



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

Original Article

Cite this article: Peixoto AB, Bravo-Valenzuela NJM, Rolo LC, Mattar R, Moron AF, Tonni G, and Araujo Júnior E (2025) Influence of pre-existing maternal diabetes mellitus on fetal myocardial performance index and systolic-to-diastolic duration ratio: a prospective cohort study. *Cardiology in the Young* **35**: 53–59. doi: [10.1017/S1047951124025927](https://doi.org/10.1017/S1047951124025927)

Received: 23 December 2023

Revised: 21 April 2024

Accepted: 3 August 2024



First published online: 16 December 2024

Keywords:

Maternal diabetes; fetal heart function; spectral Doppler; tissue Doppler

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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-diastolic 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°. Interval of 3 cardiac cycles was determined based on the use of mitral and aortic valve clicks, as published by Hernandez-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 four-chamber view was maintained at an angle of <30°. 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

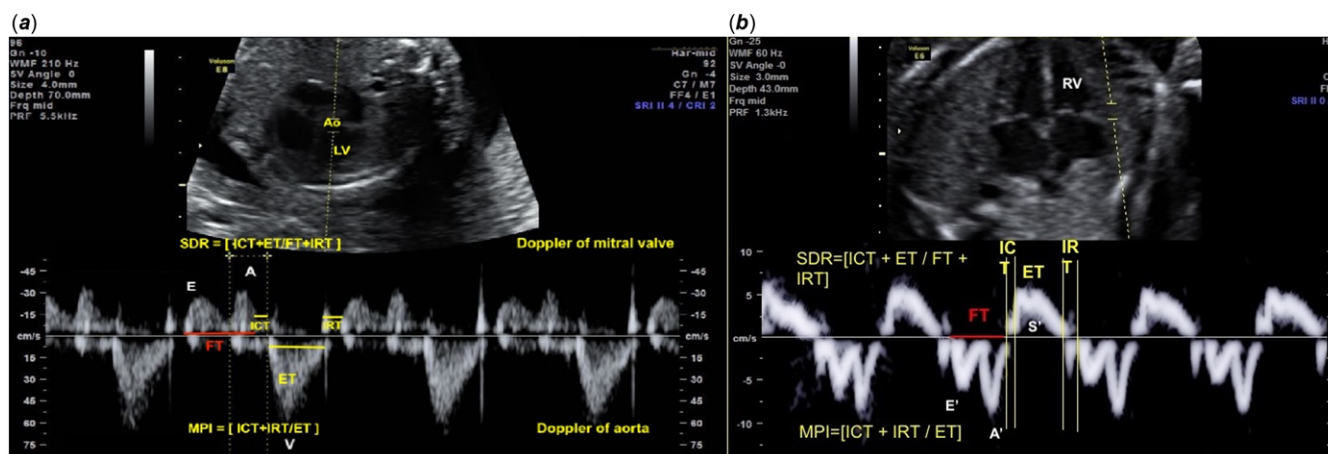


Figure 1. Fetal echocardiography showing the cardiac cycle intervals and the formulas to calculate: 1-MPI and 2-SDR. (A) MPI and SDR of the left ventricle using spectral Doppler. (B) MPI and SDR of the right ventricle using tissue Doppler. Formulas: $MPI = [ICT + IRT] / ET$ and $SDR = [ICT + ET] / FT + IRT$. 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-to-diastolic 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 1 DM) | | | Group 3 (28, type 2 DM) | | | <i>p</i> |
|---|-----------------------|--------|--------|-------------------------|--------|--------|-------------------------|--------|--------|----------|
| | Mean | Min | Max | Mean | Min | Max | Mean | Min | Max | |
| 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 | <0.001 |
| 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 | <0.001 |
| 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 | <0.001 |
| APGAR score 5th min | 9.0 ^(a,b) | 6.0 | 10.0 | 8.9 | 6.0 | 10.0 | 8.9 | 8.0 | 10.0 | <0.001 |

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. Echocardiography fetal cardiac parameters using spectral and tissue Doppler in normal and type 1 and 2 diabetes mellitus pregnant women

| | Group 1 (120, normal) | | Group 2 (31, type 1 DM) | | Group 3 (28, type 2 DM) | | <i>F</i> | <i>p</i> (1) | <i>p</i> (2) | <i>n</i> ² |
|--------------------------|------------------------|--------|-------------------------|--------|-------------------------|--------|----------|--------------|--------------|-----------------------|
| | Mean | SD | Mean | SD | Mean | SD | | | | |
| 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 the echocardiographic parameter used to assess the fetal cardiac function in type 1 and 2 diabetes mellitus pregnant women

| | OR | CI 95% | χ^2 | r^2 (Nagelkerke) | p |
|--------------------------|-------|-------------|----------|-----------------------|-------|
| 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 |

CI = confidence interval; 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; OR = odds ratio; Binary logistic regression.

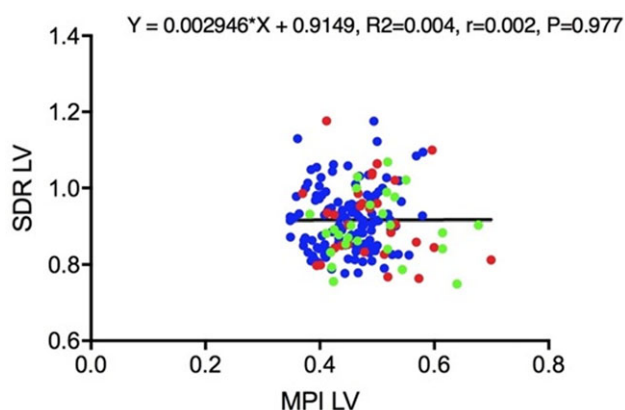


Figure 2. Correlation between left ventricular (LV) myocardial performance index (MPI) and LV systolic-to-diastolic duration ratio (SDR) of all cases included in the study. Blue: normal cases; red: type 1 diabetes mellitus, green: type 2 diabetes mellitus. Pearson's test, $p < 0.05$.

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-to-diastolic 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-to-diastolic 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 pre-existing diabetes mellitus pregnant women, myocardial performance index was altered by reduced ejection time and higher

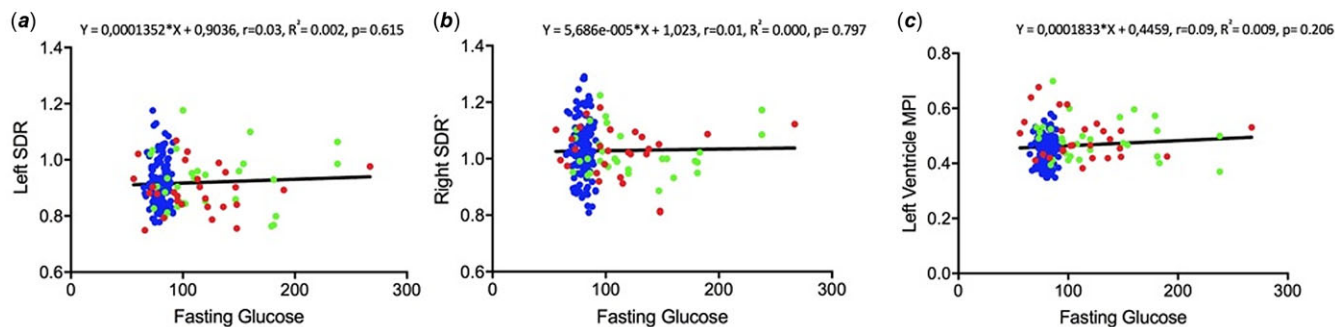


Figure 3. Correlation between fasting glucose levels in normal (blue dots), type 1 diabetes mellitus (green dots), and type 2 diabetes mellitus (red dots) pregnant women and left ventricle systolic-to-diastolic duration ratio (SDR) (A), right ventricle tissue systolic-to-diastolic duration ratio (SDR')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

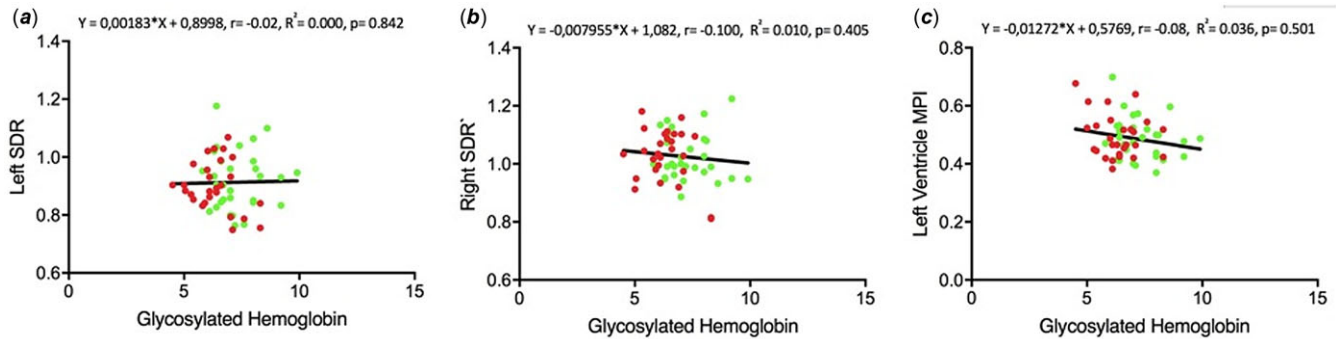


Figure 4. Correlation between glycosylated haemoglobin levels in normal (blue dots), type 1 diabetes mellitus (green dots), and type 2 diabetes mellitus (red dots) pregnant women and left ventricle systolic-to-diastolic duration ratio (SDR) (A), right ventricle tissue systolic-to-diastolic duration ratio (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-to-diastolic 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 systolic-to-diastolic duration ratio could be a useful tool for predicting adverse perinatal outcomes in fetuses of pre-existing diabetes mellitus pregnant women.

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