

Assessment of left ventricular systolic function using pressure-strain loops in offspring of women with gestational diabetes mellitus: a prospective cohort study

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Background: Gestational diabetes mellitus (GDM) increases the risk of cardiovascular abnormalities in offspring. The objective of this study is to assess changes in left ventricular myocardial work using the left ventricular pressure-strain loop (LVPSL) method in neonates born to mothers with GDM. The aim of the research is to examine early impairments in neonatal left ventricular systolic function and to investigate whether these impairments persist over time.

Methods: In a prospective cohort study, we enrolled 61 neonates born to mothers with GDM and 30 healthy neonates born to mothers without pregnancy complications between August 2021 and March 2023 using a random method. The GDM group was further subdivided based on maternal hemoglobin A1c (HbA1c) levels into those with HbA1c $\leq 6.5\%$ and those with HbA1c $> 6.5\%$. Echocardiographic assessments and left ventricular myocardial work parameters were measured and compared across the three groups using one-way analysis of variance (ANOVA) with multiple comparisons conducted using the Least Significant Difference t (LSD-T) test and multiple correction using the Bonferroni method in terms of data of normal distribution and homoscedasticity. Non-normally distributed data were presented as median (first quartile, third quartile) [M (Q1, Q3)] and compared using the Kruskal-Wallis *H* test. The correlation between myocardial work parameters in neonates born to mothers with GDM and the maternal HbA1c levels was also analyzed using Pearson correlation analysis or Spearman's rank correlation.

Results: The enrolled 61 neonates born to women with GDM comprised 34 male and 27 female neonates, with a gestational age (GA) of 38.9 ± 1.7 weeks. The control group 30 healthy neonates comprised 17 males and 13 females, with a GA of 39.1 ± 1.8 weeks. Neonates in the HbA1c $\leq 6.5\%$ and HbA1c $> 6.5\%$ groups demonstrated increased interventricular septal thickness (IVSD) ($P < 0.05$) compared to the control group. However, no significant differences in IVSD were observed among the groups after a 12-month follow-up ($P > 0.05$). At birth and during the 12-month follow-up, global longitudinal strain (GLS), global work index (GWI), and global constructive work (GCW) values were lower in both HbA1c groups compared to the control group, with the HbA1c $> 6.5\%$ group revealing significantly reduced GLS, GWI, and GCW ($P < 0.05$). Neonatal GLS exhibited a positive correlation with maternal HbA1c, whereas GWI and GCW revealed negative correlations ($r = 0.683$, $r = -0.709$, $r = -0.688$, $P < 0.001$).

Conclusions: The LVPSL method can examine early impairments in left ventricular systolic function in

neonates born to mothers with GDM. More severe impairments are associated with poorer glycemic control during pregnancy, as indicated by higher maternal HbA1c levels. These functional impairments persist in the offspring 12 months postpartum.

Keywords: Gestational diabetes mellitus (GDM); offspring; glycosylated hemoglobin; left ventricular systolic function; pressure-strain loop (PSL)

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Introduction

In recent years, the prevalence of gestational diabetes mellitus (GDM) has been increasing, driven by rising obesity rates, advanced maternal age, and lifestyle changes (1). GDM is associated with an elevated risk of obesity, metabolic disorders, and cardiovascular diseases in neonates, with cardiovascular complications being particularly severe. These complications commonly manifest as congenital heart malformations, myocardial hypertrophy, and myocardial damage, potentially elevating the risk of cardiovascular events during childhood and adulthood (2-6). Research conducted both domestically and internationally indicates that while structural changes in the hearts of neonates born

to mothers with GDM may resolve within a few months post-birth, the associated cardiac functional impairments tend to be irreversible (7,8).

The non-invasive left ventricular pressure-strain loop (LVPSL) method uses speckle tracking imaging (STI) and accounts for the influence of afterload on the myocardium without load dependence and angle dependence. LVPSL, which closely approximates the invasive pressure-volume loop, has been confirmed to have good correlation with oxygen consumption and regional myocardial glucose metabolism as assessed by fluorodeoxyglucose positron emission tomography (FDG-PET). This method enables the early and quantitative detection of changes in left ventricular myocardial function (9,10). LVPSL is currently used for the early assessment of impaired left ventricular systolic function in various conditions, including hypertension, diabetes, coronary artery disease, and heart failure (11-13). There have been few studies reporting LVPSL in neonates born to mothers with GDM. The objective of this study is to use LVPSL to assess changes in left ventricular myocardial work in neonates born to mothers with GDM, to identify early impairments in left ventricular systolic function in these neonates, and to determine, through follow-up, whether these impairments persist even later. We present this article in accordance with the STROBE reporting checklist (available at <https://cdt.amegroups.com/article/view/10.21037/cdt-24-450/rc>).

Methods

Study participants

A total of 61 neonates born to women with GDM were enrolled from the Obstetrics and Gynecology Department of the Seventh Medical Center of the Chinese People's Liberation Army (PLA) General Hospital between August 2021 and March 2023 into the case group. Based

Highlight box

Key findings

- Offspring of mothers with gestational diabetes mellitus (GDM) show early impairments in left ventricular systolic function, measured by the left ventricular pressure-strain loop method.
- Neonatal global longitudinal strain, global work index, and global constructive work are lower in GDM neonates, especially in those with maternal hemoglobin A1c (HbA1c) >6.5%.
- Impairments in myocardial function persist for 12 months.

What is known and what is new?

- GDM increases cardiovascular risk in offspring.
- This study reveals specific early myocardial work impairments in neonates from mothers with GDM, linked to maternal HbA1c levels, demonstrates the lasting impact of GDM on neonatal heart function, with more severe impairments tied to poorer maternal glycemic control.

What is the implication, and what should change now?

- Highlights the need for better glycemic control in pregnancy to reduce long-term cardiovascular risks in offspring.
- Calls for further research to explore interventions for neonatal cardiac impairments due to GDM.

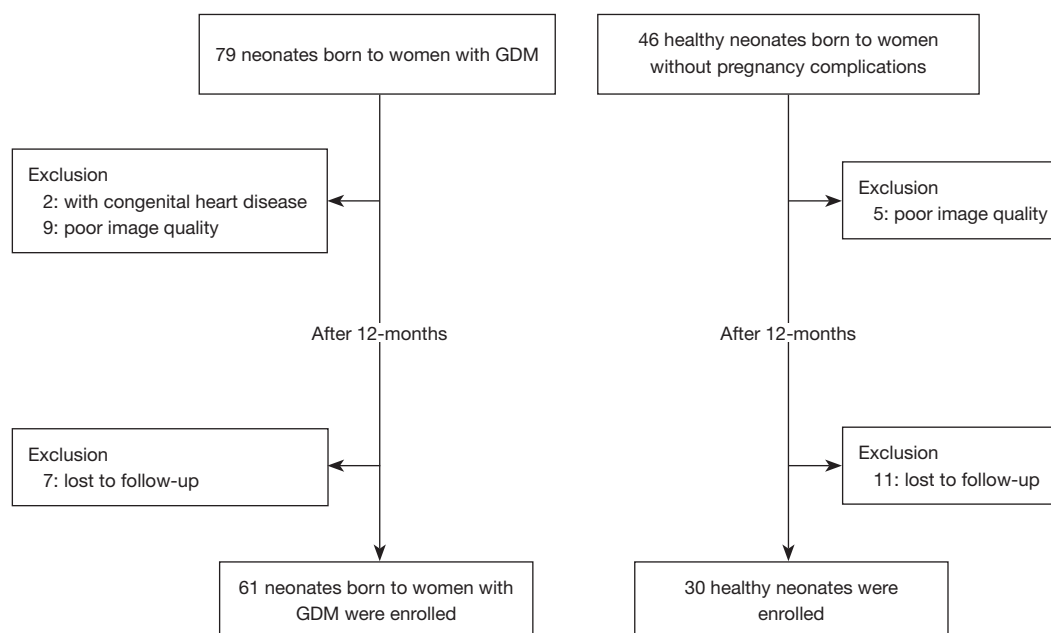


Figure 1 Flow diagram of the study. GDM, gestational diabetes mellitus.

on hemoglobin A1c (HbA1c) levels of the mothers with GDM, the neonates were further classified into those with HbA1c $\leq 6.5\%$ ($n=34$) and those with HbA1c $>6.5\%$ ($n=27$). Additionally, 30 healthy neonates born to mothers without pregnancy complications during the same period were included in the control group, which matched for age and gender. The enrolled neonates were followed up until 12 months after delivery (*Figure 1*). The diagnostic criteria for GDM included a 75 g oral glucose tolerance test (OGTT) with fasting blood glucose ≥ 5.1 mmol/L, 1-hour postprandial ≥ 10.0 mmol/L, and 2-hour postprandial ≥ 8.5 mmol/L, and the diagnosis was confirmed by meeting one or more of these criteria (14). Exclusion criteria encompassed: (I) neonates born at a gestational age (GA) <37 weeks; (II) neonates with an Apgar score <7 ; (III) congenital heart disease or other malformations; (IV) requirement for mechanical ventilation; (V) maternal pregnancy complications; and (VI) chronic maternal diseases like hypertension, hyperthyroidism, congenital heart disease, and chronic kidney disease. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and approved by the Ethics Committee of the Seventh Medical Center of Chinese PLA General Hospital (No. S2024-006-01). Informed consent was obtained from all participants' legal guardians.

Measurements and records for all neonates included

in the study encompassed length, weight, systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR). Body mass index (BMI) was calculated using the formula $BMI = \text{weight}/\text{height}^2$. Additionally, laboratory indexes, including blood glucose and HbA1c, were recorded for the mothers with GDM.

Instruments and methods

Echocardiogram examinations were conducted on all neonates included in the study between 24–48 hours after birth and at 12 months. The GE Vivid E9 ultrasound diagnostic system (GE Vingmed Ultrasound AS, Horten, Norway), equipped with a 6S probe (frequency range, 2.4 to 8 MHz) and an Echo PAC ultrasound workstation, was used for these examinations. Routine two-dimensional imaging captured echocardiographic parameters, including interventricular septal thickness (IVSD) at end-diastole, left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), and left ventricular posterior-wall thickness at end-diastole (LVPWD). The left ventricular ejection fraction (LVEF) was measured using the biplane Simpson's method. Dynamic images of the left ventricle's apical four-chamber, three-chamber, and two-chamber views were collected and stored at a frame rate of 60–80 frames per second. These images were then uploaded

Table 1 Comparison of general data among the three groups

General characteristics	Control group (n=30)	HbA1c ≤6.5% group (n=34)	HbA1c >6.5% group (n=27)	F/χ^2	P
Male	17 (56.7)	20 (58.82)	14 (51.9)	0.304	0.86
Length (cm)	47.03±2.48	47.97±2.65	47.85±2.58	1.203	0.31
Weight (g)	2,598±521	3,146±613 ^a	3,503±572 ^{ab}	18.278	<0.001
BMI (kg/m ²)	11.74±2.24	13.82±3.25 ^a	15.17±1.18 ^{ab}	14.214	<0.001
SBP (mmHg)	66.93±6.37	64.29±6.78	65.07±7.22	1.250	0.29
DBP (mmHg)	38.13±7.36	35.32±6.02	36.37±6.11	1.499	0.23
HR (BPM)	143.83±16.45	140.32±17.21	141.56±16.56	0.355	0.70

Data are presented as mean ± standard deviation or n (%). Compared to the control group, ^a, $P<0.017$; compared to HbA1c ≤6.5% group, ^b, $P<0.017$. BMI, body mass index; BPM, beats per minute; DBP, diastolic blood pressure; HbA1c, hemoglobin A1c; HR, heart rate; SBP, systolic blood pressure; 1 mmHg =0.133 kPa.

to the Echo PAC workstation, where the endocardium of the apical four-chamber, two-chamber, and three-chamber heart images were outlined. The system automatically generated regions of interest; manual adjustments were made if tracking was unsatisfactory. The opening and closing times of the mitral and aortic valves were determined, and systolic and DBPs were entered to obtain the LVPSL 17-segment myocardial work index bullseye plot and overall myocardial work parameters, including global work index (GWI), global constructive work (GCW), global wasted work (GWW), and global work efficiency (GWE). The collection, measurement, and analysis of echocardiographic images were conducted by three physicians with over ten years of clinical ultrasound experience.

Statistical analysis

Statistical analyses were conducted using SPSS version 26.0. The Shapiro-Wilk test was used to assess the normality of quantitative data. Data that followed a normal distribution were expressed as mean ± standard deviation and compared using one-way ANOVA, with multiple comparisons conducted using the Least Significant Difference t (LSD-T) test, with multiple correction using the Bonferroni method. Non-normally distributed data were presented as median (first quartile, third quartile) [M (Q1, Q3)] and compared using the Kruskal-Wallis H test. Categorical data were reported as number (percentage) and analyzed using the χ^2 test. Linear regression analysis was performed to assess the independent effect of GDM on left ventricular myocardial work parameters at birth and 12 months of age while controlling for GA, gender, mode of delivery.

The correlation between neonatal left ventricular myocardial work parameters in offspring of mothers with GDM and the HbA1c levels of the mothers was examined using Pearson correlation analysis or Spearman's rank correlation. A P value of <0.05 was considered statistically significant.

Results

Comparison of general clinical data among three groups

Sixty-one neonates born to women with GDM comprised 34 male and 27 female neonates, with GA of 38.9±1.7 weeks. The control group 30 healthy neonates comprised 17 males and 13 females, with GA of 39.1±1.8 weeks. No significant differences were observed in gender, length, SBP, DBP, or HR among the three groups of neonates (all $P>0.05$). However, neonates in the HbA1c ≤6.5% group and HbA1c >6.5% groups had higher weights and BMI compared to the control group, with statistically significant differences (all $P<0.05$). Additionally, neonates in the HbA1c >6.5% group exhibited higher weights and BMI than those in the HbA1c ≤6.5% group, with statistically significant differences (all $P<0.05$), as depicted in *Table 1*.

Comparison of routine echocardiographic parameters among groups at birth and at 12-month follow-up

No significant differences were found in LVEDD, LVESD, LVPWD, or LVEF among the three groups of neonates (all $P>0.05$). However, both the HbA1c ≤6.5% group and the HbA1c >6.5% group exhibited significantly thicker IVSD compared to the control group ($P<0.05$). The comparison

Table 2 Comparison of routine echocardiographic parameters among the three groups

Parameters	At birth					After 12 months				
	Control group (n=30)	HbA1c ≤6.5% group (n=34)	HbA1c >6.5% group (n=27)	F	P	Control group (n=30)	HbA1c ≤6.5% group (n=34)	HbA1c >6.5% group (n=27)	F	P
LVEDD (mm)	16.97±1.87	16.5±1.79	16.81±1.92	0.529	0.59	26.7±2.1	26.59±1.79	25.93±2.35	1.151	0.32
LVESD (mm)	10.57±1.68	10.41±1.42	10.67±1.59	0.209	0.81	16.37±1.61	16.29±1.8	16.04±1.58	0.302	0.74
IVSD (mm)	3.17±0.85	3.72±0.9 ^a	3.93±0.98 ^a	5.509	0.006	3.72±0.52	3.85±0.41	3.91±0.45	1.293	0.28
LVPWD (mm)	2.79±0.4	2.81±0.39	3.0±0.41	0.954	0.39	3.12±0.45	3.29±0.53	3.41±0.49	2.388	0.10
LVEF (%)	70.9±8.94	69.62±8.15	68.89±8.37	0.416	0.66	70.33±7.65	69.76±6.87	69.18±7.66	0.173	0.84

Data are presented as mean ± standard deviation. Compared to the control group, ^a, P<0.017. HbA1c, hemoglobin A1c; IVSD, inter ventricular septal thickness at end-diastolic; LVEDD, left ventricular end-diastolic diameter; LVEF, left ventricular ejection fraction; LVESD, left ventricular end-systolic diameter; LVPWD, left ventricular posterior-wall thickness at end-diastole.

of IVSD between the HbA1c ≤6.5% group and the HbA1c >6.5% group did not reveal a significant difference (P=0.36), as depicted in *Table 2*. At the 12-month follow-up, there were no significant differences in LVEDD, LVESD, IVSD, LVPWD, or LVEF among the three groups (all P>0.05), as depicted in *Table 2*.

Comparison of left ventricular myocardial work parameters among groups at birth and at 12-month follow-up

Left ventricular myocardial work parameters at birth and at 12-month follow-up are shown in *Figure 2*. Compared to the control group, both the HbA1c ≤6.5% and HbA1c >6.5% groups exhibited reductions in global longitudinal strain (GLS), GWI, and GCW, with all differences being statistically significant (all P<0.05). Furthermore, the HbA1c >6.5% group demonstrated lower GLS, GWI, and GCW compared to the HbA1c ≤6.5% group, with all differences also reaching statistical significance (all P<0.05). These findings remained significant when adjusted for GA, gender, mode of delivery. No significant differences were found in the GWW and GWE among the three groups (all P>0.05), as depicted in *Table 3*.

At the 12-month follow-up, GLS, GWI, and GCW remained lower in the HbA1c ≤6.5% and HbA1c >6.5% groups compared to the control group, with all differences being statistically significant (all P<0.05). The GLS, GWI, and GCW in the HbA1c >6.5% group continued to be lower than those in the HbA1c ≤6.5% group, with all differences being statistically significant (all P<0.05). These findings remained significant when adjusted for GA, gender, mode of delivery. No significant differences were observed in GWW and GWE among the three groups at

the 12-month follow-up (all P>0.05), as depicted in *Table 3*.

Correlation between neonatal left ventricular myocardial work parameters and maternal HbA1c in GDM pregnant women

A positive correlation was observed between the GLS and the HbA1c levels of the mothers of the neonates (r=0.683, P<0.001), as depicted in *Figure 3A*. In contrast, negative correlations were found between the GWI and GCW of the neonates and the HbA1c levels of their mothers (r=-0.709, P<0.001; r=-0.688, P<0.001), as depicted in *Figure 3B, 3C*, respectively.

Discussion

GDM is one of the most prevalent complications during pregnancy, with a prevalence rate ranging from approximately 6–25% (15). Epidemiological studies have revealed that offspring of mothers with GDM have a fivefold increase in the risk of cardiovascular abnormalities compared to offspring of mothers without GDM. These risks are closely linked to the level of glycemic control in the mother—the higher the maternal blood glucose levels, the more significant the changes in the cardiac structure and function of the offspring (16,17). Enhancing glycemic control in pregnant women with GDM can mitigate the adverse effects of the condition on the cardiac structure and function of their offspring. Compared with conventional echocardiographic parameters, STI is not affected by cardiac geometry and has no angle dependence. It has higher accuracy, sensitivity and better repeatability in the diagnosis and prognosis of a variety of cardiovascular

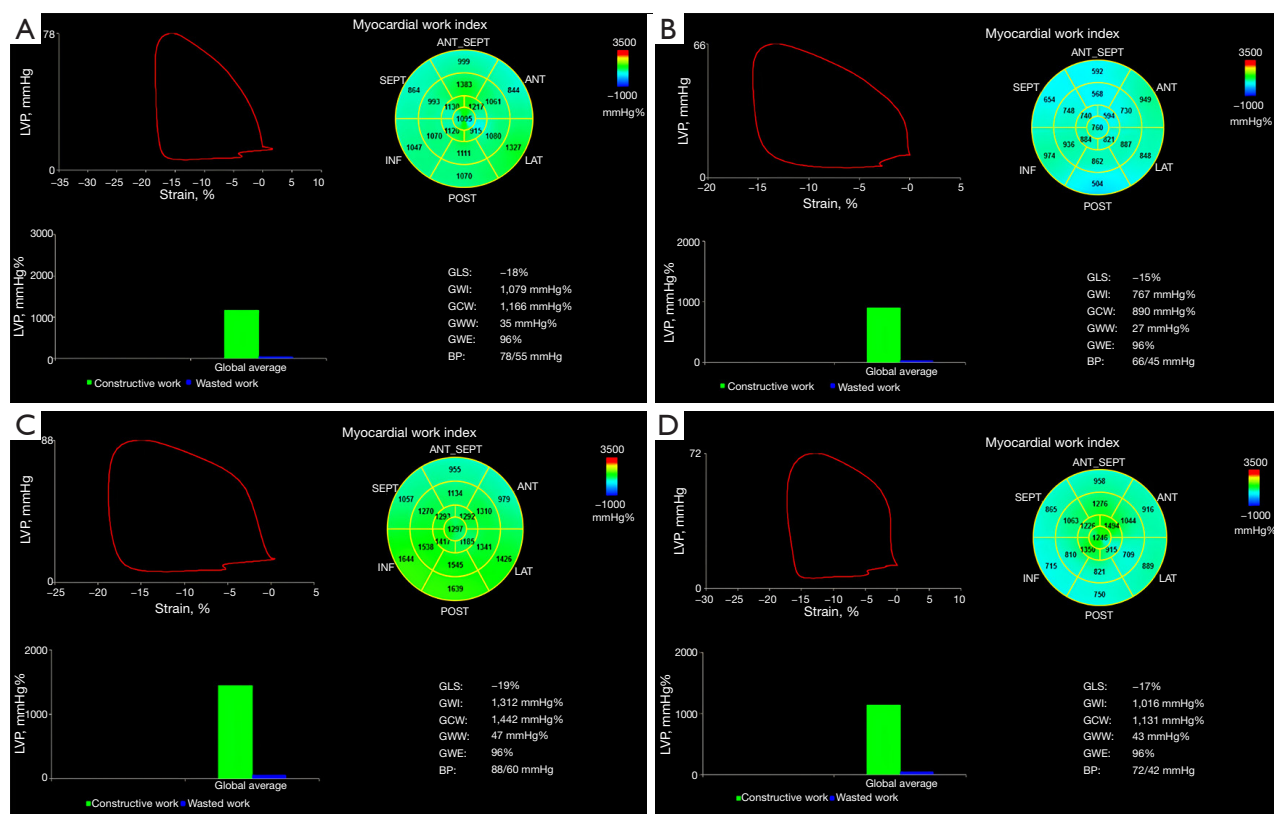


Figure 2 Representative images of left ventricular myocardial work parameters at birth and at the 12-month follow-up. (A) Representative images of left ventricular myocardial work parameters of healthy neonates from non-complicated pregnancy at birth. (B) Representative images of left ventricular myocardial work parameters of a neonate born to a mother with GDM at birth. (C) Representative images of left ventricular myocardial work parameters of a healthy neonate from a non-complicated pregnancy at the 12-month follow-up. (D) Representative images of left ventricular myocardial work parameters of neonates born to mothers with GDM at the 12-month follow-up. BP, blood pressure; GCW, global constructive work; GDM, gestational diabetes mellitus; GLS, global longitudinal strain; GWE, global work efficiency; GWI, global work index; GWW, global wasted work; LVP, left ventricular pressure; ANT, anterior; INF, inferior; LAT, lateral; POST, posterior; SEPT, septal.

Table 3 Comparison of left ventricular myocardial work parameters among the three groups

Parameters	At birth						After 12 months					
	Control group (n=30)	HbA1c ≤6.5% group (n=34)	HbA1c >6.5% group (n=27)	F/H	P	Adjusted P	Control group (n=30)	HbA1c ≤6.5% group (n=34)	HbA1c >6.5% group (n=27)	F/H	P	Adjusted P
GLS (%)	-17.83±2.1	-16.53±1.69 ^a	-14.78±1.69 ^{ab}	19.700	<0.001	<0.001	-18.83±2.32	-17.32±1.96 ^a	-15.93±1.94 ^{ab}	13.899	<0.001	<0.001
GWI (mmHg%)	893±149	816±129 ^a	679±113 ^{ab}	19.045	<0.001	<0.001	1,027±165	946±159 ^a	822±119 ^{ab}	13.471	<0.001	<0.001
GCW (mmHg%)	1,279±251	1,159±243 ^a	881±216 ^{ab}	20.700	<0.001	<0.001	1,388±162	1,254±155 ^a	1,094±170 ^{ab}	23.518	<0.001	<0.001
GWW (mmHg%)	34 [21, 56]	45 [28, 62]	47 [22, 60]	1.419	0.49	0.82	38 [25, 60]	50 [33, 69]	50 [38, 63]	2.458	0.29	0.48
GWE (mmHg%)	97 [95, 98]	96 [95, 98]	95 [92, 97]	5.304	0.07	0.16	97 [96, 98]	96 [95, 97]	96 [96, 97]	5.878	0.05	0.21

Data are presented as mean ± standard deviation or median [interquartile range]. Compared to the control group, ^a, P<0.05; compared to HbA1c ≤6.5% group, ^b, P<0.05. The analyses were adjusted for gestational age, gender, mode of delivery. HbA1c, hemoglobin A1c; GCW, global constructive work; GLS, global longitudinal strain; GWE, global work efficiency; GWI, global work index; GWW, global wasted work.

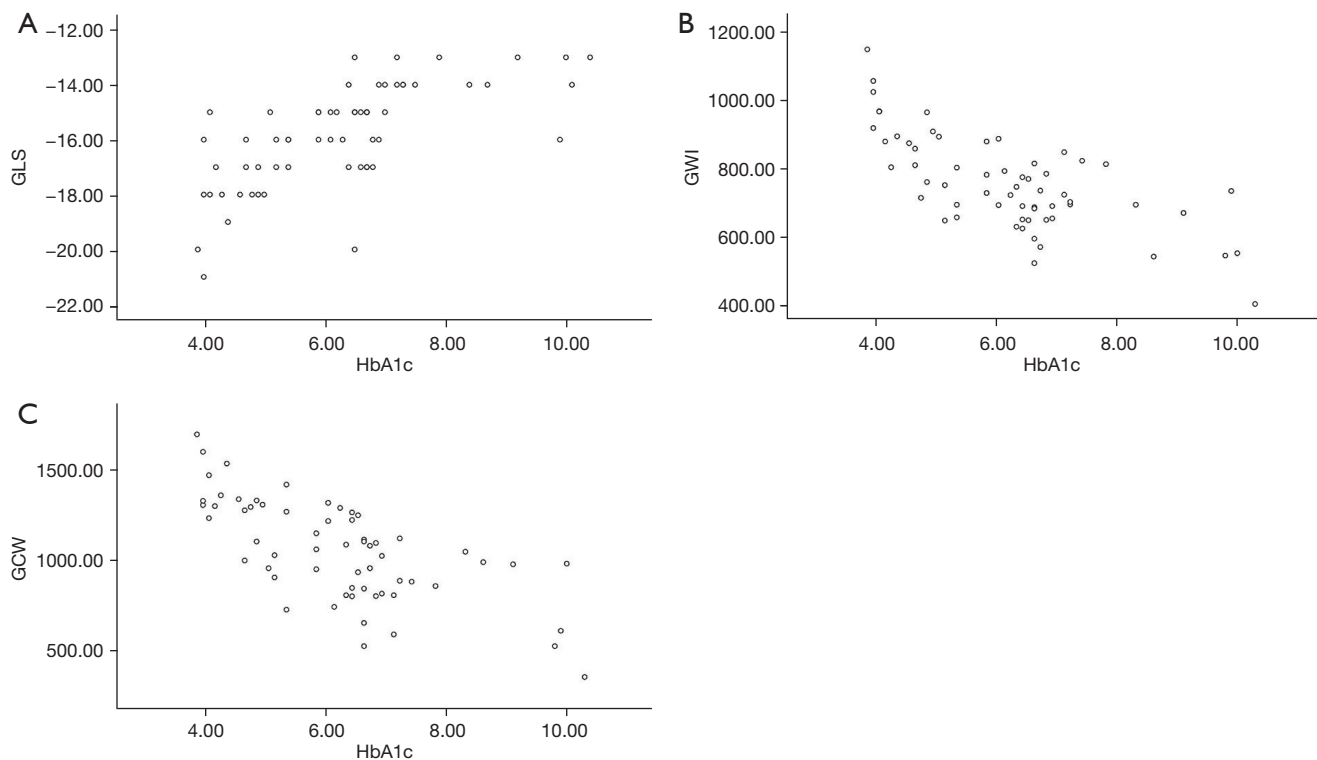


Figure 3 The relationship between neonatal left ventricular myocardial work parameters and maternal HbA1c in women with GDM. (A) Correlation between GLS and HbA1c. (B) Correlation between GWI and HbA1c. (C) Correlation between GCW and HbA1c. HbA1c, hemoglobin A1c; GCW, global constructive work; GDM, gestational diabetes mellitus; GLS, global longitudinal strain; GWI, global work index.

diseases in adults and children. It can improve the diagnostic accuracy and has incremental value independent of ejection fraction (EF) (18,19). Prior research has demonstrated that although conventional echocardiographic LVEF may appear normal in neonates born to mothers with GDM, reductions in myocardial strain parameters can indicate early left ventricular systolic dysfunction in these neonates. However, STI does not account for the influence of afterload on the myocardium (20,21). The non-invasive LVPSL method, as a new approach, incorporates the impact of afterload and allows for early and quantitative detection of changes in left ventricular myocardial function (9,10).

The results of our study indicate that neonates in both the HbA1c $\leq 6.5\%$ and HbA1c $>6.5\%$ groups exhibited increased weights and BMI compared to the control group. This may be attributed to maternal hyperglycemia during pregnancy, which can lead to fetal hyperinsulinemia. The resulting hyperinsulinemia promotes the deposition of fat and glycogen in various fetal tissues, thereby contributing to an increase in neonatal weight (22).

Furthermore, our findings revealed that neonates born

to mothers with GDM had a thicker IVSD compared to the control group ($P < 0.05$), corroborating the findings of Samanth *et al.* (7). This thickening may be due to maternal hyperglycemia during pregnancy, which causes fetal hyperinsulinemia. Hyperinsulinemia, in turn, enhances the synthesis and deposition of fats and glycogen in myocardial cells, leading to myocardial cell proliferation and hypertrophy, particularly affecting the interventricular septum (23,24). A follow-up comparison of IVSD among the three groups after 12 months revealed no significant differences ($P > 0.05$), indicating that the thickening of the IVSD in neonates born to mothers with GDM resolves within 12 months post-birth. Consistent with the findings of Samanth *et al.* and inconsistent with the results of Smith *et al.*, it is possible that the resolution of cardiac hypertrophy in infants born to pregnant women with GDM may be several months or even longer (7,25). However, the underlying mechanisms behind the spontaneous resolution of myocardial hypertrophy in infants born to mothers with GDM remain unclear and require further investigation.

The results of our study indicated that while there was

no significant change in LVEF among neonates in the HbA1c $\leq 6.5\%$ and HbA1c $> 6.5\%$ groups compared to the control group, parameters like GLS, GWI, and GCW were significantly reduced. This finding aligns with the observations of Iwashima *et al.*, indicating that changes in GLS, GWI, and GCW in neonates born to mothers with GDM occur earlier than changes in LVEF (26). This allows for more sensitive detection of subclinical left ventricular dysfunction in these neonates. The observed reductions in GLS, GWI, and GCW in neonates born to mothers with GDM, compared to the control group, may be attributed to prolonged fetal exposure to a hyperglycemic environment, leading to fetal hyperinsulinemia, increased oxidative stress, abnormalities in calcium ion channels, mitochondrial dysfunction, and disruptions in glucose and lipid metabolism, all of which contribute to myocardial injury and fibrotic changes (27,28). At the 12-month follow-up, neonates born to mothers with GDM continued to exhibit lower GLS, GWI, and GCW compared to the control group, indicating a potential long-term adverse effect of maternal diabetes on cardiac function. The mechanisms underlying this persistent cardiac dysfunction may involve intrauterine gene programming that affects the cardiac phenotype and the excessive activation of myocardial cell signaling pathways, which could extend into adulthood (29).

HbA1c is a reliable marker for assessing glycemic control in GDM; an HbA1c $\leq 6.5\%$ indicates good glycemic control, whereas an HbA1c $> 6.5\%$ indicates poor control. The results of our study reveal that neonates in the HbA1c $> 6.5\%$ group have significantly lower GLS, GWI, and GCW compared to those in the HbA1c $\leq 6.5\%$ group (all $P < 0.05$). This indicates that neonates born to mothers with poorer glycemic control exhibit more pronounced impairments in left ventricular systolic function compared to those born to mothers with better glycemic control. Correlation analysis further indicates that GLS in neonates is positively correlated with their mothers' HbA1c levels ($r = 0.683$, $P < 0.001$), while GWI and GCW are negatively correlated ($r = -0.709$, $P < 0.001$; $r = -0.688$, $P < 0.001$). International studies have revealed that the incidence of cardiac complications in offspring of GDM pregnant women is 3.4% when maternal HbA1c is $< 8.5\%$, increasing to 22.4% when HbA1c exceeds 8.5% (30). This increase in cardiac complications is likely due to higher maternal blood glucose levels in cases of poor glycemic control, which leads to more severe myocardial injury and fibrosis, resulting in greater impairments in neonatal left ventricular systolic

function (23). Consequently, maintaining optimal glycemic control is essential for women with GDM to reduce its adverse effects on the cardiac function of their offspring.

However, there are several limitations in this study. First, a relatively small sample size and the absence of extended follow-up beyond 12 months to monitor long-term changes in left ventricular myocardial contractile function in neonates limited the reliability of the conclusions. Additionally, the study faced a follow-up loss, as 7 out of 68 enrolled neonates were lost to follow-up, resulting in a loss-to-follow-up rate of 10.29%. This introduces a potential follow-up bias, despite efforts by obstetricians and pediatricians to enhance follow-up adherence through communication with the families. Second, neonatal guidelines on speckle tracking echocardiography (STE) suggest to acquire images at 80–120 frames/s, given the relatively high HR. But images were acquired with a 6S probe at a frame rate of 60–80 frames/s in the study, which might lead to measurement errors. Finally, pressure-strain loop (PSL) had not been validated in neonates.

Conclusions

The non-invasive LVPSL technique provides a quantitative assessment of changes in left ventricular myocardial work in neonates born to mothers with GDM, enabling the early detection of impairments in left ventricular systolic function. The severity of these impairments is correlated with maternal glycemic control, with poorer control associated with more pronounced dysfunction in neonatal left ventricular systolic function. Notably, this myocardial damage persists up to 12 months postnatally.

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None.

Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at <https://cdt.amegroups.com/article/view/10.21037/cdt-24-450/rc>

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013) and approved by the Ethics Committee of the Seventh Medical Center of Chinese PLA General Hospital (No. S2024-006-01). Informed consent was obtained from all participants' legal guardians.

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References

1. Sweeting A, Wong J, Murphy HR, et al. A Clinical Update on Gestational Diabetes Mellitus. *Endocr Rev* 2022;43:763-93.
2. Mitanchez D, Zyzdorzcyk C, Siddeek B, et al. The offspring of the diabetic mother--short- and long-term implications. *Best Pract Res Clin Obstet Gynaecol* 2015;29:256-69.
3. Skovsgaard CB, Møller A, Bjerre JV, et al. Diabetes in pregnancy and offspring cardiac function: a systematic review and meta-analysis. *Front Pediatr* 2024;12:1404625.
4. Akbariasbagh P, Shariat M, Akbariasbagh N, et al. Cardiovascular Malformations in Infants of Diabetic Mothers: A Retrospective Case-Control Study. *Acta Med Iran* 2017;55:103-8.
5. Di Bernardo SC, Lava SAG, Epure AM, et al. Consequences of gestational diabetes mellitus on neonatal cardiovascular health: MySweetHeart Cohort study. *Pediatr Res* 2023;94:231-8.
6. Yu Y, Arah OA, Liew Z, et al. Maternal diabetes during pregnancy and early onset of cardiovascular disease in offspring: population based cohort study with 40 years of follow-up. *BMJ* 2019;367:l6398.
7. Samanth J, Padmakumar R, Vasudeva A, et al. Persistent subclinical myocardial dysfunction among infants of diabetic mothers. *J Diabetes Complications* 2022;36:108079.
8. Aguilera J, Semmler J, Anzoategui S, et al. Cardiac function in gestational diabetes mellitus: A longitudinal study from fetal life to infancy. *BJOG* 2021;128:272-9.
9. Manganaro R, Marchetta S, Dulgheru R, et al. Correlation between non-invasive myocardial work indices and main parameters of systolic and diastolic function: results from the EACVI NORRE study. *Eur Heart J Cardiovasc Imaging* 2020;21:533-41.
10. Wang CL, Chan YH, Wu VC, et al. Incremental prognostic value of global myocardial work over ejection fraction and global longitudinal strain in patients with heart failure and reduced ejection fraction. *Eur Heart J Cardiovasc Imaging* 2021;22:348-56.
11. Edwards NFA, Scalia GM, Shiino K, et al. Global Myocardial Work Is Superior to Global Longitudinal Strain to Predict Significant Coronary Artery Disease in Patients With Normal Left Ventricular Function and Wall Motion. *J Am Soc Echocardiogr* 2019;32:947-57.
12. Liao L, Shi B, Ding Z, et al. Echocardiographic study of myocardial work in patients with type 2 diabetes mellitus. *BMC Cardiovasc Disord* 2022;22:59.
13. Chan J, Edwards NFA, Khandheria BK, et al. A new approach to assess myocardial work by non-invasive left ventricular pressure-strain relations in hypertension and dilated cardiomyopathy. *Eur Heart J Cardiovasc Imaging* 2019;20:31-9.
14. Management of Diabetes in Pregnancy: Standards of Medical Care in Diabetes-2020. *Diabetes Care* 2020;43:S183-92.
15. Zielinsky P, Piccoli AL Jr. Myocardial hypertrophy and dysfunction in maternal diabetes. *Early Hum Dev* 2012;88:273-8.
16. Turan S, Turan OM, Miller J, et al. Decreased fetal cardiac performance in the first trimester correlates with hyperglycemia in pregestational maternal diabetes. *Ultrasound Obstet Gynecol* 2011;38:325-31.
17. El-Ganzoury MM, El-Masry SA, El-Farrash RA, et al. Infants of diabetic mothers: echocardiographic measurements and cord blood IGF-I and IGFBP-1. *Pediatr Diabetes* 2012;13:189-96.
18. Voigt JU, Cvijic M. 2- and 3-Dimensional Myocardial

- Strain in Cardiac Health and Disease. *JACC Cardiovasc Imaging* 2019;12:1849-63.
19. Petoello E, Flore AI, Nogara S, et al. Global longitudinal strain is an informative index of left ventricular performance in neonates receiving intensive care. *Sci Rep* 2024;14:8881.
 20. Iwashima S, Hayano S, Murakami Y, et al. Cardiac Function in Infants Born to Mothers With Gestational Diabetes - Estimation of Early Diastolic Intraventricular Pressure Differences. *Circ Rep* 2019;1:378-88.
 21. Smith A, Franklin O, McCallion N, et al. Effect of Gestational Diabetes Mellitus on Neonatal Myocardial Function. *Neonatology* 2021;118:64-72.
 22. Semertzidou A, Grout-Smith H, Kalliala I, et al. Diabetes and anti-diabetic interventions and the risk of gynaecological and obstetric morbidity: an umbrella review of the literature. *BMC Med* 2023;21:152.
 23. Depla AL, De Wit L, Steenhuis TJ, et al. Effect of maternal diabetes on fetal heart function on echocardiography: systematic review and meta-analysis. *Ultrasound Obstet Gynecol* 2021;57:539-50.
 24. Ghandi Y, Habibi D, Nasri K, et al. Effect of well-controlled gestational diabetes on left ventricular diastolic dysfunction in neonates. *J Matern Fetal Neonatal Med* 2019;32:2101-6.
 25. Smith A, Franklin O, McCallion N, et al. Assessment of Myocardial Function in Infants of Mothers with Gestational Diabetes Mellitus Using Deformation Imaging over the First Year of Age. *J Pediatr* 2023;263:113645.
 26. Iwashima S, Yanase Y, Takahashi K, et al. Non-Invasive Myocardial Work Indices in Infants Born to Mothers With Diabetes in Pregnancy. *Circ J* 2023;87:1095-102.
 27. Al-Biltagi M, El Razaky O, El Amrousy D. Cardiac changes in infants of diabetic mothers. *World J Diabetes* 2021;12:1233-47.
 28. Mather KJ, Hutchins GD, Perry K, et al. Assessment of myocardial metabolic flexibility and work efficiency in human type 2 diabetes using 16-[18F]fluoro-4-thiapalmitate, a novel PET fatty acid tracer. *Am J Physiol Endocrinol Metab* 2016;310:E452-E460.
 29. Chen B, Du YR, Zhu H, et al. Maternal inheritance of glucose intolerance via oocyte TET3 insufficiency. *Nature* 2022;605:761-6.
 30. Nold JL, Georgieff MK. Infants of diabetic mothers. *Pediatr Clin North Am* 2004;51:619-37, viii.

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