10.5005/jp-journals-10009-1272
REVIEW ARTICLE

Three-dimensional Evaluation of the Placenta: Review of the Literature

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ABSTRACT

The introduction of the three-dimensional (3D) ultrasound made feasible the quantitative and qualitative evaluation of the placenta's characteristics like the volume, the surface rendered imaging, the vascularization and the blood flow. These novel techniques may assist the early detection of pregnancies at high risk for fetal growth restriction (FGR), pre-eclampsia (PET) and pregnancy-induced hypertension (PIH) and help clinicians to detect pregnancies at risk earlier and to assess new therapeutic strategies in order to prevent adverse pregnancy outcomes. However, in this new technique there are still limitations regarding the assessment of the placenta employing 3D ultrasound in everyday clinical practice. In the following article, we perform a review of the literature regarding the importance of 3D evaluation of the placenta in pregnancy.

Keywords: Three-dimensional ultrasound, Three dimension, Placental volume.

How to cite this article: Natsis S, Antsaklis P, Antsaklis A, Kurjak A. Three-dimensional Evaluation of the Placenta: Review of the Literature. Donald School J Ultrasound Obstet Gynecol 2013;7(1):73-79.

Source of support: Nil

Conflict of interest: None declared

INTRODUCTION

Pregnancy associated problems like intrauterine growth retardation (IUGR) or pre-eclampsia (PET) are mainly caused by a disturbed placental function. Current models suggest that these problems are related to an impaired invasion of fetal trophoblastic cells in the maternal decidua, which will leads to an impeded transformation of the spiral arteries into vessels of low resistance.[1] This causes reduced blood flow and accordingly leads to hypoxic damage of the endothelial vessels, initiating a range of disorders including placental infraction, increased maternal blood pressure (pregnancy-induced hypertension, PIH) and fetal growth restriction (FGR) among others.

Conventional two-dimensional (2D) ultrasound has been widely used for the evaluation of the placenta during pregnancy. This 2D evaluation includes the assessment of the morphology and anatomy of the placenta, identification of its location and evaluation of other placental issues, such as quality of implantation, structural or functional anomalies, placental size and more recently study of color/power and pulsed Doppler characteristics of the placenta.[2,3]

The earlier in pregnancy we identify a risk factor for obstetric complications, the higher the chance that we may find a treatment. Identifying risk factors for PET and IUGR in the first trimester of pregnancy has been a great challenge in obstetrics the last decade. New evidence show that three-dimensional (3D) evaluation of the placenta may be a possible method to detect impaired trophoblastic invasion in the first trimester might be. 3D ultrasound has the potential to provide improved visualization of the fetal anatomic morphology compared to the conventional 2D imaging. 3D ultrasound and power Doppler offer a more objective and more detailed method of evaluating placental volume and its vascular network. In 1984, the first placental volumes acquired via sonography were conducted by Brinkley et al.[4] Since, then the progress of technology and the development of 3D sonography (3DUS) imaging assisted by computer technology, has made possible the measurement and calculation of fetal and placental volumes accurately and quickly. This method has been standardized and implemented in everyday practice. What is more 3D power Doppler offers more information on the placental anatomy and function. The Doppler parameters derived from 3D interrogation of the placenta include the vascularization index (VI), the flow index (FI) and the vascularization flow index (VFI).

Aim of this paper is to review all available studies regarding 3D ultrasonographic assessment of the placental morphology, placental volume measurement, and placental vascularization and blood flow.

Evaluation of Placental Abnormality Using 3D Ultrasound

In most cases an exact diagnosis of placental abnormalities can be made using only the 2D ultrasound. However, using the 3D ultrasound, more detailed information on placental abnormalities can be obtained, especially visualization of the continuity and curvature. There have been two reports on placental diagnosis of placental abnormalities using 3D surface rendered imaging. Hata et al in 2004[5] investigated six cases with placental abnormalities and found that visualization of the continuity and curvature of structures was more easily accomplished with the 3D sonography than the 2D. In addition, Abramowicz et al suggested that 3D

surface rendered images provide an entirely new visual experience not only for the examiner, but also for patients and their families, owing to the near-photographic depiction of the placental abnormality *in utero*.[6]

Volume Measurement Using 3D Ultrasound

Volume measurements using 3D ultrasound methods are much more accurate than the methods using the 2D ultrasound for regular and irregular shaped objects. Riccabona et al observed that 3D measurement error was only 6.4 ± 4.4% whereas 2D error reached 12.6 ± 8.7% when compared the accuracy of ultrasound for volume measurement.[7] There are three techniques for the placental volume assessment; that is (a) the multiplanar method, (b) the VOCAL (virtual organ computer-aided analysis) method and (c) the XI VOCAL (extended imaging VOCAL) method. Nowac et al in 2007 in a prospective cross sectional study involving 37 pregnant women, evaluated placental volumes in early pregnancy using both multiplanar and VOCAL methods and comparing the results.[8] This study showed strong correlation between placental volume measured by the VOCAL and the multiplanar methods which are considered to be concordant. Another study by Cheong et al in 2010 showed that XI VOCAL method to be inferior to VOCAL in terms of reliability and validity.[9] The better results of the VOCAL mode can be explained by its ability to allow finer contouring of the object of interest and easier subsequent modification of the contour. In contrast the current XI VOCALmode applies a fixed slice interval and does not take into account the highly variable contour of an irregular subject.

There are several studies regarding the volume of the placenta and the prediction of the birth weight percentile. Plasencia et al in a prospective study involving 3,104 singleton pregnancies suggested that combined measurement of placental volume and serum pregnancy associated plasma protein A (PAPP-A) can improve the prediction of small (SGA) or large for gestational age (LGA) fetuses, compared to the prediction provided by maternal characteristics alone.[10] They found that an algorithm combining maternal characteristics with either placental volume or maternal serum PAPP-A can potentially identify about 30% of pregnancies with SGA or LGA, with a false positive rate (FPR) of 10%.[10] However, there was no significant improvement in the performance of screening for SGA or LGA neonates by the addition of placental volume in the combination of maternal factors and serum PAPP-A. There are also two previous studies which have studied the prediction of SGA from first trimester measurements of placental volume.[11,12] Hafner et al examined 2,489 singleton pregnancies at 11 to 13^{+6} weeks of their pregnancy and reported that the detection rate of SGA by measurement of placental volume alone was 27%, with a FPR of 10%.[11] Similarly, Law et al studied 601 pregnancies and reported that the measurement of placental volume at 11 to 13^{+6} weeks identified 23% of SGA neonates, with a FPR of 10% and the prediction rate was not improved by the measurement of uterine artery Dopplers or fetal crown rump length (CRL).[13]

There are plenty of studies regarding the prediction of adverse pregnancy outcomes including PET and pregnancy-induced hypertension, using placental volume measurement in the first trimester of pregnancy, but their results do not appear to agree on the prognostic value of placental volume measurement. Metzenbauer et al in a study involving 2,863 singleton pregnancies suggested that the median placental quotient (quotient from placental volume and CRL) in the chromosomally abnormal fetuses group, was significantly lower than that in the normal fetuses and they concluded that the assessment of placental volume may prove to be useful in first trimester risk assessment for chromosomal anomalies.[14] Obido et al suggested that the value of placental volume measurement and the interpretation of the results from the measurements depend on the pregnancy complication being studied.[18] In particular they found placental volumes to be lower in the pregnancies with PIH and SGA compared with the placentas of pregnancies with PET. This is consistent with studies that have demonstrated different morphologic characteristics of the placenta in pregnancies with growth restriction compared with PE.[18] However as a screening tool, placental volume was associated with poor predictive efficiency even for SGA and PIH in that study. On the other hand, Haffner et al stated that placental quotient (PQ) is insufficient for the screening of SGA, PET and PIH in low-risk populations.[11] They also reported that the placentas of women with pathologic uterine perfusion in the second trimester of pregnancy are already remarkably small at the end of first trimester.[20]

Several studies about the reproducibility of the placentas' volume measurement are available.[19-25] Bujold et al in 2009 concluded that evaluation of placental volume between 11 and 14 weeks of pregnancy is a feasible and reliable method.[22] In an other study by Huster et al in 2010, it was confirmed that the 3D measurements of the placental volumes are highly reproducible with the intraobserver and the interobserver correlations greater than 0.75, which is considered to be a good agreement.[23] Deurloo et al in 2006 in his study about reproducibility of 3D sonographic measurements of placental volume concluded that this method is highly reproducible both by the same and by

different operators.[24] On the other hand, Chen et al which noted that the intra- and interobserver agreement of placental volume measured by 3D ultrasound is relatively poor, which is reflected in the wide limits of agreement of acceptance in each case.[25]

3D Power Doppler Analysis of the Placenta

Conventional Doppler ultrasound study has been used as a noninvasive method to assess human fetoplacental circulation, by examining blood flow in the umbilical artery. Increased umbilical arterial resistance and reduced umbilical arterial flow studied by conventional Doppler ultrasound can be used as a predictor of adverse pregnancy outcome in high risk pregnancies. Power Doppler ultrasound uses the amplitude of the signals received to represent the number of moving blood cells. It has been found to be superior to frequency –based color Doppler ultrasonography, especially in low blood flow situations (low velocities), and has the potential to detect alterations in blood flow. In recent years power Doppler ultrasonography combined with 3D ultrasound (3D power Doppler) has been promising when it comes to evaluating morphological features of the placenta and the quantification of total blood flow in the placental vascular network in ongoing pregnancy.[26] More recently, 3D power Doppler indices such as, (a) VI which means the proportion of the volume showing a flow signal in the placenta; (b) FI which is the average flow signal intensity inside the placenta; (c) vascularization flow index (VFI) which is a combination of the information concerning vessel presence and the level of flow obtained by multiplying VI and FI, have been used to assess placental perfusion. Differences in these indices have been shown to exist between the different populations that are studied and the different gestational ages.[27] With the exception of first trimester of pregnancy, 3D power Doppler technology does not allow the evaluation of the whole placental vascular tree.[26,28] To avoid this technical difficulty, Merce et al have suggested a different method based on 3D power Doppler which they called 'placental vascular biopsy' or 'placental vascular sonobiopsy' (PVS) or 'virtual placental biopsy' and have confirmed with their studies its clinical reproducibility.[29,33] For the measurement of PVS the power Doppler window is placed over the placenta, including its total thickness, from the basal to chorionic plates.[30] The spherical 3D volume is obtained between the basal and chorionic plates. The VOCAL program automatically calculates gray scale and color values (VI, FI and VFI) from the acquired sphere. A sequence of three placental sections separated by successive rotation of 60° is obtained and 3 or 4 spherical sampling sites are chosen in each plane.

Several studies have been conducted to determine the reference values and the ranges of the VI, FI and VFI during pregnancy. Paula et al in a prospective study of 295 singleton, low-risk women found that the placental vascular indicesestimated by 3D power Doppler ultrasonography presented constant distribution throughout gestation, despite the significant increase of the placental volume.[31] This finding suggests that placental vascularization may increase proportionally to the organ volume, contributing to maintaining the placental vascular indices constant throughout gestation. Similar findings were observed by Guiot et al.[27] The results of these studies are considerably different when compared to other studies reported in the literature. Yu et al in 2003 in a study involving 100 normal placentas found that both VI and VFI increased throughout pregnancy.[32] In a later study by Merce et al it was demonstrated that 3D indices correlated significantly with gestational age, although each of them exhibited different behavior.[33] Whereas FI increased in a linear and progressive manner along gestation, the VI increased up to 30 weeks maintaining a plateau up to the 37th week and decreasing after that week of pregnancy. The VFI reflected the behavior of both indices. One possible explanation for these differences in the previous studies is the different sampling method of volume acquisition in the placenta. For example, Yu et al did not describe the volume applied and the place selected to obtain a representative sample of placental vascularization, while Merce et al used the previous reported method of sonobiopsy. Another explanation is the different machines and the machine setting used. There are investigations which provide evidence that machines settings affect VI, FI and VFI calculations.[34] It has been also demonstrated that the position of the placenta attachment in the uterine cavity may affect the measurements.[35] Some authors have stressed that only anterior placentas should be included in their studies to avoid the risk of Doppler signal attenuation.[30] Jones et al suggested that when undertaking 3D ultrasound and power Doppler angiography (3D-PDA) several technical aspects must be considered and she documented that depth depended attenuation of the signal needs to be accounted for in any *in vivo* work where the probe is not in direct contact with the tissue of interest.[36]

Vascularization Indices and Adverse Pregnancy Outcome Prediction

Several articles have studied the importance of first trimester placental vascularization indices for the prediction of adverse pregnancy outcomes (Table 1). Odeh et al[37] in a study with 308 pregnant women during 11 to 13^{+6} weeks of gestation

Table 1: Studies regarding usefulness of 3D measurement of the placenta in first trimester of pregnancy for the prediction of adverse pregnancy outcome[15-17]

Study	*Year*	*N*	*Gestation*	*Parameter used*	*Prediction*	*Screening*
Schuchter[12]	2001	380	11-14	PQ	PIH, PET, FGR	Useful
Hafner[20]	2001	1060	11-13	PV, PQ	Uterine perfusion	Useful
Metzenbauer[14]	2002	2863	10-13	PQ	Chromosomal abnormalities	Useful
Metzenbauer[15]	2002	1476	NG	PQ	LBW	Promising
Hafner[11]	2006	2489	11-13	PQ	PIH, PET, FGR	Insufficient
Rizzo[16]	2008	348	11-14	PV	PET	Useful
Law[13]	2009	619	11-13	PV	SGA	Useful
Rizzo[38]	2009	84	11-14	PV+PAPP-A	Pregnancy outcomes	Insufficient
Schwartz[17]	2010	135	11-14	PQ	PET, SGA	Promising
Plasencia[10]	2011	3104	11-13	PV+PAPP-A	Birth weight	Useful
Obido[18]	2011	388	11-14	PV,VI,FI,VFI	PIH, PET, FGR	Insufficient
Odeh[37]	2011	308	11-14	PV,VI, FI,VFI	SGA, PET	Insufficient

NG: Not given; PQ: Placental quotient; PV: Placental volume; PIH: Pregnancy induced hypertension; FGR: Fetal growth restriction; LBW: Low birth weight; SGA: Small for gestational age fetus; PET: Pre-eclampsia; PAPP-A: Pregnancy associated plasma protein A

suggested that VI may be of some potential in detection of PIH. Obido et al[18] found that the mean vascular indices of first trimester placentas were lower in pregnancies that subsequently developed PET compared to pregnancies who did not develop PET. In addition those pregnancies with both PET and SGA had a significantly lower FI compared tothe control group of unaffected pregnancies. The prediction models for PET using these indices were however, associated with only modest discriminatory ability. These findings were not as significant as previous studies, which had suggested better prediction of PET and SGA using placental volumes and vascularization indices. Rizzo et al[38] in a study with 84 singleton pregnancies which had low PAPP-A levels during the first trimester of pregnancy found that among pregnancies with low serum PAPP-A levels, significant decrease in the 3D power Doppler vascularization indices at 11 to 13^{+6} weeks was shown in those pregnancies who had low PAPP-A but also developed IUGR fetuses. A second finding of this study was the significant association between the degree of reduction in the 3D placental Doppler indices and the severity of the growth defects at birth. In another study Bozkurt et al[39] reported that VI values in the placenta at 11 to 14 weeks of gestation show a positive linear correlation with the newborn weight.

Table 2: Studies regarding the value of different parameters from 3D assessment for the prediction of adverse pregnancy outcome

Study	*Year*	*N*	*Week*	*Population*	*Parameter*	*Prediction*	*Screening*
Merce[33]	2005	99	14-40	Normal	PB, VI, FI, VFI	Correlation with GA	Useful
Zalud[40]	2007	199	14-25	Normal	VI, FI, VFI	Definition of indices in 2nd trimester	Useful
Guiot[27]	2008	45	23-37	Normal & FGR	VI, FI, VFI	FVW in Normal and IUGR	Useful
Zalud[41]	2008	199	14-25	Normal	VI, FI, VFI	Correlation with maternal age and parity	Parity influences indices
De Paula[31]	2009	295	12-40	Normal	VI, FI, VFI	Quantitative analysis of PV	Placental indices have constant distribution
Rizzo[38]	2009	84	11-14	Low PAPP-A	PV, VI, FI, VFI	Pregnancy outcome	Altered 3D placental indices, useful
Noguchi[30]	2009	208	12-40	Normal	PB, VI, FI, VFI	FGR	Useful
Tuuli[43]	2010	120	11-14	Normal	VI, FI, VFI	Correlation of indices ± PB	VI & VFI more reliable than FI in PB
Hafner[21]	2010	383	11-14	Normal	PV, PQ, VI, FI, Uterine art. Doppler	Pregnancy outcome	Useful for IUGR and PE
Yigiter[44]	2011	310	11-14	Normal	PV, VI, FI, VFI, uterine art. Doppler	PAPP-A, IGF-1, free β-hCG	Significant correlation
Obido[18]	2011	388	11-14	Normal	PV, VI, FI, VFI	Adverse pregnancy outcomes	Useful

PB: Placental sonobiopsy; VI: Vascularization index; FI: Flow index; VFI: Vascularization flow index; PV: Placental volume; PQ: Placental quotient; PE: Pre-eclampsia; FGR: Fetus growth restriction; FVW: Flow velocity waveforms

Other studies on 3DPD indices of the placenta on the later half of the pregnancy for adverse pregnancy outcomes have been conducted (Table 2). Guiot et al in 2008[27] studied 45 pregnant women from 23 to 37 weeks of gestation and concluded that 3D power Doppler sonography can provide new insights about the placental pathophysiology and FI appears to be the most reliable index, because of its low intraplacental variability. The VI and VFI were significantly lower in pregnancies complicated by FGR and had positive end diastolic umbilical artery flow velocity waveforms while in pregnancies with absent or reversed end diastolic umbilical artery flow velocity waveforms compared with normal pregnancies, while the FI decreased only in those with absent or reversed end diastolic umbilical artery flow velocity waveforms. On the other hand Nogucchi et al[30] showed that VI, FI and VFI in FGR pregnancies decrease throughout pregnancy and suggested that the FI is the least reliable index despite the fact it has a low intraplacental variability. One possible explanation is the heterogenity of the study populations between these two papers.

With respect to maternal characteristics and vascularity indices, Zalud et al in 2008[40,41] found that maternal age influenced uterine spiral vasculature volume, whereas parity influenced all placental 3DPD indices. Rizzo et al[38] found lower values of the vascular flow indices among women who smoked over 10 cigarettes per day. Obido et al[18] on the other hand found that maternal smoking did not affect the placental vascular indices.

Several studies have demonstrated the reproducibility of 3DPD ultrasound placental index measurements. Several authors obtained good intra- and interobserver reproducibility employing 3DPD parameters in the placenta.[22,30,36] When the visualization of the entire placental tree is not feasible a valid alternative could be placental vascular indices from PVS which show a good correlation with those of the entire placenta.[42]

CONCLUSION

It is well-established that PET and IUGR is caused by abnormal trophoblastic invasion and pathologic formation of the spiral arteries leading to increased placental resistance and decreased blood flow to the intervillous space. This abnormality in placentation can indirectly be measured and assessed via 2D ultrasound and more specifically through uterine artery Doppler.[44] However, studies show that conventional 2D ultrasound cannot provide the same information as 3D assessment of the placenta. Indeed 3D ultrasonography offers a more direct evaluation of blood flow to the placenta, and it has been shown by many studies that it may lead to earlier recognition of placentas at risk for adverse pregnancy outcomes, such as PET and IUGR or even chromosomal abnormalities.[43] We are now able using this new technique to evaluate more precisely the surface of the placenta, its volume and the placental vascular tree. However, lack of standardization of a universal method that would assess placenta with 3D ultrasound, has delayed the gathering of sufficient data that would allow this method to be applied as a screening tool in everyday clinical practice. Further work is required to establish the effect of other confounding parameters before valid conclusions may be made and a better understanding of 3D power Doppler ultrasound imaging achieved.[38] More studies with standardized machine settings are needed in current practice, in order to draw safe conclusions on the usefulness of 3D assessment of the placenta.

REFERENCES

1. Pijnenborg R, Bland JM, Robertson WB, Brosens I. Uteroplacental arterial changes related to interstitial trophoblast migration in early human pregnancy. Placenta 1983 Oct-Dec;4(4):397-413.
2. Abramowicz J, Sheiner E, Ultrasound of the placenta: A systematic approach. Part I: Imaging placenta 2008;29;225-40.
3. Matijevic R. The placenta. In: Kurjak A, Chervenak FA (Eds). Donald school textbook of ultrasound and gynecology (2nd ed). New Delhi: Jaypee; 2008;452-64.
4. Brinkley JF, McCallum WD, Muramatsu SK, et al. Fetal weight estimation from lengths and volumes found by 3D ultrasonic measurements. J Ultrasound Med 1984;3:163.
5. Hata T, Kanenishi K, Inusbashiri E, Tanaka H, Senoh D, Manabe A, et al. Three dimensional sonographic features of placental abnormalities. Gynecol Obstet Invest 2004;57:61-65.
6. Abramowicz JS, Sheiner E. In utero imaging of the placenta: Importance for diseases of pregnancy. Placenta 2007 Apr;28(Suppl A):S14-22.
7. Riccabona M, Nelson TR, Pretorius DH. Three-dimensional ultrasound: Accuracy of distance and volume measurements. Ultrasound Obstet Gynecol 1996;7:429-34.
8. Nowak PM, Nardozza LMM, Araujo Jr, Rolo LC, Moron AF. Comparison of placental volume in early pregnancy using multiplanar and VOCAL methods. Placenta 2008;29:241-45.
9. Cheong KB, Leung KY, Li TKT, Chan HY, Lee YP, Tang HY. Comparison of inter and intraobserver agreement and reliability between three different types of placental volume measurement technique (XI VOCAL, VOCAL and multiplanar) and validity in the in vitro setting. Ultrasound Obstet Gynecol 2010;36; 210-17.
10. Plasencia W, Akolekar R, Dagklis T, Veduta A, Nicolaides K. Placental volume at 11 to 13 weeks' gestation in the prediction of birth weight percentile. Fetal Diagn Ther 2011;30:23-28.
11. Hafner E, Metzenbauer M, Hofinger D, Stonek F, Schuchter K, Waldhor T, et al. Comparison between three dimensional placental volume at 12 weeks and uterine artery impedance/notching at 22 weeks in screening for pregnancy-induced hypertension, pre-eclampsia and fetal growth restriction in a low risk population. Ultrasound Obstet Gynecol 2006;27:652-57.

12. Schuchter K, Metzenbauer M, Hafner E, Philipp K. Uterine artery Doppler and placental volume in the first trimester in the prediction of pregnancy complications. Ultrasound Obstet Gynecol 2001;18:590-92.
13. Law LW, Lewng TY, Sahota DS, Chan LW, Fung TY, Lau TK. Which ultrasound or biochemical markers are independent prediction of small-for-gestational age? Ultrasound Obstet Gynecol 2009;34:283-87.
14. Metzenbauer M, Hafner E, Schuchter K, Philipp K. First–trimester placental volume as a marker for chromosomal anomalies: Preliminary results from an unselected population: Ultrasoun Obstet Gynecol 2002;19:240-42.
15. Metzenbauer M, Hafner E, Hoefinger D, Schuchter K, Philipp K. Association between birth weight and placental volume in the first trimester. Z Geburtsch Neonatol 2002;206:138-41.
16. Rizzo G, Capponi A, Cavicchioni O, Vendola M, Arduini D. First trimester uterine Doppler and three dimensional ultrasound placental volume calculation in predicting pre-eclampsia. Eur J Obstet Gynecol Reprod Biol 2008 Jun;138(2):147-51.
17. Schwartz N, Coletta J, Pessel C, Feng R, Timor-Tritsch IE, Parry S, et al. Novel 3-dimensional placental measurements in early pregnancy as predictors of adverse pregnancy outcomes. J Ultrasound Med 2010;29:1203-12.
18. Obido AO, Goetzinger KR, Huster KM, Christiansen JK, Obido L, Tuuli MG. Placental volume and vascular flow assessed by 3D power Doppler and adverse pregnancy outcomes. Placenta 2011;32:230-34.
19. Mayhew TM. A stereological perspective on placental morphology in normal and complicated pregnancies. J Anat 2009 Jul;215(1):77-90.
20. Hafner E, Metzenbauer M, Dillinger-Paller B, Hoefinger D, Schuchter K, Sommer-Wagner H, et al. Correlation of first trimester placental volume and second trimester uterine artery Doppler flow. Placenta 2001;22:729-34.
21. Hafner E, Metzenbauer M, Stumpflen I, Walddhor T, Philipp K. First trimester placental and myometrial blood perfusion measured by 3D power Doppler in normal and unfavourable outcome pregnancies. Placenta 2010;31:756-63.
22. Bujold M, Effendi M, Girard M, Gouin K, Forest JC, Couturier B, et al. Reproducibility of first trimester three-dimensional placental measurements in the evaluation of early placental insufficiency. J Obstet Gynaecol Can 2009 Dec;31(12): 1144-48.
23. Huster K, Haas K, Schoenborn J, McVean D, Obido A. Reproducibility of placental volume and vasculature indices obtained by 3-dimensional power Doppler sonography. J Ultrasound Med 2010;29:911-16.
24. Deurloo K, Spreeuwenberg M, Rekoert-Hollander M, van Vugt J. Reproducibility of 3-dimensional sonographic measurements of fetal and placental volume at gestational ages of 11 to 18 weeks. J Clin Ultrasound 2007;35:125-32.
25. Chen M, Leung KY, Lee CP, Tang MHY, Ho PC. Placental volume measured three dimensional ultrasound in the prediction of α-thalassemia: A preliminary report. Ultrasound Obstet Gynecol 2006;28:166-72.
26. Hafner T, Kurjak A, Funduk–Kurjak B, Bekavac I. Assessment of early chorionic circulation by three dimensional power Doppler. J Perinat Med 2002;30:26-32.
27. Guiot C, Gaglioti P, Oberto M, Piccoli E, Rosato R, Todros T. Is three dimensional power Doppler ultrasound useful in the assessment of placental perfusion in normal and growth restricted pregnancies? Ultrasound Obstet Gynecol 2008;31:171-76.
28. Matijevic R, Kurjak A. The assessment of placental blood vessels by three dimensional power Doppler ultrasound. J Perinat Med 2002;30:33-39.
29. Merce LT, Barco MJ, Bau S. Reproducibility of the study of placental vascularization by three dimensional power Doppler. J Perinat Med 2004;32:228-33.
30. Noguchi J, Hata K, Tanaka H, Hata T. Placental sonobiopsy using three dimensional power Doppler ultrasound in normal and growth restricted fetuses. Placenta 2009;30;391-97.
31. De Paula CFS, Ruano R, Campos JADB, Zugaib M. Quantitative analysis of placental vasculature by three dimensional power Doppler ultrasonography in normal pregnancies from 12 to 40 weeks of gestation. Placenta 2009;30:142-48.
32. Yu CH, Chang CH, Ko HC, Chen WC, Chang FM. Assessment of placental fractional moving blood volume using quantitative three dimensional power Doppler ultrasound. Ultrasound Med Biol 2003;29:19-23.
33. Merce LT, Barco M, Bau S, Kupesic S, Kurjak A. Assessment of placental vascularization by three dimensional power Doppler 'vascular biopsy' in normal pregnancies. Croat Med J 2005:46:765-71.
34. Martins WP, Raine Fenning N, Ferriani RA, Nastri CO. Quantitative three dimensional power Doppler angiography: A free-flow phantom experiment to evaluate the relationship between color, gain, depth and signal artifact. Ultrasound Obstet Gynecol 2010:35:361-68.
35. Raine-Fenning NJ, Nordin NM, Ranmarine KV, Campbell BK, Clewes JS, Perkins A, et al. Determining the relationship between three-dimensional power Doppler data and true blood flow characteristics: An in vitro flow phantom experiment. Ultrasound Obstet Gynecol 2008;32;540-50.
36. Jones NW, Raine-Fenning NJ, Mousa HA, Bradley H, Bugg G. Evaluating the intra- and interobserver reliability of three-dimensional ultrasound and power Doppler angiography (3D-PDA) for assessment of placental volume and vascularity in the second trimester of pregnancy. Ultrasound Med Biol 2011;37(3):376-85.
37. Odeh M, Ophir E, Maximovsky O, Grinin V, Bornstein J. Placental volume and three dimensional power Doppler analysis in prediction of pre-eclampsia and small for gestational age between week 11 and 13 weeks and 6 days of gestation. Prenat Diagn 2011;31:367-71.
38. Rizzo G, Capponi A, Pietrolucci ME, Capece A, Arduini D. First trimester placental volume and vascularization measures by 3-dimensional power Doppler sonography in pregnancies with low serum pregnancy associated plasma protein A levels. J Ultrasound Med 2009;28:1615-22.
39. Bozkurt N, Yigiter B, Gokaslan H, Kavak ZN. Correlations of fetal maternal outcomes and first trimester 3D placental volume/ 3D Doppler calculations. Clinical Exp Obstet Gynecol 2010;37:26-28.
40. Zalud I, Shaha S. Three dimensional sonography of the placental and uterine spiral vasculature: Influence of maternal age and parity. J Clin Ultrasound 2008;36(7):391-96.

41. Zalud I, Shaha S. Evaluation of the uteroplacental circulation by three-dimensional Doppler ultrasound in the second trimester of normal pregnancy. J Maternal-Fetal Neonatal Med 2007 April;20(4):299-305.
42. Tuuli MG, Houser M, Obido L, Huster K, Macones GA, Obido AO. Validation of placental vascular sonobiopsy for obtaining representative placental vascular indices by three dimensional power Doppler ultrasonography. Placenta 2010;31:192-96.
43. Yigiter AB, Kavak ZN, Durukan B, Isci H, Uzuner A, Uyar E, et al. Placental volume and vascularization flow indices by 3D power Doppler US using VOCAL technique and correlation with IGF-1, free beta-hCG, PAPP-A and uterine artery Doppler at 11 to 14 weeks of pregnancy. J Perinat Med 2011 Mar; 39(2):137-41.
44. Gebb J, Dar P. Colour Doppler ultrasound of spiral artery blood flow in the prediction of pre-eclampsia and intrauterine growth restriction. Best Pract Res Clin Obstet Gynaecol 2011 Jun;25(3):355-66.

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