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Influence of pre-existing maternal diabetes mellitus on fetal myocardial performance index and systolic-to-diastolic duration ratio: a prospective cohort study

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Abstract

Objective: To evaluate the influence of pre-existing maternal diabetes mellitus on fetal myocardial performance index and systolic-to-diastolic duration ratio. Methods: Prospective cohort study included 179 pregnant women between 20 and 36w6d, divided into 3 groups: Group 1 (120, normal), Group 2 (31, type 1 diabetes mellitus), and Group 3 (28, type 2 diabetes mellitus). Systolic-to-diastolic duration ratio was calculated as the sum of isovolumic contraction time and ejection time divided by the sum of isovolumic relaxation time and ventricular filling time. Spectral Doppler was used to assess left ventricle systolic-to-diastolic duration ratio. Tissue Doppler was used to assess right ventricular filling time. Using spectral Doppler, left ventricle myocardial performance index was calculated as the sum of isovolumic contraction time and isovolumic relaxation time divided by ejection time. Results: Pre-existing maternal diabetes mellitus had a significant influence on fasting glucose levels (p < 0.001), left ventricle isovolumic contraction time (p < 0.001), left ventricle ejection time (p = 0.025), and left ventricle myocardial performance index (p < 0.001). Group 2 had higher left ventricle isovolumic contraction time (0.036 vs. 0.031 sec, p = 0.001) and left ventricle myocardial performance index (0.487 vs. 0.453, p = 0.003) compared with Group 1. Group 3 showed higher left ventricle myocardial performance index (0.492 vs. 0.449, p = 0.006) and lower left ventricle ejection time (0.161 vs. 0.169 sec, p = 0.038) than Group 1. Left ventricle systolic-to-diastolic duration (p = 0.704), right ventricle systolic-to-diastolic duration ratio' (p = 0.757), left ventricle isovolumic contraction time (p = 0.163), left ventricle ejection time (p = 0.093), and left ventricle myocardial performance index (p = 0.087) were not useful parameters in predicting composite neonatal outcomes. Conclusion: Pre-existing maternal diabetes mellitus had significant influence on fetal left ventricle myocardial performance index, but no effect on systolic-to-diastolic duration ratio. Systolic-to-diastolic duration ratio was not useful in predicting adverse perinatal outcomes.

Introduction

Prenatal assessment of cardiac function is critical, especially in fetuses at risk for heart failure. In this setting, a variety of two- and three-dimensional and Doppler ultrasound parameters can be combined to assess fetal cardiac function. However, there is no consensus on the selection of the most appropriate parameters to be used to perform a functional assessment of the fetal heart.^{1–5} Fetal heart disease (anatomical or functional cardiovascular defects, arrhythmias) and no heart disease (maternal diabetes, placental insufficiency) can lead to fetal heart failure.⁶

Based on the haemodynamic condition that causes heart failure, several parameters have been proposed to assess fetal cardiac function. Estimation of cardiac output is important in conditions such as arterial-venous malformations, vascular masses, and twin-to-twin transfusion syndrome, among others.^{7,8} In these situations, and in those with increased preload, there is usually cardiomegaly, which can be assessed by the cardio-thoracic index.⁹ Either in conditions of increased preload and high afterload, venous Doppler and myocardial performance index (or Tei index) are altered.¹⁰

In addition, myocardial performance index has been shown to be an early marker of myocardial dysfunction (subclinical phase of cardiac dysfunction) and to have high sensitivity and specificity for predicting perinatal morbidity and mortality in diabetes mellitus, fetal growth restriction, and twin-to-twin transfusion syndrome (recipient fetus). The myocardial performance index is a Doppler ultrasound parameter that includes measurements of cardiac cycle intervals such as isovolumetric contraction, isovolumetric relaxation, and ejection times, and is capable of analysing both systolic and diastolic ventricular function.^{11,12} However, the calculation of the myocardial performance index does not include all times of the cardiac cycle and overlooks ventricular filling time. The most recent update on fetal echocardiography from the American Society of Echocardiography describes diastolic filling time corrected for heart rate (total duration of the inflow Doppler spectral trace divided by heart rate) as a parameter that shows progressive shortening in twin-to-twin transfusion syndrome as fetal diastolic function deteriorates.⁵

The systolic-to-diastolic duration ratio is an index that differs from the myocardial performance index in that it includes ventricular filling time. This index is calculated as the sum of the isovolumetric ejection time, isovolumetric contraction time, and isovolumetric relaxation time divided by the isovolumetric filling time.^{13,14} While indices that include ventricular filling time may be more sensitive in detecting cardiac dysfunction, another index known as the systolic-to-diastolic duration ratio has been developed. The systolic-to-diastolic duration ratio consists of the relationship between the ventricular systolic and diastolic duration using the following formula: isovolumic contraction time + ejection time/isovolumic relaxation time + filling time. Reference values for fetal systolic-to-diastolic duration ratio using both spectral and tissue Doppler have been established from 20 to 36 weeks of gestation as a useful parameter for assessing systolic and diastolic fetal heart.15

In fact, the Cardiovascular Profile Score, known as the 10-point score, is becoming a "heart failure score" because it includes ultrasound markers of fetal cardiovascular distress. This score includes the ventricular filling time waveform pattern and has been validated to correlate with myocardial performance index in hydrops, fetal growth restriction, fetal cardiomyopathy, and other conditions.^{16,17} Therefore, in this study, we evaluated left ventricle myocardial performance index and ventricular systolic-to-dia-stolic duration ratio in fetuses from pre-existing maternal diabetes mellitus with the aim of demonstrating the applicability of the latter parameter in the assessment of cardiac function.

Methods

We carried out a prospective cohort study at the Service of Gynecology and Obstetrics, University of Uberaba, and Department of Obstetrics, Paulista School of Medicine – Federal University of São Paulo. This study was approved by the Local Ethics Committee (CAE: 87111116.4.0000.5505). Mothers signed an informed consent and were divided into 3 groups: Group 1, normal; Group 2, type 1 diabetes mellitus; and Group 3, type 2 diabetes mellitus.

We included mothers with singleton pregnancy, gestational age based on the last menstrual period and confirmed by ultrasonography up to 13w6d of gestation, normal fetal heart evaluation according to the screening of our service, absence of maternal chronic diseases or obstetrical complication such as arterial hypertension and collagenosis, and absence of fetal malformations diagnosed on ultrasound.

The ultrasound examinations were performed by a single examiner (ABP) using two devices Voluson E6 and E8 (General Electric Medical System, Zipf, Austria) equipped with a convex probe (C1-5-D).

The following clinical data were collected: age, ethnicity, gestational age at ultrasound examination, parity, weight, height, body mass index, systolic blood pressure, diastolic blood pressure, last fasting serum glucose level during antenatal care, gestational age at delivery, type of delivery, birth weight, and APGAR score at 1st and 5th min. The following variables were considered adverse perinatal outcomes: fetal death, neonatal death, APGAR score at 5th min <7, neonatal ICU admission, macrosomia, respiratory distress syndrome, hyperglobulinaemia, hyperbilirubinaemia, hypocalcaemia, neonatal sepsis, and hypoglycaemia. The presence of at least one adverse perinatal outcome was considered a composite neonatal outcome. We did not consider caesarean section as an adverse perinatal outcome because of the high rate of caesarean section in Brazil.

The fetal myocardial performance index was calculated using the formula isovolumic contraction time + isovolumic relaxation time/ejection time. To calculate the left ventricle myocardial performance index, spectral Doppler probe was positioned on the lateral wall of the ascending aorta, below the aortic valve and just above the mitral valve in the left ventricle outflow view of the heart. The devices were coded with the following presets: spectral Doppler sample size (2–4 mm), Doppler sweep speed of 5 cm/sec, gain -10 dB, filter (wall motion filter) of 210 Hz, and insonation angle <20°.¹⁸ Interval of 3 cardiac cycles was determined based on the use of mitral and aortic valve clicks, as published by Hernandes-Andrade et al.¹⁹

To calculate the left ventricle systolic-to-diastolic duration ratio, three consecutive heartbeats were obtained during maternal apnoea using the mitral and aortic valve clicks. The filling time was measured from the beginning of the opening click of the mitral valve to the closing click of the mitral valve (i.e., the interval from the E wave to the A wave of the mitral valve). The systolic-to-diastolic duration ratio was calculated with the following formula: isovolumic contraction time + ejection time/ isovolumic relaxation time + filling time. To obtain the left ventricle systolic-to-diastolic duration ratio, the pulsed Doppler sample was positioned below the aortic valve and just above the mitral valve in the left ventricle outflow view of the fetal heart. To obtain the right ventricle systolic-to-diastolic duration ratio', the tissue Doppler sample size (2-4 mm) was placed at the junction between the right ventricle wall at the level of its atrioventricular valve (tricuspid annulus). The Doppler sweep speed was adjusted to 5 cm/sec, and the gain was adjusted to -25 dB to clearly see the Doppler velocity waveform. The insonation ultrasound beam at the apical or basal cardiac fourchamber view was maintained at an angle of $<30^{\circ}$. The right ventricle systolic-to-diastolic duration ratio' was calculated using the formula: isovolumic contraction time + ejection time/ isovolumic relaxation time + filling time (Figure 1).¹⁵

The data were analysed in an Excel 2010 (Microsoft Corp., Redmond, WA, USA) using SPSS 20.0 (SPSS Inc., Chicago, IL, USA) and Prisma GraphPad 7.0 (GraphPad Software, San Diego, CA, USA). Variables with a normal distribution were presented as means and standard deviations. Non-normally distributed variables were presented as medians and minimum and maximum values. Categorical variables were described as absolute and percentage frequencies. Analysis of variance tests were used to assess the effect of types 1 and 2 diabetes mellitus on continuous variables. General linear model with fetal heart rate as covariate was applied to assess the influence of diabetes mellitus on fetal

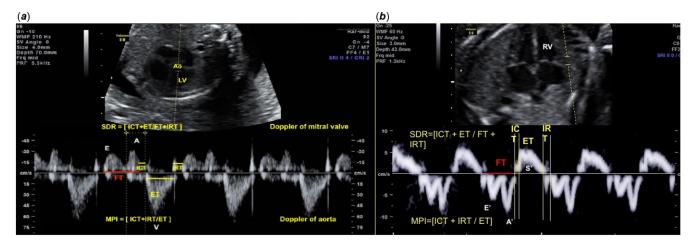


Figure 1. Fetal echocardiography showing the cardiac cycle intervals and the formulas to calculate: 1-MPI and 2-SDR. (*A*) MPI and SDR of the left ventricle using spectral Doppler. (*B*) MPI and SDR of the right ventricle using tissue Doppler. Formulas: MPI = ICT + IRT/ET and SDR = ICT + ET/FT + IRT. SDR = systolic-to-diastolic duration ratio by spectral Doppler; SDR' = systolic-to-diastolic duration ratio by tissue Doppler; MPI = myocardial performance index; ET = ejection time; FT = filling time; ICT = isovolumetric contraction time; IRT = isovolumetric relaxation time; E = E wave of mitral valve flow; A = A wave of mitral valve flow; E' = E wave of tricuspid valve flow by tissue Doppler; A' = A wave of tricuspid valve flow; S' = pulmonary artery flow by tissue Doppler (systolic wave).

cardiac function parameters. Fisher's exact test was used to assess the association of myocardial performance index and systolic-todiastolic duration ratio parameters with adverse perinatal outcomes. Binary logistic regression was applied to examine the capability of spectral Doppler to predict composite neonatal outcomes. The Spearman and Pearson correlation tests were used to assess the correlation between fetal cardiac function parameters, fasting glucose levels, and glycosylated glucose levels. The significance level for all tests was p < 0.05.

Results

The 179 mothers were divided into 3 groups: Group 1 (120, normal), Group 2 (type 1 diabetes mellitus, 31), and Group 3 (type 2 diabetes mellitus, 28). Table 1 presents the maternal and neonatal characteristics of the study population. Group 2 had significantly higher fasting glucose levels (108.0 vs. 80.0 mg/dl, p < 0.001), lower gestational age at delivery (36.6 vs. 39.6 weeks, p < 0.001), lower APGAR score at 1st min (8.0 vs. 9.0, *p* < 0.001), and lower APGAR score at 5th min (8.9 vs. 9.0 p < 0.001) than Group 1. Group 3 had significantly higher maternal age (32.0 vs. 28.0 years, p = 0.005), body mass index (29.8 vs. 27.0 kg/m², p = 0.001), and fasting glucose (104.0 vs. 80.0 mg/dl, *p* < 0.001) than Group 1. Group 3 had significantly lower gestational age at delivery (37.6 vs. 39.6 weeks, p < 0.001), lower APGAR score at 1st min (8.0 vs. 9.0, p = 0.005), and lower APGAR score at 5th minute (8.9 vs. 9.0, p = 0.008) than Group 1. Group 2 had significantly lower maternal age (26 vs. 32 years, p = 0.009), number of pregnancies (1.0 vs. 2.0, p = 0.016), parity (0.0 vs. 1.0, p = 0.011), body mass index (25.6 vs. 26.8 kg/m², p = 0.003), and gestational age at delivery (36.6 vs. 37.6 weeks, p = 0.008) than Group 3. Group 2 had significantly higher fetal heart rate (108 vs. 104 bpm, p = 0.010) than Group 3.

We observed that maternal diabetes mellitus had significant influence on left ventricle isovolumic contraction time (F(2) = 7.31, p < 0.001, $n^2 = 0.076$), left ventricle ejection time (F(2) = 4.21, p = 0.025, $n^2 = 0.034$), and left ventricle myocardial performance index (F(2) = 8.75, p < 0.001, $n^2 = 0.028$) parameters. There was no influence of maternal diabetes mellitus on left ventricle systolic-to-diastolic duration ratio (p = 0.210) and right

ventricle systolic-to-diastolic duration ratio (p = 0.976). Group 2 had significantly higher left ventricle isovolumic contraction time (0.036 vs. 0.031 sec, p = 0.001) and left ventricle myocardial performance index (0.487 vs. 0.453, p = 0.003) than Group 1. Group 3 had significantly higher left ventricle myocardial performance index (0.492 vs. 0.449, p = 0.006) and lower left ventricle ejection time (0.161 vs. 0.169 sec, p = 0.038) than Group 1 (Table 2).

Regarding adverse perinatal outcomes, Group 2 had higher prevalence of vascular alterations (p < 0.0001), neonatal ICU admission (p < 0.0001), macrosomia (p < 0.0001), hyperbilirubinaemia (p < 0.0001), hypoglycaemia (p < 0.0001), and composite neonatal outcome (p < 0.0001) compared to the Group 1.

We found that left ventricle systolic-to-diastolic duration ratio (p = 0.704), right ventricle systolic-to-diastolic duration ratio' (p = 0.757), left ventricle isovolumic contraction time (p = 0.163), left ventricle ejection time (p = 0.093), and left ventricle myocardial performance index (p = 0.087) were not good predictors of composite neonatal outcomes. Table 3 shows the odds ratio and the respective confidence intervals 95% for each parameter.

Considering all the normal cases included in the study, there was no significant correlation between left ventricle myocardial performance index and left ventricle systolic-to-diastolic duration ratio (r = 0.002, p = 0.977) (Figure 2).

There was no significant correlation between fasting glucose levels and left ventricle systolic-to-diastolic duration ratio (r = 0.03, p = 0.615), right ventricle systolic-to-diastolic duration ratio' (r = 0.01, p = 0.797), and left ventricle myocardial performance index (r = 0.09, p = 0.206) (Figure 3). There was no significant correlation between glycosylated haemoglobin levels and left ventricle systolic-to-diastolic duration ratio' (r = -0.02, p = 0.842), right ventricle systolic-to-diastolic duration ratio' (r = -0.100, p = 0.405), and left ventricle myocardial performance index (r = -0.08, p = 0.501) (Figure 4).

Discussion

Although there is no classical standardisation for assessing fetal cardiac function, the Cardiovascular Profile Score has been used to

Table 1. Maternal and neonatal characteristics of the study population

	Group 1 (120, normal)			Group	2 (31, type	e 1 DM)	Group 3 (28, type 2 DM)			
	Mean	Min	Мах	Mean	Min	Мах	Mean	Min	Мах	р
Maternal age (years)	28.0 ^(b,c)	15.0	44.0	26.0	17.0	41.0	32.0	23.0	42.0	0.011
Number of pregnancies	2.0	1.0	8.0	1.0 ^(c)	1.0	4.0	2.0	1.0	4.0	0.047
Parity	1.0	0.0	4.0	0.0 ^(c)	0.0	2.0	1.0	0.0	3.0	0.040
Abortion	0.0	0.0	5.0	0.0	0.0	1.0	0.0	0.0	1.0	0.958
Gestational age at ultrasound examination (weeks)	30.2	20.6	36.8	29.7	22.0	35.1	31.1	22.6	36.6	0.382
Weight (Kg)	71.4	41.0	121.5	68.0	50.8	94.3	76.0	48.6	109.5	0.050
Height (m)	1.6	1.5	1.8	1.6	1.5	1.7	1.6	1.4	1.7	0.067
Body mass index (Kg/m ²)	27.0 ^(b)	17.3	40.1	25.6 ^(c)	21.9	34.6	29.8	20.9	41.0	0.003
Systolic blood pressure (mmHg)	110.0	90.0	140.0	110.0	80.0	140.0	110.0	90.0	150.0	0.579
Diastolic blood pressure (mmHg)	70.0	50.0	80.0	70.0	50.0	90.0	70.0	50.0	100.0	0.074
Fasting glucose (mg/dl)	80.0 ^(a,b)	65.0	91.0	108.0	71.0	238.0	104.0	56.0	190.0	<0.00
Glycosylated haemoglobin (%)				7.0	5.8	9.9	6.0	4.5	8.3	0.002
Estimated fetal weight (grams)	1429.5	345.0	2625.0	1516.0	412.0	2876.0	1620.0	471.0	3126.0	0.288
Largest vertical pocket (cm)	4.9	3.2	7.5	5.4	3.1	8.3	4.8	2.8	8.6	0.052
Fetal heart rate (bpm)	141.0	119.0	168.0	140.0 ^(c)	122.0	162.0	147.0	117.0	163.0	0.034
Cardio-thoracic ratio	0.2	0.2	0.5	0.2	0.2	0.3	0.0	0.2	0.3	0.981
Interventricular septum (mm)	2.3	1.4	4.0	2.3	1.0	3.7	2.5	1.4	4.3	0.380
Gestational age at delivery (weeks)	39.6 ^(a,b)	34.3	42.0	36.6	33.7	38.8	37.6	36.7	38.6	<0.00
Birth weight (grams)	3190.0	2075.0	4225.0	3360.0	2160.0	4400.0	3375.0	2120.0	4575.0	0.824
APGAR score 1st min	9.0 ^(a,b)	2.0	10.0	8.0	2.0	9.0	8.0	3.0	9.0	<0.00
APGAR score 5th min	9.0 ^(a,b)	6.0	10.0	8.9	6.0	10.0	8.9	8.0	10.0	<0.00

DM = diabetes mellitus. (a) Group 1 versus Group 2, (b) Group 1 versus Group 3, (c) Group 2 versus Group 3. p value assessed by the Kruskal-Wallis test and Dunn's post hoc test.

Table 2. Echo	ocardiography fetal c	ardiac parameters	using spectral and	l tissue Doppler in n	ormal and type 1 and 2 di	iabetes mellitus pregnant women

	Group 1 (120, normal)			Group 2 (31, type 1 DM)		Group 3 (28, type 2 DM)				
	Mean	SD	Mean	SD	Mean	SD	F	p (1)	p (2)	n ²
Left ventricle SDR	0.918	0.81	0.923	0.103	0.899	0.848	1.575	0.525	0.210	0.018
Right ventricle SDR'	1.028	0.009	1.030	0.018	1.024	0.019	0.025	0.997	0.976	0.001
Left ventricle ICT (sec)	0.032 ^(a)	0.005	0.036	0.006	0.034	0.006	7.31	<0.001	<0.001	0.076
Left ventricle IRT (sec)	0.043	0.0049	0.044	0.0061	0.044	0.0057	1.18	0.309	0.31	0.013
Left ventricle ET (sec)	0.168 ^(b)	0.0097	0.166	0.011	0.161	0.0139	4.21	0.016	0.025	0.034
Left ventricle MPI	0.449 ^(a,b)	0.053	0.487	0.071	0.492	0.075	8.75	<0.001	0.02	0.028

SDR = systolic-to-diastolic duration ratio; SDR' = tissue systolic-to-diastolic duration ratio; ICT = isovolumetric contraction time; IRT = isovolumetric relaxation time; ET = ejection time; MPI = myocardial performance index; SD = standard deviation; DM = diabetes mellitus. F = Fisher calculated by general linear model; n^2 = eta squared. (a) Group 1 versus Group 2, (b) Group 1 versus Group 3, (c) Group 2 versus Group 3, p(1) = analysis of variance; p(2) = general linear model, Tukey's post hoc test.

assess signs of fetal heart failure. The Cardiovascular Profile Score, known as the 10-point score, may predict outcome by describing the degree of fetal cardiovascular heart failure. The Cardiovascular Profile Score combines various cardiac ultrasound and Doppler parameters to assess cardiovascular status, with the highest score being 10 and the highest risk of perinatal mortality when lower than 7.^{16,20,21} Among the variety of Doppler ultrasound parameters, the Cardiovascular Profile Score includes the ventricular filling Doppler pattern obtained by spectral Doppler at the right or

left atrioventricular valve, which reinforces the value of analysing this period of the cardiac cycle. The systolic-to-diastolic duration ratio is a ratio between the sum of the isovolumic contraction time and the ejection time and the sum of the isovolumic relaxation time and the filling time. Reference ranges for systolic-to-diastolic duration ratio have been established in fetuses from low-risk pregnant women.¹⁵ Therefore, in this study, we aimed to demonstrate its applicability in fetuses of pre-existing diabetes mellitus pregnant women.

Table 3. Risk of composite neonatal outcomes according to theechocardiographic parameter used to assess the fetal cardiac function in type1 and 2 diabetes mellitus pregnant women

				r ²	
	OR	CI 95%	X ²	(Nagelkerke)	р
Left ventricle SDR	0.46	0.008-25.28	0.14	0.001	0.704
Right ventricle SDR'	1.73	0.53–57.29	0.09	0.001	0.757
Left ventricle IRT (sec)	0.61	0.000-165	8.31	0.000	0.845
Left ventricle ICT (sec)	0.0	0.0–167.0	1.94	0.018	0.163
Left ventricle ET (sec)	0.0	0.0–121.3	2.85	0.026	0.093
Left ventricle MPI	108.5	0.48–244.8	2.92	0.027	0.087

 $\label{eq:CI} CI = \text{confidence interval; SDR} = \text{systolic-to-diastolic duration ratio; SDR'} = \text{tissue systolic-to-diastolic duration ratio; ICT} = \text{isovolumetric contraction time; IRT} = \text{isovolumetric relaxation time; IRT} = \text{ejection time; MPI} = \text{myocardial performance index; OR} = \text{odds ratio; Binary logistic regression.}$

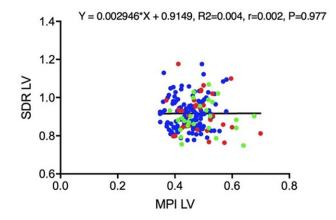


Figure 2. Correlation between left ventricular (LV) myocardial performance index (MPI) and LV systolic-to-diastolic duration ratio (SDR) of all cases included in the study. Blue: normal cases; red: type 1 diabetes mellitus, green: type 2 diabetes mellitus. Pearson's test, p < 0.05.

The myocardial performance index or Tei index has been widely used to assess cardiac function because it combines systolic and diastolic myocardial performance.19,22 The myocardial performance index is a useful tool in conditions with increased preload and afterload such as severe atrioventricular valve, tetralogy of Fallot with absent pulmonary valve, complete atrioventricular block, truncal valve stenosis, twin-to-twin transfusion syndrome, and ductus arteriosus stenosis.^{23,24} Bhorat et al. (2015)²⁵ demonstrated increased values of myocardial performance index in fetuses of poorly controlled diabetic mothers compared to controls and a cut-off value >0.52 to predict poor perinatal outcomes. Similarly, in the current study, we observed increased values of left ventricle myocardial performance index in the type 1 and 2 diabetes mellitus pregnant women compared to controls, with a significant correlation between myocardial performance index and systolic-to-diastolic duration ratio (0.848-unit increase in left ventricle systolic-to-diastolic duration ratio for 1-unit increase in left ventricle myocardial performance index). Similar to myocardial performance index, systolic-todiastolic duration ratio can be abnormal due to systolic and/or diastolic abnormalities, and it is important to identify each interval of the cardiac cycle that is altered.

Previously, our group has established reference values for fetal left ventricle systolic-to-diastolic duration ratio (spectral Doppler) and right ventricle systolic-to-diastolic duration ratio' (tissue Doppler) in a low-risk population with mean values of 1.4 for left ventricle systolic-to-diastolic duration ratio and 1.56 for right ventricle systolic-to-diastolic duration ratio'. In this study, left ventricle systolic-to-diastolic duration ratio showed a negative correlation with gestational age, but right ventricle systolic-todiastolic duration ratio' did not show a significant decrease with gestational age. Similar to the other studies, we have observed a strong positive correlation between myocardial performance index and gestational age. Classically, myocardial performance index has been used to assess cardiac performance in fetal growth restriction, maternal diabetes mellitus, and twin-to-twin transfusion syndrome.²⁶⁻²⁸ In addition, the myocardial performance index has been shown to detect preclinical stages of myocardial dysfunction.²⁹ In agreement with other studies, we showed that myocardial performance index was significantly higher in the pre-existing diabetes mellitus pregnant women than in the controls. In preexisting diabetes mellitus pregnant women, myocardial performance index was altered by reduced ejection time and higher

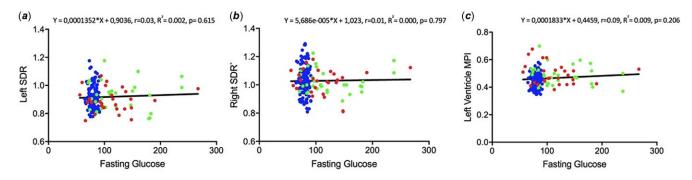


Figure 3. Correlation between fasting glucose levels in normal (blue dots), type 1 diabetes mellitus (green dots), and type 2 diabetes mellitus (red dots) pregnant women and left ventricle systolic-to-diastolic duration ratio (SDR) (A), right ventricle tissue systolic-to-diastolic duration ratio (SDR') (B), and left ventricle myocardial performance index (MPI) (C).

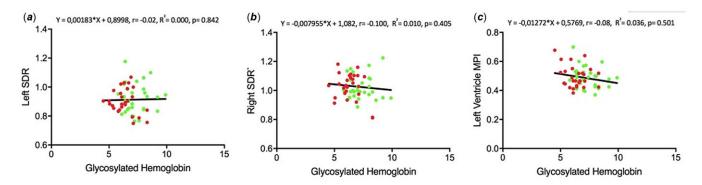


Figure 4. Correlation between glycosylated haemoglobin levels in normal (blue dots), type 1 diabetes mellitus (green dots), and type 2 diabetes mellitus (red dots) pregnant women and left ventricle systolic-to-diastolic duration ratio (SDR) (A), right ventricle tissue systolic-to-diastolic duration ratio (SDR') (B), and left ventricle myocardial performance index (MPI) (C).

isovolumic contraction time. However, no significant correlation between pre-existing maternal diabetes mellitus and left ventricle systolic-to-diastolic duration ratio/right ventricle systolic-todiastolic duration ratio' was observed, being not a useful echocardiographic parameter in predicting composite neonatal outcomes.

In summary, pre-existing maternal diabetes mellitus had a significant effect on fetal left ventricle myocardial performance index. Conversely, no significant correlation was observed between systolic-to-diastolic duration ratio and pre-existing maternal diabetes mellitus. Accordingly, we did not believe that systolicto-diastolic duration ratio could be a useful tool for predicting adverse perinatal outcomes in fetuses of pre-existing diabetes mellitus pregnant women.

References

- Rocha LA, Rolo LC, Araujo Júnior E. How to perform a functional assessment of the fetal heart: a pictorial review. Ultrasonography 2019; 38:365–373.
- Donofrio MT, Moon-Grady AJ, Hornberger LK et al. Diagnosis and treatment of fetal cardiac disease: a scientific statement from the American Heart Association. Circulation 2014; 129: 2183–2242.
- AIUM practice parameter for the performance of fetal echocardiography. J Ultrasound Med 2020; 39: E5–E16.
- Carvalho JS, Axt-Fliedner R, Chaoui R et al. ISUOG practice guidelines (updated): fetal cardiac screening. Ultrasound Obstet Gynecol 2023; 61: 788–803.
- Moon-Grady AJ, Donofrio MT, Gelehrter S et al. Guidelines and recommendations for performance of the fetal echocardiogram: an update from the American Society of Echocardiography. J Am Soc Echocardiogr 2023; 36 : 679–723.
- Srisupundit K, Luewan S, Tongsong T. Prenatal diagnosis of fetal heart failure. Diagnostics (Basel) 2023; 13: 779.
- 7. Van MieghemT, LewiL, GucciardoLet al. The fetal heart in twin-to-twin transfusion syndrome. Int J Pediatr 2010; 2010: 379792.
- Moon-Grady AJ. Fetal echocardiography in twin-twin transfusion syndrome. Am J Perinatol 2014; 31 Suppl 1: S31–S38.
- Iwagaki S, Takahashi Y, Chiaki R et al. Cardiomegaly of the larger twin in monochorionic twin pregnancies warrants neonatal intensive care even without twin-to-twin transfusion syndrome. Eur J Obstet Gynecol Reprod Biol 2019; 241: 82–87.
- Ortiz JU, Torres X, Eixarch E et al. Differential changes in myocardial performance index and its time intervals in donors and recipients of twinto-twin transfusion syndrome before and after laser therapy. Fetal Diagn Ther 2018; 44 :305–310.
- 11. Hernandez-Andrade E, Benavides-Serralde JA, Cruz-Martinez R, Welsh A, Mancilla-Ramirez J. Evaluation of conventional doppler fetal cardiac

function parameters: E/A ratios, outflow tracts, and myocardial performance index. Fetal Diagn Ther 2012; 32 : 22–29.

- Hernandez-Andrade E, Figueroa-Diesel H, Kottman C et al. Gestationalage-adjusted reference values for the modified myocardial performance index for evaluation of fetal left cardiac function. Ultrasound Obstet Gynecol 2007; 29: 321–325.
- Nawaytou HM, Peyvandi S, Brook MM, Silverman N, Moon-Grady AJ. Right ventricular systolic-to-diastolic time index: hypoplastic left heart fetuses differ significantly from normal fetuses. J Am Soc Echocardiogr 2016; 29 : 143–149.
- Friedberg MK, Silverman NH. Cardiac ventricular diastolic and systolic duration in children with heart failure secondary to idiopathic dilated cardiomyopathy. Am J Cardiol 2006; 97 : 101–105.
- Peixoto AB, Bravo-Valenzuela NJM, Mattar R et al. Reference values for left and right ventricular systolic-to-diastolic duration ratio (SDR) found using both spectral and tissue Doppler of fetal heart between 20 and 36+6 weeks of gestation. Int J Cardiovasc Imaging 2021; 37 : 2717–2726.
- Hofstaetter C, Hansmann M, Eik-Nes SH, Huhta JC, Luther SL. A cardiovascular profile score in the surveillance of fetal hydrops. J Matern Fetal Neonatal Med 2006; 19: 407–413.
- 17. Huhta JC. Diagnosis and treatment of foetal heart failure: foetal echocardiography and foetal hydrops. Cardiol Young 2015; 25 Suppl 2 : 100–106.
- Lobmaier SM, Cruz-Lemini M, Valenzuela-Alcaraz B et al. Influence of equipment and settings on myocardial performance index repeatability and definition of settings to achieve optimal reproducibility. Ultrasound Obstet Gynecol 2014; 43 ; 632–639.
- Hernandez-Andrade E, Lopez-Tenorio J, Figueroa-Diesel H 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 : 227–232.
- Huhta JC. Fetal congestive heart failure. Sem Fetal Neonatal Med 2005; 10: 542–552.
- Mäkikallio K, Räsänen J, Mäkikallio T, Vuolteenaho O, Huhta JC. Human fetal cardiovascular profile score and neonatal outcome in intrauterine growth restriction. Ultrasound Obstet Gynecol 2008; 31: 48–54.
- Tei C, Ling LH, Hodge DO et al. New index of combined systolic and diastolic myocardial performance: a simple and reproducible measure of cardiac function- a study in normals and dilated cardiomyopathy. J Cardiol 1995; 26: 357–366.
- 23. Flood K, Unterscheider J, Daly S et al. The role of brain sparing in the prediction of adverse outcomes in intrauterine growth restriction: results of the multicenter PORTO study. Am J Obstet Gynecol 2014; 211: 288.e1–288.e5,
- Votava-Smith JK, Habli M, Cnota JF et al. Diastolic dysfunction and cerebrovascular redistribution precede overt recipient twin cardiomyopathy in early-stage twin-twin transfusion syndrome. J Am Soc Echocardiogr 2015; 28 : 533–540.

- 25. Bhorat IE, Bagratee JS, Pillay M, Reddy T. Use of the myocardial performance index (MPI or Tei index) as a prognostic indicator of adverse fetal outcome in poorly controlled gestational diabetic pregnancies. Prenat Diagn 2014; 34:1301–1306.
- 26. 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 : 400–405.
- 27. Peixoto AB, Bravo-Valenzuela NJM, Martins WP, Mattar R, Moron AF, Araujo Júnior E. Reference ranges for the left ventricle modified myocardial

performance index, respective time periods, and atrioventricular peak velocities between 20 and 36 + 6 weeks of gestation. J Matern Fetal Neonatal Med 2021; 34 456–465.

- Rychik J, Tian Z, Bebbington M et al. The twin-twin trans- fusion syndrome: spectrum of cardiovascular abnormality and development of a cardiovascular score to assess severity of disease. Am J Obstet Gynecol 2007; 197 : 392.e1–392.e8,
- 29. Willruth A, Steinhard J, Enzensberger C et al. Fetal color tissue Doppler imaging (cTDI): biventricular reference ranges for the time segments of the cardiac cycle in second and third trimesters of gestation. Arch Gynecol Obstet 2016; 294 : 917–924.