Original Article

The Correlation of Myocardial Performance Index, Doppler Ultrasound Indices of Fetal Blood Vessels with Perinatal Mortality and Early Neonatal Morbidity in Small-for-Gestational Age Fetuses

Wirada Hansahiranwadee MD[1], Somsri Pitukkijronnakorn MD[1], Panyu Panburana MD[1], Sakda Arj-Ong Vallibhakara MD PhD[2]

[1] Division of Maternal Fetal Medicine, Department of Obstetrics and Gynaecology, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

[2] Section for Clinical Epidemiology and Biostatistics, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok, Thailand

Objective: To assess the correlation of Myocardial Performance Index (MPI), Doppler ultrasound indices of fetal blood vessels with perinatal mortality and early neonatal morbidity in small-for-gestational age (SGA) fetuses.

Materials and Methods: The cross-sectional study of singleton pregnancies with small for gestational age fetuses with perinatal mortality and early neonatal morbidity was conducted from March 1st to November 30th, 2014. Forty-nine cases of singleton pregnancies with SGA fetuses were enrolled by excluding chromosome abnormality, major organ anomaly or intrauterine infection. MPI, Doppler ultrasonography of umbilical artery, middle cerebral artery, aortic isthmus, ductus venosus and umbilical vein were performed within 48 hours before delivery. The Z-scores were calculated for Doppler indices. The delivery method and the indication of delivery, data regarding perinatal mortality, bronchopulmonary dysplasia (BPD), interventricular hemorrhage (IVH) and necrotizing enterocolitis (NEC) were recorded. The correlation and multiple logistic regression analyses was used to find the significant factors of perinatal mortality and early neonatal morbidity in SGA fetuses.

Results: Total 38 pregnant women and newborns were analyzed. No perinatal mortality was detected but found some of early neonatal morbidity. 6 newborns needed to admit in NICU (15.8%), 3 of which had BPD (7.9%). Neither IVH nor NEC was detected. This study did not demonstrate the correlation between MPI, all Doppler parameters after dichotomous branching and early neonatal morbidity, with individual adjusted R^2 = -0.027 (p-value= 0.951) for UA S/D ratio ≥ 95th percentile, -0.005 (p-value= 0.819) for UA PI ≥ 95th percentile, 0.091 (p-value=0.368) for cerebroplacental ratio ≤ 1.08, 0.088 (p-value= 0.996) for aortic isthmus flow index ≤ 5th percentile, 0.160 (p-value= 0.058) for MPI ≥ 95th percentile. Only, the gestational age (GA <38 wks) was the only significant factor associated with early neonatal morbidity with adjusted R^2 of 0.620 (p-value <0.05, Odd ratios 7.0, 95%CI: 0.61-79.87).

Conclusion: There was no significant correlation between perinatal mortality and early neonatal morbidity in small-for-gestational age (SGA) fetuses with Doppler ultrasound parameters in terms of MPI, UA S/D ratio, UA pulsatility index, MCA pulsatility index, DV waveform, aortic isthmus flow index and UV waveform in SGA fetuses. Gestation age was the most significant associated factor with early neonatal morbidity in SGA fetuses. However, no conclusion could be drawn regarding the correlation of perinatal mortality with MPI and Doppler ultrasound parameters due the lack of fetal and neonatal death.

Keywords: Myocardial performance index, MPI, Doppler ultrasound, Venous Doppler, Perinatal mortality, Early neonatal morbidity, SGA

J Med Assoc Thai 2018; 101 (6): 765-71
Website: http://www.jmatonline.com

Fetal growth restriction (FGR) is one of the common problems in obstetrics. This condition leads to perinatal morbidity and mortality in neonatal period[1]. Impaired cognitive function in childhood and increased cardiovascular risk in adult were reported as the long term sequelae of fetal growth restriction fetus[2].

Small-for-gestational-age (SGA) fetus is diagnosed by ultrasonography to estimate the fetal weight, which is less than the 10^{th} percentile of gestation age in customized growth chart [3]. Many etiologies can cause SGA fetuses such as constitutionally small fetus,

Correspondence to:
Vallibhakara SA. Section for Clinical Epidemiology and Biostatistics, Faculty of Medicine, Ramathibodi Hospital, Mahidol University. 270 Rama VI Road, Ratchathewi, Bangkok 10400, Thailand.
Phone: +66-2-2011269, Fax: +66-2-2011284
Email: dr.sakda@gmail.com

How to cite this article: Hansahiranwadee W, Pitukkijronnakorn S, Panburana P, Vallibhakara SA. The correlation of myocardial performance index, Doppler ultrasound indices of fetal blood vessels with perinatal mortality and early neonatal morbidity in small-for-gestational age fetuses. J Med Assoc Thai 2018;101:765-71.

uteroplacental insufficiency, congenital infection, chromosome abnormality and congenital anomaly[2].

The universal recommendations of fetal surveillance in FGR are ultrasonography for fetal growth evaluation, amount of amniotic fluid or biophysical profile[2]. The role of Doppler ultrasonography in FGR is umbilical artery (UA) Doppler velocimetry used in conjunction with standard fetal surveillance to improve perinatal outcome. But middle cerebral artery (MCA) velocimetry does not provide the correlation with perinatal outcome[3]. Beside either UA or MCA alone, the cerebroplacental ratio (CPR) is used to detect "brain sparing effect", and used to predict adverse outcomes in preterm FGR fetuses[4]. Regarding Doppler assessment in ductus venosus (DV) investigation, recent studies showed the correlation with perinatal death especially in early onset fetal growth restriction. But the aortic isthmus flow (AoI) investigation in early onset fetal growth restriction in combination with DV had no benefit to predict the perinatal death. While the myocardial performance index (MPI) may stratify the probability of death [5].

The hypothesis of this study was whether the MPI, arterial and venous Doppler ultrasound parameters in SGA fetus had the correlation with perinatal morbidity and mortality or not. The result may be useful in clinical practice of Doppler ultrasonography essential for SGA fetus. The population of this study included SGA fetus from constitutionally small fetus and fetal growth restriction from uteroplacental insufficiency.

The primary objective of this study was to assess the correlation between MPI, aortic isthmus flow index (IFI), Doppler parameters of fetal blood vessel (UA, MCA, DV, umbilical vein) with perinatal mortality in small-for-gestational age (SGA) fetus. Secondary objective was to assess the correlation of the MPI and these Doppler parameters with early neonatal morbidity in SGA fetus.

Materials and Methods

This prospective study was conducted during March to November 2014 and approved by the Committee on Human Rights Related to Research Involving Human Subjects of Faculty of Medicine, Ramathibodi Hospital, Mahidol University (MURA2014/13-ID01-57-13). Study population was pregnant women with small-for-gestational-age fetus who delivered at Ramathibodi Hospital, Mahidol University. Written informed consents were obtained. Gestational age was confirmed by first or second trimester ultrasound scanning. Small-for-gestational age fetus was defined as an estimated fetal weight below 10th percentile of gestational age according to customized growth curve after excluding SGA from chromosomal abnormality, major congenital anomaly and congenital infection following our standard protocol for SGA investigation. Normal newborn appearance from physical examination by neonatologist presumed that fetus did not have chromosome abnormality, congenital infection and congenital anomaly.

The ultrasound assessment was performed by two maternal fetal medicine specialists for standardization, using two-dimension transabdominal 2-5 MHz curvilinear transducer, Voluson E8 (GE Medical Systems, Zipf Austria) by comparing the MPI and Doppler parameters with 30 cases of normal pregnancy. Ultrasonography was performed to estimate fetal weight and amniotic fluid volume before Doppler assessment.

Doppler parameters of UA, MCA, DV, IFI, MPI and umbilical vein (UV) were obtained in the absence of fetal movement. Doppler of umbilical artery was performed at free loops of umbilical cord [6] and the data were collected as systolic/diastolic (S/D) ratio and pulsatility index (PI) (Figure 1). Middle cerebral artery Doppler assessment was performed in transverse view of fetal skull at the level of Circle of Willis. Sample volume was placed at 2 mm after branching from internal carotid artery[6], measured as MCA PI (Figure 2). CPR was calculated by MCA PI divided by UA PI[7]. DV Doppler assessment was obtained from transverse section from fetal abdomen[6] and collected as PI and present or absent of atrial flow (Figure 3). Aortic isthmus flow Doppler was measured from midsagittal view of aortic arch or alternatively a three vessel trachea view with comparable result[8]. Sample volume was placed few millimeters beyond the origin of left subclavian artery in midsagittal view (Figure 4) or placed just before the confluence of aorta with the ductus arteriosus in the V configuration[8]. The data was collected as aortic isthmus flow index (IFI) which was systolic velocity integrals minus diastolic velocity integrals and divided by systolic velocity integral (S-D/S)[9]. Doppler of UV was also performed at free loops of umbilical cord[6] (Figure 5) and data was collected as present or absent pulsation flow. MPI was obtained from apical or basal four chamber view in a cross section of fetal thorax by using high frequency preset cardiac mode. Sample volume was placed just beyond the mitral valve in medial wall and below the aortic valve. The aortic and mitral valve clicks were used for isovolumetrics contraction time (ICT) and

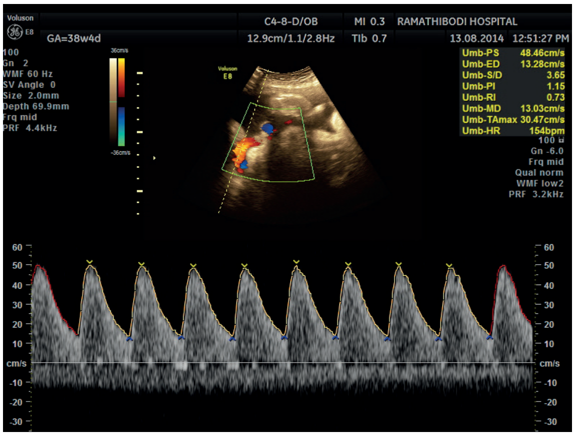

Figure 1. Measurement of umbilical artery Doppler at free loop.

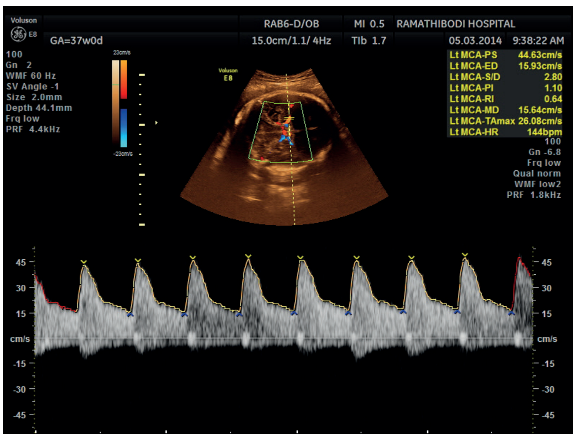

Figure 2. Measurement of middle cerebral artery Doppler.

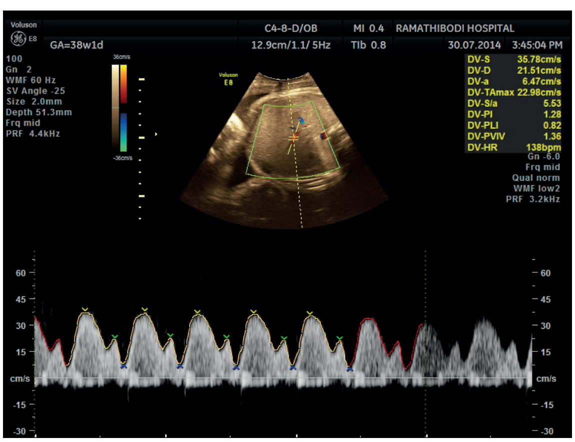

Figure 3. Measurement of ductus venosus Doppler.

isovolumetrics relaxation time (IRT) and ejection time (ET) calculation[10] (Figure 6). ICT was the time from closure of mitral valve to opening of aortic valve. IRT was the time from closure of aortic valve to opening of mitral valve. Ejection time was the time from opening to closure of aortic valve. The MPI was calculated as (ICT+IRT)/ET. All Doppler parameters were converted to Z-scores according to normal reference in previously published data[7, 11-15]. Previous study found the risk of perinatal death according to cardiovascular Doppler indices performed within 72 hours. All of the Doppler ultrasonography were performed within 48 hours before delivery[16].

The mode and indication of delivery, gestational age, birth weight, Apgar scores and Ballard score were recorded. The mortality and morbidity data of pregnancy, perinatal mortality and early neonatal morbidity; NICU admission, intraventricular hemorrhage, necrotizing enterocolitis, bronchopulmonary dysplasia were also recorded and analyzed.

The data analysis was performed by Stata Statistical Software: Release 13. (College Station, TX: StataCorp LP). Means of Z scores of all Doppler parameters were compared between SGA with early neonatal morbidity group and SGA without early neonatal morbidity group. Then Z scores of all parameters were categorized into dichotomous group as normal or abnormal values. The UA S/D ratio, UA PI and MPI equal or above the 95th percentile were considered as abnormal and those below 95th percentile were considered as normal[6]. CPR above 1.08 was normal and equal or below 1.08 was abnormal[7]. Ductus venosus with positive a wave considered as normal. An absent or reversed a wave considered as abnormal[6]. IFI below the 5th percentile and equal or above 5th percentile were considered as normal and abnormal respectively[14]. UV Doppler with pulsation was considered as abnormal while that without pulsation was normal[6]. Gestational age at delivery was collected and used as one of parameters. Perinatal mortality was defined as stillbirth or death within 28 days of life. Early neonatal morbidity included NICU admission, intraventricular hemorrhage, necrotizing enterocolitis and bronchopulmonary dysplasia. Multiple logistic regression was used to find the association between these parameters and early neonatal morbidity. $P<0.05$ was considered statistically significance.

Results

A total of 49 singleton pregnancies with small for gestational age were enrolled into this study. Eleven

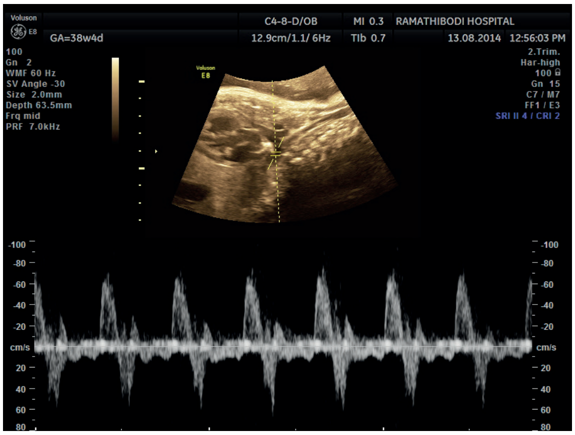

Figure 4. Measurement of aortic isthmus Doppler.

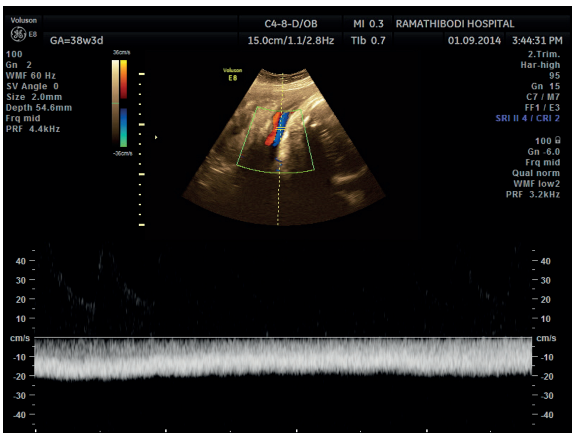

Figure 5. Measurement of umbilical venous Doppler.

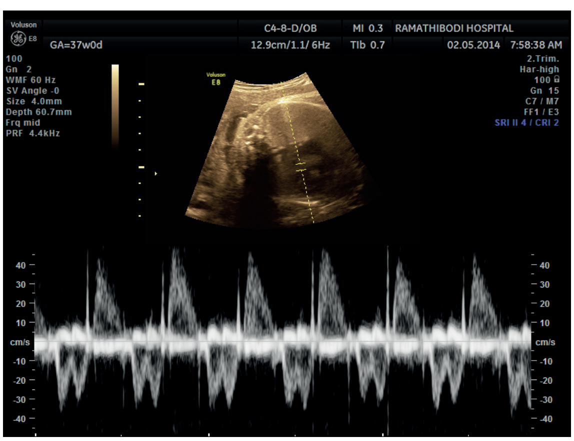

Figure 6. Measurement of myocardial performance index.

cases (22.4%) were excluded because the birth weights were appropriate for gestational age after re-evaluated and validated from consensus. Therefore, total 38 cases were analyzed. Maternal characteristics, delivery data and perinatal outcomes of the groups of SGA fetuses were shown in Table 1. The median of maternal age, numbers of nulliparity and maternal comorbidity were not significantly different between both groups (*p*-value = 0.45, p-value=0.47 and p-value 0.80, respectively). No smoker was found in this study population. The median of gestational age at delivery (38 (35-40) weeks vs. 30 (29-38) weeks) and birth weight (2,405 (1,520-2840) gram vs. 1,030 (790-2,325) gram) in SGA with early neonatal morbidity group were significantly lower than SGA without early neonatal morbidity (both of p-values < 0.001). However, percentage of severe small-for-gestational fetus (birthweight below 3rd percentile) and percentage of low Apgar score were not significantly different between these two groups. No perinatal mortality was found in this study. Total early neonatal morbidity was 15.8% (6/38). All 6 newborns were needed to admit in NICU. Three of them had bronchopulmonary dysplasia (7.9 %). No case of intraventricular hemorrhage or necrotizing enterocolitis was found.

The mean Z scores of all Doppler parameters were not significantly different between the group of SGA newborns with early neonatal morbidity and the group of SGA newborn without early neonatal morbidity (see Table 2), except the Aortic isthmus flow index (IFI) which was significantly lower in SGA newborn with early neonatal morbidity group (Mean ± SD of IFI; -3.04 (±0.97) vs. -5.01 (±0.92), *p*-value <0.001).

When authors focusing on SGA with early neonatal morbidity group. All Doppler parameters demonstrated no significant correlation with early neonatal morbidity in multivariate analysis after dichotomous branching as previously described (Table 3). But gestational age showed significant correlation with early neonatal morbidity (adjusted $R^2 = 0.620$, *p*-value <0.001). This confirmed the result of previous study [5,17].

Discussion

This study evaluated myocardial performance index (MPI) and Doppler parameters of UA, MCA, CPR, IFI, DV and UV in prediction of perinatal mortality, and early neonatal morbidity of the SGA newborns which had the pathology from uteroplacental insufficiency. The pathophysiology of SGA began with increased vascular resistance of placental arteries which was able to be observed by increasing in S/D

Table .1 Maternal characteristics and perinatal outcome data

Characteristics	SGA without early neonatal morbidity (n = 32)	SGA with early neonatal morbidity (n = 6)	***p*-value**
Maternal characteristics			
Maternal age (year)	30 (19 to 38)	31 (28 to 39)	0.45
Nulliparity	68.8 % (22)	100% (6)	0.47
Preeclampsia	18.8% (6)	33.3% (2)	0.80
SLE**	3.1% (1)	0	1.00
Smoking	0	0	-
Delivery data			
GA at delivery (week)	38 (35 to 40)	30 (29 to 38)	<0.001*
Birth weight <3rd percentile	46.9% (15)	83.3% (5)	0.23
Birth weight (g)	2405 (1,520 to 2840)	1030 (790 to 2,325)	<0.001*
Apgar score at 5 min. <7	0	16.7% (1)	0.34
Perinatal outcome			
NICU*** admission	-	100% (6)	-
Bronchopulmonary dysplasia	-	50% (3)	-
Intraventricular hemorrhage	-	0	-
Necrotizing enterocolitis	-	0	-

Data are present as median (range) or proportion (%, n)

* *p*-value <0.05 was assigned as statistically significance.

** SLE = systemic lupus erythromatosus, *** NICU = neonatal intensive care unit

Table 2. Z-scores of myocardial performance index and Doppler parameters of SGA with and without early neonatal morbidity

Doppler indices	SGA without morbidity (n = 32) mean (± SD)	SGA with morbidity (n = 6) mean (± SD)	*p*-value
UA S/D ratio	0.98 (±2.10)	1.61 (±1.14)	0.30
UA PI	0.70 (±1.70)	1.98 (±1.41)	0.09
MCA PI	0.43 (±1.45)	1.25 (±4.30)	0.67
CPR	-0.82 (±1.18)	-0.81 (±2.23)	0.99
IFI	-3.04 (±0.97)	-5.01 (±0.92)	<0.001*
MPI	4.34 (±2.37)	2.48 (±1.84)	0.06
DV PI	- 0.10 (±2.97)	-0.04 (±2.50)	0.96
Pulsatile of UV	0	0	-

Abbreviations: UA = Umbilical artery, PI = Pulsatility index, IFI = Isthmus Flow Index, MCA = Middle cerebral artery, CPR = Cerebroplacental ratio, MPI = Myocardial performance index, DV = Ductus venosus, UV=Umbilical vein.

ratio and PI in umbilical artery[2], which was the first abnormal parameter. Then fetuses had adaptation by centralization of the blood to vital organs; heart, brain and adrenal gland. This "brain sparing effect" characterized by MCA vascular resistance which was lower than UA vascular resistance as shown in decreased cerebroplacental ratio[7]. If the pathology progressed, the cardiac function would decrease. Then the venous Doppler parameters were lastly affected by the effect of increased afterload pressure[6]. Absent and reversed a waves of ductus venosus (DV) as well as pulsation of umbilical vein (UV) were the abnormal forms of venous Doppler. So the abnormalities of precordial veins were the most predictive parameters for perinatal mortality. Many previous studies evaluated the fetal cardiovascular Doppler parameters to predict the intrauterine growth retardation perinatal morbidity and mortality[17-19].

Aortic isthmus flow index (IFI) was used to detect the difference between resistance of umbilical artery, which received the blood from right ventricle and resistance of middle cerebral artery which received the blood from left ventricle[9]. In uteroplacental insufficiency which the umbilical arterial resistance increased, the aortic isthmus flow showed negative wave. Previous study showed the correlation between negative IFI and postnatal neurological morbidity since

Table 3. Correlation between variables estimated by multivariate analysis with early neonatal morbidity in SGA fetuses after dichotomization of Doppler variables

Variables	Adjusted R^2	p-value
UA S/D ratio ≥95th	-0.027	0.91
UA PI ≥95th	-0.005	0.82
CPR ≤1.08	0.091	0.37
IFI ≤5th	0.088	0.99
MPI ≥95th	0.160	0.06
GA <38 weeks	0.620	<0.001

Abbreviations: UA = Umbilical artery, PI = Pulsatility index, IFI = Isthmus Flow Index, MCA = Middle cerebral artery, CPR = Cerebroplacental ratio, MPI = Myocardial performance index, DV = Ductus venosus, UV = Umbilical vein, GA = Gestational age it was a marker of brain centralization[17,18]. In this study, when comparing between SGA with and without early neonatal morbidity, all Doppler parameters were not statistically different except the IFI (p-value < 0.001). The UA S/D ratio and pulsatility index were non-significantly increased in morbidity group. MCA PI and CPR, which represented the brain sparing effect, were not significantly different. The MPIs were also indifferent between both groups. But MPIs in both groups were still higher than the normal value thus confirmed previous study[19,20]. This study showed that the mean of IFI in SGA without early neonatal morbidity was significant higher than in SGA with early neonatal morbidity. The Z scores of IFI in both groups of study were lower when compared to the normal reference[14,20]. Flow across isthmic part of aorta is linked between two arterial systems. Thus lower than normal value of IFI reflected decreased forward flow to umbilicus and lower part of the body leads to fetal hypoxemia. The hypoxemia causes vasoconstriction of mesenteric, renal and skeletal arteries[9]. This pathophysiology may explain the difference of IFI between groups. The abnormal of DV and UV were not detected in this population.

Even though the IFI is significantly different between both groups, after setting IFI ≤ 5th as the standard cut off to abnormality according to Raskamp[14] and Cruz-Lemini[20], there was no correlation to early neonatal morbidity. Our result confirmed previous studies[5,17] showing that the gestational age was the only factor that was able to predict early neonatal morbidity. The finding of this study showed that the gestational age (GA < 38 weeks) was 62 percent related with early neonatal morbidity (adjusted $R^2 = 0.620$, p-value <0.05, Odd ratios 7.0, 95%CI: 0.61-79.87) that consist of NICU admission and bronchopulmonary dysplasia in SGA newborn independently of the Doppler parameter. In early onset fetal growth restriction that needed to be delivered remotely from term had the neonatal morbidity of preterm such as NICU admission, respiratory distress syndrome, necrotizing enterocolitis and intraventricular hemorrhage from prematurity. So after analyzed by univariate analysis the IFI did not has the correlation with early neonatal morbidity. The pathology in early onset FGR had more severity leading to more neonatal morbidity. In previous study, MPI, IFI and DV in early onset fetal growth restriction had association with perinatal mortality [5,17,19]. But in this study we were not able to find the correlation of MPI, all arterial and venous Doppler parameters with early neonatal morbidity. The limitation of the study was no perinatal mortality, we were not able to conclude the correlation between perinatal mortality of SGA fetus and MPI and all Doppler parameters. Also we were not able to find the correlation between early neonatal morbidity of SGA fetus and these Doppler parameters. The larger sample size may establish the significant association between the Doppler parameters and MPI with early neonatal morbidity and perinatal mortality. Therefore, this approach can be integrated into the standard protocol. The combination of Doppler parameter for the prediction of perinatal morbidity and mortality should be the further step of study.

Conclusion

There was no correlation between early neonatal morbidity and Doppler ultrasound parameters in terms of MPI, UA S/D ratio, UA pulsatility index, MCA pulsatility index, DV waveform, aortic isthmus flow index and UV waveform in SGA fetuses. However, no conclusion could be drawn regarding the correlation of perinatal mortality with MPI and Doppler ultrasound parameters due no fetal and neonatal death detection.

What is already known on this topic?

Umbilical artery Doppler was only one parameter to use in conjunction with other fetal surveillance to improve perinatal outcome in SGA fetus. Myocardial performance index in SGA fetuses were higher than AGA fetus in comparable gestational age

What this study adds?

This study confirmed previous study result that GA is one of the most powerful predictor for early neonatal morbidity of SGA fetus, no other Doppler parameters unless umbilical artery Doppler correlate with neonatal morbidity.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Cunningham FG, Leveno KL, Bloom SL, Hauth JC, Rouse DJ. Fetal growth disorders In: Cunningham FG, Leveno KL, Bloom SL, Hauth JC, Rouse DJ, editors. Williams obstetrics. 23rd ed. NewYork: McGraw-Hill; 2010. p. 872-90.
2. Resnik R, Creasy RK. Intrauterine growth restriction. In: Creasy RK, Resnik R, Iams JD, Lockwood CJ, Moore TR, Greene MF, editors. Creasy and Resnik's maternal-fetal medicine:

principles and practice. 7th ed. Philadelphia, PA: Saunders Elsevier; 2013. p. 743-55.
3. American College of Obstetricians and Gynecologists. ACOG Practice bulletin no. 134: fetal growth restriction. Obstet Gynecol 2013;121:1122-33.
4. Bahado-Singh RO, Kovanci E, Jeffres A, Oz U, Deren O, Copel J, et al. The Doppler cerebroplacental ratio and perinatal outcome in intrauterine growth restriction. Am J Obstet Gynecol 1999;180:750-6.
5. Hernandez-Andrade E, Crispi F, Benavides-Serralde JA, Plasencia W, Diesel HF, Eixarch E, et al. Contribution of the myocardial performance index and aortic isthmus blood flow index to predicting mortality in preterm growth-restricted fetuses. Ultrasound Obstet Gynecol 2009;34:430-6.
6. Bahtiyar MO, Copel JA. Doppler ultrasound: Select fetal and maternal applications. In: Creasy RK, Resnik R, Iams JD, Lockwood CJ, Moore TR, Greene MF, editors. Creasy and Resnik's maternal-fetal medicine: principles and practice. 7th ed. Philadelphia, PA: Saunders Elsevier; 2013. p. 211-7.
7. Baschat AA, Gembruch U. The cerebroplacental Doppler ratio revisited. Ultrasound Obstet Gynecol 2003;21:124-7.
8. Del Rio M, Martinez JM, Figueras F, Bennasar M, Palacio M, Gomez O, et al. Doppler assessment of fetal aortic isthmus blood flow in two different sonographic planes during the second half of gestation. Ultrasound Obstet Gynecol 2005;26:170-4.
9. Fouron JC. The unrecognized physiological and clinical significance of the fetal aortic isthmus. Ultrasound Obstet Gynecol 2003;22:441-7.
10. Hernandez-Andrade E, Lopez-Tenorio J, Figueroa-Diesel H, Sanin-Blair J, Carreras E, Cabero L, et al. A modified myocardial performance (Tei) index based on the use of valve clicks improves reproducibility of fetal left cardiac function assessment. Ultrasound Obstet Gynecol 2005;26:227-32.
11. Kofinas AD, Espeland MA, Penry M, Swain M, Hatjis CG. Uteroplacental Doppler flow velocity waveform indices in normal pregnancy: a statistical exercise and the development of appropriate reference values. Am J Perinatol 1992;9:94-101.
12. Kurmanavicius J, Florio I, Wisser J, Hebisch G, Zimmermann R, Muller R, et al. Reference resistance indices of the umbilical, fetal middle cerebral and uterine arteries at 24-42 weeks of gestation. Ultrasound Obstet Gynecol 1997;10:112-20.
13. Baschat AA. Relationship between placental blood flow resistance and precordial venous Doppler indices. Ultrasound Obstet Gynecol 2003;22:561-6.
14. Ruskamp J, Fouron JC, Gosselin J, Raboisson MJ, Infante-Rivard C, Proulx F. Reference values for an index of fetal aortic isthmus blood flow during the second half of pregnancy. Ultrasound Obstet Gynecol 2003;21:441-4.
15. Hernandez-Andrade E, Figueroa-Diesel H, Kottman C, Illanes S, Arraztoa J, Acosta-Rojas R, et al. Gestational-age-adjusted reference values for the modified myocardial performance index for evaluation of fetal left cardiac function. Ultrasound Obstet Gynecol 2007;29:321-5.
16. Cruz-Lemini M, Crispi F, Van Mieghem T, Pedraza D, Cruz-Martinez R, Acosta-Rojas R, et al. Risk of perinatal death in early-onset intrauterine growth restriction according to gestational age and cardiovascular Doppler indices: a multicenter study. Fetal Diagn Ther 2012;32:116-22.
17. Baschat AA, Gembruch U, Reiss I, Gortner L, Weiner CP, Harman CR. Relationship between arterial and venous Doppler and perinatal outcome in fetal growth restriction. Ultrasound Obstet Gynecol 2000;16:407-13.
18. Cruz-Martinez R, Figueras F, Tenorio V, Valsky DV, Arranz A, Crispi F, Hernandez-Andrade E, et al. Combination of the aortic isthmus with ductus venosus improves the prediction of neurological damage in early-onset intrauterine growth restricted fetuses. Ultrasound Obstet Gynecol 2010;36 Suppl 1:40.
19. Cruz-Martinez R, Figueras F, Hernandez-Andrade E, Oros D, Gratacos E. Changes in myocardial performance index and aortic isthmus and ductus venosus Doppler in term, small-for-gestational age fetuses with normal umbilical artery pulsatility index. Ultrasound Obstet Gynecol 2011;38:400-5.
20. Comas M, Crispi F, Cruz-Martinez R, Figueras F, Gratacos E. Tissue Doppler echocardiographic markers of cardiac dysfunction in small-for-gestational age fetuses. Am J Obstet Gynecol 2011;205:57-6.