REVIEW ARTICLE

Primary Care in Obstetrics and Gynecology — A Place for Advanced Ultrasound?

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Abstract

The evaluation of adnexal masses based on transvaginal sonography (TVS) and when their size is too big- transabdominal US can be facilitated and refined by using color Doppler (CD), power Doppler (PD), and pulsed Doppler(PW), including three-dimensional ultrasound (3D US). With these modes, we obtain information about vascularity and flow indices, and their distribution within a mass. Considering the fact that neoangiogenesis is a main feature of malignancy, this is essential information. Thus, we are able to assume the benign or malignant character of an adnexal mass, make the right choice of additional imaging or biochemical tests, and then channel the treatment appropriately. This is subsequently demonstrated for simple cyst, hemorrhagic cysts, endometrioma, dermoid, serous papillary cystoma, ectopic pregnancy, and ovarian carcinoma.

Abnormal uterine bleeding (AUB) is a common problem in primary care. Compared to transabdominal approach, TVS improves the detection rate of underlying uterine pathology. In conditions like endometrial hyperplasia, polyps, submucous leiomyoma, and endometrial cancer, CD, PD, PW and contrast enhanced transvaginal ultrasound may optimize sonographic evaluation. Saline infusion sono-hysterography (SISH) in out patient department (OPD) is an alternative to invasive diagnostic hysteroscopy in patients with AUB.

Care for maternal and fetal well-being during pregnancy is a main task in OPD. The assessment of fetal pathology is almost entirely based on Ultrasound. Several illustrations of fetal anomalies detected during 1st trimester and 2nd trimester screening, of abnormal findings in feto-maternal Doppler ultrasound, and fetal pathology demonstrated in 3D/4D ultrasound mode, conclude this review of advanced ultrasound in primary care.

Keywords: Adnexal mass, power Doppler, transvaginal ultrasound, saline infusion sonohysterography, obstetric ultrasound screening, primary care.

INTRODUCTION

Ultrasound has turned out as the main diagnostic tool in modern obstetrics and gynecology. When the first medical ultrasound-related institution, the American Institute for Ultrasound in Medicine (AIUM), was established in 1952, the founders most probably could not anticipate this development. Another two decades had to pass, until in 1973 the World federation for ultrasound in medicine and biology (WFUMB) initiated the foundation of many national ultrasound organizations. Medical ultrasound was on its way! The revolution in computer science accelerated the progress of ultrasound technology with incredible results. In our days, new machines, with refined software for image – perfection, set new standards in diagnostic centers around the world. Every month, interesting articles about new applications of ultrasound technology are published in journals dealing exclusively with sonography. This process is to continue if we believe the words of one of the most prominent members of the International Society for Ultrasound in Obstetrics and Gynecology (ISUOG), Prof. Kypros Nicolaides: "…the future is ultrasound, ultrasound, and…ultrasound!"

International conferences in ultrasound focus on 3D/4D, spatio-temporal image correlation (STIC), enhanced power Doppler, tissue block ultrasound and 3D vascularization Index, while the average gynecologist and obstetrician, sonographer and radiologist is still comfortable with the B-mode images. There was always a gap between the scientific avant-garde, their discoveries, and the majority of "users " in primary health care. To bridge this gap and help apply the progress of ultrasound in primary health care by " teaching ultrasound " is a most honorable and rewarding privilege. We owe our teachers who dedicate themselves to this task!

In this article, the impact of "learning ultrasound" on quality of images, diagnostic approach, and certainty of diagnose may be appreciated. The review includes a selection of cases illustrating advanced ultrasound in primary care.

Table 1: Sensitivity for various diagnostic tools in differentiation of adnexal masses[1]

Bimanual examination	45-90%
Ultrasound morphology	68-91%
MRI	87-91%
CT	75-90%
PET	67-79%
Ca 125 > 35 U/ml	78%

ULTRASOUND IN THE EVALUATION OF ADNEXAL MASSES

Diagnostic evaluation of adnexal masses is based on two principles: first-adnexal masses mainly arise from the ovary; second-their chances to be malignant need to be evaluated. The challenge is ever the same: ovarian malignancy is mostly diagnosed in advanced stages, a fact which has not changed in the last few decades. Diagnostic evaluation begins with the patients history and physical examination and, is then followed by ultrasound imaging and biochemical tests. How to distinguish a benign from a malignant adnexal mass (Table 1)?

Ultrasound examination is the cheapest, fastest, and most conclusive diagnostic tool in the evaluation of an adnexal or pelvic mass.[2,16] Simple cysts, hemorrhagic cysts (Figs 1A and 1B), endometrioma (Figs 2A to C), and dermoid cysts (Fig. 3) often have their characteristic sonographic features, highly predictive of histological diagnose.

Occasionally, follow-up scans are needed to differentiate a functional ovarian cyst from a persistent pelvic mass. Scoring systems based on the analysis of B-mode images of the adnexal mass have been introduced almost two decades ago[3] and can now be improved by adding PW, PD and 3D-PD (Table 2).[4]

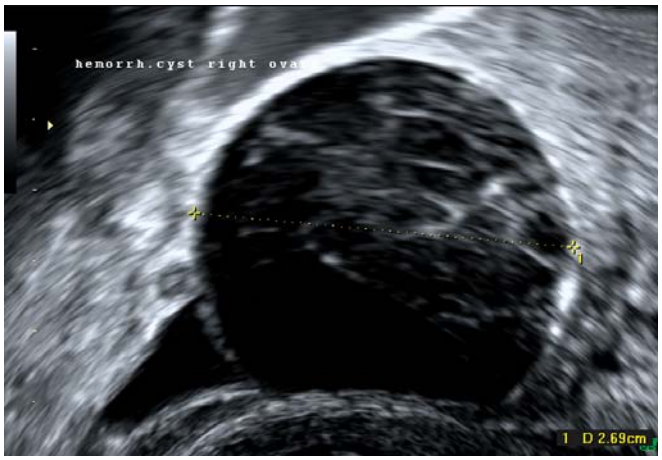


Fig: 1A: Network of echogenic strands after hemolysis in a hemorrhagic cyst

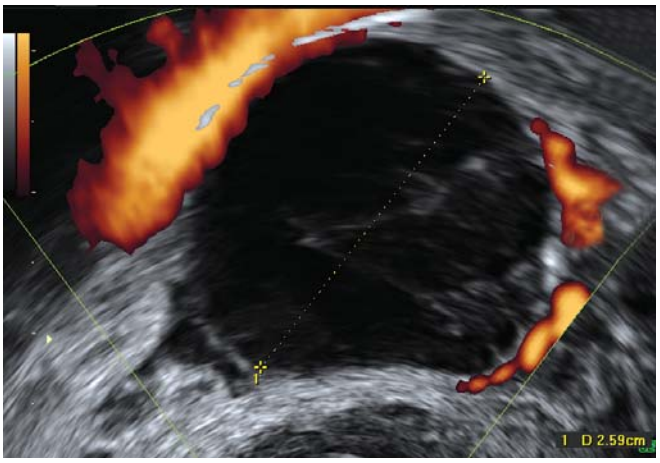


Fig. 1B: Power Doppler mode in a hemorrhagic cyst demonstrates the absence of blood vessels

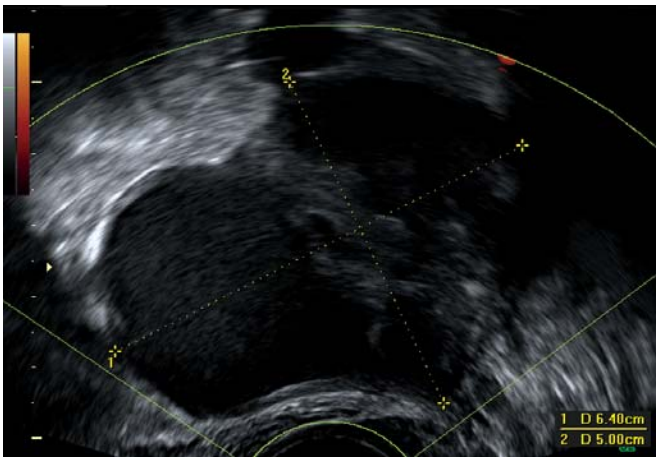


Fig. 2A: Endometrioma right ovary with homogenous distribution of low to medium fine echoes in a cystic mass with only one septation, no solid components

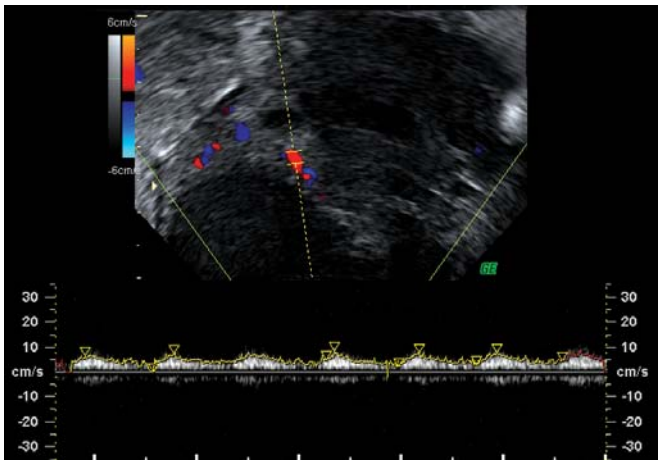


Fig. 2B: Endometriosis right ovary, no blood flow within the mass, peripheral RI above 0.42

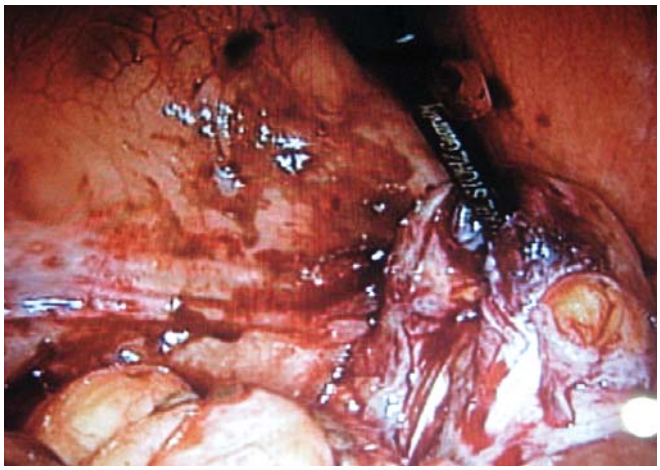


Fig. 2C: Laparoscopic picture of the endometrioma right ovary

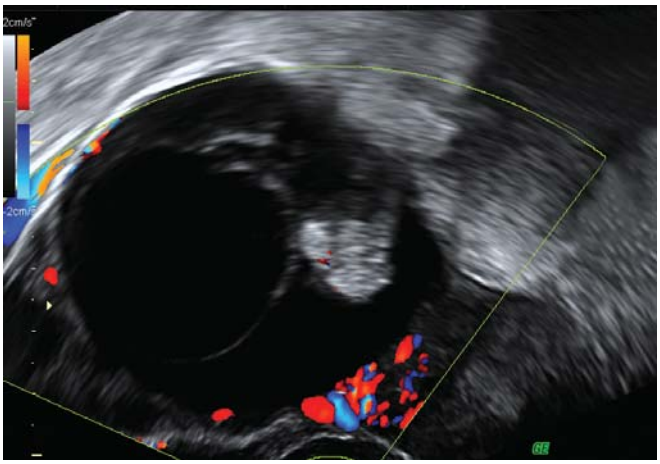


Fig. 3: Rokitansky protuberance in a dermoid, appearing as echogenic area with low vascularity

Table 2: Sonographic features of benign adnexal masses[5-7]

Cyst filled with anechoic fluid, with dorsal enhancement *Power Doppler* : No/low vascularity of cystic wall	**Simple cyst**
Homogenous distribution of low to medium fine echoes in a cystic mass with/without septation, in absence of solid components *Power Doppler* : Vascularity only at ovarian hilus *PW-Doppler* : RI above 0.42	**Endometrioma**
Fishnet-like pattern of intracystic echoes *Power Doppler* : No intracystic vessels	**Hemorrhagic cyst**
Intermixed hypoechoic areas, fluid/fluid levels, often markedly hyperechoic nodule with dorsal shadowing (Rokitansky protuberance) *Power Doppler*: No/low vascularization, solid/hyperechoic areas: no randomly dispersed and increased blood flow *PW-Doppler*: RI above 0.42	**Dermoid cyst**

COLOR-DOPPLER, PULSED WAVE-DOPPLER AND POWER DOPPLER IN THE EVALUATION OF PELVIC MASSES

Color-Doppler flow imaging is useful in evaluating the malignancy risk of an adnexal mass.[17,18] Malignancies are rich in neovascularization and therefore have a lower resistance-and pulsatility index. Tumor neoangiogenesis, as described in 1971, by J. Folkman,[8] is associated with improper vascular architecture. Intratumoral vessels have no media and are permanently dilated. This results in lower vascular resistance, detectable by pulsed Doppler. Resistance Indices (RI) less than 0.42 are considered to be predictive of malignancy.[9] Similar changes in vascularization and RI may result as well from neoangiogenesis in physiological processes. The rapid tissue phasing of the corpus luteum for example, through the four stages of vascularization, maturation, organization and regression, is accompanied by physiological neoangiogenesis,[10] and may give reason to wrong assumptions of malignancy because of rich vascularization and low RI.

The same applies for ectopic pregnancy, tubo-ovarian abscess, and pelvic inflammatory disease (Figs 5A and B).

Aseptic inflammatory processes in ruptured dermoid cysts, or endometriosis with frequently raised Ca125 level as sign for peritoneal reaction, may create similar diagnostic difficulties by showing rich blood flow with low resistance index.

3D-Power Doppler (3D-PD) displays the total blood flow in the examined region of interest (ROI). It shows the degree of vascularization and gives an insight into the architecture of the vascular tree (arborisation) (Table 3).[11,12]

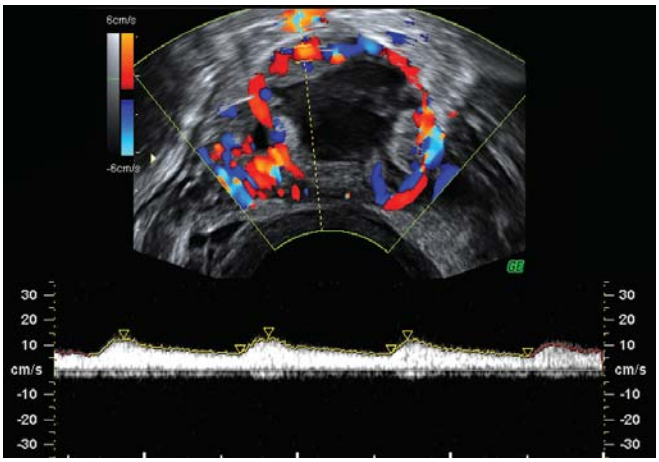


Fig. 4: Corpus luteum color-PW Doppler shows rich diastolic flow and low RI

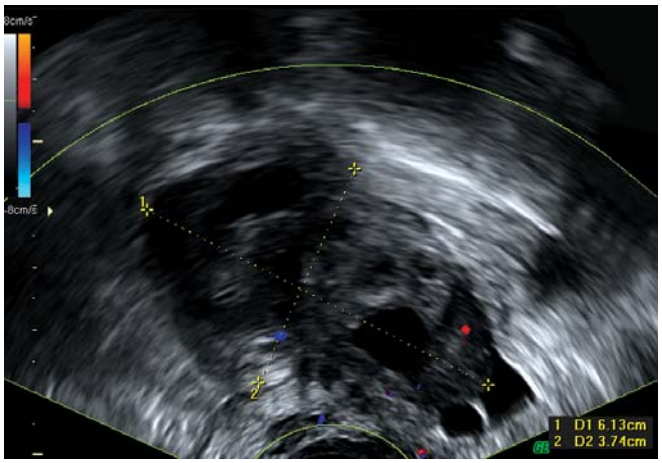


Fig. 5A: Right adnexal mass 7 over 3 cm, Ca 125 152 U per ml, histology chlamydia salpingitis

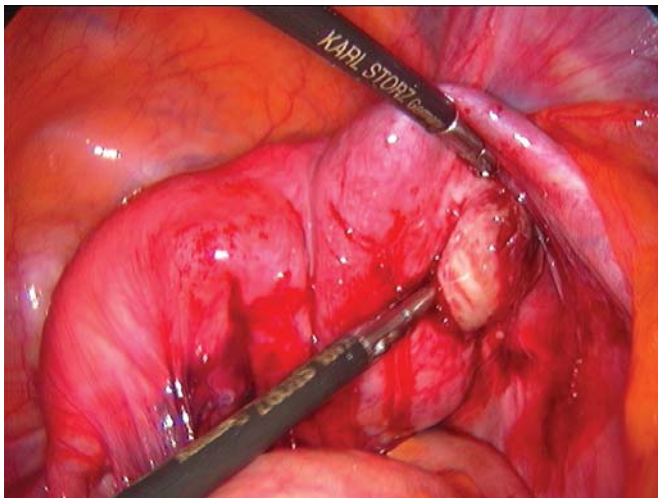


Fig. 5B: Laparoscopic aspect of chronic chlamydia salpingitis

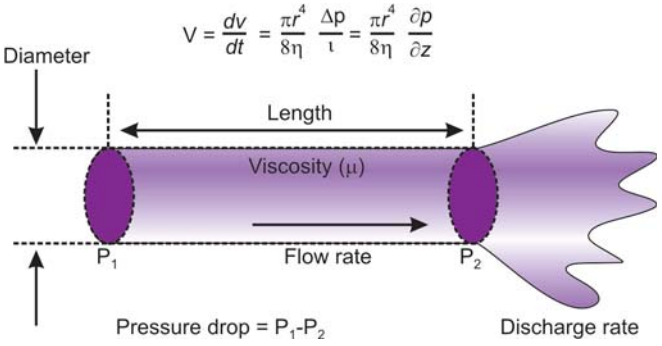


Fig. 6: Hagen Poiseuille equation, physical determinants of laminar flow

With magnification, tumor-typical vascular features like blind endings, aneurysms, tumoral lakes and stenosis can be depicted. Smaller vessels may remain invisible because their radius does not allow the passage of sound wave-reflecting erythrocytes. A. Kurjak and S. Kupesic in 2000 described the use of sonocontrast agents in enhanced 3D power Doppler.[13]

Blood viscosity, pressure gradient, hematocrit, and mainly the radius of a vessel raised to the power of 4 determine the flow in a blood vessel (Fig. 6).

Enhanced PD can visualize new tumor vessels with small radius by using microbubbles instead of erythrocytes for the sound wave reflection. Especially adnexal masses with features of malignancy but uncharacteristic low vascularization, need additional enhanced PD evaluation. A Kurjak documented several cases of early Stage 1 diagnosis of ovarian cancer[14] using enhanced PD, with an impressive increase of power Doppler flow in the tumor, after intravenous application of contrast agent.

Currently, morphological assessment of suspected ovarian malignancy appears to be optimal as a multimodal approach using B-mode, 3D-mode including ovarian volume calculation, 3D power Doppler, and PW-Doppler for RI-measurement, desirably completed with enhanced PD-sonoangiography of the tumor (Fig. 7). This may look as an overloaded diagnostic approach, but means practically just pushing a button on the machine while keeping the ROI in focus. The settings of the ultrasound machine are important to standardize the results in the relatively new technique of 3D power Doppler: for ovarian examination with Voluson 730, RIC 5-9 H transvaginal probe, settings could be standardized as proposed by M Kudia and JL Alcazar in January 2009: PRF = 0.6 kHz, and gain 0.8 (Figs 8A and B).[15]

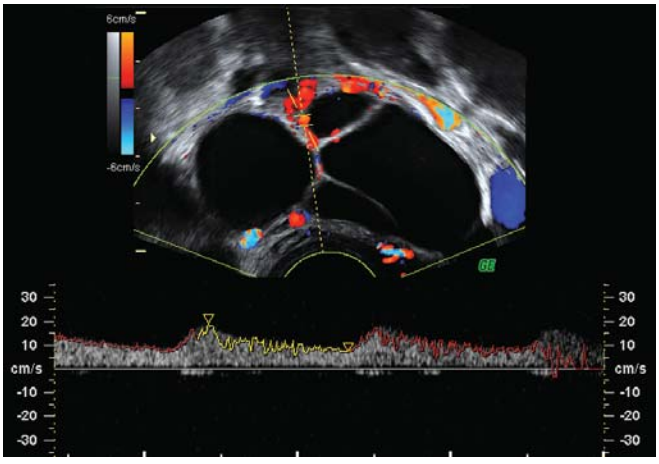


Fig. 7: Left ovarian papillary serous cystoma in a patient of 55 years, RI above 0.42, sharp margins, thin internal septations, moderate vascularization

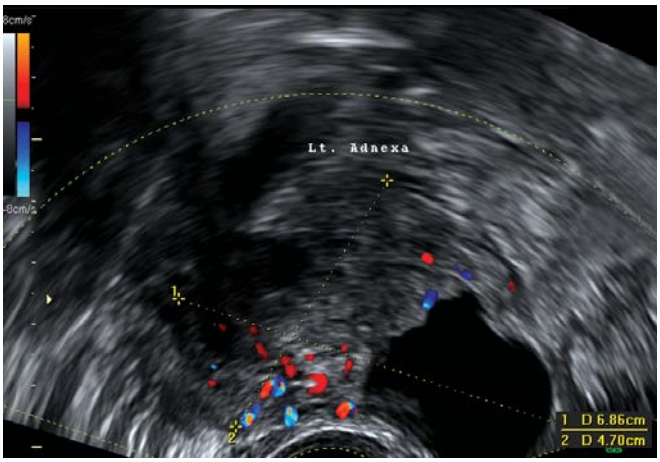


Fig. 8A: TVS image left ovary. 48-year-old patient with bilateral serous papillary ovarian carcinoma. She had a normal gynecological check-up without ultrasound one year prior to diagnosis. Randomly dispersed vessels in the echogenic area of the adnexal mass

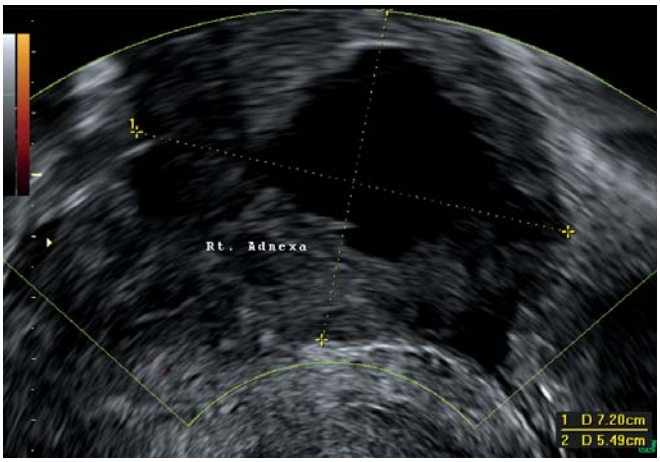


Fig. 8B: TVS of the other ovary, same patient. B-mode features typical ovarian malignancy. Ca125 preoperative 1404 U per ml, postoperative staging FIGO III

Table 3: Sonographic criteria for malignancy of an adnexal mass[7-10]

B-mode	– Multilocular or multiple cysts
	– Thick or irregular septae or walls
	– Poorly defined borders
	– Papillary projections
	– Solid components, echogenic elements
	– Presence of ascites
Color Doppler, PW-Doppler	– Resistance indices below 0.42
Power Doppler	– Central vascularization of the mass
	– Disorganized, randomly dispersed blood vessels in the solid component

ECTOPIC PREGNANCY AS ADNEXAL MASS

In the evaluation of an adnexal mass, the possibility of an ectopic pregnancy should never be neglected. Together with the information about the last menstrual period (LMP), clinical symptoms, and serum beta HCG levels, transvaginal sonography is of great support for the clinician. The corpus luteum can impress as a gestational sac-like structure. Color Doppler helps in identification of the corpus luteum by demonstrating a ring of increased vascularity due to high endocrine activity, known as the "ring of fire". Visualization of the characteristic corpus luteum blood flow may aid in diagnosis of ectopic pregnancy, since about 85% of all ectopic pregnancies are found on the very same side of the corpus luteum. This explains why in the majority of cases with proven ectopic pregnancy, luteal flow is detected ipsilateral of the ectopic pregnancy. Luteal color-or power Doppler flow may be used as a guide while searching for an ectopic pregnancy, and could be called the "light house-effect" of corpus luteum, which directs the investigator to the color Doppler signals of the ectopic pregnancy (Figs 9A to 10).[19]

The color Doppler image of the ectopic pregnancy usually presents randomly dispersed multiple small vessels within the adnexe, which are clearly separated from the ovarian tissue and corpus luteum. The pronounced vascularity is proof of the trophoblast vitality and its invasive neo-angiogenesis, apart from the vasodilatation of the fallopian vessels under the influence of maternal progesterone.[20]

UTERINE BLEEDING (AUB) AND TRANSVAGINAL SONOGRAPHY (TVS)

Abnormal uterine bleeding is one of the most common complaints in OPD. It may be a symptom of hormonal dysfunction, benign uterine pathology, or the first sign of endometrial, cervical, even ovarian carcinoma.[21] As per recommendation of the American College of Obstetricians and Gynecologists and the Society of Radiologists, both TVS and endometrial biopsy have equal efficacy as a first diagnostic step in women with postmenopausal bleeding.[22,23]

The two diagnostic modalities have similar sensitivity for detecting endometrial carcinoma. Transvaginal sonographic measurement of endometrial thickness of less than 5 mm from one myometrial-endometrial interface to another is associated with a low risk of endometrial cancer.[24,25] Approximately 10% of *asymptomatic* postmenopausal women have an endometrial thickness of 8 mm or more, and out of these, 1 to 3% can be expected to have endometrial carcinoma.[26,2]

If endometrial thickness exceeds 5 mm, regardless the patient is bleeding or not, we should differentiate between focal (polyp) and symmetrical (hyperplasia) thickness.[28]

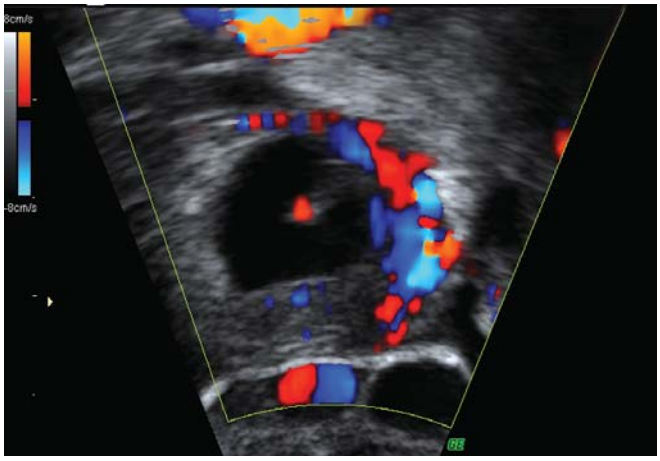


Fig. 9A: Viable embryo left tube with heart action shown by color Doppler. Only 5-8% of all ectopic pregnancies present with a viable embryo

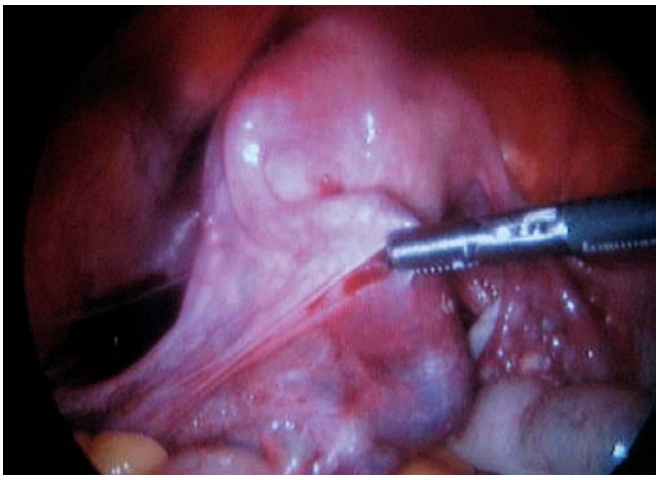


Fig. 9D: Laparoscopic picture of the viable ectopic in the left tube. (*Courtesy:* Dr Susheela Anilkumar)

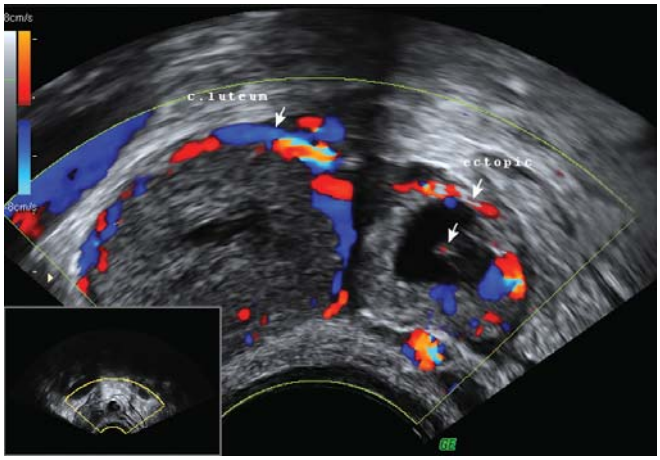


Fig. 9B: Corpus luteum "ring of fire" next to the color Doppler signals of the ectopic pregnancy. Viability with high beta HCG requested laparoscopic salpingectomy

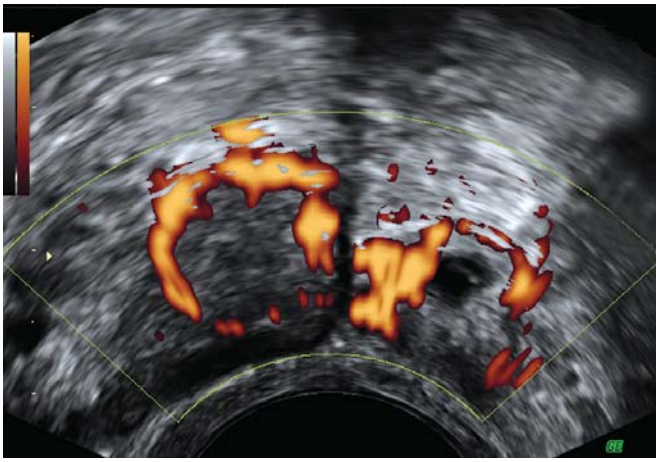


Fig. 10: Ectopic blighted ovum pregnancy with corpus luteum in power Doppler mode. Nonviability with low serum beta HCG made methotrexate first choice- therapy

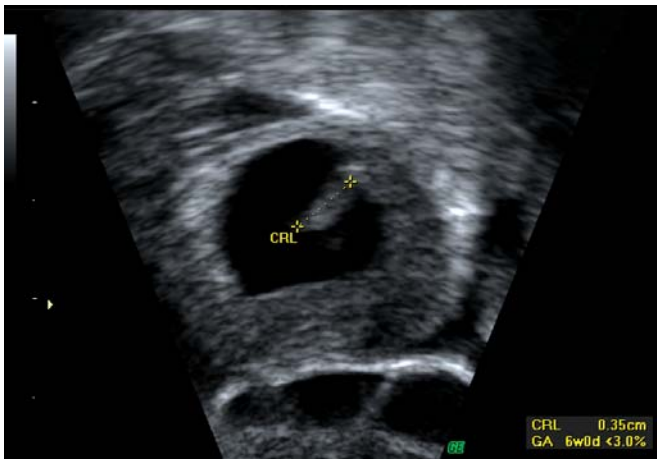


Fig. 9C: Crown rump length (CRL) equivalent to 6 weeks of the viable embryo in the left fallopian tube

Saline infusion sonohysterography (SISH) can be a valuable diagnostic tool in such cases.[29]

By means of color Doppler velocimetry, we can increase the specifity of TVS in the differentiation of thickened postmenopausal endometrium. No flow can be detected in the normal, atrophic endometrium of the postmenopause. But if color Doppler is used to interrogate thickened endometrium in cases of endometrial cancer, angiogenesis can be demonstrated, with a visualization rate of 100% of abnormal blood flow. In contrast to endometrial hyperplasia, blood flow patterns in endometrial carcinoma will be characteristically low with an RI near or below 0.40.[30]

In premenopausal women, there is no clinical cut-off value for abnormal endometrial thickness. Often enough, patients with abnormal uterine bleeding present with

unremarkable endometrial findings in TVS. A polyp can "hide" in a thick mid-cyclic endometrial lining, and might be only visualized by means of color – or power Doppler, demonstrating it's vascular stem. TVS should therefore be performed on day 4, 5, or 6 of the menstrual cycle, when proliferation is just beginning and endometrium is still thin. In one study of 200 premenopausal women with abnormal uterine bleeding (AUB), 16 of 80 women (20%) with an endometrial stripe < 5 mm had an endometrial polyp or submucosal leiomyoma as the source of their bleeding.[31]

Following TVS including color Doppler and power Doppler, further evaluation by means of saline infusion sonohysterography (SISH) or hysteroscopy with endometrial biopsy, should be based on the clinical situation: if there is persistent AUB, or if structural uterine abnormalities are suspected such as a polyps, SIHS may be the next noninvasive diagnostic step.

In patients with hormonal replacement therapy (HRT), persistent uterine bleeding will always require endometrial biopsy, regardless of ultrasound findings.

In cases of suspected endometrial cancer, endometrial biopsy with dilatation and fractionated curettage is preferable, since hysteroscopy and SISH imply the risk of flushing fluid with malignant viable cells from the endometrial cavity through the fallopian tubes into the peritoneal cavity.[32]

ENDOMETRIAL POLYPS AND SALINE INFUSION SONOHYSTEROGRAPHY (SISH)

Endometrial polyps are localized hyperplastic proliferations of endometrial glands and stroma around a vascular core-"single vessel arrangement" –A Kurjak –[33] that either forms sessile or pedunculated projection from the lining into the uterine cavity. The sizes range from a few millimeters to several centimeters, of single or multiple polyps. The majority are benign. In a series of 509 women with hysteroscopically removed endometrial polyps, histology was benign in 70%, hyperplasia without atypia in 26%, atypical hyperplasia in 3%, and cancer in 0.8%.[34]

Like leiomyoma, polyps can have an abnormal karyotype.[35,36]

In 25%, endometrial polyps are the cause of abnormal vaginal bleeding in both pre- and postmenopausal women.[37] Hysteroscopic removal following diagnosis of endometrial polyp seems to improve pregnancy rates after intrauterine insemination, with pregnancy rates of 63% *versus* 28% in the control group (Figs 11.A to C).[38]

Saline Infusion Sonohysterography (SISH) is a useful minimal invasive technique to find endometrial polyps in women with abnormal uterine bleeding. This method is significantly more accurate in the detection of endometrial polyps than TVS alone.[39] Five to 10 ml of 0.9% sodium chloride, transcervically instilled into the uterine cavity under sonographic control (TVS) through a catheter (for example neonatal intensive care feeding sonde), will substantially enhance endometrial visualization.

Single vessel arrangement such as the vascularization pattern of a polyp becomes visible by switching on CW or PD, flow indices by PW. SIHS is well-tolerated, free of complications, and cheap.

Not only polyps, but other pathologies such as hyperplasia, leiomyoma, synechia (Asherman-Syndrome) are much better visualized with SISH than by TVS alone (Fig. 12).

Whether SISH should be used if endometrial cancer is suspected, seems controversial and needs further discussion.

ESTIMATION OF GESTATIONAL AGE, FIRST TRIMESTER SCREENING

Enough evidence has been accumulated to suggest that routine ultrasound examinations give more accuracy in assessment of the expected date of delivery (EDD) than LMP dating or physical examination, even in women with certain menstrual dates.[40] Determination of the EDD is most important in obstetrics to avoid inappropriate intervention after false diagnosis of preterm or postdates pregnancy. Correct assessment of gestational age logically results in avoidance of false positive diagnosis of IUGR and preterm labor, as well as unjustified induction of labor.

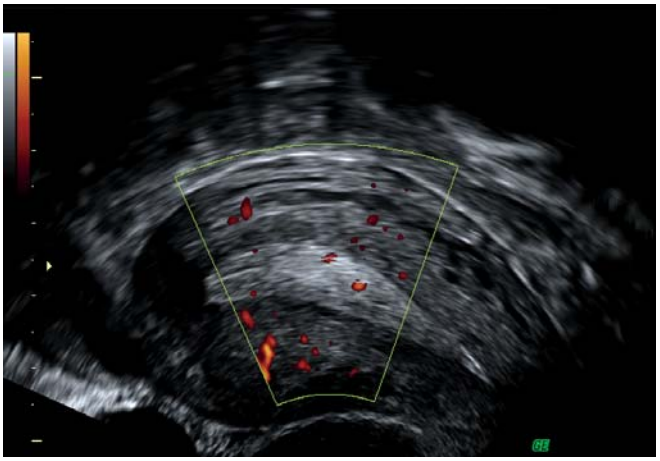


Fig. 11A: TVS of an endometrial polyp hidden within a secretorial endometrium

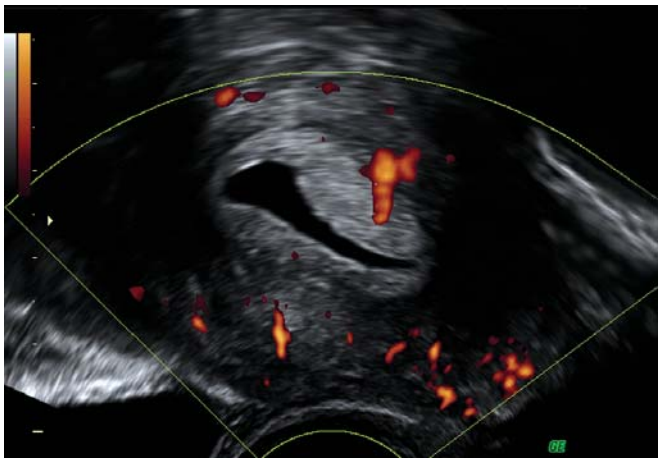


Fig. 11B: After transcervical instillation of saline (SISH), applying power Doppler, a polyp with single vessel arrangement can be seen

Reliable identification of multiple pregnancy including correct assessment of chorionicity (intertwin peak *versus* T-sign) as an important prognostic factor and predictor of specific pathology like twin-to-twin transfusion syndrome (TTTS), is an added value to early pregnancy ultrasound. Ultrasound technology is rapidly progressing, and assessment of fetal anatomy in the first trimester, especially by means of transvaginal ultrasound, is becoming a reality (Figs 13 A to D).[41]

The nuchal translucency (NT) measurement in the first trimester in combination with serum screening of free beta HCG and PAPP-A can detect over 90% of fetuses with Down's syndrome, as well as fetuses with other aneuploidies and/or congenital heart malformation (Figs 14 A to C).

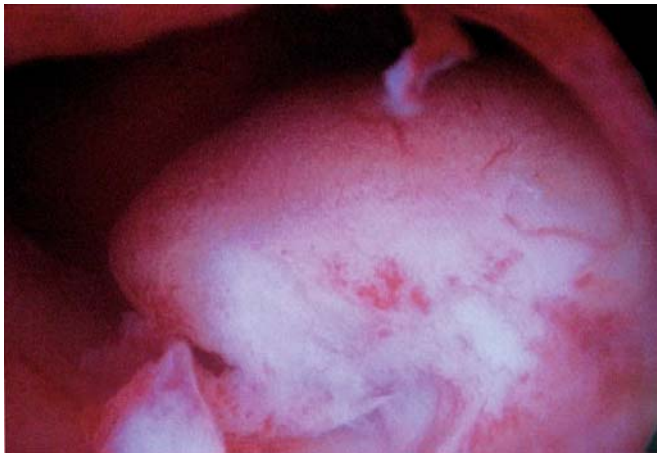


Fig. 11C: Hysteroscopic view of the polyp before ablation

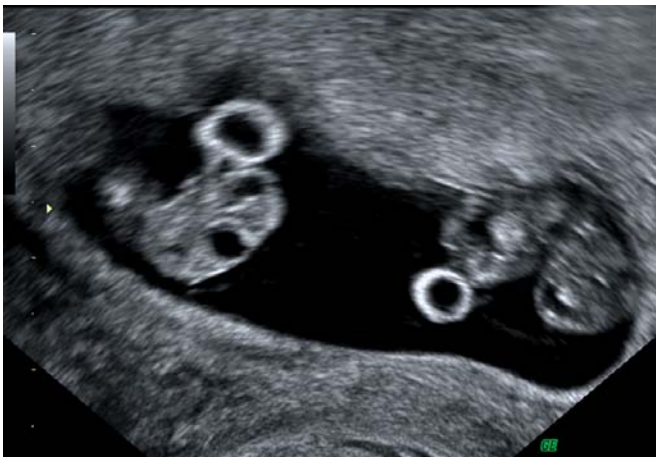


Fig. 13A: Triplets 9 weeks, *in vitro* fertilization (IVF). The hyperechoic yolk sacs are suspicious of aneuploidy

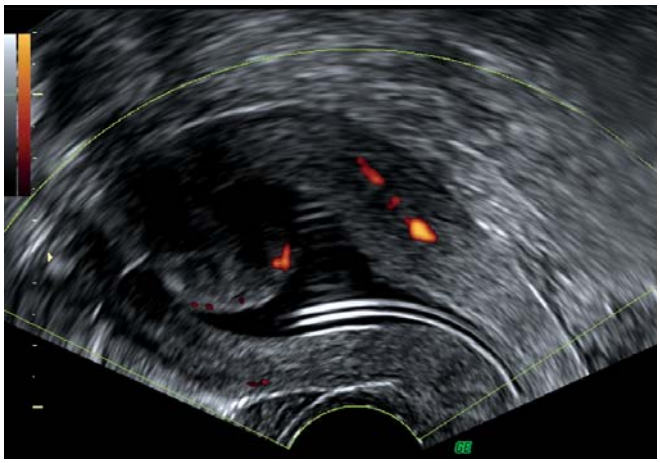


Fig. 12: SISH allows the assessment of a submucous fibroid

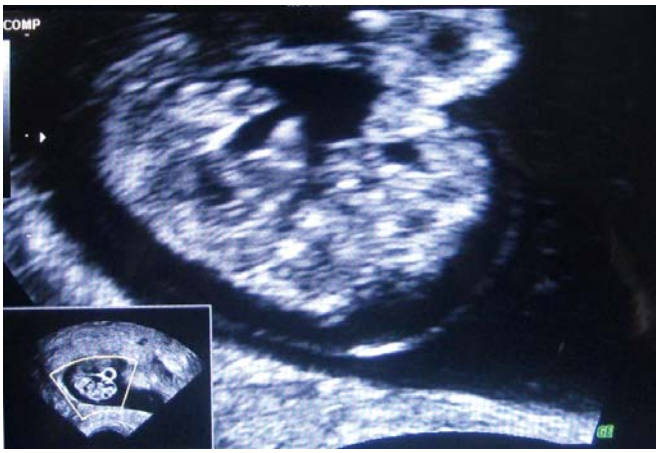


Fig. 13B: Cine loop-extracted B-mode picture. Lateral view of the fetus, outlining a triangular pulsating mass protruding from the anterior thorax of one of the triplets

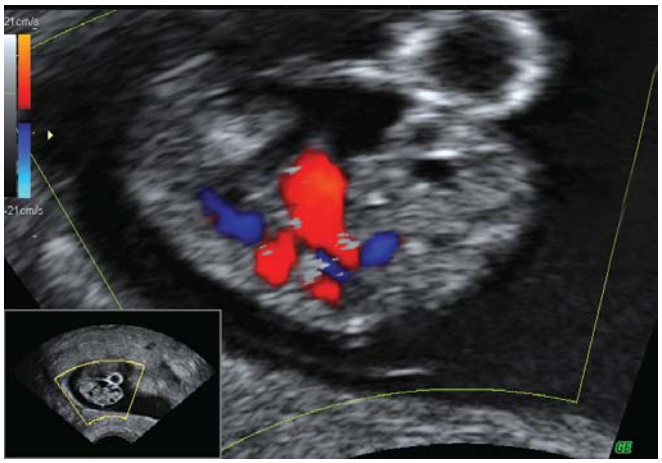


Fig. 13C: Color Doppler and cine loop demonstrate malformation suspicious of ectopia cordis in this triplet

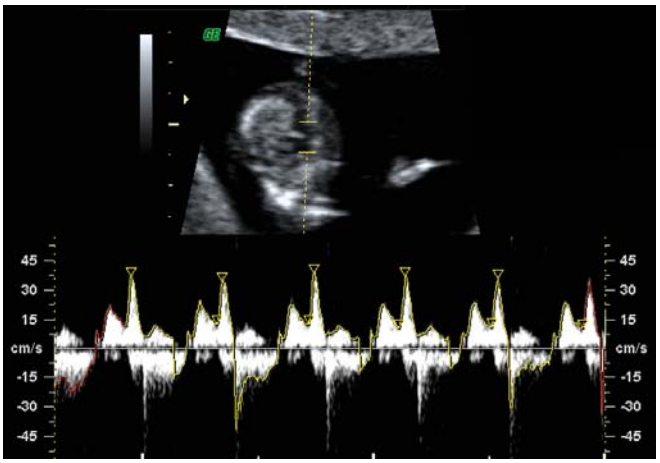


Fig. 14B: First trim combined NT screening, the same fetus: Tricuspid valve regurgitation, as seen in 65% of fetuses with Down's syndrome

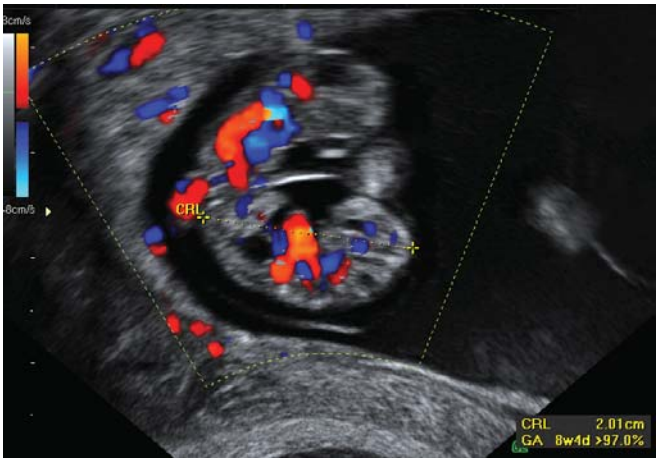


Fig. 13D: B-mode and CD suggest caudal conjunction of the triplet with suspected ectopia cordis and the next fetus. Fetal demise of all triplets followed a week later, with dilatation and vacuum-curettage

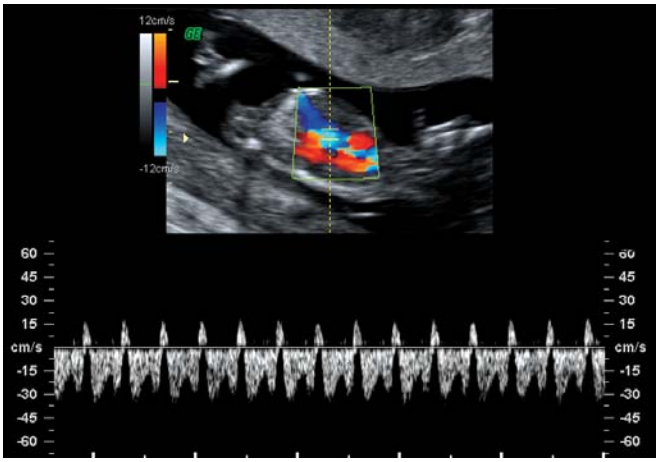


Fig. 14C: First trim combined NT screening, ductus venosus Doppler: reverse flow during atrial contraction

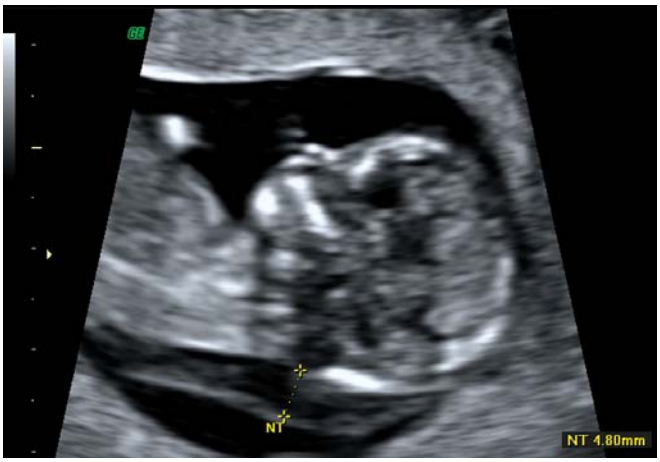


Fig. 14A: First trim combined screening shows increased NT, absent nasal bone. Adjusted risk for Down's syndrome calculated as 1:5. Karyotype trisomia 21 confirmed by amniocentesis at 16 w

Second trimester screening between 18 and 23 weeks for detection of fetal anomalies[42] at a gestational age that allows good visualization of anatomy, requires experienced sonographers. Yet certain skeletal and heart anomalies may evolve only in the late 2nd or 3rd trimester. The efficacy of this screening has been confirmed by the Helsinki, RADIUS and Eurofetus trials (Figs 15 A to F).[43-45]

Patients with anomalies such as hypoplastic left heart[46] and transposition of the great arteries[47] have better outcomes if the diagnosis is made prenatal rather than postnatal, because these fetuses will be delivered in specialized clinical set-ups (Fig. 16). This also applies to anomalies of the renal system, where, early treatment of prenatal diagnosed abnormalities helps to avoid long-term morbidity (Figs 17A and B).

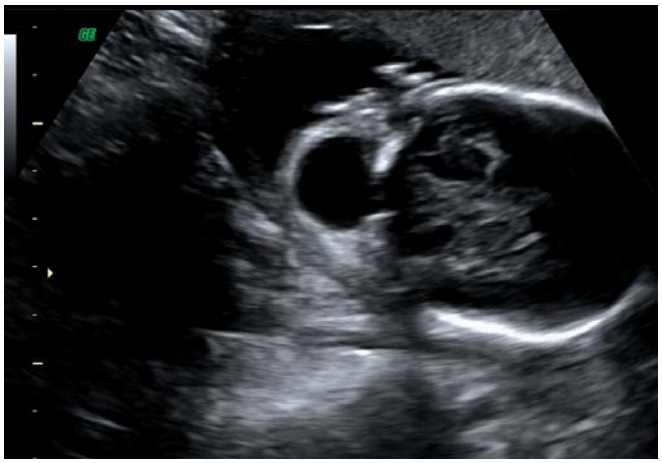


Fig. 15A: Second trim screening showing a covered defect of the os occipitale, without herniation of brain tissue

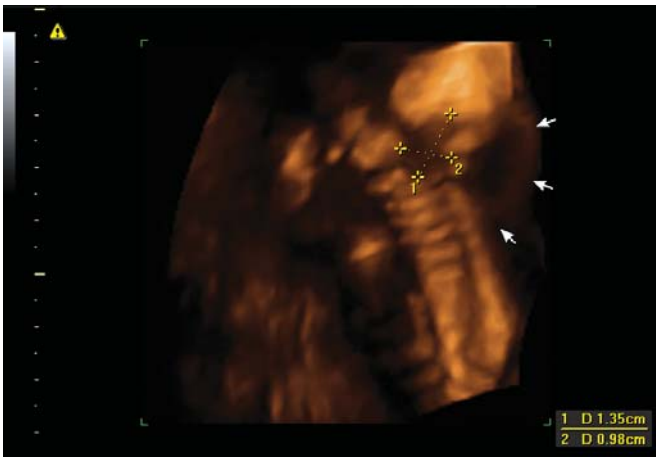
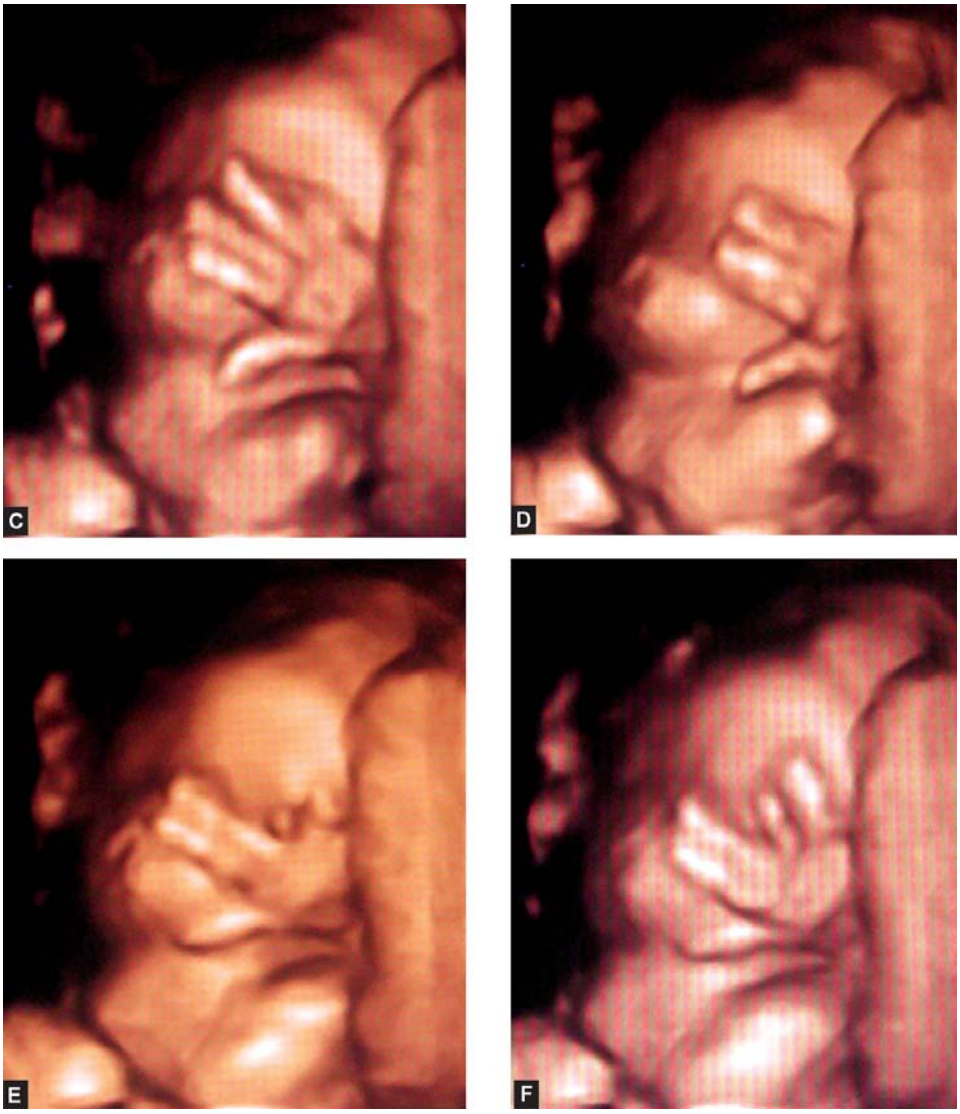


Fig. 15B: Occipital encephalocele in maximum mode depicting the occipital bone defect



Figs 15 C to F: A 4D KANET neurological test in the same fetus with encephalocele demonstrates smooth, complex and variable finger movements as sign of normal neurological function[48]

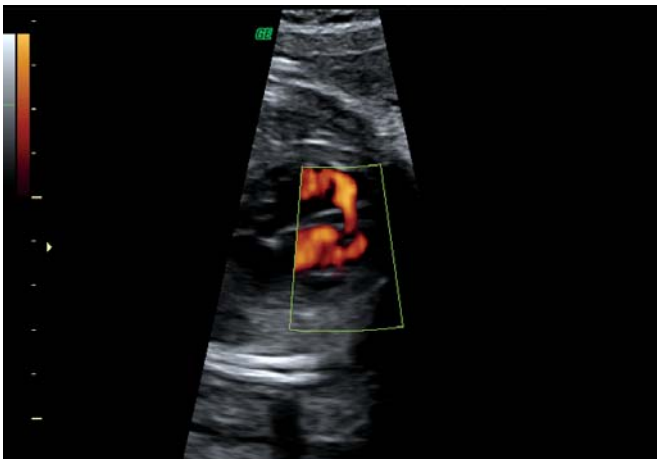


Fig. 16: Muscular VSD in power Doppler mode

DOPPLER ULTRASOUND IN OBSTETRICS

Doppler flow measurement is used to detect redistribution in the fetal circulation when growth restriction is suspected. The method helps anticipate decompensation of fetal adaptation to placental insufficiency or hemodynamic burden of TTTS. For the best delivery timing of a compromised fetus, Doppler velocimetry assists in finding the correct way between the risk of prematurity on one side, and long-term morbidity caused by severe intrauterine growth retardation (IUGR) on the other, and is meant to avoid intrauterine fetal death (IUFD) as the most negative outcome. The predictive range and accuracy of Doppler is still unmatched by any other form of fetal surveillance (Figs 18 A to D).[49]

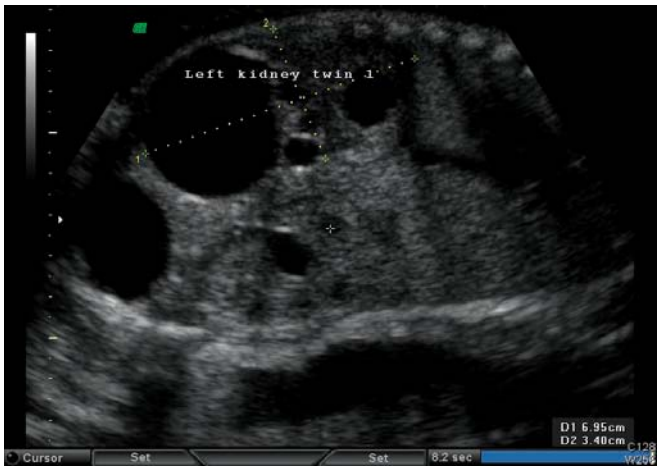


Fig. 17A: Twin pregnancy, 29W-5D, unilateral multicystic left kidney of twin 1. In multicystic kidneys, renal function is normal, with normal amniotic fluid volume

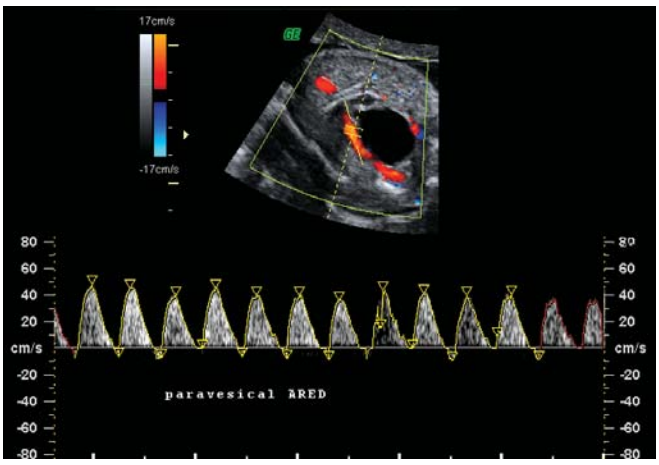


Fig. 18A: Feto-maternal Doppler with paravesical umbilical artery ARED flow in a 27 weeks fetus with severe early IUGR

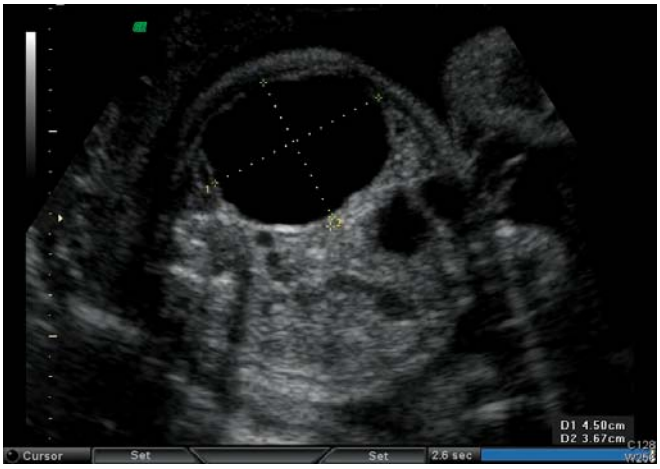


Fig. 17B: Multicystic kidney has good prognosis with surgical correction by means of nephrectomy. If not diagnosed antenatal, infection and hypertension will develop

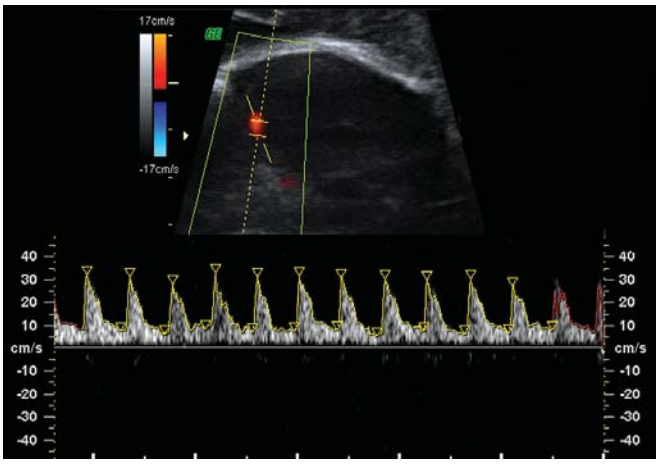


Fig. 18B: The same fetus with increased diastolic flow in the middle cerebral artery as sign of redistribution in the fetal circulation in favor of brain and adrenals

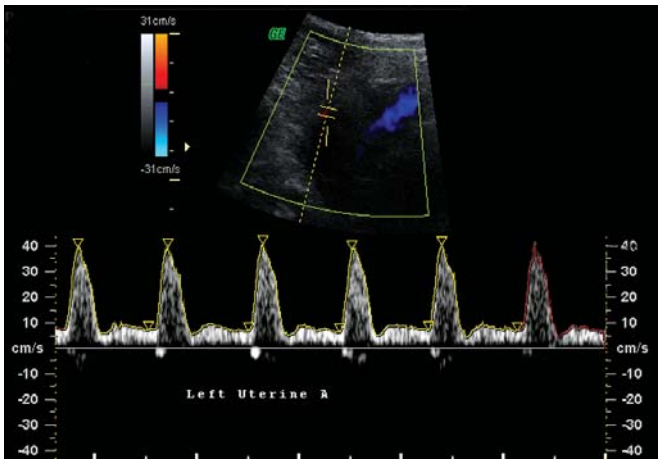


Fig. 18C: Left uterine artery with increased resistance index (RI) and notching, indicating failure of second trophoblast invasion around 20 weeks

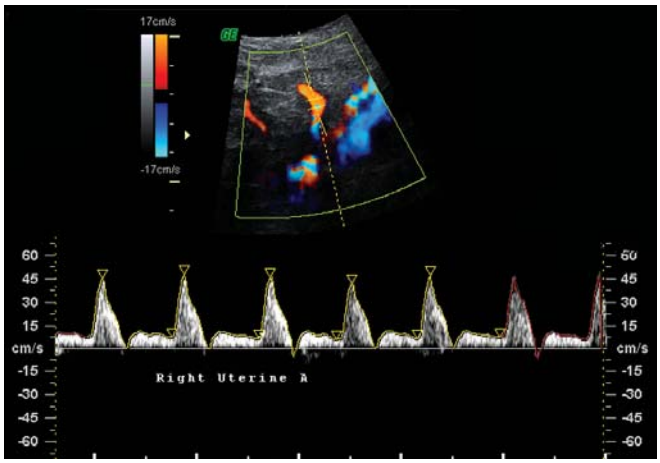


Fig. 18D: Right uterine artery with similar findings

CONCLUSION

The out patient department (OPD) of obstetrics and gynecology is the venue where, patients meet the specialist to present their symptoms hoping for a quick diagnosis and relief. If necessary, hospital admission is planned after diagnosis, for conservative or surgical in-patient treatment. Finding the right diagnosis often depends on ultrasound. Pregnancies are confirmed and surveyed, conveniently including 1st and 2nd trimester screening if the physician is qualified.

Pregnancy risks have to be identified and management strategies need to be developed, before the delivery mode is chosen. During any clinic day, decisions have to be made from the first consultation to the last, and one of the main pillars they are based upon is ultrasound. Primary care would certainly benefit from the availability of advanced ultrasound! The obstetrics and gynecologist specialist while seeing a patient should have the ultrasound machine right next to the examination bed or chair. Transvaginal ultrasound-the concept of the "seeing finger" as it was introduced by A Kurjak into our clinical routine more than twenty years ago-is today an essential diagnostic tool for clinicians. The misanthropic statement "life is nothing but a chain of missed opportunities" should certainly not apply for diagnostic efforts in primary care!

Modern ultrasound with medium-range machines provides the opportunity of cost-effective, quick and substantial contribution to the diagnosis under one essential condition: the user has to be well trained! The ultrasound machine alone remains nothing but a prestigious object, unless it becomes a reliable helper in the hands of the one who has been taught how to use it. The meaning of the rule "we know what we look for, and we look for what we know" can change from limitation to amplification only through "learning ultrasound". Advanced ultrasound in primary care would certainly be desirable, but ultimately depends on the expertise of the clinician and expensive top-of-the-line equipment. A more realistic, cost/benefit orientated view of the role of ultrasound in primary care would suggest a sound training of the primary care physicians in basic sonography, and equipment with medium-range machines.

Advanced ultrasound with high-end machines and cutting-edge knowledge and performance of dedicated specialists will remain an option available only in specialized centers.

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