



Subclinical myocardial dysfunction assessed by two-dimensional speckle-tracking echocardiography in children and adolescents with prediabetes

Cardiac function in children with prediabetes

Gülçin Arslan¹ Müge Nasırlı¹ Hakan Dedecengiz² Barış Güven³ Eren Er¹ Bumin Nuri Dündar⁴

¹Department of Pediatric Endocrinology, İzmir City Hospital, İzmir, Türkiye.

²Department of Pediatric Cardiology, İzmir City Hospital, İzmir, Türkiye.

³Department of Pediatric Cardiology, İzmir Tepecik Training and Research Hospital, University of Health Sciences, İzmir, Türkiye.

⁴Department of Pediatric Endocrinology, Faculty of Medicine, İzmir Kâtip Çelebi University, İzmir, Türkiye.

Abstract

Aim: Prediabetes is associated with an increased risk of cardiovascular morbidity. Although cardiovascular dysfunction is well documented in diabetes, evidence regarding cardiac involvement in children with prediabetes remains limited. This study aimed to evaluate subclinical myocardial dysfunction using two-dimensional speckle-tracking echocardiography (2D-STE) in asymptomatic children and adolescents with prediabetes.

Methods: Thirty-two children with obesity and prediabetes and 28 controls underwent laboratory evaluation and echocardiographic assessment, including conventional echocardiography, tissue Doppler imaging, and 2D-STE.

Results: Prediabetic children demonstrated significantly higher left ventricular end-systolic volume, left ventricular mass, left ventricular internal diameters, and posterior wall thickness. Diastolic function parameters were impaired, with lower tricuspid E/A ratios and reduced mitral septal and lateral e' velocities. Global longitudinal strain values were also significantly lower in the prediabetes group. In contrast, conventional systolic function parameters, including left ventricular ejection fraction, fractional shortening, and tricuspid annular plane systolic excursion, were similar between groups. After adjustment for body mass index and age, only the association between prediabetes and the tricuspid E/A ratio remained significant.

Conclusion: Children with prediabetes showed subtle differences in selected echocardiographic parameters despite preserved conventional systolic function. However, after adjustment for body mass index (BMI) and age, only the tricuspid E/A ratio remained significantly associated with prediabetes. These findings should be considered exploratory, and their clinical significance requires confirmation in larger longitudinal studies.

Keywords

global longitudinal strain, 2D-STE, prediabetes, subclinical myocardial dysfunction

DOI: 10.4328/ACAM.00021

Ann Clin Anal Med 2026;17(10):1117-1121

Received: 12.08.2026

Accepted: 12.09.2026

Published Online: 06.09.2026

Printed: 01.10.2026

Corresponding Author: Gülçin Arslan, Department of Pediatric Endocrinology, İzmir City Hospital, İzmir, Türkiye.

Email: gulcinak_005@hotmail.com P.: +90 555 811 95 77

Corresponding Author ORCID: <https://orcid.org/0000-0003-4506-2654>

Other Authors ORCID: Müge Nasırlı, <https://orcid.org/0000-0001-6540-9809> • Hakan Dedecengiz, <https://orcid.org/0000-0003-3088-7311> • Barış Güven, <https://orcid.org/0000-0002-4520-5574> • Eren Er, <https://orcid.org/0003-4770-0365> • Bumin Nuri Dündar, <https://orcid.org/0000-0002-7506-061X>

Introduction

The majority of existing studies have focused on cardiovascular risks associated with prolonged duration of diabetes.¹ Therefore, these observations raise the question of whether similar abnormalities may also be present during the prediabetic stage. Although comparatively limited data are available regarding outcomes during the prediabetic stage, several studies have identified prediabetes as a strong predictor of cardiovascular disease (CVD).²

Diabetes mellitus adversely affects myocardial structure and function, contributing to both systolic and diastolic impairment, yet the exact mechanisms underlying these alterations are still not fully clarified.³ Most research on myocardial dysfunction in diabetes has predominantly focused on left ventricular involvement. However, growing evidence suggests that right ventricular involvement also contributes significantly to cardiac function and prognosis in diabetic cardiomyopathy, especially in cases accompanied by left ventricular diastolic dysfunction and/or reduced ejection fraction, pathological hypertrophy, and interstitial fibrosis. It is widely thought that diabetic cardiomyopathy initially manifests as left ventricular diastolic dysfunction, while systolic dysfunction develops as the disease progresses.⁴

Prediabetes refers to a metabolic state in which blood glucose levels are above the normal range but do not meet the diagnostic criteria for diabetes mellitus. The prediabetic state includes isolated impaired fasting glucose (IFG), isolated impaired glucose tolerance (IGT) that is associated with insulin resistance in individuals with obesity, and the coexistence of IFG and IGT.⁵ These entities represent different phenotypic expressions of a single pathological process and are associated with an increased risk of developing type 2 diabetes mellitus (T2DM), although they may have distinct associations with clinical outcomes and mortality.⁶ Prediabetic individuals often present with cardiovascular risk profiles commonly observed in type 2 diabetes mellitus.⁷

This emphasizes the need for early identification of prediabetic patients and primary prevention of atherosclerotic cardiovascular disease (ASCVD). The components of metabolic syndrome are often found in prediabetic patients, long before the transition to T2DM. The metabolic syndrome doubles the risk of ASCVD and is accountable for increasing the risk of progression to diabetes four to five times.⁸ Furthermore, mechanisms other than hyperglycemia that coexist and are interdependent are involved in the onset and progression of diabetes and its complications, especially cardiovascular disease. Therefore, in addition to the hyperglycemic environment, increased secretion of adipocyte cytokines (adipokines) and oxidative stress with secondary chronic inflammation that promotes vascular endothelial dysfunction, hypertension, atherogenic dyslipidemia, and a prothrombotic status also contribute to the development of CVD, even in the absence of progression to overt diabetes.⁷

Reports have shown that two-dimensional (2D) speckle tracking technology is an effective method for evaluating left ventricular function.⁹ It also allows quantitative analysis of myocardial deformation and strain, enabling the detection of subtle myocardial dysfunction before overt clinical manifestations and providing detailed assessment at global, regional, and segmental levels. The objective of this study was to determine whether asymptomatic children and adolescents with prediabetes exhibit early myocardial dysfunction detectable by two-dimensional speckle-tracking echocardiography (2D-STE).

Materials and Methods

This prospective case-control study included all consecutive eligible patients with obesity and prediabetes who presented to the Pediatric Endocrinology Clinic at our hospital during the study period (October 2025 to April 2026), for a total sample size of 32. In addition, we enrolled 28 healthy controls. Prediabetes was defined according to the American Diabetes Association criteria as impaired fasting glucose (100–125 mg/dL) and/or HbA1c levels of 5.7–6.4%.¹⁰ We excluded patients with genetic/syndromic or endocrine causes of obesity and those receiving medications that may affect body weight, blood glucose, and insulin levels. Height, weight, body mass index (BMI), and corresponding standard deviation score (SDS) values were measured using a stadiometer and electronic scale, and SDS was calculated using the Childmetrics tool of the Turkish Pediatric Endocrinology and Diabetes Society, based on growth data by Olcay Neyzi.^{11,12} Obesity was defined per World Health Organization (WHO) growth standards: BMI-for-age z-score > +2 SD for those 5–19 years.¹³ Blood samples, collected after 12-hour fasting in the early morning, were reviewed for complete blood count, lipid profile, glycated hemoglobin (HbA1c), fasting plasma glucose and insulin levels, and the Homeostatic Model Assessment of Insulin Resistance (HOMA-IR). Insulin resistance was estimated using HOMA-IR, calculated from fasting blood samples as fasting glucose [mg/dL] × fasting insulin [μU/mL] / 405.¹⁴

The same experienced pediatric cardiologist performed a comprehensive echocardiographic evaluation, including conventional echocardiography, tissue Doppler imaging, two-dimensional strain, and 2D-STE, blinded to participants' metabolic status, to assess cardiac function. Echocardiographic examinations were performed using a GE HealthCare Vivid E95 ultrasound system equipped with an M5Sc transducer (GE HealthCare, Horten, Norway). Two-dimensional speckle-tracking echocardiography (2D-STE) is an advanced, angle-independent imaging modality that enables quantitative assessment of myocardial deformation by tracking natural acoustic markers ("speckles") within the myocardium throughout the cardiac cycle. Compared with conventional echocardiographic methods, 2D-STE is more sensitive in detecting subtle and subclinical myocardial dysfunction before overt systolic impairment becomes apparent.¹⁵ For 2D-STE analysis, high-quality apical and short-axis images obtained over consecutive cardiac cycles are analyzed using dedicated software after manual delineation of the endocardial border. The software automatically segments the myocardium and calculates strain and strain rate parameters reflecting regional and global myocardial mechanics, including global longitudinal strain (GLS), a sensitive marker of early myocardial dysfunction.¹⁵ Previous studies have demonstrated the utility of 2D-STE in identifying early myocardial alterations associated with diabetes and prediabetes, suggesting its potential role in the early detection of diabetic cardiomyopathy and metabolic cardiac remodeling.¹⁵

Ethical Approval

This study was approved by the Institutional Clinical Research Ethics Committee (Date: 26.09.2025, Decision No: 2025/292).

Statistical Analysis

All analyses were performed using SPSS Statistics version 27.0 (IBM Corp., Armonk, NY, USA). We assessed the distribution of continuous variables using histograms, Q-Q plots, and skewness-kurtosis values. Normally distributed variables were expressed as mean (SD), while non-normally distributed variables were presented as median (Q1–Q3). Categorical variables were presented as counts and

Table 1. Comparison Of Anthropometric Measurements And Laboratory Data Between The Prediabetes Group And The Control Group

Parameters	Patient group	Control group	P value
Sex, female/male	18/14	10/18	.128
Age, y	14.03 ± 2.40	12.28 ± 2.69	.01*
Body weight, kg	85.93 ± 27.12	44.78 ± 14.07	<.001*
Weight SDS	2.85 ± 1.86	−0.21 ± 1.01	<.001*
Height, cm	161.79 ± 11.63	151.72 ± 15.73	.006*
Height SDS	0.30 ± 1.26	0.03 ± 1.02	.365
BMI, kg/m ²	31.83 ± 7.93	18.88 ± 3.44	<.001*
BMI SDS	2.44 ± 1.41	−0.18 ± 1.15	<.001*
Fasting plasma glucose, mg/dL	97.44 ± 13.66	88.76 ± 7.34	.019*
Insulin, µIU/mL	41.01 ± 27.79	9.30 ± 4.16	<.001*
HOMA-IR	9.89 ± 6.87	2.08 ± 1.08	<.001*
HbA1c, %	5.84 ± 0.30	5.12 ± 0.27	<.001*
Triglycerides, mg/dL	109.33 ± 55.42	72.93 ± 29.00	.006*
HDL cholesterol, mg/dL	47.68 ± 12.61	52.66 ± 12.88	.222
LDL cholesterol, mg/dL	83.61 ± 26.84	85.42 ± 23.01	.825
Total cholesterol, mg/dL	152.56 ± 29.45	152.78 ± 33.53	.983

Abbreviations; BMI, body mass index; BMI SDS, body mass index standard deviation score; HOMA-IR, homeostasis model assessment of insulin resistance; HbA1c, glycated hemoglobin; *Statistically significant (*P* < .05).

Table 2. Comparison Of Echocardiographic Measurements Between The Prediabetes Group And The Control Group

Parameters	Patient group	Control group	P value
LVEDV index, mL/m ²	91.88 ± 29.20	79.14 ± 22.99	.068
LVESV index, mL/m ²	29.28 ± 9.10	24.39 ± 6.55	.021*
LVM, g	107.54 ± 39.71	85.88 ± 32.41	.026*
LVMI, g/m ²	28.66 ± 8.67	26.52 ± 5.53	.268
LVEF, %	67.63 ± 4.44	68.93 ± 4.30	.255
Tricuspid E/A ratio	1.54 ± 0.28	1.81 ± 0.39	.003*
Mitral E/A ratio	1.74 ± 0.40	1.87 ± 0.35	.210
Mitral septal e', cm/s	15 ± 1	16 ± 2	.048*
Mitral septal a', cm/s	9.3 ± 1	9 ± 1	.374
Mitral septal s', cm/s	10 ± 1	9 ± 1	.007*
Mitral lateral e', cm/s	16 ± 2	18 ± 2	.033*
Mitral lateral a', cm/s	8 ± 1	7 ± 1	.015*
Mitral lateral s', cm/s	11 ± 1	10 ± 1	.338
TAPSE, mm	2.30 ± 0.35	2.20 ± 0.34	.291
LVIDd, cm	4.42 ± 0.64	4.10 ± 0.57	.044*
LVIDs, cm	2.75 ± 0.37	2.55 ± 0.27	.022*
FS, %	37.50 ± 3.77	38.36 ± 3.64	.376
LVPWd, cm	0.80 ± 0.16	0.70 ± 0.12	.016*
ICT, ms	59.84 ± 6.51	59.14 ± 7.30	.696
IRT, ms	53.91 ± 6.76	51.07 ± 7.59	.132
LVGLS, %	−17.13 ± 2.37	−18.43 ± 2.60	.046*

Abbreviations; LVEDV, left ventricular end-diastolic volume index; LVESV, left ventricular end-systolic volume index; LVM, left ventricular mass; LVMI, left ventricular mass index; LVEF, left ventricular ejection fraction; TAPSE, tricuspid annular plane systolic excursion; LVIDd, left ventricular internal diameter at end-diastole; LVIDs, left ventricular internal diameter at end-systole; FS, fractional shortening; LVPWd, left ventricular posterior wall thickness at end-diastole; ICT, isovolumetric contraction time; IRT, isovolumetric relaxation time; LVGLS, left ventricular global longitudinal strain. *Statistically significant (*P* < .05).

percentages. Comparisons between groups were performed using Student’s t-test for normally distributed continuous variables and the Mann–Whitney U test for non-normally distributed variables. Categorical variables were analyzed using the Chi-square test or Fisher’s exact test, as appropriate. Linear regression analysis was performed to assess the association between prediabetes status and echocardiographic parameters after adjustment for BMI and age. Unstandardized regression coefficients (B), 95% confidence

intervals (CIs), and *P* values were reported.

Reporting Guidelines

This study was reported according to the STROBE guidelines.

Results

The mean (SD) age of the 32 prediabetic patients was 14.03 (2.40) years, and 18 (56.2%) were female; the 28 controls had a mean (SD)

age of 12.28 (2.69) years, and 10 (35.7%) were female. Compared with healthy controls, children with prediabetes had significantly higher body weight SDS (mean [SD], 2.85 [1.86] vs. -0.21 [1.01]), greater height (mean [SD], 161.79 [11.63] cm vs. 151.72 [15.73] cm), higher height SDS (mean [SD], 0.30 [1.26] vs. 0.03 [1.02]), increased BMI (mean [SD], 31.83 [7.93] kg/m² vs. 18.88 [3.44] kg/m²), and higher BMI SDS (mean [SD], 2.44 [1.41] vs. -0.18 [1.15]). Anthropometric and laboratory data are presented in Table 1, and echocardiographic data in Table 2. Echocardiographic evaluation showed significantly higher left ventricular end-systolic volume index, left ventricular mass, left ventricular internal diameters, and posterior wall thickness in children with prediabetes compared with healthy controls (all $P < .05$). Significant differences were also observed in several diastolic and myocardial tissue Doppler parameters; the tricuspid E/A ratio was significantly lower, and mitral septal and lateral e' velocities were significantly reduced in the study group. Left ventricular global longitudinal strain (LVGLS) values were also significantly lower in prediabetic children. In contrast, conventional systolic function parameters—including left ventricular ejection fraction, fractional shortening, and TAPSE—were similar between the two groups. Comparison of echocardiographic parameters between patients with severe obesity (BMI SDS $> +3$) and those with obesity (BMI SDS $+2$ to $+3$) revealed no statistically significant differences. In linear regression analysis adjusted for body mass index and age, we identified a mild but significant inverse association between prediabetes status and the tricuspid E/A ratio ($B = -0.20$, 95% CI [-0.38, -0.01], $P = .035$).

Discussion

In this study, children and adolescents with prediabetes demonstrated evidence of early subclinical myocardial alterations despite preserved conventional systolic function. Prediabetic patients exhibited increased left ventricular dimensions and mass, impaired diastolic parameters, and reduced LVGLS values compared with healthy controls. Notably, after adjustment for BMI and age, only the tricuspid E/A ratio remained significantly associated with prediabetes status. However, residual confounding related to obesity, insulin resistance, and other metabolic factors cannot be excluded.

Children with prediabetes had significantly higher fasting plasma glucose, insulin, HOMA-IR, HbA1c, and triglyceride levels than healthy controls, reflecting impaired glucose metabolism and increased insulin resistance in this population. In particular, markedly elevated insulin and HOMA-IR values support the presence of substantial insulin resistance, which is considered a key pathophysiological mechanism in the development of prediabetes and progression toward type 2 diabetes mellitus.¹⁶ Higher triglyceride levels observed in the prediabetes group are also consistent with the dyslipidemic profile commonly associated with insulin resistance and metabolic dysfunction.¹⁷ Although HDL cholesterol levels were lower in the prediabetes group, the difference was not statistically significant. Similarly, LDL and total cholesterol levels were comparable between groups.

Echocardiographic assessment revealed significantly higher left ventricular end-systolic volume, left ventricular mass, left ventricular internal diameters, and posterior wall thickness in children with prediabetes compared with controls. The increased left ventricular mass, ventricular dimensions, and posterior wall thickness observed in our prediabetes cohort may reflect early cardiac remodeling associated with insulin resistance and metabolic dysregulation.¹⁸ Similar structural alterations have

previously been reported in children and adolescents with obesity and impaired glucose metabolism, suggesting that adverse myocardial changes may begin before the development of overt diabetes.^{19–21} Insulin resistance, hyperinsulinemia, and low-grade inflammation have been proposed as potential mechanisms contributing to myocardial hypertrophy and ventricular remodeling in this population.^{18,19} In addition, preserved conventional systolic parameters despite impaired LVGLS values support the concept that subclinical myocardial dysfunction may precede overt systolic impairment in children with metabolic abnormalities.^{19,20}

Our findings demonstrated significant alterations in several diastolic and myocardial tissue Doppler parameters in prediabetic children, including lower tricuspid E/A ratios and reduced mitral septal and lateral e' velocities, suggesting early impairment in ventricular relaxation and diastolic function. In addition, the significantly lower LVGLS values in the prediabetic group support subclinical myocardial dysfunction, even in the absence of overt systolic impairment detected by conventional echocardiographic parameters. These findings may reflect the combined influence of obesity and metabolic disturbances associated with prediabetes on cardiac function. These findings are consistent with previous studies reporting impaired diastolic indices and reduced myocardial strain parameters in children and adolescents with prediabetes, insulin resistance, and other metabolic abnormalities, suggesting that myocardial involvement may begin early in the course of metabolic dysregulation.^{20,22} In contrast to the altered diastolic and deformation parameters, conventional systolic function indices, including left ventricular ejection fraction, fractional shortening, and TAPSE, remained preserved in prediabetic children, suggesting that subclinical myocardial involvement may occur before overt systolic dysfunction becomes detectable by standard echocardiographic measurements. Furthermore, after adjustment for BMI and age, only the association between prediabetes status and the tricuspid E/A ratio remained significant. This finding should be interpreted cautiously, as residual confounding by obesity, insulin resistance, and other metabolic abnormalities cannot be excluded. These findings are in line with previous studies demonstrating impaired myocardial strain and diastolic function despite preserved conventional systolic parameters in individuals with prediabetes and diabetes, supporting the concept of early diabetic cardiomyopathy and subclinical ventricular dysfunction.^{23–25}

Limitations

Although this study provides important insights into early myocardial alterations in pediatric prediabetes, several limitations should be acknowledged. First, the relatively small sample size and single-center design may limit the generalizability of the findings. Second, the prediabetes group had significantly higher BMI values and differed in age compared with controls; although regression analysis was adjusted for both BMI and age, residual confounding related to obesity, insulin resistance, and other metabolic factors cannot be completely excluded. The slight age difference between the groups and the absence of age-normalized echocardiographic Z-scores may have influenced some of the observed differences. Moreover, no correction for multiple echocardiographic comparisons was applied, which may increase the risk of type I error, and the observational design precludes conclusions regarding an independent or causal effect of prediabetes on myocardial function. In addition, we did not evaluate advanced metabolic and inflammatory biomarkers potentially associated with myocardial dysfunction. Finally, strain measurements obtained by 2D-speckle

tracking echocardiography may be influenced by image quality and vendor-specific variability. In this study, preserved left ventricular ejection fraction despite impaired myocardial strain parameters has been considered an indicator of early subclinical myocardial dysfunction in metabolic disorders. Further longitudinal studies with larger cohorts are needed to determine whether these subclinical alterations have clinical or prognostic significance.

Conclusion

In conclusion, children and adolescents with prediabetes showed subtle differences in selected echocardiographic parameters despite preserved conventional systolic function. However, after adjustment for BMI and age, only the tricuspid E/A ratio remained significantly associated with prediabetes. Therefore, these findings should be considered exploratory and do not establish an independent or causal effect of prediabetes on myocardial function. Larger longitudinal studies are needed to determine their clinical and prognostic significance.

Declarations

Animal and Human Rights Statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed Consent

Written informed consent was obtained from the parents/legal guardians of all participants.

Data Availability

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflict of Interest

The authors declare no conflict of interest.

Funding

None.

Author Contributions (CRediT Taxonomy)

Conceptualization: G.A.
Methodology: G.A.
Formal Analysis: G.A., E.E.
Investigation: G.A., M.N., H.D.
Data Curation: G.A., M.N., H.D.
Writing – Original Draft Preparation: G.A.
Writing – Review & Editing: B.G., B.N.D.
Supervision: B.G., B.N.D.

AI Usage Disclosure

The authors declare that no AI-assisted technologies were used.

Acknowledgements

The authors thank all patients and their families for participation in the study.

Abbreviations

BMI: Body mass index
BMI SDS: Body mass index standard deviation score
HbA1c: Glycated hemoglobin
HOMA-IR: Homeostasis model assessment of insulin resistance

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How to Cite

Gülçin Arslan, Müge Nasırlı, Hakan Dedeçengiz, Barış Güven, Eren Er, Bumin Nuri Dündar. Subclinical myocardial dysfunction assessed by two-dimensional speckle-tracking echocardiography in children and adolescents with prediabetes. *Ann Clin Anal Med* 2026;17(10):1117-1121. doi:10.4328/ACAM.00021