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The Techniques of IVF Made Easy®

Editors
Manish R Pandya
Vijaykumar Chelur



Forewords
Zsolt Peter Nagy
Sadhana Desai

2nd Edition

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DVD Contents

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2. Placement in Incubator
3. Pick-up Transvaginal Sonography (TVS)
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Chapter 6

In Vitro Fertilization and Follicle

Ritu Jain

FOLLICULOMETRY IN IVF-FOLLICULAR ASSESSMENT FROM ANTRAL FOLLICLE TO TRIGGER IN IVF

Transvaginal sonography (TVS) is the best standard diagnostic and treatment guiding modality in infertility management. Follicular assessment by TVS is the core component of assisted reproductive technology right from counting antral follicles till oocyte retrieval from mature follicle.

It provides accurate information:

- Regarding ovarian reserve
- Choosing appropriate protocol for stimulation
- Deciding the time of antagonist in flexible protocol
- Guiding the gonadotropin schedule during cycle
- Knowing the time of hCG trigger
- Deciding the sequence of hCG in batch IVF
- Taking appropriate preventive measures in suspected OHSS
- Ruling out any infection
- Mapping the accessibility of ovaries for pick up.

Anatomically ovaries are placed in ovarian fossa just anterior to internal iliac vessels. Sonographically they are recognized as ellipsoid structure with multiple hypoechoic areas as follicle. Scrolling from one pole to the other systematically scans each ovary. Measuring the maximal diameters on three dimentional plane assessed each follicle.

Accuracy of follicles assessment is different in normal and hyper-stimulated ovary. The reliability of follicular measurements decreases

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as the number of follicles increase as it becomes ellipsoidal from spherical and there is a lot of observer bias.

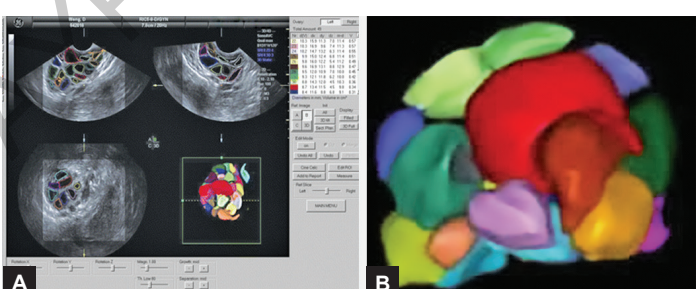
3D/2D USG

SonoAVC 3D folliculometry is ideal:

- As it measures volume (follicle is a 3D structure) which is the best parameter for size rather than diameter which is an imperfect surrogate marker.
- Volume-based criteria seems to be a better indicator of oocyte maturity and increase mature oocyte yield.
- SonoAVC makes it possible to save raw ovarian volumes and make them available for retrieval and analysis.
- It is well standardized and eliminates interobserver bias providing a quality control system.

Most of gynaecologists routinely prefer 2D scan in TVS as there is good agreement between SonoAVC and 2D measurements (Figs. 6.1A and B).

Ovarian stromal blood flow velocity after 2–3 weeks of pituitary suppression is a true representative of baseline ovarian flow because ovaries are quiescent. It correlates well with intraovarian perfusion and delivery of gonadotrophins.



Figs. 6.1A and B: 2D and 3D view of hyperstimulated ovary.

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Antral Follicle Count

- Folliculometry in IVF starts from antral follicle which marks the start of gonadotropin dependent phase.
- Antral follicle count (AFC) is considered the best biomarker for predicting ovarian response along with age and AMH.
- AFs are measured by transvaginal ultrasonography in the early follicular phase, by taking the mean of two perpendicular measurements.
- 3D ultrasound does not have any advantage over 2D ultrasound in the assessment of ovarian reserve.
- It is the follicle of 2–6 mm in size declines with age and correlates well with FSH and CCCT than that of 7–10 mm size which remains constant.
- Antral follicles of 2–6 mm relates to reproductive age and could well reflect the size of the remaining primordial follicle pool.
- The numbers of follicles in both ovaries are added for the total AFC. A count of 5–10/ovary is considered as a predictor of a normal response.
- More than 10 AFs are considered to be a good predictor of hyper-response.
- A low follicle count (less than 5/6 in total) predicts a poor response with more chances of cancellation.

Criteria for triaging different responders:

AFC	*Response*	*Gonadotropins*
5–10/ovary	Normal responder	225–300 IU
>10/ovary	Hyper-responder	75–150 IU
< 5/ovary	Poor responder	375–450 IU

Ovarian Volume

- During folliculometry, ovarian volume is not considered much significant as it remains unchanged till the perimenopausal period and does not add to the predictive value of AFC.
- A decline in the ovarian volume is a late event noticed in women > 40 years.

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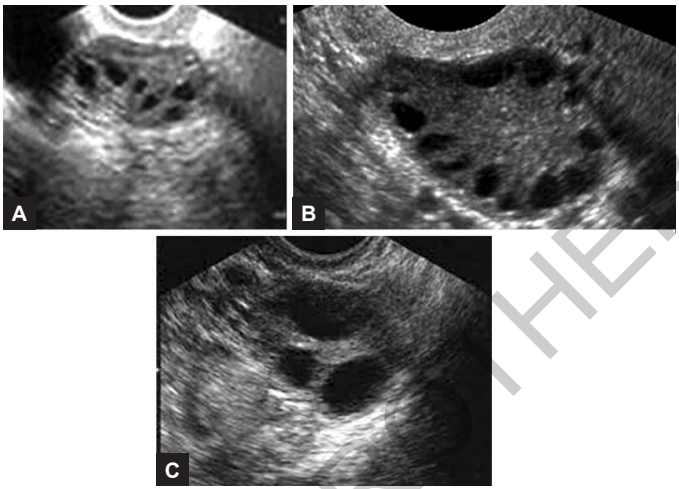

Figs. 6.2A to C: Images of ovary. (A) Normal; (B) Hyper (PCOS); (C) Poor.

- Small ovaries < 3 ml, measured on TVS are associated with poor response to ovulation induction.
- The volume of each ovary is calculated by measuring in three perpendicular directions and applying the formula for an ellipsoid (D1 × D2 × D3 × 0.52) (Figs. 6.2A to C).

SERIAL FOLLICLE STUDY IN IVF STIMULATION

- Serial ultrasound examinations are performed to assess the number and size of follicles during controlled ovarian stimulation (COS) for IVF.
- Usually followed schedule is counting antral follicles and then on D4, D6, D8 and D10.
- Number of recruited follicles on D4 actually predicts the expected number of oocytes.
- Intermediate and small sized follicles are also counted and tracked as they also contribute to E2 levels and account for OHSS.

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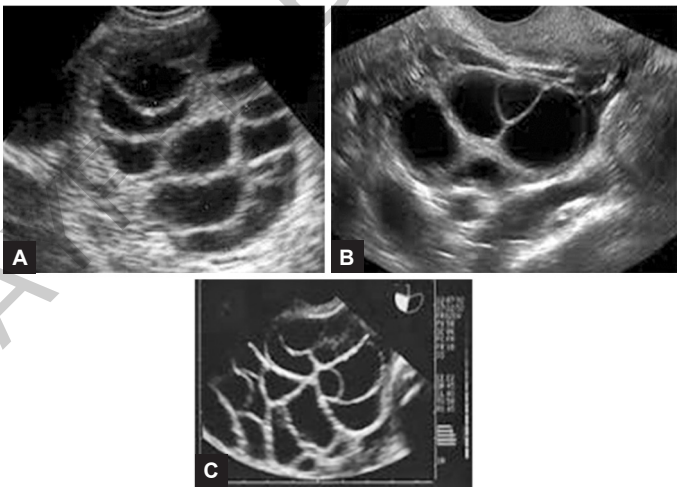
- "The rate of follicular growth is dependent on the phase of the stimulation cycle." As stimulation is started , early growth of follicle may be slow, but once the follicle(s) have committed to 'active' growth, then they may grow 1–3 mm per day.
- Soon thereafter, the follicles start to grow and once they reach about 12 to 14 mm, they will grow fairly predictably at a rate of 2 mm per day.
- Measuring E2 levels in blood is a direct reflection of growing follicles and hence granulosa cell activity.
- The likelihood of a follicle containing a mature oocyte is related to its size. The fertilization rate was higher in oocytes collected from follicles with internal echoes (87%) compared to echo-free follicles (50%).
- In antagonist cycle, once the follicle reaches 14 mm, antagonist is added as in flexible schedule to prevent LH surge.



Figs. 6.3A to C: Normal, poor, and hyper-responding ovary in stimulated phase.

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- During follicle study it is important to measure endometrium thickness and take appropriate measures.
- Fluid in pelvis with normal growing follicles and probe tenderness is suggestive of infection and needs treatment.
- If growing follicles per ovary are 15 or more, with disproportionate rise in E2, coasting is started and daily E2 monitoring and follicle study is started.
- Fluid in pelvis with hyperstimulated ovaries need correlation with E2 levels to rule out OHSS (*see* Figs. 6.3A to C).
- Sometimes ovaries are stuck up high in pelvis and may need transabdominal ultrasound, but always the best guide is internal iliac vessels.
- In batch IVF, patient having the large sized follicle is taken first in sequence.
- Folliculometry significantly predicts the ovarian response to COH and the outcome of ARTs in the current treatment cycle.

POINTS TO REMEMBER

1. TVS is best guide for standard diagnostic and treatment modality for managing infertility and IVF.
2. Folliculometry done by TVS is core component for IVF as ovum pick is done with help of USG only.
3. TVS will give accurate information regarding ovarian reserve, choosing appropriate protocol for perticular cycle and patient, use of gonadothrophine either increase in dose or decrease, time for trigger with hCG or antagonist, suspect OHSS, rule out infection, doing mapping for pick up of ovum.
4. Sono AVC is 3D reconstuction of ovarian follicluar volume with each follicle color coaded with different color with all measurements like size volume and shape.
5. AFC is done on day 2 of cycle before starting donadothrophine and is considered best boimarker with age and AMH.
6. AFC is very good guide for starting dose of gonadothrophine like 5-10/ovary is normal and start 225-300 IU, >10/ovary hyper responder start with low dose 75-150 IU, <5/ovary is poor responder start with high dose 375-450 IU.

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7. Ovarian volume is not considered much significant and is declined after age of 40, small volume < 3 ml is associated with poor response, always measure volume by HxWxLX0.52.
8. Usually TVS was done on D2/D4/D8/D10 for serial monotoring of follicle, D4 is actual predictor of number of expevted follicle, rate of follicular growth is dependant n phase of stimulation cycle, and active follcle grows at 1-3 mm per dya and after reaching 12 to 14 mm will grow at 2 mm per day.
9. During folliculomtery we have to measure endometrium (ET) also and take appropriate action to make it around 8 mm.
10. Always take large sized follicle ovary first for pick up.
11. Folliculometrty significantly predicts the ovarian response to COH and outcome of ART in current cycle.

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Manish R Pandya MD FICOG FICMCH (Gynecologist) Endoscopy (CICE France) ART (EART—Mumbai, CRM—Cleveland) is Professor and Head, Obstetrics and Gynecology, Scientific Research Institute, Surendranagar, Gujarat, India, practicing since 24 years. He has done more than 9000 endoscopic surgeries by special umbilical technique. He was trained in endoscopy surgery at BEAMS and Johnson and Johnsons institute, Mumbai in 2001 and he has also been trained at Clermont Ferrand, France in CICE in the year of 2007 (Centre International de Chirurgic Endoscopique). He is Co-author of *Step by Step Infertility Practice, Step by Step Gynecological Endoscopy Surgery* and *Step by Step Active Management of Labour*. He is Principal-author of *Step by Step Male Infertility Management* and *Atlas of Fetal Echocardiography* published by Jaypee Brothers Medical Publishers, New Delhi. He has written three chapters in postgraduate series of BI Publication and one chapter on DUB in ECAB clinical update by Elsevier Publication. Four research paper published in UBCP journal. He is Editor-in-Chief of Indian Journal of Obstetric and Gynecological Research (IJOGR), Innovative Publication, New Delhi, and Open Assess Journal in Gynecology (OAJG), Medwin Publication USA. He has published 44 research papers and case report in IJOGR and one systemic review in OAJG. He has a FOGSI-recognized USG Training Center and ART Training Center at Surendranagar, for basic advance color Doppler and 3D 4D USG with small parts and IUI, IVF and ICSI. His center is NARCHI-recognized for DFW/DRCH/DGO (Diploma in Obs & Gyne) and College of Physician and Surgeons (CPS), Mumbai, MCI-GMC recognized 4 seat for DGO. He had done 534 CME and DGM in all over India and internationally as faculty till date. He has been awarded with "The Dynamic Indian of the Millennium" award by KG Foundation, Coimbatore by Padma Shree Dr Bhaktavatsalam and "Gynec Excellence award by AOGS and FOGSI. His Mahavir Hospital is only ISO-certified hospital in Surendranagar, Gujarat.
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Vijaykumar Chelur MSc PhD is renowned Embryologist of India. He passed his BSc (1995) and MSc (Microbiology, 1988) from Kuvempu University, Karnataka, India. He has done his PhD from NIMS, Jaipur, Rajasthan. He received his training in embryology from Dr Joshua Peter and Dr Judith Menezes. He was trained in micromanipulation by Mr Michael Robert Herbert, Monash University, Australia. He got trained in Embryo Biopsy, PGD/PGS by FISH, PCR and aCGH from University College of London. He is the board certified Embryologist (EMB-Level IV) from American College of Embryology, USA. He has trained more than 300 professionals through EART and set-up about 16 labs, both across the World. He is an invited speaker to many national and international seminars and conferences. He is Consultant to more than eight ART centers over India and Africa. He and Dr Manish Pandya are Life Member to many organizations such as Indian Society of Reproduction (ISAR), Indian Fertility Society (IFS) and Academy of Clinical Embryologists (ACE), India.

Printed in India

Available at all medical bookstores or buy online at www.jaypeebrothers.com



JAYPEE BROTHERS
Medical Publishers (P) Ltd.
EMCA House, 23/23-B, Ansari Road,
Daryaganj, New Delhi - 110 002, INDIA
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OBSTETRICS & GYNECOLOGY

ISBN 978-93-5270-330-2

