Reliability of automated volumetric measurement of multiple growing follicles in controlled ovarian hyperstimulation

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Objective: To evaluate the reliability of a computer-assisted approach for automatically measuring ovarian follicles during controlled ovarian hyperstimulation (COH).
Design: Prospective, comparative study.
Setting: Hospital Béclère, Clamart, France.
Patient(s): Twenty-seven infertile IVF-ET candidates undergoing COH.
Intervention(s): Just before the oocyte retrieval, growing follicles (n = 72) had their mean diameters measured and their volumes determined semimanually by virtual organ computer-aided analysis (VOCAL) and automatically by SonoAVC. Follicles were sorted in small (12–16 mm; n = 35) and large (>16 mm; n = 37) growing follicles. Measures were compared with the follicular fluid volume.
Main Outcome Measure(s): Concordance of results using intraclass correlation coefficient and limits of agreement methods, respectively.
Result(s): Overall, VOCAL (median: 3.42 mL; range: 0.98–9.68 mL) and SonoAVC (3.25 mL; 0.98–8.63 mL) measurements were equivalent to the corresponding actual follicle volume (3.20 mL; 0.80–10.20 mL). The intraclass correlation coefficient values between follicular fluid volume and mean diameter, VOCAL, and SonoAVC were 0.51, 0.95, and 0.98, respectively, for small follicles, and 0.80, 0.93, and 0.92, respectively, for large follicles. 95% limits of agreement between actual volume and VOCAL (−1.09 to +1.07 mL) and SonoAVC (−1.08 to +0.84 mL) measurements were comparable in both groups.
Conclusion(s): Automated measurement of multiple follicular volumes using SonoAVC is a simple technique, which reliability is superior to usual diameter measurements and comparable to VOCAL. This technologic refinement invites us to switch toward volumetric monitoring of follicle growth during COH. (Fertil Steril® 2010;94:2172–6. ©2010 by American Society for Reproductive Medicine.)

Key Words: SonoAVC, VOCAL, 3D ultrasound, follicle volume, in vitro fertilization, controlled ovarian hyperstimulation

The foremost objective of controlled ovarian hyperstimulation (COH) in in vitro fertilization-embryo transfer (IVF-ET) cycles is the achievement of multiple, reproductively competent oocytes. From a morphologic standpoint, the adequate appraisal of follicle readiness to ovulation triggering is essentially based on the exhaustive scanning of the ovaries by transvaginal ultrasonography. Yet, when performed on a routine basis, such a procedure has long been restricted to two-dimensional (2D), manual determination of follicle diameters, as follicle volume assessment remained unreliable (1), complex, and time consuming. The improvement in the reliability and simplicity of follicle measurements, in particular, of volumetric data, presumably will refine the assessment of ovarian response to COH and maybe lead to the improvement of the reproductive outcome of oocytes.

An emerging approach to achieve these objectives is SonoAVC technology (General Electric Healthcare, Kretz, Austria) (2–5). This software is based on an algorithm that identifies hypoechogenic structures and their approximate shape (ovarian follicles) in the selected 3D matrix. Then, after having recognized the center of each structure, SonoAVC is able to progressively calculate the exact number of surrounding voxels toward the structure borders (growth function) and extrapolate its mean diameter and volume. Yet, whereas some studies indicated that SonoAVC is useful to assess ovarian follicle diameters (6), volumes of follicle-like structures (2), and growing antral follicles (3), its reliability to determine multiple growing follicle volumes during COH is a key issue and requires further confirmation. In a previous investigation including patients undergoing IVF-ET in monodominant follicle cycles, we showed that both the reproducibility and reliability of SonoAVC are comparable to the reference technique (virtual organ computer-aided analysis [VOCAL]) (7, 8) for the measurement of single preovulatory follicle volumes (4). However, according to that study's design (4), the molding effect of interfollicle compression in the antral follicle shape usually observed in controlled hyperstimulated ovaries is barely

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absent. Indeed, when multiple preovulatory follicles coexist in the same ovary, their shape tends to be more complex and less recognizable than in monodominant follicle cycles.

To clarify this issue, in the present investigation, we aimed at evaluating the concordance between actual volumes and 2D follicle diameter, VOCAL, and SonoAVC volume measurements of multiple developing follicles obtained after COH.

MATERIALS AND METHODS

Subjects

Twenty-seven infertile women, 26 to 39 years of age, were studied prospectively. All of them met the following inclusion criteria: both ovaries present, deprived of morphologic abnormalities, and adequately visualized in transvaginal ultrasound scans; menstrual cycle length range between 25 and 35 days; no current or past diseases affecting ovaries or gonadotropin or sex steroid secretion, clearance, or excretion; no clinical signs of hyperandrogenism; body mass indexes (BMI) ranging between 18 and 25 kg/m^2. An informed consent was obtained from all women, and this investigation received the approval of our internal institutional review board.

Protocol for COH

All women underwent COH with GnRH agonist and exogenous gonadotropins as described elsewhere (9). Administration of hCG to trigger final follicle maturation and ovulation was performed when at least four follicles exceeded 16 mm in diameter and estradiol levels were higher than 1,000 pg/mL. Ooocyte retrieval was performed approximately 36 hours after hCG administration by transvaginal ultrasound-guided aspiration.

Ultrasonographic Measurement of the Growing Follicle Volumes

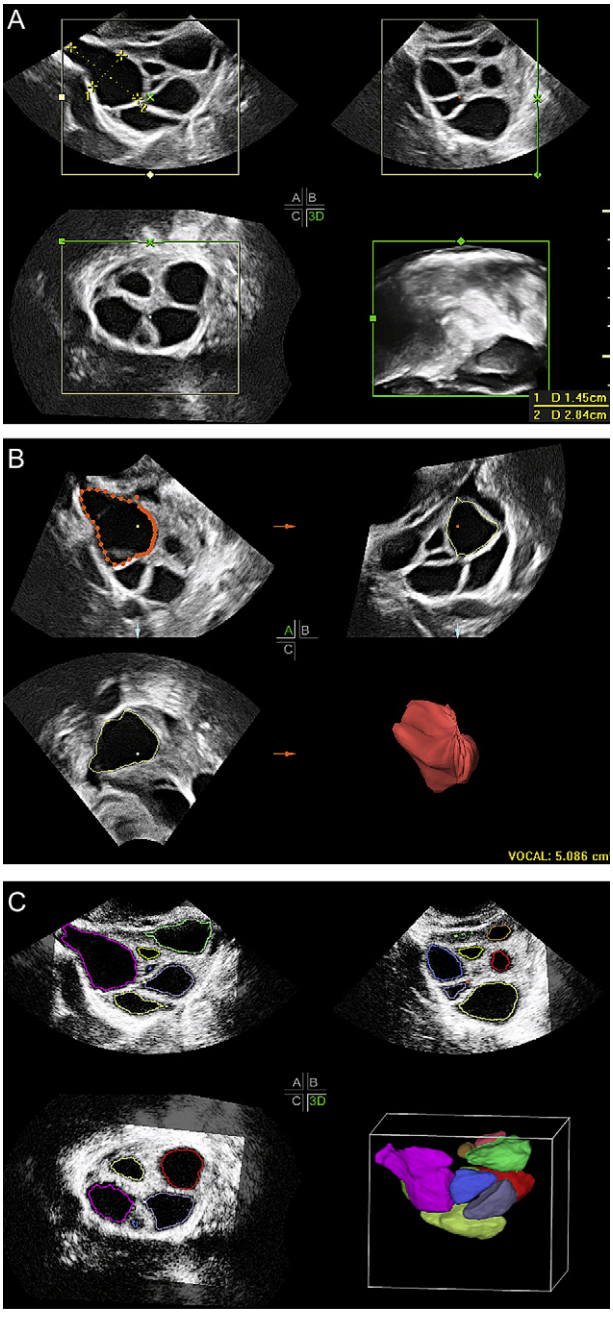
Just before oocyte retrieval (approximately 9:00 A.M.), using a 3.7 to 9.3 MHz transvaginal ultrasound probe (RIC5-9H, General Electric Medical Systems, Paris, France), a single operator (F.L.) selected for each ovary one or two growing follicles that met the following inclusion criteria: mean diameter >12 mm, adequate visualization of follicle borders, placed as close as possible to the transducer, and distributed side by side in a row at the same ultrasonographic plane. Each selected follicle had its mean diameter measured (manual diameter measurement) (Fig. 1). For this, the two orthogonal diameters (d1 and d2) were determined at the largest follicle plane using 2D ultrasound by placing calipers at the inner follicle borders. Mean follicle diameter corresponded to (d1 + d2)/2 and results were expressed in millimeters. Incidentally, the operator was given enough time to carefully select the largest follicle plane of each follicle so that 2D measurements would be as accurate as possible. A 2D picture including all selected follicles was then obtained and, in the print, each follicle was respectively numbered to allow their subsequent identification. Thereafter, departing from the same ultrasonographic plane that served to follicle selection and picture, each ovary was 3D-reconstructed using the same transvaginal ultrasound probe equipped with a 146-angle rotating head.

Under transvaginal ultrasound guidance, for the present's study purposes, follicular fluid (FF) from each selected growing follicle was thoroughly aspirated using a 10-mL syringe connected to a 35-mm, 17-gauge needle then maintained at steady temperature conditions (37°C) until the oocyte was found and isolated. Actual growing follicle volumes were extrapolated from FF volume. For the first selected follicle, FF volume was estimated by adding the volume contained in the aspiration syringe to the residual volume contained in the needle (0.5 mL). Yet, the residual volume was not added in the estimation of actual volume calculation of the following follicles as the same needle was used for their aspiration.

After the oocyte retrieval, volumes of selected follicles were determined manually using offline 3D reconstruction by means of a virtual organ computer-aided analysis (VOCAL) technology (General Electric Healthcare, Kretz, Austria). For this, the region of interest in the 3D volume, which corresponded to the inner follicle border, was manually and progressively (every 15°) set (VOCAL measurement) (Fig. 1). The same follicle volume was reassessed automatically, in the same 3D reconstructed images, using SonoAVC (General Electric Healthcare) (Fig. 1). Volumes were expressed in milliliters and diameters were expressed in millimeters.

FIGURE 1

The three types of measurements performed in the same selected growing follicles: (**A**) mean follicle diameter, (**B**) VOCAL volume, and (**C**) SonoAVC volume calculation.



Lamazou. Automatic measurement of follicles. Fertil Steril 2010.

Definition of Groups According to Growing Follicle Diameters

To refine the analysis of concordance between actual volumes and mean follicle diameter, VOCAL, and SonoAVC volume measurements of