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The Reproducibility of 3D power Doppler in Intrauterine Growth Restriction

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Abstract:

Objective: it is to examine the reproducibility of 3D power Doppler in the management of intrauterine growth restriction compared with the conventional 2d Doppler.

Patients and Methods: This study was performed between Jan 2021 and Feb 2022 and included 100 pregnant women recruited from outpatient clinic at Elgalaa Teaching Hospital, 3D power Doppler US was done for assessment of IUGR and compare the findings with 2D Doppler.

Results: it is found that 3D Power Doppler parameters were significant in prediction of poor neonatal outcome regarding development of respiratory complications, neurological complications and IUFD as complications to IUGR comparing to 2D colour Doppler parameters which were non-significant in these cases. Our results also showed that the only parameter of 2D Colour Doppler that showed significance and positive correlation to birth weight among these cases was Middle Cerebral Artery Pulpability Index.

Conclusion: 2D Doppler flow-velocity waveforms are of limited value in the prediction of poor neonatal outcome in IUGR except for MCAPI. 3D power Doppler was superior in the diagnosis and prediction of neonatal outcome.

Keywords: 3D power doppler; 2D colour doppler; IUGR

Introduction

Doppler ultrasound is a noninvasive technique commonly used to evaluate maternal and fetal hemodynamics. Continuous, adequate perfusion of the maternal and fetal sides of the placenta is necessary for normal fetal growth. FGR is associated with diminished flow and abnormal Doppler waveforms in both maternal and fetal vessels. Assessment of Doppler flow with appropriate intervention can reduce perinatal mortality in pregnancies complicated by FGR (Todros et al., 1999).

Although useful for monitoring pregnancies complicated by FGR, Doppler of any vessel is not useful as a screening tool for identifying these pregnancies (Berkley et al., 2012).

Arteries, particularly the umbilical artery, are the vessels most commonly insonated. Venous Doppler assessment has been studied less extensively, and is used for monitoring, rather than diagnosis, of FGR.

Umbilical artery Doppler velocimetry has become the clinical standard for identifying early-onset fetal growth restriction, i.e., at <34 weeks' gestation (ACOG, 1997, RCOG, 2011, Gagnon et al., 2003).

Doppler ultrasound determination of umbilical artery blood flow reveals impedance in the fetoplacental circulation, with absent or reversed end-diastolic blood flow diagnostic of severe fetal growth restriction. The use of umbilical artery Doppler ultrasound has led to reductions in perinatal death related to complications of placental insufficiency and iatrogenic preterm delivery (Maulik et al., 2010).

However, umbilical artery Doppler is not reliable for the identification of late onset growth restriction and associated complications. Unfortunately, late-onset fetal growth restriction is more prevalent than growth restriction of early onset, and most adverse outcomes attributable to late-onset growth restriction occur in fetuses with normal umbilical artery Doppler waveforms (Mayer & Joseph, 2014).

Middle cerebral artery Doppler waveform analysis is emerging as a promising diagnostic tool for the diagnosis of late third-trimester growth restriction among fetuses with normal umbilical artery Doppler waveforms, but further studies are required to support its widespread use (Chang et al., 1994).

Szilard (1974) developed a mechanical three-dimensional (3D) display system to see a fetus three dimensionally in 1974. (Brinkley et al., 1982(and colleagues developed a (3D) position sensor for a probe. They acquired many tomographic images of a stillbirth-baby under water, traced its outline manually and showed its wire-framed (3D) image.

A modern (3D) ultrasound system was first developed by Baba and colleagues in 1986 and a live fetus in utero was depicted three-dimensionally (Baba et al., 1986).

Doppler examinations of intraplacental blood circulation appear to be an efficient method for diagnosing and managing pregnancies complicated by fetal intrauterine growth restriction (IUGR), especially because the changes in maternal Doppler findings (i.e., uterine artery) and in fetal Doppler (i.e., umbilical artery) are secondary to the changes in the placental vascular tree (Abramowicz & Sheiner, 2007, 2008).

During the first trimester, all placental 3DPD indices in the case of IUGR were similar to those measured in normal pregnancies in three studies (Hafner et al., 2010, Odibo et al., 2011, Odeh et al., 2011). However, a positive correlation was confirmed between 3DPD indices and IUGR severity (Luria et al., 2012).

Patients and Methods:

It is a prospective observational study that performed between Jan 2021 and Feb 2022 including 100 pregnant women gathered from outpatient clinic of Elgalaa Teaching Maternity Hospital attending for routine antenatal care. All participating women signed an informed written consent.

All the patients were selected from the group of women with singleton pregnancies with intrauterine fetal growth restriction diagnosed by 2D ultrasound between 24 and 36 weeks of gestation based on the date of their last menstrual period according to Naegele's rule.

All included women after informed consent was taken, they subjected to:

• Full history, Abdominal examination to assess the fundal height and estimated fetal weight.

• Ultrasound assessment of fetal anatomy and fetal biometry including:

1. Biparietal (BPD), that was measured on a transverse axial section of the fetal head which includes the falx cerebri anterior and posterior, the cavum septum pellucidum anteriorly in the midline and the thalami. The BPD was measured from the outer edge of the nearer parital bone to the inner edge of the more distant parital bone.
2. Femur length (FL) was measured with the bone across the beam axis, the strong acoustic shadow behind the femoral shaft and the visualization of both cartilaginous ends indicates that the image plane is on the longest axis and is the optimal measurement plane. The calipers were placed along the diaphyseal shaft excluding the epiphysis.
3. Abdominal circumference (AC) was measured at the level of the liver and stomach including the left portal vein at the umbilical region.
4. Head circumference (HC) was measured along the maximal horizontal plane with the following reference points: occipital prominence at the back, above the ear at the side and above the eyebrows at the front.
5. Then the estimated fetal weight was calculated.

• IUGR cases was be obtained based on an ultrasound-estimated fetal weight below the 10th centile (P10) for gestational age according to the Hadlock 4 equation for fetal weight estimation (1) using biparietal diameter, head circumference, abdominal circumference and femur length (2).

• An expert perinatalogist measured the PI (pulsatility index) of the uterine arteries, umbilical artery middle cerebral artery and ductus venosus using 2D color Doppler ultrasound in the fetomaternity unit between 24 and 36 weeks of gestation.

• Then the same perinatologist assessed the placental vascularity by measuring flow index (FI), vascularization index (VI) and vascularization flow index (VFI) by using 3D power Doppler ultrasound at the same sitting.

• Follow up of the cases was done according to outcome after delivery based on (time of delivery, place of delivery, mode of delivery, fetal weight and gestational age at time of delivery, living or dead fetus at delivery time, whether the baby admitted to NICU or not and cause of admission if present.

Statistical analysis:

Data were analyzed using Statistical Program for Social Science (SPSS) version 20.0. Quantitative data were expressed as mean± standard deviation (SD). Qualitative data were expressed as frequency and percentage.

The following tests were done:

 Independent-samples t-test of significance was used when comparing between two means.

 Chi-square (X2) test of significance was used in order to compare proportions between two qualitative parameters.

 Pearson's correlation coefficient (r) test was used for correlating data.

 Probability (P-value)

– P-value <0.05 was considered significant.

– P-value <0.001 was considered as highly significant.

– P-value >0.05 was considered insignificant.

(SPSS 15.0.1 for windows; SPSS Inc, Chicago, IL, 2001)

Results

Demographic data	Mean ± SD
Maternal Age (years)	27.1±5.6
Number of primiparas	17
BMI	22.5 ±1.6
GA at examination (weeks)	27.1±3.2
EFW at examination	743.5±112.2
GA at delivery	35.2±2.1
Interval between examination and delivery (weeks)	10.5±5.4
Birth weight	1930.2±230.8
Respiratory complications	18
Development of sepsis	2
Neurological complications	2
Intrauterine fetal death	3
DM	14
Hypertension	17
Preeclampsia	24
Admission to NNICU	37

Table 1: Demographic data and risk factors distribution of the study group.

	Mean±SD
2D Color Doppler Parameters	
Umbilical Artery Pulsatility Index (UA PI)	0.79±0.23
Uterine Artery Pulsatility Index (UT A PI)	0.81±0.14
Middle Cerebral Artery Pulsatility Index (MCA PI)	1.52±0.31
Ductus Venosus (DV PV IV)	0.60±0.197
3D Power Doppler Parameters	
Vascularization Index (VI)	8.28±5.47
Flow Index (FI)	29.87±4.07
Vascularization Flow Index (VFI)	4.76±2.05

Table 2: Descriptive data of 2D Color Doppler and 3D Power Doppler parameters of the study group.

	GA at delivery (Term vs Preterm)	Birth weight (< 2kg vs ≥ 2kg)	Respiratory complications	Sepsis	IUFD	Neurological complications
UA PI	0.0817	0.411	0.87	0.165	0.34	0.57
UT A PI	0.945	0.256	0.73	0.567	0.673	0.87
MCA PI	0.681	**0.011**	0.893	0.753	0.916	0.46
DV PV IV	0.521	0.912	0.439	0.964	0.086	0.75
VI	0.872	**0.019**	**0.022**	0.2698	**0.029**	0.45
FI	0.845	**0.031**	**0.034**	0.934	**0.023**	0.844
VFI	0.654	**0.022**	**0.011**	0.468	**0.033**	0.723

Table 3: P-value of neonatal outcome according 2D Color Doppler and 3D Power Doppler parameters of the study group.

Discussion

The entity of fetal growth-restriction (FGR) remains challenging and complex in modern obstetrics. FGR pathophysiology is clear when FGR is caused by severe placental dysfunction, resulting in impaired transfer of oxygen and nutrients to the fetus that may lead to fetal hypoxia and early growth impairment. However, FGR pathophysiology is unclear in cases of less severe placental dysfunction that exhibit different patterns of deterioration and later clinical manifestation [19-22].

As fetal growth restricted pregnancies are caused by defective placentation. This may result in abnormalities of blood flow in umbilical vessels ranging from reduced to absent/reverse UA end-diastolic flow (24). Therefore, evaluation of placental function by umbilical artery Doppler (UAD) is a clinical standard to distinguish between small for gestational age and fetal growth restriction (FGR) (25). The umbilical artery pulsatility index (PI) and systolic to diastolic (S/D) ratio remain the most widely used assessments of fetal well-being [26].

Thanks to great technological progress over the last few years, it is now possible to quantitatively evaluate intraplacental blood circulation and placental volume by means of 3D Power Doppler and VOCAL technique. Intraplacental blood circulation is described by three vascular indices: vascularization index (VI), flow index (FI), and vascularization flow index (VFI). Vascularization index is the ratio of the number of color voxels to the total number of voxels in the sampled tissue, thus it represents the percentage of vascularized tissue. Flow index is the average color value of all color voxels and it describes the mean velocity of flow in the sampled tissue. The vascularization-flow index is the average color value of all color and gray voxels and describes both: the vascularization and the blood flow [27].

There is only a small number of studies evaluating placental vasculature with the use of 3D Power Doppler technique have been conducted. They differed from one another in respect of the applied methodologies of measuring the placental vasculature [28].

Some authors evaluated placental vasculature only in selected parts of the placenta introducing a technique called the 'vascular biopsy' [27].

However, not unlike in the study performed by de Paula et al [29], Pomorski et al applied a method allowing for measuring vascular indices for the entire placental volume [30]. This allowed them to gather full information on placental vasculature and should not be underestimated as, due to high regional variability of placental perfusion; there are significant differences in the values of vascularization index, flow index, and vascularization-flow index between different regions of the placenta [30].

In the current study, the aim was to investigate the role of 3D power Doppler ultrasonography in the assessment of FGR with various degrees of severity and onset, and compare the results with conventional analysis of 2D Doppler.

Motivation for this study rose from publications reporting a decrease in MCA PI in fetuses having normal umbilical artery 2D indices in late and mild FGR [10]. These data could not be explained by conventional 2D power Doppler. No information currently provides answers to questions such as: does the decrease in MCA PI in these cases result from an expression of different hemodynamic mechanisms other than placental vascular compromise? Or is the 2D Doppler assessment of limited sensitivity in detecting milder placental compromise? [31].

To address these questions, the current study was designed to analyze the role of 3D power Doppler ultrasonography and to compare the results with conventional analysis of 2D Doppler in FGR pregnancies for detecting placental compromise and how could the Doppler findings predict neonatal outcome.

In the current study, three-dimensional Doppler-flow indices were found to be significantly lower in pregnancies complicated by FGR, irrespective of gestational age, severity or onset of FGR.

These findings were also demonstrated by Luria et al., 2012 where they demonstrated that the indices examined by 3D Doppler flow were significantly lower in pregnancies complicated by FGR as compared with normal pregnancies as they worked on two groups, a FGR group and a normal control one. Significant differences in 2D indices between FGR and control pregnancies were observed only in parameters that are not routinely measured, such as the Cerebral to Umbilical ratio (C/U ratio), Ductus Venosus (DV), Inferior Vena cava (IVC), and Superior Vena Cava (SVC) and Mitral Valve (MIT) early diastolic filling (E) to atrial contraction (A) ratio (E/A) ratio. However, other routinely used indices measurements in clinical practice, such as the UA PI and MCA PI, were not different between the FGR and the control groups [4].

Also, these findings were also demonstrated by Guiot et al on 2008 were they compared placental vasculature in normal pregnancy to placental vasculature in IUGR pregnancy by means of 3D Power Doppler and VOCAL technique has been the study by [27].

The study was performed on a group of 45 pregnant women between 23 and 37 weeks of gestation gathered from obstetric outpatient attending for routine antenatal care, including 30 IUGR and 15 normal pregnancies. Placental vascular indices were calculated for five different regions of the placenta. The authors stated that VI, FI, and VFI values were significantly lower in the IUGR pregnancies [27].

Another study presented by Pomorski et al. placental vasculature in normal and IUGR pregnancies were compared, while all measures were derived from the entire placental volume by using 3D Power Doppler technique and this is the same technique used in ours. Based on our and their findings, they were able to show that the values of VI, FI, and VFI are statistically significantly lower in the IUGR group compared to those in the normal group. Their results clearly show that placentas of IUGR complicated pregnancies have fewer blood vessels (reduced VI) and decreased blood flow (reduced FI) as well [30].

Another study presented by Moran et al., on 2015 suggested that there may be a role for 3-Dimensional Power Doppler (3DPD) placental assessment of volume, vascularization and blood flow and computer analysis of placental calcification in the identification and management of Pre-eclampsia and Intrauterine growth restriction (PET/IUGR) pregnancy (32).

Also, our findings were noticed by Artunc Ulkumen et al., on 2014 and Abule´ et al., on 2016 where they also noticed decrease the placental volume and placental vascular indicies in growth restricted fetuses [33,34].

Doppler velocimetry parameters of growth-restricted fetuses associated with the most frequent complications of pregnancy, hypertension and diabetes, were correlated to the corresponding parameters of fetuses not presenting these complications by Piazze et al., on 2005 where they found that Values for Umbilical artery pulsitility index (UA PI), Umbilical artery to Middle cerebral artery pulsitilty index ratio (UA/MCA PI ratio), and mean Uterine artery resistance index (Ut RI) were significantly higher in women with hypertension than in those with no hypertension. The UA/MCA PI ratio of fetuses with growth restriction was significantly higher when the mother had diabetes [35].

While Kovo et al. on 2014 strengthened the hypothesis that FGR with or without preeclampsia are 2 distinct entities. Worse pregnancy outcome and more placental vascular lesions observed in FGR with preeclampsia versus FGR without preeclampsia suggest different pathophysiology in the development of these 2 disorders [36].

Our finding was also noticed by Luria et al., on 2012 where they found a Positive correlation was found between all the 3D indices and the severity of FGR, as expressed in centiles of birth weight. Correlation coefficients were r = –0.25 (P=0.03), r = –0.28 (P= 0.01) and r = –0.26 (P= 0.02) for VI, FI, and VFI, respectively. Umbilical artery PI showed negative correlation and MCA PI showed positive correlation to birth weight percentile (r = –0.23, P=0.15 and r = 0.23, P = 0.16, respectively) [4].

Previously, the Doppler fetal examination was applied stepwise starting with the umbilical artery and followed by the MCA [37]. This approach has been questioned as recent studies show that IUGR cases with normal flow in the umbilical artery might present signs of brain vasodilatation [38]. So, Hernandez-Andrade et al., on 2012 demonstrated that Fetal Brain vasodilatation is a risk factor of neurological complications, other fetal brain vessels as the anterior and posterior cerebral arteries are first affected in intrauterine growth restricted fetuses. Small for gestational age fetuses with normal flow in the umbilical artery but reduced pulsatility index in the anterior and/or middle cerebral arteries, have an increased risk of neurological complications. Evaluation of fetal brain blood perfusion with two- and three-dimensional power Doppler ultrasound might help in identifying earlier cases of brain vasodilatation [39].

On the other hand, Romero Gutiérrez et al., on 2009 showed that The Doppler fluxometry of the umbilical artery have better predictive value than the middle cerebral artery for predicting bad perinatal outcome. And they recommended the assessment of umbilical artery as first choice in order to determine the well-being in fetuses with intrauterine growth restriction [40].

Our findings regarding development of respiratory and neurological complications and composite outcome were also noticed by Piazze et al on 2005 & Sovio et al on 2015 where they found that no 2D Color Doppler velocimetry parameter predicted the presence of neonatal respiratory distress syndrome, intraventricular hemorrhage, and retinopathy of prematurity [22,40].

While Leppänen et al., on 2010 noticed that Pathological antenatal Doppler flow (UA PI and MCA PI) was associated with adverse cognitive outcome but not with motor development at 2 years of corrected age. That study supported the hypothesis that inadequate circulation impairs the growth potential of the developing brain, which leads to reduced cerebral volume. This reduced cerebral volume is associated with poorer neurodevelopment in Very Low Birth Weight (VLBW) infants at 2 years of age [41].

In spite of that Unterscheider et al., on 2014 noticed that Perinatal deaths occurred more commonly among infants with severe growth restriction and associated abnormal umbilical artery Doppler values which highlights the fact that fetuses with EFW <3rd centile and/or abnormal UA Doppler are a greater risk of poor perinatal outcome [20].

Conclusion and recommendation:

Two-dimensional (2D) Doppler flow-velocity waveforms are of limited value in the evaluation of placental compromise and prediction of poor neonatal outcome in fetal growth restriction (FGR) except for MCAPI that was able to predict poor neonatal outcome. Three-dimensional (3D) power Doppler ultrasonography provides new insights into placental pathophysiology, enabling the investigation of placental vascularization and blood flow. Abnormal low 3D Power Doppler vascular indices (VI, FI, VFI) as well as low placental volumes were present in IUGR cases and were significant in prediction of poor neonatal outcome.

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