REVIEW ARTICLE

To Doppler or Not to Doppler: From Doppler Ultrasound to Color Doppler to Doppler in 3D and Beyond

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ABSTRACT

This review aims to provide the reader with an update on the present and potential clinical applications in Doppler ultrasound in perinatal medicine. Umbilical artery Doppler plays an important role in the management of intrauterine growth restriction (IUGR) and pre-eclampsia and aids in twin-to-twin transfusion syndrome management while notching in the waveform is a predictor of umbilical cord abnormalities. Middle cerebral artery Doppler reliably detects fetal anemia and may be useful in the assessment of IUGR as well. Abnormal uterine artery Doppler may play a role in predicting growth restriction, hypertensive disorders of pregnancy and preterm delivery. Abnormal ductus venosus waveforms can also be used to predict adverse fetal outcome and may allow for better timing of delivery while umbilical venous pulsations may be a sensitive marker for fetal heart failure in hydropic pregnancies. 3D power Doppler allows better small vessel visualization that is not affected by angle of insonation and has been used to diagnose placental and cord abnormalities. Significant improvements have recently occurred, improving the visualization and evaluation of placental vascularity, resulting from enhancements in delineation of tissue detail through electronic compounding and harmonics as well as enhancements in signal processing of frequency- and/or amplitude-based color Doppler ultrasound. Spatial representation of vascularity can be improved by utilizing 3D processing. Greater sensitivity of 3D Doppler ultrasound to macro- and microvascular flow has provided improved anatomic and physiologic assessment throughout pregnancy. The rapid development of these new ultrasound techniques will continue to enlarge the scope of clinical applications in placental studies. As clinical experience with these new technologies increases and as the technology improves further, it is reasonable to expect that 3D Doppler and 4D ultrasound will be complementary addition to well-established 2D Doppler ultrasound imaging.

Keywords: Pulsed Doppler, Color/power Doppler, 3D Doppler, Pregnancy.

INTRODUCTION

Christian Doppler first reported on the Doppler effect in 1842, describing the changes in the frequency of a light or sound wave produced by a changing relationship between two objects. The traditional example given to describe the Doppler principle is the sound level when a train approaches and then departs from a station. The frequency of the sound is higher in pitch when the train approaches the station and lower when it departs. The change in sound pitch is also termed as frequency shift and is proportional to the speed of movement of the sound (or light) emitting source.² Clinically, the combination of real-time ultrasound with pulse wave Doppler allows the identification of a specific area or blood vessel for sampling. When an ultrasound beam with a certain frequency is used to insonate a blood vessel, the reflected frequency shift is proportional to blood flow velocity within that blood vessel. The frequency shift is highest in systole when blood flow is the fastest and lowest in diastole when flow is slowest. The frequency shift is also angle dependent and velocity is measured accurately when the angle of incidence (cosine θ) is as small as possible. When

a sound beam is perpendicular to the direction of flow, the measured velocity is zero since the cosine of 90° is zero. Using ratios of frequency shifts of flows in systole and diastole, Doppler indices can be made independent of the effects of the angle of the ultrasound beam. The indices used in Doppler ultrasound reflect vascular resistance and include the systolic/diastolic (S/D ratio), the resistance index (RI = systolic velocity-diastolic velocity/systolic velocity) and the pulsatility index (PI = systolic velocity—diastolic velocity/mean velocity). The S/D ratios are used frequently in the United States to assess arterial waveforms though some experts feel that the PI is a more reproducible index.

Pulsed Doppler Ultrasound in Maternal Fetal Medicine

Umbilical Artery Doppler

Umbilical artery Doppler is easy to obtain (Figs 1 and 2). Using a combination of pulsed echo and continuous wave Doppler ultrasound, Stuart et al first characterized umbilical artery (UA) velocity waveforms in normal pregnancies from 16 to 20 weeks

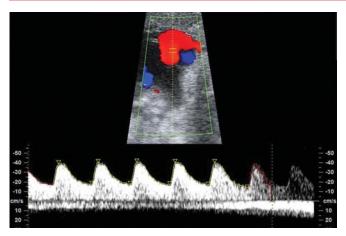


Fig. 1: Umbilical artery Doppler: Normal blood flow

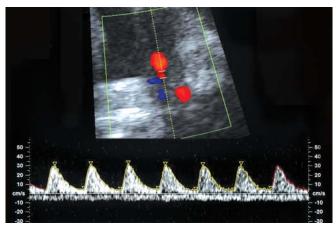


Fig. 2: Umbilical artery Doppler: Abnormal blood flow with increased resistance

of gestation and showed that umbilical artery angle independent indices decreased with advancing gestation.4 Trudinger et al then showed that ratios of peak systolic to least diastolic flow velocities in umbilical arteries became abnormal in pathologic conditions, such as intrauterine growth restriction (IUGR).⁵ A meta-analysis of UA Doppler in the management of high-risk pregnancies for pre-eclampsia and IUGR has been shown to reduce antenatal admissions by 44%, labor induction by 29%, cesarean section for nonreassuring fetal heart tracings by 52% and more importantly perinatal mortality by 38%. 6 Absent or reverse end diastolic flow in the UA is now clearly shown to be associated with advanced fetal compromise and associated with increased perinatal morbidity and mortality and is an indication for delivery. The measurement of Doppler flow in the UA is also an excellent tool to aid in prognosis in pregnancies complicated by twin-twin transfusion syndrome (TTTS). Absent end diastolic flow in the donor twin is associated with a higher risk of intrauterine fetal demise of the donor when patients are undergoing either amnioreduction or laser therapy for TTTS. Kontopoulos et al have recommended assessment of AEDV in the preoperative evaluation of TTTS patients.⁷

Middle Cerebral Artery (MCA) Doppler

The MCA is the most studied cerebral artery because it is the most accessible cerebral vessel and it carries 80% of the cerebral

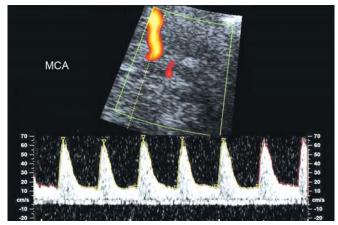


Fig. 3: Abnormal MCA Doppler with high peak velocity blood flow

blood flow. It can be sampled at an angle of 0° between the ultrasound beam and the direction of blood flow, and the real velocity of blood flow is actually measured in the form of a peak systolic velocity (PSV). One of the most important applications of Doppler technology in obstetrics has been the detection of fetal anemia in pregnancies complicated by red cell isoimmunization or other causes (Fig. 3). There appears to be excellent reproducibility when the proximal vessel is sampled after its origin from the internal carotid artery. A PSV above 1.5 MoM for the fetus' gestational age has been shown to have a 100% sensitivity for detecting fetal anemia.8 The MCA PSV is actually more reliable than the delta OD450 in the diagnosis of fetal anemia leading ACOG to issue a statement that Doppler ultrasound evaluation in the management of alloimmunization allows for a more thorough and less invasive workup with fewer risks to mother and fetus. 9 Besides diagnosis and management of fetal anemia, MCA PSV may also be helpful in the management of monochorionic diamniotic pregnancies complicated by twin anemia polycythemia sequence (TAPS). About 5% of monochorionic diamniotic pregnancies are complicated by large intertwin hemoglobin differences in the absence of amniotic fluid discordances. Slaghekke et al have shown that the recipient twin in these pregnancies have MCA PSVs < 0.8 MoM. ¹⁰ In addition to donor anemia, the diagnosis of TAPS is important because the recipient twin is at risk for thrombocytopenia and polycythemia-hyperviscosity syndrome. The MCA PSV is also a new parameter in the assessment of IUGR. Mari et al showed that MCA waveforms change in growth restricted fetuses and is more significantly related to fetal hypoxemia and hypercapnia. 11 These changes are suggestive of fetal brain autoregulation.

Uterine Artery (UtA) Doppler

The uterine artery can be assessed as it crosses over the external iliac artery (Fig. 4). Inter and intraobserver variability has been reported to be about 10%. Significant decrease in the S/D ratio of the UtA occurs with advancing gestation until 26 weeks as diastolic velocities increase. This is a result of normal trophoblastic invasion leading to spiral artery remodeling



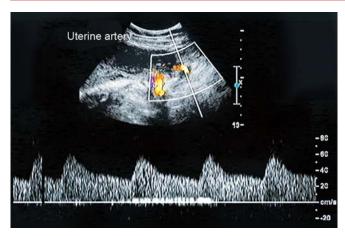


Fig. 4: Uterine artery Doppler in normal pregnancy

resulting in a low resistance system that allows for the normal maternal-fetal exchange of nutrients, waste and metabolites. Phupong and Dejthevaporn showed that a disruption of this transition from high to low impedance is associated with an increased risk of pre-eclampsia and small for gestational age infants in previously healthy nulliparous women. 13 Onwudiwe et al also showed that UtA Doppler screening played a significant role in the prediction of a small for gestational age (SGA) neonate, pre-eclampsia and also gestational hypertension. ¹⁴ In the presence of obstetric complications, such as fetal growth restriction, UtA Doppler identifies the fetus at higher risk for preterm delivery and lower birth weight. Li et al showed that bilateral UtA notching is a more significant predictor of adverse pregnancy outcome when compared to umbilical artery Doppler. 15 Ferrazzi et al showed that abnormal UtA Doppler in pregnancies complicated by IUGR is an important indicator of hypoxic or ischemic placental lesions.¹⁶ Abnormal UtA Dopplers in fetus with growth restriction also identify mothers with an increased risk of the development of pre-eclampsia later in pregnancy.¹⁷ In addition, abnormal UtA Doppler in highrisk pregnancies appear to be a significant predicator of the need for cesarean section, SGA neonate and prematurity that was independent and superior to that of umbilical artery Doppler. 18 UtA Doppler studies are considered investigational in the USA.

Umbilical Cord Compression

Abnormalities of the umbilical cord (e.g. velamentous insertions, true knots and strictures) are usually only noted postpartum. Abuhamad et al first showed the umbilical artery Doppler waveforms can be abnormal in monoamniotic twin pregnancies complicated by cord entanglement. ¹⁹ In a prospective trial, Abuhamad et al showed that UA waveform notching appears to be a strong predictor of cord entanglement, true knots, cord stricture, velamentous insertion, tight nuchal cords and abnormal cord coiling. ²⁰

Venous Doppler

Doppler applications in obstetrics have largely focused on arterial flow profiles which give information on downstream impedance and upstream pressure. Venous Doppler evaluation allows estimation of forward cardiac function and venous distribution.²¹ With the exception of the umbilical vein, all veins have a four phase flow pattern. Forward velocity is highest during ventricular systole (S) and early diastole (D). Velocity is lower during the ascent of the atrioventricular ring (v) and especially during atrial systole (A).

Ductus Venosus (DV)

The fetal circulation consists of two parallel blood streams that are uniquely partitioned. The single umbilical vein carries oxygenated blood from the placenta to the fetus reaching the fetal liver as the first major organ. 55% of the blood flow is diverted to the left lobe, 20% to the right lobe and 25% to the (ductus venosus) DV towards the heart. The DV acts as the first partition determining the proportion of umbilical venous blood diverted to the heart and it carries the most rapidly moving blood in the venous system and is thus easily identifiable on Doppler ultrasound (Fig. 5). Rizzo et al studied Doppler indices from both the inferior vena cava (IVC) and DV and compared these values to cordocentesis derived blood sampling in IUGR fetuses and showed that abnormal DV S/A ratios could predict hypoxemia in this subgroup.²² Several authors have reported on the use of DV studies in the prediction of fetal compromise in IUGR and other vascular abnormalities allowing for delivery prior to changes in biophysical profile scores. Baschat et al showed that DV Doppler parameters combined with IVC and UV Doppler measurements correctly predicted acid-base status in a significant proportion of IUGR neonates.²³ Similarly, Schwarze et al showed that abnormal DV waveforms in preterm IUGR fetuses along with ARED was strongly associated with adverse fetal and perinatal outcome less than 32 weeks allowing for better timing of delivery.²⁴ Mari et al caution that DV waveforms alone cannot be used as the sole indicator for delivery, especially in the IUGR fetus less than 30 weeks.²⁵ They recommend using MCA PSV along with DV reversed flow as indicators for delivery, given the high perinatal mortality rates when IUGR fetuses are delivered less than 29 weeks of gestation.

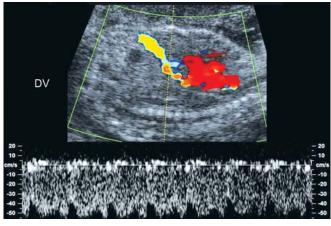


Fig. 5: Normal ductus venosus blood flow

Umbilical Vein

Umbilical vein Doppler provides information on fetal forward cardiac flow. Until 15 weeks, the umbilical vein has pulsations which are related to IVC patterns. After this gestational age, pulsations may be associated with fetal heart accelerations, breathing and cord constriction. Pulsations may also be seen in the presence of severe IUGR and fetal hydrops. Hofstaetter et al showed umbilical vein pulsations were a more sensitive indicator of heart failure in fetal hydrops compared to heart size, cardiac function, arterial Doppler and DV measurements.

Other Veins

The hepatic veins and IVC share characteristics with the DV but is not easily interpreted. The portal veins have no pulsations, and respond to fetal hypoxemia.²⁹ The ease of measuring the DV, however, makes it the vessel of choice in venous Doppler measurements currently.

Color and Power Doppler Imaging

Doppler imaging has provided velocity information when their beams are directed at blood vessels and this technology has been available for many years. However, real time Doppler imaging only became available with fast signal processing which produces several images per second of the scanned region. Fast signal processing allows for the production of color Doppler velocity images and power Doppler images. Color Doppler shows the direction of flow of information extracted by the electronics from the sequence of returning echoes (red denoting flow towards the transducer and blue away). Power Doppler images are generated when the power level at each image pixel is presented as a level of brightness. Image brightness is uniform except at vessel walls or in turbulent areas making power Doppler a sensitive technique for depicting flow in small vessels.

Color and power Doppler ultrasound have been used to image the vasculature of the fetal lung, kidney and brain (Fig. 6).³¹ Since power Doppler has the advantage of displaying intensity of a returning Doppler signal, it is less dependent on the orientation of the blood vessel and is a useful technology to use in obstetrical imaging. Guerriero et al used transvaginal



Fig. 6: Renal artery color Doppler

color Doppler imaging to diagnose prenatal intracranial hemorrhage in the second trimester³² and Pilu et al have used this technology to correctly identify discrepant intracranial vasculature allowing for prenatal microcephaly diagnosis.³³ Fetal sacrococcygeal teratomas have been diagnosed prenatally using amplitude-based color Doppler sonography.³⁴ Other applications of color Doppler imaging in pregnancy include fetal echocardiography³⁵ and the identification of renal arteries in pregnancies complicated by oligohydramnios.³⁶

A major application of color Doppler in obstetrics is the evaluation of the placenta and is useful for the antenatal diagnosis of placenta previa, placenta accreta and vasa previa. The accuracy of *in vivo* detection of arterio-arterial anastomoses in monochorionic twins and its protection against the development of twin-to-twin transfusion syndrome was found to be highly specific with the use of power Doppler ultrasound technology and has been advocated as having a role in the stratification of antenatal assessment of monochorionic twins. ³⁹

Doppler Ultrasound in 3D

Three-dimensional (3D) ultrasound is a natural development in the evolution of ultrasound technology. The acquisition of data points throughout an entire volume of interest is required to produce a 3D ultrasound picture. ³¹ Slow acquisition speeds yield more scanned slices and volume data points, and are used to image static organs whereas fast speeds are used for imaging moving structures, such as fetuses. Ultra fast acquisition allows for four-dimensional (4D) real time imaging. 3D imaging reconstruction is voxel-based with the voxel being the smallest 3D picture unit. This allows for each pixel (smallest 2D picture unit) to be placed in the correct position in 3D volume reconstruction.

3D Power Doppler

This technology allows for the three-dimensional reconstruction of vessels after their visualization using power Doppler ultrasound (Fig. 7). Instead of frequency shifts, 3D power Doppler analyzes amplitude signals and has been shown to be three to five times more sensitive than conventional color Doppler in visualizing small vessels and slower flows.³⁹ Additionally, vessel visualization is not affected by angle of insonation and is not susceptible to aliasing. Three-dimensional quantification of blood flow from color Doppler is not possible. A new method for blood flow and vascularization has been developed to better depict overall blood flow in 3D power Doppler studies. 40 The vascularization index (VI) = color voxels/(total voxels -background voxels), and measures flow in a region of interest. Flow index (FI) = weighted color voxels/ (color voxels – border voxels), and measures the intensity of color flow in a region of interest and is not an indicator of perfusion. The vascularization flow Index (VFI) = weighted color voxels/(total voxels - background voxels) and combines the percent of color voxels and intensity in a region of interest and therefore represents both blood flow and vascularization.



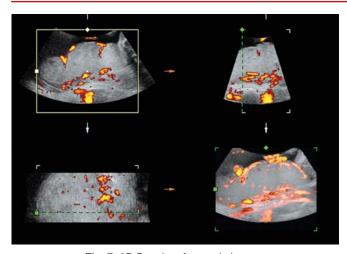


Fig. 7: 3D Doppler of normal placenta

3D Doppler ultrasound is advantageous for the study of normal uterine, placental and fetal cardiovascular development. The 3D Doppler reconstruction of ultrasound images has become an available option on ultrasound equipments. Several clinical applications are feasible in all parenchymatous organs (mainly the liver and kidneys), peripheral vessels (supra-aortic trunks and limb vessels) and central (the aorta and iliac arteries) or cerebral vessels. Moreover, tumoral vessels in parenchymatous organs can be reconstructed, and the fetal blood flow can be seen with excellent detailing. The introduction of 3D has permitted to study normal and abnormal peripheral, central and parenchymatous vessels with similar patterns to those obtained with digital angiography. The spatial relationships between the vascular structures of the placenta were studied with 3D ultrasound angiograms. The applications of this new technique include the analysis of vascular anatomy and the potential assessment of organ perfusion in the future.

Doppler ultrasound waveform analysis of the maternal-fetal circulation has emerged to add useful information in the determination of fetal well-being. One of potential application of 3D Doppler could be in the study of vascular changes in patients with IUGR and pre-eclampsia. It is a known fact that IUGR and pre-eclampsia are commonly associated with deficient trophoblastic invasion of the maternal spiral arteries during the first and second trimester. This problem can produce abnormally increased resistance to flow through the uterine circulation, and the resulting placental insufficiency can significantly reduce the delivery of oxygen to the fetus. Abnormal placental development is associated with fetal and neonatal morbidity, growth impairment, incidence of major congenital anomalies, increased incidence of preterm birth, fetal nonreassuring status in labor, neonatal intensive care admissions and overall mortality. If proven clinically useful in large scale prospective studies, 3D Doppler evaluation of placenta could establish a foundation for earlier in vivo recognition of homodynamic changes in pre-eclampsia and possibly in IUGR. Three-dimensional power Doppler sonography has the potential to study the process of placentation and evaluate the development of the embryonic and fetal cardiovascular system.42

Matijevic and Kurjak compared the performance of 2D and 3D power Doppler ultrasound in the visualization of the placental vascular network during ongoing pregnancy. ⁴³ There was no difference in the visualization of primary placental stem vessels by 2D and 3D power Doppler. However, 3D power Doppler performed better distally with statistically significant differences at the level of secondary stem, and even more prominent differences at the level of tertiary stem vessels. There was no difference in the visualization rate of radial and spiral arteries. The authors concluded that 3D Doppler was superior to 2D Doppler in the determination of the distal vascular branches of the fetal placental blood vessels.

The relationship of large and vascularized chorioangiomas and adverse pregnancy outcome is well recognized. Shih et al studied a patient with a large placental tumor and signs of impending fetal cardiac failure. The angioarchitecture of the tumor depicted by three-dimensional (3D) power Doppler ultrasound enabled them to accurately diagnose a placental chorioangioma. During the follow-up period, quantitative flow data obtained using 3D power Doppler indicated altered hemodynamics in the tumor and concomitant improvement in the condition of the fetus, enabling them to manage the mother conservatively. Spontaneous delivery occurred at 38 weeks without any complications. This report demonstrates the potential value of 3D power Doppler in prenatal diagnosis and monitoring of pregnancies complicated by large, vascularized chorioangioma.

3D Doppler ultrasound is a new method which allows the spatial presentation of fetal vessels in utero. Hartung et al have examined the feasibility of this technique in prenatal diagnosis.⁴⁵ The aim of their study with normal human fetuses was to determine the adjustment of the system presets, the optimal insonation planes and the regions of interest. Seven regions of interest were examined in three different planes. Best examinations were achieved in the vessels of the umbilical cord (successful rate 100%), followed by the placental and abdominal (84% each), cerebral (80%), pulmonary (64%) and renal vessels (51%). The most difficult conditions for examination and the most unreliable results were found for the fetal heart with a success rate of only 31% of the cases. Similar to the experience in 2D power Doppler, a plane with blood flow towards the transducer was the best insonation plane. In this study, the authors were able to show that 3D Doppler of fetal vessels is possible. The feasibility is limited by fetal movements and unfavorable fetal positioning. The possible benefit of the method is to diagnose complex fetal vascular malformations in the future.

Ritchie et al have developed a system for producing 3D angiograms from a series of two-dimensional power-mode Doppler ultrasound. Two-dimensional Doppler scans were acquired using a commercial scanner and image-registration hardware. Two-dimensional images were then digitized, and specially designed software reconstructed 3D volumes and displayed volume-rendered images. Scanning a flow phantom constructed from tubing assessed the geometric accuracy of their

system. The system was tested on patients by scanning native and transplanted kidneys and placentas. Three-dimensional images of the phantoms depicted the spatial relationships between blood flows within the tubing segments and contained less than 1 mm of geometric distortion. Three-dimensional images of the kidney and placenta demonstrated that spatial relationships between vasculature structures could be visualized with 3D Doppler ultrasound. Applications of this new technique include analysis of vascular anatomy and the potential assessment of organ perfusion.

Chaoui et al wanted to assess the fetal cardiovascular system using 3D power Doppler in normal and abnormal conditions during the second half of pregnancy.⁴⁷ The following regions of interest were assessed: placental, umbilical, abdominal, renal, pulmonary and intracranial vessels together with the heart and great arteries. Satisfactory visualization of the fetal vascular system using 3D Doppler could be achieved in normal pregnancies. The main difficulty during the learning curve was the optimization of the power Doppler image prior to 3D data acquisition. Despite good visualization conditions, the reconstruction of satisfactory images was only possible in 56 out of the 87 (64%) pregnancies with abnormal vascular anatomy. These were abnormalities of placenta and umbilical vessels, intra-abdominal and intrathoracic anomalies, renal malformations, central nervous system and cardiac defects. The main reasons for the lack of information were fetal position and movements, overlapping with signals from neighboring vessels as well as technical limitations of the online system.

Zalud and Shaha have evaluated uteroplacental circulation using 3D power Doppler and established norms for placental and spiral artery blood flow in normal pregnancies between 14 and 25 weeks of gestation. 48 They showed that VI, FI and VFI all increased slowly in placental and spiral arteries with advancing gestation though these indices were all elevated with increasing parity. 49 Merce et al noted that the use of 3D power Doppler is akin to a vascular biopsy and is an appropriate tool for the routine evaluation of the placenta vascular tree during gestation and that these indices are significantly related to fetal biometry and umbilical artery Doppler velocimetry.⁵⁰ Bartha et al used 3D power Doppler to evaluate fetal cerebral circulation in both normal and IUGR fetuses and showed that on average, VI, FI and VFI were all increased in fetuses with growth restriction suggesting hemodynamic redistribution that was higher than expected by conventional Doppler flow studies.⁵¹ Even the fetal hepatic and portal system can be evaluated by 3D power Doppler. Kalache et al identified absent ductus venosus, direct connection of the umbilical vein to the right atrium and umbilical vein to the inferior vena cava using 3D power Doppler.⁵²

Placenta accreta has become the leading cause of emergency peripartum hysterectomy and the rates have increased markedly in the last few decades.⁵³ The resulting blood loss and surgery results in significant maternal and neonatal morbidity and occasionally mortality and is becoming a significant problem

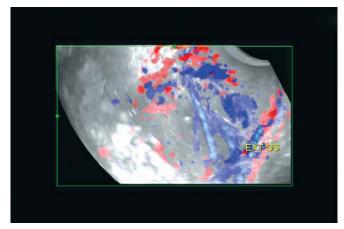


Fig. 8: 3D Doppler of placenta accreta

in obstetrics today. The antepartum diagnosis of accreta is essential and has been shown to result less blood transfusions, intensive care unit (ICU) admissions, genitourinary tract injuries and a decrease in neonatal intensive care unit (NICU) length of stay, respiratory distress syndrome (RDS) and surfactant use.⁵⁴ The addition of 3D power Doppler imaging of the placenta, especially in the basal view, may be a useful complementary technique for the antenatal diagnosis or exclusion of placenta accreta (Fig. 8).⁵⁵

CONCLUSION

Doppler ultrasound of the umbilical artery plays an important role in the management of IUGR and pre-eclampsia and aids in prognostication in twin-to-twin transfusion syndrome while notching in the waveform is a predictor of umbilical cord abnormalities. Middle cerebral artery Doppler reliably detects fetal anemia and may be useful in the assessment of IUGR as well. Abnormal uterine artery Doppler may play a role in predicting growth restriction, hypertensive disorders of pregnancy and preterm delivery. Abnormal ductus venosus waveforms can also be used to predict adverse fetal outcome and may allow for better timing of delivery while umbilical venous pulsations may be a sensitive marker for fetal heart failure in hydropic pregnancies. 3D power Doppler allows better small vessel visualization that is not affected by angle of insonation and has been used to diagnose placental and cord abnormalities. As clinical experience with these new technologies increase and as the technology improves further, it is reasonable to expect that 3D Doppler and 4D ultrasound will be complementary addition to well-established 2D Doppler ultrasound imaging.

REFERENCES

- Doppler C. Uber das farbige. Licht der Dopplersterne und einigr anderer Gestirne des Himmels. (On the coloured light of double stars and certain other stars of the heavens). Royal Bohemian Society 1842;2:465.
- Callen P. Ultrasonography in obstetrics and gynecology (5th ed). Saunders Elsevier 2008.



- 3. Hoffman S, Galan H. Assessing the 'at-risk' fetus: Doppler ultrasound. Curr Opin Obstet Gynecol 2009;21:161-66.
- Stuart B, Drumm J, Fitzgerald D, Duignan N. Fetal blood velocity waveforms in normal pregnancy. Br J Obstet Gynaecol Sep 1980;87(9):780-85.
- Trudinger B, Giles W, Cook C, Bombardieri J, Collins L. Fetal umbilical artery flow velocity waveforms and placental resistance: Clinical significance. Br J Obstet Gynaecol Jan 1985;92(1):23-30.
- Alfirevic Z, Neilson J. Doppler ultrasonography in high-risk pregnancies: Systematic review with meta-analysis. Am J Obstet Gynecol May 1995;172(5):1379-87.
- 7. Kontopoulous E, Quintero R, Chmait R, Bornick P, Russell Z, Allen M. Percent absent end-diastolic velocity in the umbilical artery waveform as a predictor of intrauterine fetal demise of the donor twin after selective laser photocoagulation of communicating vessels in twin-twin transfusions syndrome. Ultrasound Obstet Gynecol Jul 2007;30(1):35-39.
- 8. Mari G, Adrignolo A, Abuhamad Z, Pirhonen J, Jones D, Ludomirsky A, et al. Diagnosis of fetal anemia with Doppler ultrasound in the pregnancy complicated by maternal blood group isoimmunization. Ultrasound Obstet Gynecol Jun 1995;5(6):400-05.
- 9. ACOG Practice Bulletin No. 75: Management of alloimmunization. Obstet Gynecol Aug 2006;108(2):457-64.
- 10. Slaghekke F, Kist W, Oepkes D, Pasman S, Middeldorp J, Klumper F, et al. Twin anemia-polycythemia sequence: Diagnostic criteria, classification, perinatal management and outcome. Fetal Diagn Ther Mar 2010.
- Mari G, Hanif F, Kruger M, Cosmi E, Santolaya-Forgas J, Treadwell M. Middle cerebral artery peak systolic velocity: A new Doppler parameter in the assessment of growth-restricted fetuses. Ultrasound Obstet Gynecol Mar 2007;29(3):310-16.
- 12. Ghidini A, Locatelli A. Monitoring of fetal well-being: Role of uterine artery Doppler. Semin Perinatol 2008;32:258-62.
- 13. Phupong V, Dejthevaporn T. Predicting risks of pre-eclampsia and small for gestational age infant by uterine artery Doppler. Hypertens Pregnancy 2008;27:387-95.
- Onwudiwe N, Yu C, Poon L, Spiliopoulos I, Nicolaides K. Prediction of pre-eclampsia by a combination of maternal history, uterine artery Doppler and mean arterial pressure. Ultrasound Obstet Gynecol Dec 2008;32(7):877-83.
- Li H, Gudnason H, Olofsson P, Dubiel M, Gudmundsson S. Increased uterine artery vascular impedance is related to adverse outcome of pregnancy but is present in only one-third of late third-trimester pre-eclamptic women. Ultrasound Obstet Gynecol May 2005;25(5):459-63.
- Ferrazzi E, Bulfamante G, Mezzopane R, Barbera A, Ghidini A, Pardi G. Uterine Doppler velocimetry and placental hypoxicischemic lesion in pregnancies with fetal intrauterine growth restriction. Placenta Jul-Aug 1999;20(5-6):389-94.
- McCowan L, North R, Harding J. Abnormal uterine artery Doppler in small-for-gestational-age pregnancies is associated with later hypertension. Aust N Z J Obstet Gynaecol Feb 2001;41(1):56-60.
- Gudmundsson S, Korszun P, Olofsson P, Dubiel M. New score indicating placental vascular resistance. Acta Obstet Gynecol Scand Sep 2003;82(9):807-12.
- 19. Abuhamad A, Mari G, Copel J, Cantwell C, Evans A. Umbilical artery flow velocity waveforms in monoamniotic twins with cord entanglement. Obstet Gyencol Oct 1995;86(4 Pt 2):674-77.
- Abuhamad A, Sclater A, Carlson E, Moriarity R, Aguiar M. Umbilical artery Doppler waveform notching: Is it a marker for cord and placental abnormalities. J Ultrasound Med Aug 2002;21(8):857-60.

- Baschat A, Harman C. Venous Doppler in the assessment of fetal cardiovascular status. Curr Opin Obstet Gynecol 2006;18:156-63.
- Rizzo G, Capponi A, Talone P, Arduini D, Romanini C. Doppler indices from inferior vena cava and ductus venosus in predicting pH and oxygen tension in umbilical blood at cordocentesis in growth retarded fetuses. Ultrasound Obstet Gynecol Jun 1996;7(6):401-10.
- 23. Baschat A, Guclu S, Kush M, Gembruch U, Weiner C, Harman C. Venous Doppler in the prediction of acid-base status of growth-restriction fetuses with elevated placental blood flow resistance. Am J Obstet Gynecol Jul 2004;191(1):277-84.
- 24. Schawarze A, Gembruch U, Krapp M, Katalinic A, Germer U, Axt-Fliedner R. Qualitative venous Doppler flow waveform analysis in preterm intrauterine growth-restricted fetuses with ARED flow in the umbilical artery—correlation with short term outcome. Ultrasound Obstet Gynecol Jun 2005;25(6):573-79.
- Mari G, Hanif F, Treadwell M, Kruger M. Gestational age at delivery and Doppler waveforms in very preterm intrauterine growth-restricted fetuses as predicators of perinatal mortality. J Ultrasound Med May 2007;26(5):555-59.
- Rizzo G, Arduini D, Romanini C. Umbilical vein pulsations: A physiologic finding in early gestation. Am J Obstet Gynecol Sep 1992;167(3):675-77.
- Mari G, Hanif F. Fetal Doppler: Umbilical artery, middle cerebral artery and venous system. Semin Perinatol Aug 2008;32(4): 253-57.
- Hofstaetter C, Hansmann M, Eik-Nes S, Huhta J, Luther S. A cardiovascular profile score in the surveillance of fetal hydrops. J Matern Fetal Neonatal Med Jul 2006;19(7):407-1330.
- 29. Bellotti, Pennati G, De Gasperi C, Bozzo M, Battaglia F, Ferrazzi E. Simultaneous measurements of umbilical venous, fetal hepatic and ductus venosus blood flow in growth-restricted human fetuses. Am J Obstet Gynecol May 2004;190(5):1347-58.
- McDicken W, Anderson T. The difference between colour Doppler velocity imaging and power Doppler imaging. Eur J Echocardiography 2002;3:240-44.
- 31. Fortunato S. The use of power Doppler and color power angiography in fetal imaging. Am J Obstet Gynecol 1996;174:1828-33.
- 32. Guerriero S, Ajossa S, Mais V, Risalvato A, Angiolucci M, Labate F, et al. Color Doppler energy imaging in the diagnosis of fetal intracranial hemorrhage in the second trimester. Ultrasound Obstet Gynecol Sep 1997;10(3):205-08.
- 33. Pilu G, Falco P, Milani V, Perolo A, Bovicelli L. Prenatal diagnosis of microphaly assisted by vaginal sonography and power Doppler. Ultrasound Obstet Gynecol May 1998;11(5):357-60.
- 34. Fox D, Bruner J, Fleischer A. Amplitude-based color Doppler sonography of fetus with sacrococcygeal teratoma. J Ultrasound Med 1996;15:785-87.
- 35. Chua L, Twining P. A comparison of power color flow with frequency based color flow Doppler fetal echocardiography. Clin Radiol Sep 1997;52(9):712-14.
- 36. DeVore G. The value of color Doppler sonography in the diagnosis of renal agenesis. J Ultrasound Med Jun 1995;14(6):443-49.
- 37. Chou M, Ho E, Lee Y. Prenatal diagnosis of placenta previa accreta by transabdominal color Doppler ultrasound. Ultrasound Obstet Gynecol Jan 2000;15(1):28-35.
- 38. Devesa R, Munoz A, Torrents M, Carrera J. Prenatal diagnosis of vasa previa with transvaginal color Doppler ultrasound. Ultrasound Obstet Gynecol Aug 1996;8(2):139-41.
- Chaoui R, Kalache K, Hartung J. Application of threedimensional power Doppler ultrasound in prenatal diagnosis. Ultrasound Obstet Gynecol 2001;17:22-29.

- 40. Pairleitner H, Steiner H, Hasenoehrl G, Staudach A. Three-dimensional power Doppler sonography: Imaging and quantifying blood flow and vascularization. Ultrasound Obstet Gynecol 1999;14:139-43.
- 41. Pretorius DH, Nelson TR, Baergen RN, et al. Imaging of placental vasculature using three-dimensional ultrasound and color power Doppler: A preliminary study. J Perinat Med 2002;30:48-56.
- 42. Chaoui R, Hoffmann J, Heling KS. Three-dimensional (3D) and 4D color Doppler fetal echocardiography using spatio-temporal image correlation (STIC). Ultrasound Obstet Gynecol 2004;23:535-45.
- 43. Matijevic R, Kurjak A. The assessment of placental blood vessels by three-dimensional power Doppler ultrasound. J Perinat Med 2002;30:26-32.
- 44. Shih JC, Ko TL, Lin MC, et al. Quantitative three-dimensional power Doppler ultrasound predicts the outcome of placental chorioangioma. Ultrasound Obstet Gynecol 2004;24:202-06.
- 45. Hartung J, Kalache KD, Chaoui R. Three-dimensional power Doppler ultrasonography (3D-PDU) in fetal diagnosis. Ultraschall Med 2004;25:200-05.
- Ritchie CJ, Edwards WS, Mack LA, et al. Three-dimensional ultrasonic angiography using power-mode Doppler. Ultrasound Med Biol 1996;22:277-86.
- 47. Chaoui R, Kalache K, Hartung J. Application of three-dimensional power Doppler ultrasound in prenatal diagnosis. Ultrasound Obstet Gynecol 2001;17:22-29.

- Zalud I, Shaha S. Evaluation of the utero-placental circulation by three-dimensional Doppler ultrasound in the second trimester of normal pregnancy. J Matern Fetal Neonatal Med Apr 2007;20(4):299-305.
- 49. Zalud I, Shaha S. Three-dimensional sonography of the placenta and uterine spiral vasculature: Influence of maternal age and parity. J Clin Ultrasound Sep 2008;36(7):391-96.
- Merce L, Barco M, Bau S, Kupesic S, Kurjak A. Assessment of placental vascularization by three-dimensional power Doppler "Vascular Biospy" in normal pregnancies. Croat Med J 2005;465:765-71.
- 51. Bartha J, Moya E, Hervias-Vivancos B. Three-dimensional power Doppler analysis of cerebral circulation in normal and growth restricted fetuses. J Cereb Blood Flow Metab Sep 2009;29(9):1609-18.
- Kalache K, Romero R, Goncalves L, Chaiworapongsa T, Espinoza J, Schoen M, et al. Three-dimensional color power imaging of the fetal hepatic circulation. Am J Obstet Gynecol Nov 2003;189(3):1401-06.
- Miller D, Chollet J, Goodwin T. Clinical risk factors for placenta previa-placenta accreta. Am J Obstet Gynecol 1997;177: 210-14.
- Warhak C, Ramos G, Eskander R, Benirschke K, Saenz C, Kelly T, et al. Effect of predelivery diagnosis in 99 consecutive cases of placenta accreta. Obstet Gynecol Jan 2010;115(1):65-69.
- 55. Shih J, Jaraquemada P, Su Y, Shyu M, Lin C, Lin S, et al. Role of three-dimensional power Doppler in the antenatal diagnosis of placenta accreta: Comparison with gray-scale and color Doppler techniques. Ultrasound Obstet Gynecol 2009;33: 193-203.