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The Role of Three Dimensional Ultrasonography in Female Infertility

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Introduction

Ultrasonography has been a valuable diagnostic tool in most fields of medicine since the early 1970s and it is widely used by physicians in clinical practice. Conventional two-dimensional (2D) ultrasound has the ability to visualize only sagittal and transverse planes. Reflections are obtained in transverse planes in 2D ultrasounds while at certain angles in three-dimensional (3D) ultrasounds thus the images produced by 3D ultrasounds are more accurate. However, translation of 2D scan to 3D scan takes time (approximately 15 minutes). One of the new applications in this field is automatic measurements with software called sonography-based automated volume calculation (SonoAVC). The application of SonoAVC is employed in observation of follicle growth in controlled ovarian hyperstimulation (COH) and in pregnancy for evaluation for embryo and fetus.

In recent years, 3D ultrasonography has been actively used in follow-up of *in vitro* fertilization procedures and evaluation of infertile patient. Moreover there is literature suggesting 3D ultrasonography as an alternative to invasive procedures such as hysteroscopy [1]. Furthermore, 3D ultrasonography is not only used in COH but also in evaluation of ovarian and uterine pathologies and congenital syndromes. Also there is increasing evidence that 3D sonography yields highest reliability for ovarian and follicular volume [2-4].

The aim of this review is to analyse the recent update of application of 3D ultrasonography in female infertility.

Material and Methods

We defined a literature search using the keywords '3D ultrasound, SonoAVC, sonography-based automated volume calculation, follicle volume, *in vitro* fertilization, controlled ovarian hyperstimulation, congenital uterine anomalies' and carried out a systematic search of the databases listed below in January 2016 and updated in March 2016 to investigate the role of 3D ultrasonography in female infertility.

Medical Literature Analysis and Retrieval System Online (MEDLİNE).

Cochrane Database of Systematic Reviews.

PUBMED.

Taylor and Francis Database.

Wiley Online Library.

Oxfort Journals Database.

Clinical Trial.

The literature review was conducted for this topic only. All the literature in English language was screened. Reference lists from relevant studies were scanned to identify further literature. Also manuscript of all the articles was obtained in full text. During review, 32 articles were screened and 12 of these articles were Cited.

Most of the studies were enrolled in IVF centers to investigate the use of 3D ultrasonography for follicle measurements. Patients who had previous ovarian surgery including ovarian cystectomy, ovarian drilling and unilateral oophorectomy, were excluded.

SonoAVC: The Technology

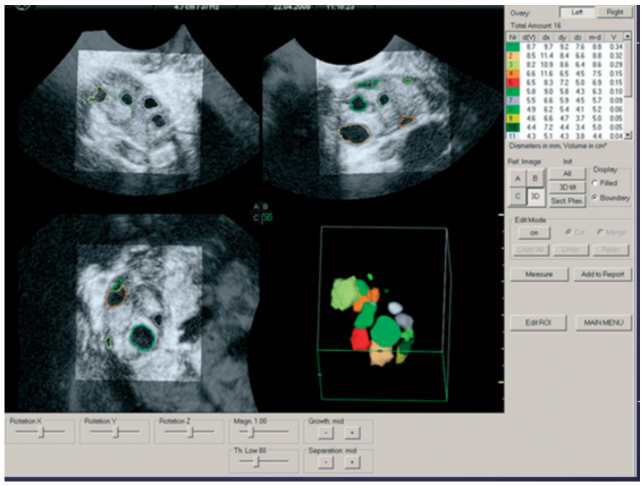

Figure 1: SonoAVC of follicule.

After visualization of the whole ovary, SonoAVC automatically calculates ovarian volume and accurate dimensions of follicles. SonoAVC codes every follicle with a different colour thus prevents counting one follicle twice. Therefore, colour coding increases the accuracy of the follicle counting especially when the number of follicles is high (Figure 1).

SonoAVC enables not only the visualization of single follicles but also calculates mean follicle diameter (MFD), follicular volume (V) and volume based diameter of the follicle d(V). d(V) refers to the volume of a sphere having the same diameter with the follicle.

The software has growth and separation settings. The setting of growth enables measurement of distances between hypoechoic and echoic areas while separation mode measures distance between two hypoechoic areas. Because this software displays and calculates hypoechoic structures, it may be used not only for ovary but also for other areas.

Discussion

Absolute folliculometry is vital for effective infertility treatment. Ultrasound technology is utilised for follicle count and the monitoring of ovarian response. 3D ultrasound technology provides additional information in addition to the basic data obtained by 2D ultrasounds.

3D Evaluation of ovaries

In a study enrolled in U.K. in 2010, antral follicle counts and dimensions were evaluated in 24 patients aged<40 years undergoing *in vitro* fertilization (IVF) treatment [2]. 3D ultrasound measurement of the 2-10 mm antral follicle count was compared with conventional 2D scan between the days 2-5 of COH. 3 patients having follicles larger than 10 mm were excluded. There was no significant difference on 3-4 mm and 4-5 mm follicle counts between two methods. However, 2-10 mm follicle counts were significantly lower in 3D ultrasound evaluation. Campbell and his colleagues suggested that in conventional 2D scans the same follicle was counted more than once leading to a greater count and concluded that 3D measurement has higher accuracy for follicle count. In 3D analysis of antral follicles, SonoAVC software was used and SonoAVC took significantly less time to measure the size and record the number of antral follicles than did 2D ultrasound imaging. This is the first study comparing 2D method with 3D automated volume calculation for the measurement of antral follicle number and size. However, the limitation of this study is the absence of a data such as anti-mullerian hormone levels to be compared with the accuracy these measurements.

Fenning et al. evaluated follicle volumes with SonoAVC in 51 patients undergoing controlled ovarian hyperstimulation as part of IVF treatment [3]. After oocyte pickup, true follicle volumes were determined and compared with SonoAVC measurements. 244 follicles were analysed and the researchers concluded that SonoAVC provides measurements of follicular diameter that are more accurate than the manual measures and has the potential to improve the clinical work flow because the time taken for the measurements is significantly shorter. Two different studies enrolled in Brazil and France in 2010 found that SonoAVC volume measurements failed to be statistically different from the corresponding actual follicle volumes and suggested that automated measurement of multiple follicular volumes using SonoAVC is a simple technique, which reliability is superior to usual diameter measurements [4,5]. Respectively, 15 and 27 infertile women were studied, 26 to 41 years of age. All of them met the following inclusion criteria: both ovaries present; menstrual cycle length range between 25 and 35 days; no clinical signs of hyperandrogenism; BMI ranging between 18 and 25 kg/m^2.

Ata and co-workers compared automated and manual follicle monitoring in a population of 100 women undergoing controlled ovarian stimulation for IVF who had received gonadotropins for more than 5 days and found that SonoAVC measurements had very good reproducibility, with intraclass correlation coefficient ≥ 0.8 for most evaluations [6]. The main indication for IVF was male factor in 24, unexplained infertility in 24, decreased ovarian reserve in 22, PCO in 10, tubal factor in 7 and endometriosis in 7 women. Deutch et al. reviewed 3D ultrasonographic ovarian volumes retrospectively and 3D volumes of gonadotropin-stimulated ovaries and simulated ovarian follicles of known volume were evaluated with SonoAVC. They found measurements obtained by the SonoAVC correlated extremely well with the manual measurements and concluded that SonoAVC was a very accurate and efficient way to measure ovarian follicles [7]. In another study, SonoAVC was suggested to help establish new criteria for timing hCG administration based on follicular volume estimation rather than follicular size [8]. Fifty-eight women undergoing ovulation induction for IVF underwent monitoring using both conventional 2D ultrasound and 3D automated follicle count on the day of hCG administration. Follicular monitoring of each ovary was first performed manually using conventional 2D measurements with documentation of the two greatest diameters of each follicle. This was followed by a 3D volume acquisition of each ovary. The time required to analyse patients with more than 10 follicles was maximally 7.6 minutes less for the automated method. Moreover time needed for each examination was four minutes less. A relatively small number of study populations were the most important limitation of this study. Nevertheless the automated method seems to be advantageous for major IVF centers. Although, SonoAVC measurements seem to be accurate and time saving, the software doesn't appear to improve IVF outcomes. In a study where 72 women undergoing assisted reproduction treatment were enrolled, the timing of final follicle maturation and oocyte retrieval were evaluated based on follicle tracking with use of either conventional 2D ultrasound or SonoAVC (Table 1). The authors found that timing final follicle maturation and egg retrieval on the basis of these automated measures does not appear to improve the clinical outcome of assisted reproduction treatment [9].

	Positive	Negative
Antral Follicle	Saves time	Requires post processing
	Highly reproducible	
	Provides size of antral follicle	
Follicle tracking	Saves time	Requires post processing
	Highly reproducible	Does not improve clinical outcome when conventional hCG criteria are used
	Accurately measures true follicle size	

Table 1: Advantages and disadvantages of SonoAVC.

3D Evaluation of uterus and endometrium

Although much of the interest in 3D ultrasonography in infertility has focused on ovaries, uterus and endometrium can be evaluated with 3D ultrasonography for volume calculations, multiplanar reconstruction and image manipulation. Images acquired by 3D ultrasonography are displayed in three planes. Coronal plane is the best anatomical plane that uterus can be viewed because both fundus and lower uterine segment are evaluated [10]. This is essential for evaluation of congenital uterine anomalies. 3D ultrasonography with MRI is now the imaging modality of choice for the assessment of congenital uterine anomalies.

In a 2012 study, 143 patients with recurrent implantation failure *in vitro* fertilization cycles underwent 3-dimensional sonohysterography (3D-SHG) followed by vaginoscopic hysteroscopy (VH) to estimate the degree of agreement between 3D-SHG and VH in detection of uterine cavity abnormalities. The results showed that there is a substantial degree of concordance between 3D-SHG and VH in diagnosing uterine cavity anomalies. The authors also found that 3D-SHG took significantly less time and induced less patient discomfort than did VH. They suggested 3D-SHG should be the method of first choice for outpatient evaluation of the uterine cavity [1].

Since 1980s, ultrasound has been used as a guide to embryo transfer and aids for an easier transfer, and more accurate placement of the embryos within the cavity. There are many studies suggesting ultrasound guided embryo transfer increases pregnancy rates [1]. In a 2005 study, Gergely and colleagues evaluated the use of maximal implantation potential (MIP) point in conjunction with a 3D ultrasound during embryo transfers in order to facilitate transfers and increase pregnancy rates. They suggested that the uterine cavity was well visualized using 3D ultrasonography and the MIP point was well identified and embryo transfers at the MIP were associated with good implantation and pregnancy rates [11].

Conclusion

In recent years, application of 3D ultrasonography has greatly increased in obstetrics and gynaecology. It is a safe and non-invasive technique for evaluation of female genitalia. 3D ultrasonography has some advantages beyond those of conventional scanning.

As it has proven advantages for its accuracy, easy application and being timesaving, for the assessment of infertility 3D ultrasonography appears to be a first-line imaging technique. However, further research should be conducted on application of 3D ultrasonography in female infertility.

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