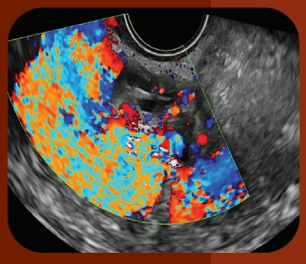
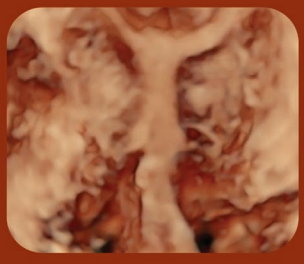
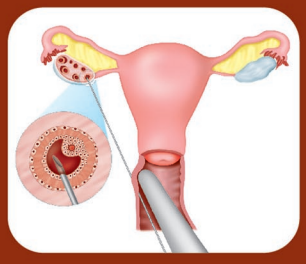


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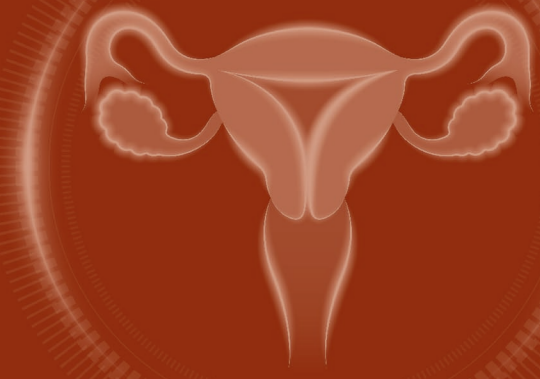

Sonal Panchal
Chaitanya Nagori

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Chapter

Preovulatory Assessment

INTRODUCTION

Ultrasound (US) and hormonal assessment are considered two primary investigations for evaluation of female factor of infertility. With advancing US technology, Doppler and 3D US have eliminated the need for majority of other investigations for cycle monitoring. When US is used with Doppler, it gives precise idea about not only the morphological changes but also vascular changes occurring during the entire cycle. Vascular changes are instantaneous to hormonal changes and occur before morphological changes.

WHEN IS THE FOLLICLE FUNCTIONALLY MATURE?

Follicle gains dominance at a mean diameter of approximately 10 mm and it grows at a rate of 2–3 mm per day. As the dominant follicle grows, it starts pulling vascularity toward itself.[1,2] This is to allow the exposure of the follicle to follicle-stimulating hormone (FSH) and development of FSH receptors on the follicle.

Follicle, that grows to >16–17 mm **(Fig. 1)** in diameter [follicular diameter is measured as single anteroposterior (AP) diameter, when the follicle is seen as a spherical structure or three longest orthogonal diameters must be measured in two orthogonal planes and the mean is used as follicular diameter] has anechoic contents, thin isoechoic wall, is round or oval, and grows at a rate of 2–3 mm/day could be considered a mature follicle on 2D US alone. A thin hypoechoic rim can be seen surrounding the follicle 24–36 hours before ovulation. Cumulus-like shadow may be seen at same time (in about 35–40% of mature follicles—not a mandatory sign for follicle maturity evaluation).

Low-level echogenicities are seen inside the follicle parallel to the wall about 6–10 hours before rupture, due

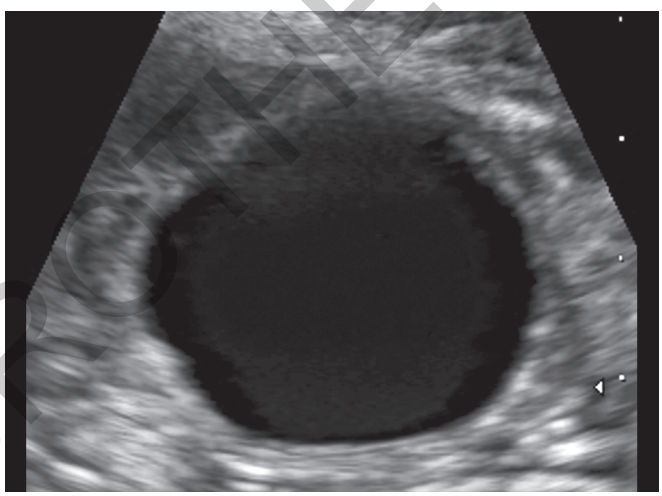


Fig. 1: B-mode ultrasound image of a mature follicle.

to separation of the inner wall **(Fig. 2)**. Around the same time, irregularity of the follicle wall is seen due to triangular anechoic niche-like shadows. And both these later signs are considered to be signs of impending ovulation.

On Doppler:

The blood vessels that have started growing toward the dominant follicle gradually increase to cover 2/3–3/4 of follicular circumference **(Fig. 3)**. Fall in perifollicular resistance index (RI) starts 2 days before ovulation.[3] These vessels show RI of 0.4–0.48[4] and this correlates with the preovulatory estrogen surge. It speaks about the adequacy of estrogen production by the follicle and thus about follicle quality. Then peak systolic velocity (PSV) starts rising and when PSV reaches 10 cm/sec, it is the time for the natural surge or the time to give surrogate surge in case a patient is under fertility treatment **(Fig. 4)**. Preovulatory perifollicular PSV correlates with the luteinizing hormone (LH) levels.

But when assessing perifollicular flows, ovarian stromal flows, corpus luteal flows, and endometrial flows,

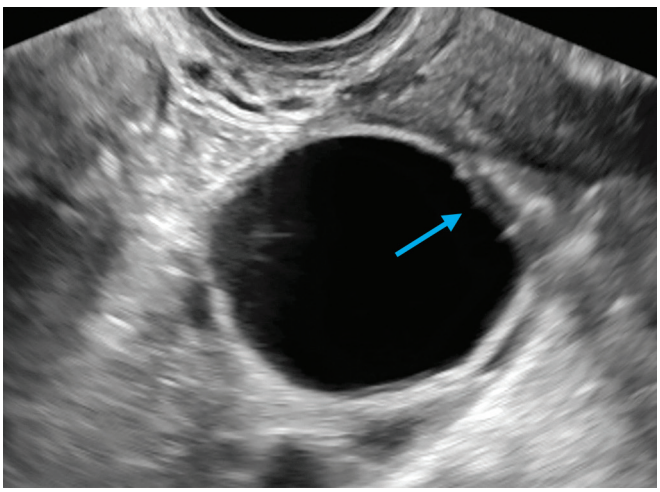


Fig. 2: B-mode ultrasound image of a follicle of which rupture is impending showing mild separation of inner wall (blue arrow) at 2 o'clock and 6 o'clock positions.

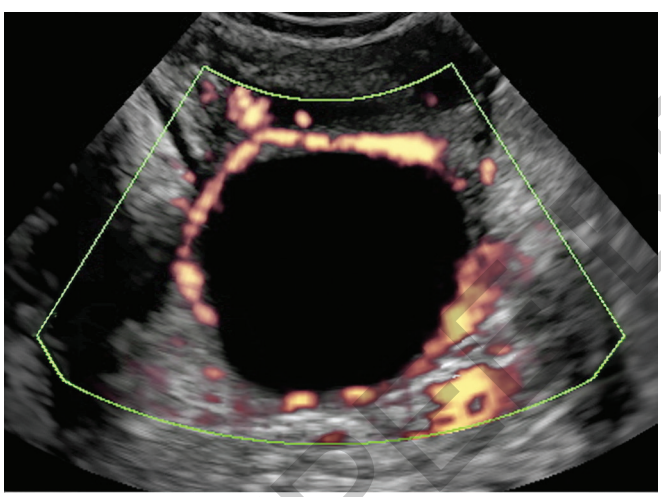


Fig. 3: Perifollicular vascularity seen on color Doppler.

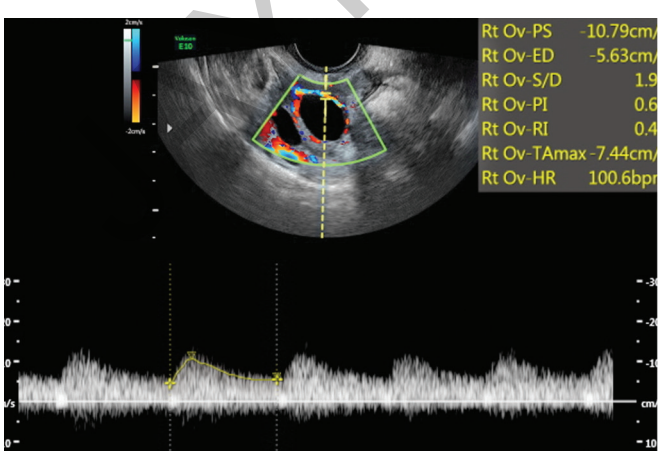


Fig. 4: Pulse Doppler image of the low resistance perifollicular flow.

remember that the pulse repetition frequency (PRF) is always set at 0.3 for color and power Doppler, with wall motion filter at the latest and gains once set in the preset should not be changed. Also, remember that the vessels that overlap on the follicular wall are perifollicular vessels. Flow may be assessed on the brightest color spots. RI and PSV matching only in one vessel with 2/3 to 3/4 circumference of the follicle covered by blood vessels is sufficient to confirm follicle maturity.

Why is Doppler assessment essential?

- Ovarian flow correlates well with oocyte recovery rates.
- Embryos produced by fertilization of the ova obtained from the follicles that had a perifollicular PSV of <10 cm/sec are less likely to be grade I embryos and also have higher chance of chromosomal malformations.[5,6]
- Oocytes from severely hypoxic follicles are associated with high frequency of abnormalities of organization of chromosomes on metaphase spindle and may lead to segregation disorders and catastrophic mosaics in embryo.[7]

On 3D ultrasound:

Follicular volume of 3–7.5 cm^3, calculated by virtual organ computer-aided analysis (VOCAL) software of 3D US has been found to be optimum in our study.[8] This agrees with the study by Wittmaack et al,[9] which says that in in vitro fertilization–embryo transfer (IVF–ET) cycles, follicles with mean follicular diameter of 12–24 mm are associated with optimal rates of oocyte recovery, fertilization, and cleavage.[9] This corresponds to the follicular volumes of between 3.77 and 7.54 mL **(Fig. 5)**. Volume assessment of the follicles is especially important when there is multifollicular development and the follicles are compressed by each other leading to irregular shape. In such a situation, mean diameter of three longest orthogonal diameters is not precise and neither the VOCAL nor the sonography-based automated volume count (SonoAVC) software of 3D US.

Follicles containing oocytes capable to produce a pregnancy have a perifollicular vascular network more uniform and distinctive.[10] In our study,[8] perifollicular vascularization index (VI) of 6–20 and perifollicular flow index (FI) >35 are most optimum. 3D power Doppler gives the most precise information about the vascularization and follicular blood flow.[11]

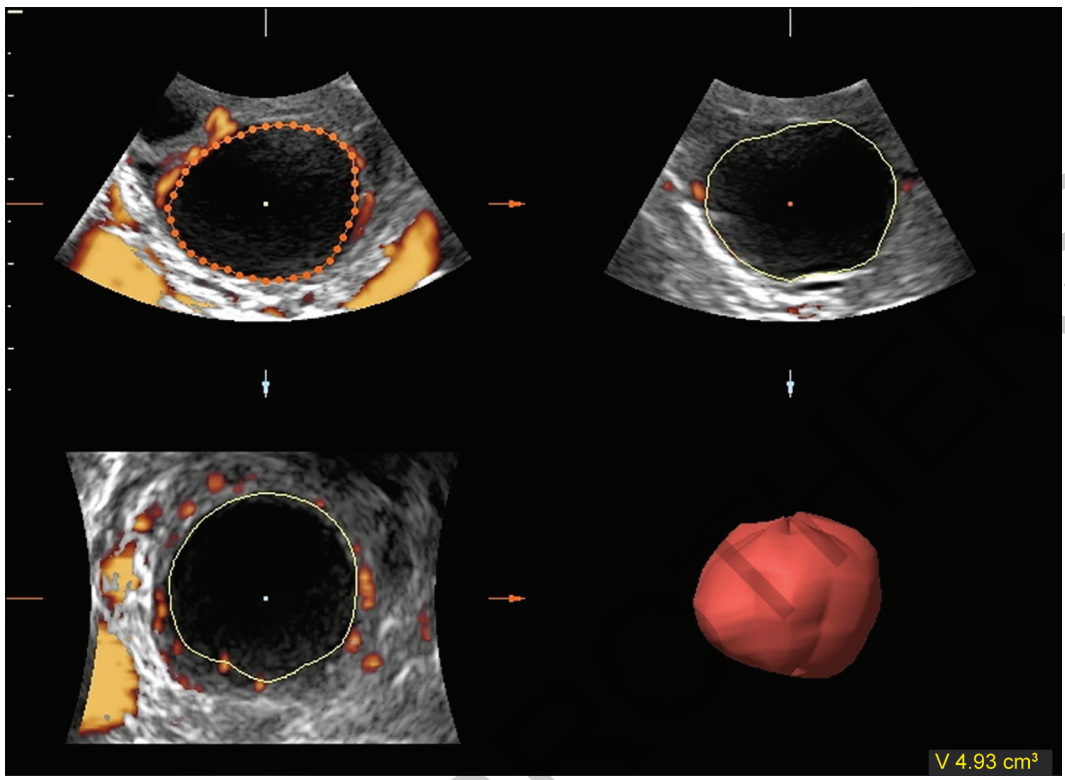


Fig. 5: 3D ultrasound acquired, virtual organ computer-aided analysis (VOCAL) calculated volume of follicle.

After surge starts:
When perifollicular PSV is 10 cm/sec, it is the time when the LH surge starts and under the effect of that LH, the perifollicular PSV keeps on rising constantly.[12] Vascular changes at the time of impending ovulation include increased vascularity of the inner wall of the follicle and a coincident surge in blood velocity just prior to eruption.[12] This derives that a rising PSV with steady low RI suggests that the follicle is close to rupture. Therefore, in cases where on pretrigger scan, the follicular PSV is high with low RI, it is an indication of the start of the surge, which means ovulation starting earlier than 36–42 hours and in these cases, earlier intrauterine insemination (IUI) gives better results. One may also plan double IUI, one at 12–14 hours and another at 36–38 hours after trigger. This covers the entire period of likely ovulation and the results of IUI are better.

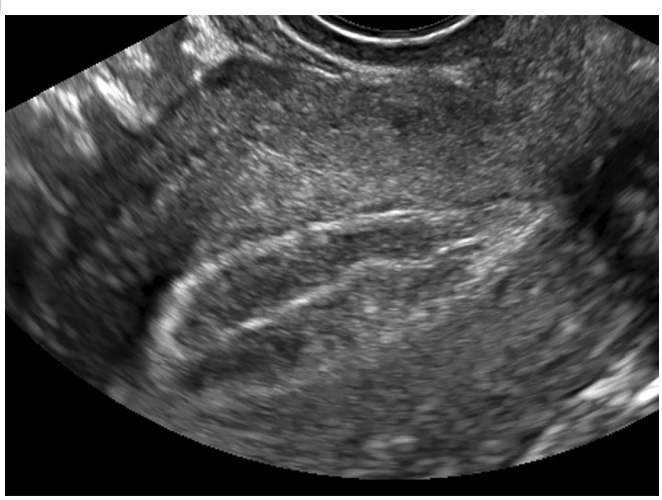


Fig. 6: B-mode ultrasound image of grade-A endometrium.

WHAT INDICATES GOOD ENDOMETRIAL RECEPTIVITY?

B-mode features of endometrium with good receptivity:

- Minimum endometrial thickness of 6 mm but 8–10 mm is optimum. The endometrial morphology may be grade A, B, or C. Grade A, when it is a triple line endometrium with the intervening area as echogenic as the anterior myometrium and usually relates with 3–5 mature follicles **(Fig. 6)**. Grade B **(Fig. 7),** when it is multilayered or triple line with hypoechoic intervening area and relates with 1–2 mature follicles. Grade C, when it is homogeneous isoechoic endometrium[13] and represents **(Fig. 8)**. It is important to remember

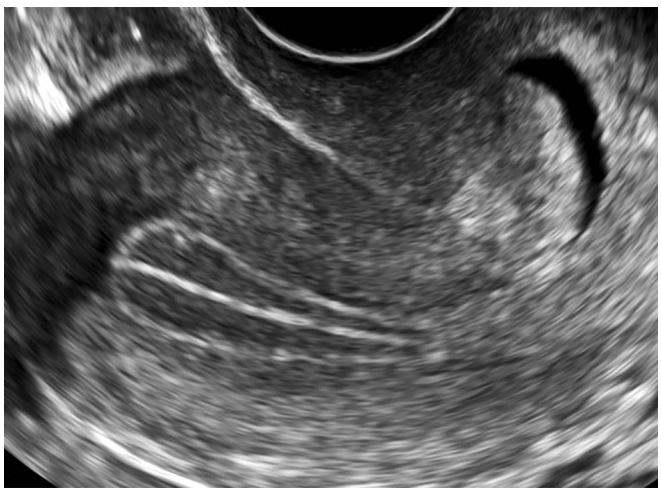


Fig. 7: B-mode ultrasound image of grade-B endometrium.

Fig. 8: B-mode ultrasound image of grade-C endometrium.

here that even grade C is a pure estrogen-dominated endometrium and relates with multifollicular development, and the changes in morphology indicate the amount of estrogen.

Doppler features of endometrium with good receptivity:
Implantation rates correlate more to the vascularity of the endometrium rather than the thickness and morphology of the endometrium.

On Doppler, endometrium shows vascularity in zones 3 and 4 or maybe called subendometrial and endometrial layers **(Figs. 9A to D)**.

The zones of vascularity are defined according to Applebaum[14] as zone 1, when the vascularity on power Doppler is seen only at endometriomyometrium junction; zone 2, when vessels penetrate through the hyperechogenic endometrial edge; zone 3, when it reaches intervening hypoechogenic zone; and zone 4, when they reach the endometrial cavity and only covers at least 5 mm^2 area of that zone.

Absent flow in the endometrial and subendometrial zones on the day of trigger indicates total failure of implantation.[15]

These arteries should have an RI <0.6. On pulse Doppler of the uterine artery, pulsatility index (PI) should be <3.2 **(Fig. 10)**.[16,17]

Endometrial Vascularity: Its Relation to Implantation Rates (Nagori and Panchal)[18]

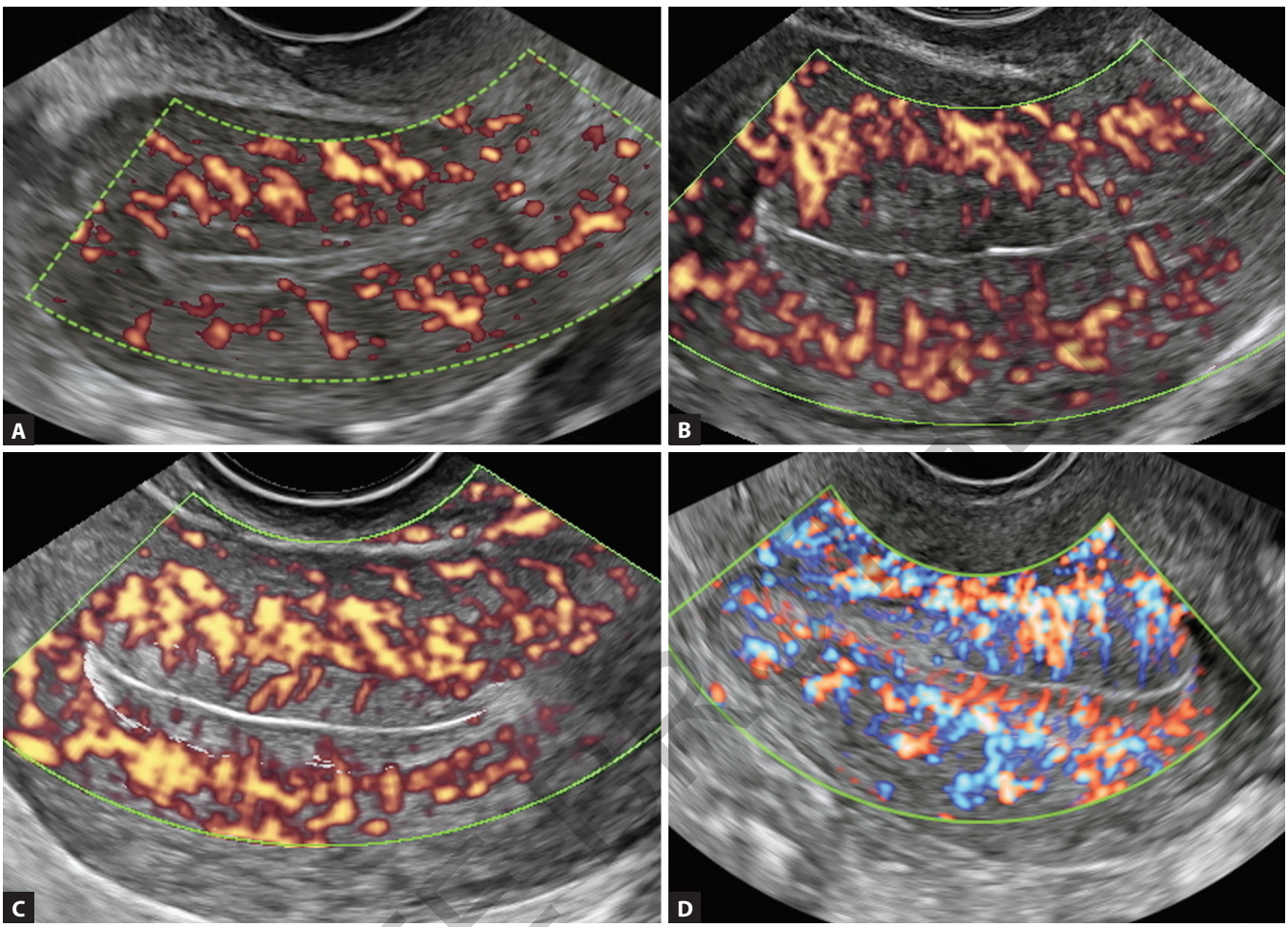
Endometrial vascularity is given in **Table 1.**

On 3D ultrasound:
Endometrial volume assessment by 3D US volume calculation correlates the cycle outcome with quantitative parameter rather than endometrial thickness.[9] This is done by a software called VOCAL. Pregnancy and implantation rates were significantly lower when endometrial volume was <2 mL.[19,20]

To summarize **(Table 2)***:*
If these parameters are not reached, the cycle is not canceled, only trigger is delayed. Stimulation is continued till these parameters are achieved. In case if the PSV of the follicle starts rising with low RI, it means the ovulation is impending. In such a situation, in spite of inadequate endometrial parameters, the trigger is given, but the patient is also explained that the result cannot be as good as it would be if every parameter was optimal. If the follicle grows beyond 23–24 mm and still perifollicular flow is not adequate, trigger is planned and patient may be given a choice of either timed intercourse or IUI, after proper explanation about the results.

After the surge has started:
The PSV of the perifollicular vessels increases, and higher PSV indicates advanced surge and ovulation earlier than 36–42 hours. In such cases, it is an IUI cycle; IUI needs to be planned earlier than 36–38 hours to achieve the best possible conception rate.

With the advancing LH surge, estrogen level falls leading to decrease in endometrial thickness by 0.5 mm and there is also decrease in endometrial vascularity. Progesterone normally also rises before ovulation, after



Figs. 9A to D: Power Doppler images of the grade 1–4 endometrium.

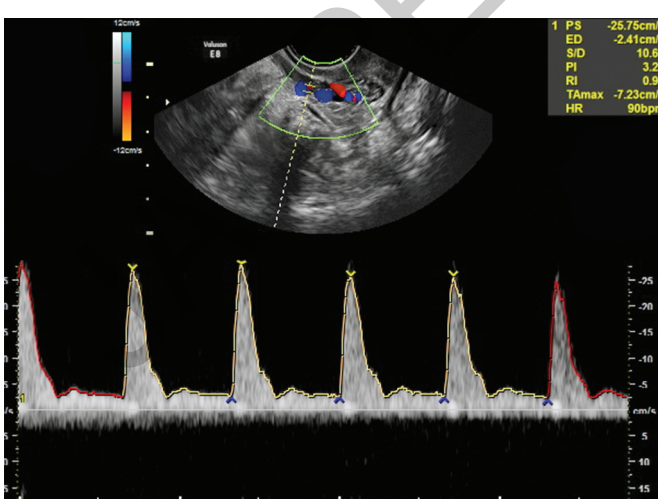


Fig. 10: Pulse Doppler image showing high resistance uterine artery flow waveform.

TABLE 1: Endometrial vascularity.

Vascularity in	Zone 1	Zone 2	Zone 3	Zone 4
% of patients	6.69%	20.73%	58%	14.47%
+ βhCG	19%	21.87%	39.77%	70.14
Gestational sac	9.6%	14.58%	36.8%	68.65%
Abortions	50%	23.8%	5.6%	1.5%

(hCG: human chorionic gonadotropin)

the surge starts. This shows fluffiness of outer margin of multilayered endometrium **(Fig 11)**. This indicates physiological level of progesterone and exposure duration of up to 24 hours. It also indicates good endometrial receptivity. With this, there is also rise in uterine artery PI on the dominant side.

When the progesterone level rises beyond the physiological levels or exposure of progesterone to

TABLE 2: Preovulatory follicle and endometrium.

	Follicle	*Endometrium*
Size/thickness	16–18 mm	8–10 mm
Morphology	Thin wall, no internal echoes, halo	Grade A/B
Vascularity	3/4th circumference	Zone 3–4
Resistance index	0.4–0.48	<0.5
Peak systolic velocity	>10 cm/sec	–
Uterine artery pulsatility index	–	<3.2
Volume	3–7 cm^3	3–7 cm^3
3D morphology	Cumulus	Intact endometriomyometrium junction
3D Power Doppler	More symmetrical the better	Higher the better

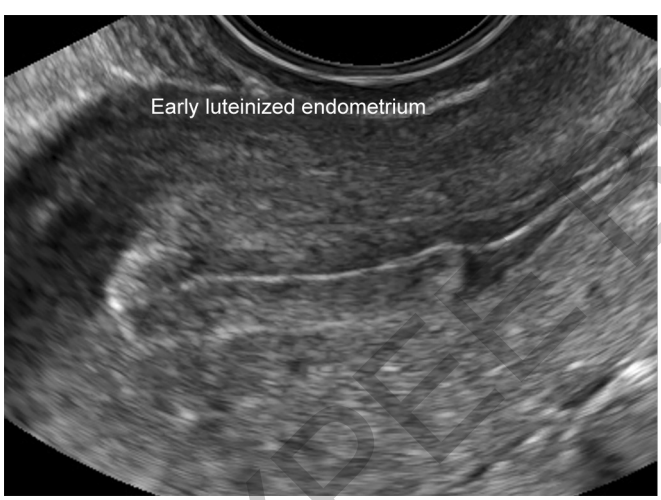


Fig. 11: Endometrium of early luteal phase seen on B-mode ultrasound. It shows fluffiness of outer margins of multilayered endometrium.

endometrium is too long, and starts deteriorating the endometrial receptivity, the outer margin of endometrium starts becoming hyperechoic.

These changes in the endometrium with immature follicle indicate premature LH surge whereas with rupture of the follicle indicates recent ovulation.

Preovulatory scan:

- Confirm dominance of the follicle by perifollicular blood flow and not by 10 mm size.
- *Good quality follicle (2D):* Anechoic, thin isoechoic wall, round/oval shape, and growth rate of 2–3 mm a day
- *Pretrigger follicle:* Apart from above-mentioned criteria
- *On 2D:* Mean follicular diameter of 16–18 mm at least
  - Hypoechoic halo starts appearing before 24–36 hours of ovulation.
  - Cumulus-like shadow starts appearing before 24–36 hours of ovulation.
  - *Low-level internal echogenicities in follicle lumen, parallel to follicular wall:* 6–12 hours before ovulation
  - *Rosebush thorn sign:* 5–10 hours before ovulation
- *On color Doppler (CD):* Vascularity covering at least 2/3 preferable 3/4 of the circumference
  - Perifollicular RI <0.48
  - Perifollicular PSV >10 cm/sec
- *On 3D:* Follicular volume of 3–7cm^3 correlates with diameter of 18–24 mm.
  - SonoAVC gives precise count and size of these follicles.
  - 3D power Doppler gives better idea about global vascularity of the follicle.
  - Cumulus may be visualized in more percentage of mature follicles.
- **Good quality endometrium**
- *On 2D ultrasound:*
  - Thickness at least 6 mm, preferable 8–10 mm
  - Grade A, B, or C
- *On CD:* Intraendometrial flow
  - 5 mm^2 area vascularized
  - Spiral RI <0.6
  - Uterine PI <3.2
- *On 3D:* Endometrial volume at least 2 cc
  - Endometrial global vascularity

CONCLUSION

Ultrasound is an excellent tool to decide the time of trigger and time of IUI. Doppler adds to the information available and for the final fine-tuning of the treatment cycle.

REFERENCES

1. Zaidi J, Barber J, Kyei-Mensah A, Bekir J, Campbell S, Tan SL. Relationship of ovarian stromal blood flow at the baseline ultrasound scan to subsequent follicular response in an in vitro fertilization program. Obstet Gynecol. 1996;88:779-84.
2. Engmann L, Sladkevicius P, Agrawal R, Bekir JS, Campbell S, Tan SL. Value of ovarian stromal blood flow velocity measurement after pituitary suppression in the prediction of ovarian responsiveness and outcome of in vitro fertilization treatment. Fertil Steril. 1999;71(1):22-9.

3. Jokubkeine L, Sladkevicius P, Rovas L, Valentine L. Assessment of changes in volume and vascularity of ovaries during the normal menstrual cycle using three-dimensional power Doppler ultrasound. Hum Reprod. 2006;21(10):2661-8.
4. Kurjak A, Kupesic-Urek S. Infertility. In: Kurjak A (Ed). Transvaginal Color Doppler. Carnforth, UK: Parthenon Publishing; 1991. pp. 33-8.
5. Nargund G, Doyle PE, Bourne TH, Parsons JH, Cheng WC, Campbell S, et al. Ultrasound-derived indices of follicular blood flow before HCG administration and prediction of oocyte recovery and preimplantation embryo quality. Hum Reprod. 1996;11(11):2512-7.
6. Nargund G, Bourne TH, Doyle P, Parsons J, Cheng W, Campbell S, et al. Association between ultrasound indices of follicular blood flow, oocyte recovery and preimplantation embryo quality. Hum Reprod. 1996;11(1):109-13.
7. Van Blerkom J, Antezak M, Schrader R. The developmental potential of human oocyte is related to the dissolved oxygen content of follicular fluid: Association with vascular endothelial growth factor levels and perifollicular blood flow characteristics. Hum Reprod. 1997;12(5):1047-55.
8. Panchal SY, Nagori CB. Can 3D PD be a better tool for assessing the pre-HCG follicle and endometrium? A randomized study of 500 cases. Presented at 16th World Congress on Ultrasound in Obstetrics and Gynecology, 2006, London. J Ultrasound Obstet Gynecol. Sept. 2006; 28(4):504.
9. Wittmaack FM, Kreger DO, Blasco L, Tureck RW, Mastroianni L Jr Lessey BA. Effect of follicular size on oocyte retrieval, fertilization, cleavage and embryo quality in in vitro fertilization cycles: A 6-year data collection. Fertil Steril. 1994;62(6):1205-10.
10. Vlaisavljević V, Reljic M, Gavrić Lovrec V, Zazula D, Sergent N. Measurement of perifollicular blood flow of the dominant preovulatory follicle using three-dimensional power doppler. Ultrasound Obstet Gynecol. 2003;22(5):520-6.
11. Mercé LT, Barco MJ, Kupesic S, Kurjak A. 2D and 3D power doppler ultrasound: From ovulation to implantation. In: Kurjak A, Chervenak F (Eds). Textbook of Perinatal Medicine. London: Parthenon Publishing; 2005.
12. Bourne TH, Jurkovic D, Waterstone J, Campbell S, Collins WP. Intrafollicular blood flow during human ovulation. Ultrasound Obstet Gynecol. 1991;1(1):53-9.
13. Smith B, Porter R, Ahuja K, Craft I. Ultrasonic assessment of endometrial changes in stimulated cycles in an in vitro fertilization and embryo transfer program. J In Vitro Fert Embryo Transf. 1984;1:233-8.
14. Applebaum M. The 'steel' or 'teflon' endometrium–ultrasound visualization of endometrial vascularity in IVF patients and outcome. Presented at the third World Congress of Ultrasound in Obstetrics and Gynecology. Ultrasound Obstet Gynecol 1993;3(Suppl 2):10.
15. Zaidi J, Campbell S, Pittrof R, Tan SL. Endometrial thickness, morphology, vascular penetration and velocimetry in predicting implantation in an in vitro fertilization program. Ultrasound Obstet Gynecol. 1995;6(3):191-8.
16. Steer CV, Campbell S, Tan SL, Crayford T, Mills C, Mason BA, et al. The use of transvaginal color flow imaging after in vitro fertilization to identify optimum uterine conditions before embryo transfer. Fertil Steril. 1992;57(2):372-6.
17. Zaidi J, Pittrof R, Shaker A, Kyei-Mensah A, Campbell S, Tan SL. Assessment of uterine artery blood flow on the day of human chorionic gonadotrophin administration by transvaginal color Doppler ultrasound in an in vitro fertilization program. Fertil Steril. 1996;65(2):377-81.
18. Nagori C, Panchal S. Endometrial vascularity: Its relation to implantation rates IJIFM. 2012;3(2):48-50
19. Raga F, Bonilla-Musoles F, Casañ EM, Klein O, Bonilla F. Assessment of endometrial volume by three-dimensional ultrasound prior to embryo transfer: Clues to endometrial receptivity. Hum Reprod. 1999;14(11):2851-4.
20. Kupesic S, Bekavac I, Bjelos D, Kurjak A. Assessment of endometrial receptivity by transvaginal color Doppler and three-dimensional power doppler ultrasonography in patients undergoing in vitro fertilization procedures. J Ultrasound Med. 2001;20:125-34.

Decision Making in TRANSVAGINAL SONOGRAPHY

Decision Making in Transvaginal Sonography is a book specifically designed for very busy gynecologists who are practicing ultrasound and for the students specializing in gynecology and infertility. Ultrasound is a highly descriptive subject and to compile it into algorithms seemed to be a difficult task. But this book of algorithms in ultrasound has truly turned out to be a very useful, easy-to-refer and easy-to-apply book. It has made the differential diagnosis in transvaginal ultrasound short, swift, and meaningful.

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