOS assessed on day 2 or day 3 of the menstrual cycle using 3D power Doppler ultrasound [15]. This result may explain the excessive response observed during gonadotropin administration in women with PCOS, which leads to ovarian hyperstimulation syndrome. Ovarian VI and VFI measured by 3D power Doppler are significantly higher in PCOS women in the study of Mala et al [16], which is similar to our results. In a recent case–control 4D STIC-HDF transvaginal ultrasound study, mean VI(sys) and mean VI(diast) of ovarian stroma were significantly higher in PCOS women compared with controls [17]. Increased uterine artery PI and RI and lower ovarian PI and RI measured by 2D Doppler imaging in PCOS women are found when compared with controls [16]. Furthermore, median v5s/D, mean vRI and median vPI of ovarian stroma are also significantly lower in PCOS women by 4D STIC-HDF study [17]. These results suggest lower impedance to flow in ovarian stromal vessels in PCOS women. However, stromal volume, echogenicity (mean gray value) and vascularity (FI) of 3D ultrasound measurements in Chinese women with PCOS are significantly lower than those in Caucasian women with PCOS [18]. This supports the concept that ovarian characteristics of PCOS by 3D ultrasound may be influenced by ethnicity or phenotypic expression. Similarly, genetic variation may be another cause of different PCOS expression. In our study, there were ethnic and racial variations in the prevalence of insulin receptor substrate (IRS)-2 Gly1057Asp polymorphisms [19]. The homozygous IRS-2 Asp1057 allele was the common genotype in IRS-2 Gly1057Asp polymorphisms in the Taiwanese female population. The frequency of this IRS-2 polymorphism is higher in PCOS patients when compared with normal controls. However, there is no difference between PCOS and normal women for this polymorphism, and women homozygous for the Gly1057 allele is the common genotype in Greek populations [20].

Laparoscopic ovarian drilling for clomiphene-resistant PCOS women increases ovulation rate and cumulative pregnancy rate. It may result in a transient increase, with a subsequent significant reduction, in ovarian volume by 3D ultrasound evaluation after laparoscopic ovarian drilling [21]. In young PCOS women who received laparoscopic ovarian drilling, the parameters in intraovarian stroma after operative treatment demonstrated significantly decreased VI and VFI by 3D transabdominal power Doppler ultrasound in our study [22]. Laparoscopic ovarian drilling treatment affects ovarian stromal blood flow dynamics in short-term follow-up that may be beneficial to endocrine profiles and intraovarian stromal flow in PCOS patients. In addition, there is a positive correlation between plasma levels of anti-Müllerian hormone and ovarian stromal blood flow changes using 3D power Doppler ultrasonography in PCOS women, including before and after laparoscopic ovarian drilling treatment [23]. Plasma level of anti-Müllerian hormone is increased in PCOS women and is significantly decreased after laparoscopic surgery, similar to the changes in ovarian stromal blood flow Doppler indices.

Ovarian endometriosis

Endometriosis is a polygenic disease with a complex, multifactorial etiology that reduces the quality of life due to chronic pelvic pain, dysmenorrhea, and dyspareunia [24]. Ultrasound is an easy and noninvasive tool used in the differential diagnosis of endometriosis, especially before surgical intervention of ovarian endometrioma [25]. Most of the cases with ovarian endometrioma can be found through abdominal or transvaginal ultrasound with good accuracy. The classical pictures of ovarian endometrioma present as cysts with homogeneous hypoechochogenic content (such as ground glass appearance) and are often referred as chocolate cysts. Sometimes, it is necessary to differentiate various benign and malignant tumors with ovarian endometrioma. When an ovarian cyst contains a fluid—fluid level or fishnet appearance from ultrasound imaging, it needs to be differentiated from the possibility of a hemorrhagic functional cyst. When the endometriotic cyst contains a solid appearance or internal septation, it may be due to reactive fibrosis or retracted blood clots without vascularity, by Doppler analysis. The typical vascularity pattern of ovarian endometrioma is the pericystic flow near the ovarian hilus. The use of color Doppler imaging does not improve the accuracy of the diagnosis of ovarian endometrioma, but can reduce the likelihood of malignancy.

The sonographic tissue characterization can be assessed with mean gray value (MGV) of the 3D volume, which represents the mean intensity of gray-scale voxels (the smallest unit of volume) within the ovary. When assessing...
the cyst content using MGV with the VOCAL system, in differentiating ovarian endometriomas from other ovarian cysts, cyst content MGV is higher in ovarian endometrioma than in other unilocular ovarian cysts that may contribute to the diagnosis of ovarian endometrioma [26]. In addition, about 7% of adnexal masses cannot be classified as benign or malignant using subjective assessment of gray-scale and Doppler ultrasound findings [27]. 3D ultrasonography can easily localize the distribution of vascularity via rotation of the 3D ultrasound planes, which helps to discriminate benign from malignant ovarian tumors [28].

The gold standard method for the diagnosis of endometriosis is laparoscopy, but surgery for ovarian endometrioma may decrease ovarian reserve, which may impair fertility. Laparoscopic excision of ovarian endometrioma is still associated with a high recurrence rate, and surgical treatment prior to in vitro fertilization (IVF) has no additional benefit over expectant management [29]. The use of laparoscopy for women undergoing assisted reproductive technology has recently been challenged. We use 3D power Doppler scan to demonstrate the dynamic vascularity and to provide a prognostic tool for IVF outcomes in patients with endometriomas. Decreased oocyte retrieval numbers and pregnancy rates are found in women undergoing IVF after laparoscopic surgery for ovarian endometriomas compared with women with tubal infertility [30]. Intra-ovarian stromal blood flow parameters using 3D power Doppler ultrasound demonstrate decreased VI, FI and VFI in the endometriotic group. It may be an initial predictor of a decreased ovarian reserve before the increase of follicle stimulating hormone in early follicular phase. These results may be due to a diminished ovarian reserve after conservative surgery for endometrioma, which leads to ovarian damage and decreased intravascular vascularity. In addition, the follicular fluid leptin level is negatively correlated with ovarian stromal FI in women with tubal infertility, however, there is no such correlation in women with endometrioma after surgery [30]. This decreased FI, which may be secondary to reduced blood flow through the ovarian stroma, leads to follicular hypoxia followed by the secretion of several angiogenic factors, such as leptin, in the ovarian follicles. Deficient angiogenic responses in the ovarian cortices in women with endometrioma after surgery may lose the negative correlation between follicular fluid leptin and intraovarian FI. Therefore, women with minimal and mild endometriosis may choose simultaneous laparoscopy combined with a modified IVF (gonadotropin-releasing hormone antagonist) protocol [31]. It will shorten the time to pregnancy with a high cumulative pregnancy rate after complete surgical removal of all visible endometriotic lesions. Traditional gonadotropin-releasing hormone agonist IVF protocol is a valid option for those with more severe stages of endometriosis after laparoscopic treatment without restored fertility.

Ovarian malignancy

It is important to be aware of the possibility of ovarian cancer before surgical treatment for an adnexal mass. Ultrasound examination is a useful method to diagnose differentially the adnexal lesions from any chance of malignancy. Two widely used ultrasound methods, namely the risk of malignancy index and subjective assessment by ultrasound contribute to discriminating malignant from benign ovarian masses in preoperative assessment [41]. The risk of malignancy index combines ultrasound
morphological score, serum cancer antigen 125 levels and menopausal status. There are several morphological and vascular parameters to evaluate the adnexal cysts by transvaginal color Doppler ultrasound, to exclude the possibility of ovarian malignancy in preoperative evaluation, including the presence of vessels and its location (central or peripheral), peak systolic velocity, RI and PI of the lesion vascularity [42]. However, there is still an overlap of these parameters between benign and malignant tumors. The best parameters to differentiate malignant cancers from benign lesions are the lowest Doppler RI with a cutoff value of 0.45 and central tumor vessel location.

3D ultrasound is a reproducible imaging technique to improve diagnostic accuracy for assessing ovarian cancers. It has both a higher sensitivity and specificity for preoperative identification of suspicious adnexal mass when compared to conventional 2D ultrasonography [43]. Using 3D power Doppler ultrasound evaluation, the mean gray index and the FI, as well as the central localization of vessels in the tumor, are important parameters contributing to the differentiation between benign and malignant ovarian masses [44]. Mean VI and VFI by 3D power Doppler ultrasound are significantly higher in advanced-stage cancers and metastatic ovarian tumors as compared with early-stage ovarian cancers [45]. When using spherical sampling with the VOCAL system for calculating 3D power Doppler vascular indices, the median VI, FI and VFI for all sphere volumes are significantly higher in malignant adnexal tumors [46]. VI is significantly more specific than are VFI and FI. However, sphere volume does not affect the performance of 3D power Doppler sampling for predicting malignancy in vascularized adnexal tumors.

Conclusion

Although conventional 2D ultrasound already is an easy, noninvasive and valuable diagnostic tool in the evaluation of the ovary during clinical practice in the field of obstetrics and gynecology, 3D ultrasound is an emerging technology that allows physicians to comprehend and evaluate with ease the sophisticated anatomy of the ovary observed from any arbitrary planes. The application of 3D power Doppler and some new software programs further the clinical role of 3D ultrasound to provide substantial assistance in pelvic imaging. However, 3D ultrasound still needs more experience in training and operating than 2D ultrasound. Further research should be conducted to explore more potential uses of 3D and power Doppler ultrasonography to provide enhanced depiction of ovarian morphology and vascularity.

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