E-ISSN 2250-0944
ISSN 2250-1150
doi: 10.31838/ijprt/16.02.492

Research Article

Correlation of Myocardial Performance Index with Serum Nt-Probnp Levels in Asymptomatic Type 2 Diabetes Mellitus

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Received: 14.07.26, Revised: 11.08.26, Accepted: 09.09.26

ABSTRACT
Background: Type 2 diabetes mellitus (T2DM) may cause progressive myocardial injury before heart failure symptoms or a reduction in left ventricular ejection fraction becomes evident. The myocardial performance index (MPI) integrates systolic and diastolic time intervals, whereas N-terminal pro-B-type natriuretic peptide (NT-proBNP) reflects myocardial wall stress. Their relationship may provide a pragmatic strategy for identifying subclinical diabetic cardiac dysfunction.
Methods: This single-centre cross-sectional observational study included 80 adults with asymptomatic T2DM. Clinical characteristics, body mass index, duration of diabetes, blood pressure and glycated haemoglobin (HbA1c) were recorded. Doppler echocardiography was used to determine MPI, left ventricular ejection fraction (LVEF) and diastolic dysfunction grade. Serum NT-proBNP was measured by the institution's standardized laboratory method. Correlation analysis assessed relationships between MPI and NT-proBNP, age, HbA1c, diastolic dysfunction and LVEF. Receiver operating characteristic (ROC) analysis evaluated NT-proBNP for detecting abnormal MPI (>=0.40).
Results: Mean age was 57.3 +/- 8.4 years; 48 participants (60.0%) were male, 67 (83.75%) were obese and mean diabetes duration was 7.9 +/- 2.8 years. Abnormal MPI was present in 59 of 80 patients (73.8%), while 59 of 80 (73.75%) had diastolic dysfunction; no participant had LVEF <50%. Mean NT-proBNP increased stepwise from 54.1 +/- 7.3 pg/mL in normal MPI to 150.3 +/- 10.7 pg/mL in severe MPI abnormality ($p<0.001$). MPI correlated strongly with NT-proBNP ($r=0.926$), HbA1c ($r=0.854$), diastolic dysfunction grade ($r=0.845$) and age ($r=0.782$), and inversely with LVEF ($r=-0.716$); all reported p values were <0.001. NT-proBNP >=66 pg/mL identified abnormal MPI with an AUC of 0.982 (95% CI 0.962-1.000), 95.3% sensitivity and 90.5% specificity.
Conclusion MPI is a simple, non-invasive marker of early global cardiac dysfunction in asymptomatic patients with T2DM and shows excellent correlation with serum NT-proBNP levels. Combined use of echocardiographic and biochemical markers may improve early cardiovascular risk stratification.

Keywords: Type 2 Diabetes Mellitus, Myocardial Performance Index, Tei Index, NT-Probnp, Diabetic Cardiomyopathy, Subclinical Left Ventricular Dysfunction, Echocardiography.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is one of the defining chronic diseases of contemporary medicine. The International Diabetes Federation estimated that 536.6 million adults aged 20-79 years were living with diabetes in 2021 and projected an increase to 783.2 million by 2045 [1]. Cardiovascular disease remains the dominant determinant of premature morbidity and mortality, but the myocardial consequences of diabetes extend beyond clinically apparent atherosclerotic disease. Diabetic cardiomyopathy describes structural and functional myocardial abnormalities occurring in association with diabetes, often before overt heart failure and sometimes in the absence of recognized coronary, valvular or hypertensive heart disease [2].

The early phenotype is frequently subtle. Hyperglycaemia, insulin resistance and lipotoxicity promote mitochondrial dysfunction, oxidative stress, advanced glycation, microvascular injury, inflammation, impaired calcium handling and interstitial fibrosis. These processes increase ventricular stiffness and

prolong relaxation before they measurably reduce ejection fraction [2]. A meta-analysis of echocardiographic studies estimated left ventricular diastolic dysfunction in approximately 35% of community-based and 48% of hospital-based populations with T2DM, underscoring the magnitude of clinically silent disease [3]. Boyer et al. similarly documented a substantial prevalence of diastolic dysfunction among asymptomatic normotensive diabetic patients, despite preserved conventional systolic function [4].

Conventional left ventricular ejection fraction (LVEF) is therefore an incomplete screening measure. The myocardial performance index (MPI), or Tei index, combines isovolumic contraction time and isovolumic relaxation time relative to ejection time, thereby summarizing global systolic-diastolic performance in a dimensionless measure. In early T2DM, Pattoneri et al. demonstrated higher MPI than in matched controls and a positive relationship with glycated haemoglobin [5]. Saglam et al. reported increased MPI in asymptomatic normotensive T2DM and associations with fasting glucose, diabetes duration, body mass index and echocardiographic measures [6]. An Indian observational study by Goroshi and Chand found MPI to be highly sensitive for diabetic cardiac dysfunction and strongly related to diastolic dysfunction grade [7].

N-terminal pro-B-type natriuretic peptide (NT-proBNP) offers a complementary biological signal. Released in response to myocardial wall stress, it is established in heart failure diagnosis and prognosis, but lower concentrations may still carry information in asymptomatic diabetes. Epshteyn et al. showed that BNP could identify unsuspected ventricular dysfunction in diabetic patients, although performance differed according to the pretest clinical context [8]. The clinical proposition is attractive: a blood biomarker could enrich the population undergoing echocardiography, while MPI could identify global dysfunction before LVEF declines. However, the direct relationship between NT-proBNP and MPI in asymptomatic T2DM remains insufficiently characterized, particularly in Indian tertiary-care populations. This study therefore evaluated MPI and serum NT-proBNP in asymptomatic T2DM, examined their correlation, and assessed associations of MPI with age, glycaemic control, diastolic dysfunction and LVEF.

MATERIALS AND METHODS

Study design and setting

A cross-sectional observational study was conducted in the Department of General Medicine, The Oxford Medical College Hospital and Research Centre, Bengaluru, India, from July 2023 to January 2025 Eighty participants were evaluated. The protocol was approved by the Institutional Ethics Committee.

Participants

Adults aged 18 years or older with established T2DM who were clinically asymptomatic for overt cardiac disease were eligible. Asymptomatic status and protocol-specific eligibility were established by clinical assessment before enrolment, and written informed consent was obtained. Protocol-defined exclusion criteria were history of hypertension, ischemic heart disease, heart failure, or valvular heart disease, Symptoms suggestive of cardiac disease (chest pain, dyspnoea, palpitations), Previous coronary intervention or angiography, Chronic alcoholism, Long-term steroid therapy Pregnancy. The analysed cohort comprised all 80 participants with complete clinical, biochemical and echocardiographic measurements.

Clinical and Biochemical Assessment

Age, sex, body mass index (BMI), duration of diabetes, systolic and diastolic blood pressure, smoking status and alcohol use were recorded. BMI was classified using Asian cut-offs as normal (18.5-22.9 kg/m2), overweight (23.0-24.9 kg/m2) and obese (>=25 kg/m2). Glycaemic status was assessed using HbA1c. Serum NT-proBNP was quantified using the Finecare NT-proBNP Rapid Quantitative Test, a fluorescence immunoassay, on the Finecare FIA System (Guangzhou Wondfo Biotech Co., Ltd., China), according to the manufacturer's instructions. Venous blood samples were collected and processed as per standard laboratory protocols.

Echocardiographic Assessment

Transthoracic echocardiography included Doppler assessment of left ventricular inflow and outflow, LVEF and diastolic function. MPI was calculated as (isovolumic contraction time + isovolumic relaxation time)/ejection time [5-7]. MPI was categorized as normal (<0.40), mildly abnormal (0.40-0.49), moderately abnormal (0.50-0.59) or severely abnormal

(>=0.60). Diastolic function was graded as normal or grades I-III. LVEF was grouped as >60%, 55-60%, 50-54% and <50%.

Statistical Analysis

Continuous variables were summarized as mean +/- standard deviation and categorical variables as number and percentage. Mean NT-proBNP concentrations were compared across prespecified MPI categories using a parametric group comparison with contrasts against normal MPI. Correlation coefficients (r) quantified relationships between MPI and NT-proBNP, age, HbA1c, diastolic dysfunction grade and LVEF. ROC analysis evaluated NT-proBNP as a predictor of abnormal MPI (>=0.40); the area under the curve (AUC), optimal cut-off, sensitivity, specificity, predictive values and likelihood ratios were reported with 95% confidence intervals where available. Tests were two-sided and $p<0.05$ indicated statistical significance.

RESULTS

The study included 80 adults with asymptomatic T2DM. Mean age was 57.3 +/- 8.4 years, and 58 of 80 participants (72.6%) were aged 46-65 years. Men constituted 60.0% of the cohort. Obesity was highly prevalent: 67 patients (83.75%) had BMI >=25 kg/m2, 12 (15.0%) were overweight and only one had a normal BMI. Mean duration of diabetes was 7.9 +/- 2.8 years; 39 patients (48.8%) had diabetes for 5-7 years, 25 (31.3%) for 8-10 years and 16 (20.0%) for more than 10 years. Mean systolic and diastolic blood pressures were 124.2 +/- 6.1 and 79.6 +/- 4.1 mmHg. Sixteen participants each reported smoking and alcohol consumption. Mean HbA1c was 8.0 +/- 1.0%, and 64 patients (80.0%) had HbA1c >=7%.

NT-proBNP was <60 pg/mL in 21 patients (26.25%), 60-119 pg/mL in 40 (50.0%) and >120 pg/mL in 19 (23.75%). MPI was normal in 21 participants (26.3%); 31 (38.8%) had mild, 22 (27.5%) moderate and six (7.5%) severe abnormality. Accordingly, 59 of 80 patients (73.8%) had abnormal MPI despite the absence of reported cardiac symptoms. LVEF remained conventionally preserved: 25 patients (31.3%) had LVEF >60%, 38 (47.5%) had 55-60%, 17 (21.3%) had 50-54% and none had LVEF <50%. Diastolic dysfunction was nevertheless present in 59 participants (73.75%), most commonly grade I (40.0%), followed by grade II (26.25%) and grade III (7.5%).

A graded increase in NT-proBNP accompanied worsening MPI. Mean NT-proBNP was 54.1 +/- 7.3 pg/mL in the normal MPI group, 80.3 +/- 5.2 pg/mL with mild abnormality, 116.2 +/- 16.9 pg/mL with moderate abnormality and 150.3 +/- 10.7 pg/mL with severe abnormality; each abnormal category differed significantly from the normal reference ($p<0.001$). MPI demonstrated a very strong positive correlation with NT-proBNP ($r=0.926$). Strong positive correlations were also observed with HbA1c ($r=0.854$), diastolic dysfunction grade ($r=0.845$) and age ($r=0.782$), whereas LVEF correlated inversely with MPI ($r=-0.716$). The reported associations were statistically significant at $p<0.001$.

ROC analysis showed excellent discrimination of abnormal MPI by NT-proBNP. The AUC was 0.982 (95% CI 0.962-1.000). A cut-off of 66 pg/mL yielded 95.3% sensitivity (95% CI 88.5-98.7%) and 90.5% specificity (95% CI 69.6-98.8%). Positive and negative predictive values were 96.8% and 86.4%, respectively. The positive likelihood ratio was 10.0 (95% CI 3.4-29.2), indicating a large increase in the probability of abnormal MPI after a positive result, while the negative likelihood ratio was 0.05 (95% CI 0.02-0.13), indicating substantial probability reduction after a negative result.

Table 1. Demographic, Metabolic and Clinical Characteristics of the Study Population (N=80)

Characteristic	Value
Age, mean +/- SD, years	57.3 +/- 8.4
Age 35-45 years	7 (8.8%)
Age 46-55 years	27 (33.8%)
Age 56-65 years	31 (38.8%)
Age >65 years	15 (18.8%)
Male sex	48 (60.0%)
Female sex	32 (40.0%)
Normal BMI, 18.5-22.9 kg/m2	1 (1.25%)
Overweight BMI, 23.0-24.9 kg/m2	12 (15.0%)

Obese BMI, >=25 kg/m2	67 (83.75%)
Diabetes duration, mean +/- SD, years	7.9 +/- 2.8
Diabetes duration 5-7 years	39 (48.8%)
Diabetes duration 8-10 years	25 (31.3%)
Diabetes duration >10 years	16 (20.0%)
Systolic blood pressure, mmHg	124.2 +/- 6.1
Diastolic blood pressure, mmHg	79.6 +/- 4.1
Current smoking	16 (20.0%)
Alcohol consumption	16 (20.0%)
HbA1c, mean +/- SD, %	8.0 +/- 1.0
HbA1c <7%	16 (20.0%)
HbA1c 7-8%	26 (32.5%)
HbA1c 8-9%	22 (27.5%)
HbA1c >9%	16 (20.0%)

The cohort represented predominantly middle-aged and older adults with prolonged diabetes, marked adiposity and suboptimal glycaemic control, but without elevated mean blood pressure. The concentration of participants between 46 and 65 years and the 83.75% prevalence of obesity identify a metabolically high-risk population in whom myocardial abnormalities may develop before symptoms. Because only 20% achieved HbA1c below 7%, the subsequent cardiac associations should be interpreted within a cohort exposed to sustained glycaemic stress.

Table 2. Distribution of NT-Probnp and Echocardiographic Phenotypes

Parameter/category	**n (%)**
NT-proBNP <60 pg/mL	21 (26.25%)
NT-proBNP 60-119 pg/mL	40 (50.0%)
NT-proBNP >120 pg/mL	19 (23.75%)
Normal MPI (<0.40)	21 (26.3%)
Mildly abnormal MPI (0.40-0.49)	31 (38.8%)
Moderately abnormal MPI (0.50-0.59)	22 (27.5%)
Severely abnormal MPI (>=0.60)	6 (7.5%)
LVEF >60%	25 (31.3%)
LVEF 55-60%	38 (47.5%)
LVEF 50-54%	17 (21.3%)
LVEF <50%	0 (0.0%)
Normal diastolic function	21 (26.25%)
Grade I diastolic dysfunction	32 (40.0%)
Grade II diastolic dysfunction	21 (26.25%)
Grade III diastolic dysfunction	6 (7.5%)

Three-quarters of participants had abnormal MPI and an almost identical proportion had diastolic dysfunction, although every patient retained LVEF of at least 50%. This discordance illustrates the limited sensitivity of conventional ejection fraction for early diabetic myocardial disease. Mild MPI abnormality and grade I diastolic dysfunction were the dominant phenotypes, suggesting that most detected disease remained at a potentially preclinical stage rather than representing advanced systolic failure. NT-proBNP elevation paralleled this subclinical functional burden.

Table 3. NT-Probnp across MPI Categories and Correlations with MPI

Analysis	**Category/parameter**	**Estimate**	**p value**
NT-proBNP by MPI	Normal (<0.40)	54.1 +/- 7.3 pg/mL	Reference
NT-proBNP by MPI	Mildly abnormal (0.40-0.49)	80.3 +/- 5.2 pg/mL	<0.001
NT-proBNP by MPI	Moderately abnormal (0.50-0.59)	116.2 +/- 16.9 pg/mL	<0.001
NT-proBNP by MPI	Severely abnormal (>=0.60)	150.3 +/- 10.7	<0.001

		pg/mL	
Correlation with MPI	NT-proBNP	r = 0.926	<0.001
Correlation with MPI	Age	r = 0.782	<0.001
Correlation with MPI	HbA1c	r = 0.854	<0.001
Correlation with MPI	Diastolic dysfunction grade	r = 0.845	<0.001
Correlation with MPI	LVEF	r = -0.716	<0.001

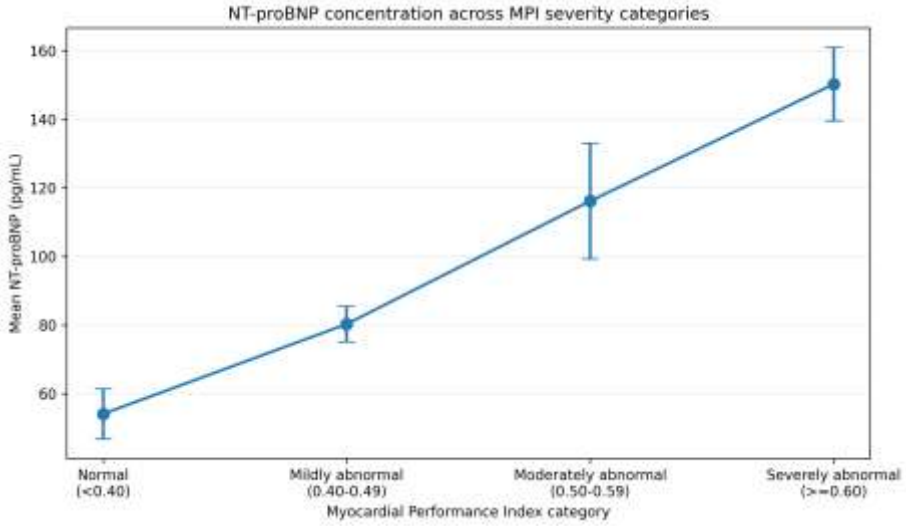
NT-proBNP rose monotonically across MPI categories, with an almost threefold difference between normal and severely abnormal global performance. The exceptionally strong correlation between MPI and NT-proBNP indicates that Doppler-derived prolongation of non-ejection intervals tracked closely with biochemical myocardial wall stress. Associations with age, HbA1c and diastolic dysfunction support a cumulative metabolic and ventricular-stiffness pathway. The inverse relationship with LVEF further demonstrates that MPI worsened even within the conventionally preserved ejection-fraction range.

Table 4. Diagnostic Performance of NT-Probnp for Abnormal MPI (>=0.40)

Parameter	**Estimate**	**95% confidence interval**
AUC	0.982	0.962-1.000
Optimal cut-off	66 pg/mL	Not reported
Sensitivity	95.3%	88.5%-98.7%
Specificity	90.5%	69.6%-98.8%
Positive predictive value	96.8%	90.1%-99.3%
Negative predictive value	86.4%	65.1%-97.1%
Positive likelihood ratio	10.0	3.4-29.2
Negative likelihood ratio	0.05	0.02-0.13

The ROC findings suggest that a serum NT-proBNP threshold of 66 pg/mL could identify abnormal MPI with high sensitivity and specificity in this dataset. A positive likelihood ratio of 10.0 provides strong rule-in information, whereas a negative likelihood ratio of 0.05 provides strong rule-out information. However, the cut-off was derived and evaluated in the same 80-patient cohort; therefore, apparent performance may be optimistic and should be validated prospectively across different ages, renal function levels and obesity profiles.

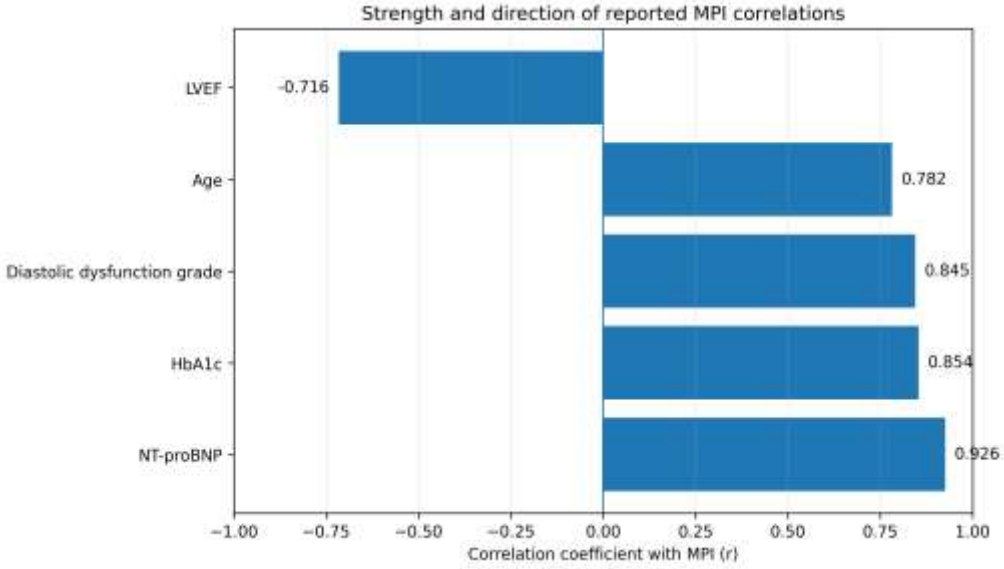
Figure 1. Mean Nt-Probnp Concentration across Mpi Severity Categories



The stepwise NT-proBNP gradient provides a visually coherent biological dose-response relationship rather than an isolated threshold effect. Error bars show that separation between adjacent MPI categories remained substantial despite within-group variability,

especially between normal, mild and moderate dysfunction. This pattern strengthens the internal plausibility of the reported correlation and suggests that NT-proBNP may reflect severity as well as presence of abnormal global function. Nevertheless, patient-level scatter is unavailable, precluding assessment of outliers, non-linearity or heteroscedasticity.

Figure 2. Correlation Coefficients between Mpi and Selected Variables



The correlation profile places NT-proBNP closest to MPI, followed by HbA1c, diastolic grade and age, while LVEF moves in the opposite direction. The hierarchy supports a model in which metabolic exposure and impaired relaxation precede overt reduction in pump function. Correlation does not establish independent causation, and several variables are interrelated; age, obesity, renal function and diabetes duration could influence both NT-proBNP and echocardiographic indices. Multivariable modelling is therefore needed to determine whether NT-proBNP contributes information beyond these covariates.

DISCUSSION

This study demonstrates a high burden of subclinical myocardial dysfunction in asymptomatic T2DM and a close concordance between Doppler-derived MPI and circulating NT-proBNP. Nearly three-quarters of participants had MPI >=0.40, while no patient had LVEF below 50%. This pattern is consistent with the established natural history of diabetic cardiomyopathy, in which impaired relaxation and global time-interval abnormalities precede a reduction in conventional ejection fraction. Boyer et al. reported frequent diastolic dysfunction in asymptomatic normotensive diabetes [4], and the pooled prevalence estimates of Bouthoorn et al. confirm that such abnormalities are common across hospital and community cohorts [3].

The magnitude and direction of the MPI findings are supported by several echocardiographic studies. Pattoneri et al. found MPI values of approximately 0.49 in early T2DM compared with 0.39 in controls and reported a correlation with HbA1c [5]. Saglam et al. similarly observed higher MPI in asymptomatic normotensive T2DM, with associations involving glucose, diabetes duration, BMI and LVEF [6]. Goroshi and Chand found diabetic cardiac dysfunction in 65% of 100 patients and reported strong concordance between MPI and diastolic dysfunction grade [7]. Kalkan et al. showed higher MPI in newly diagnosed diabetes and correlations with HbA1c (r=0.476), coronary flow reserve and LVEF [12]. The present HbA1c correlation (r=0.854) was considerably stronger, possibly because of the broad glycaemic range, the absence of a control group or shared confounding by disease duration and adiposity.

The NT-proBNP results also align with evidence that natriuretic peptide concentrations identify occult cardiac risk in diabetes. Magnusson et al. found higher NT-proBNP in 253 T2DM patients without overt cardiovascular disease than in 230 controls, independent of age, blood pressure, BMI and

renal markers [9]. Epshteyn et al. reported BNP AUCs of 0.91 in clinically referred and 0.81 in non-referred diabetic patients for ventricular dysfunction [8]. Cosson et al. found that NT-proBNP >=38 pg/mL independently predicted silent coronary disease, although sensitivity and specificity were only 59% and 67% [11]. Thus, the AUC of 0.982 and cut-off of 66 pg/mL in the present study are impressive but exceed most prior estimates and should be regarded as internally derived rather than transportable.

Not all studies support natriuretic peptides as stand-alone screening tests. Fang et al. identified subclinical cardiomyopathy in 24 of 66 patients after excluding hypertrophy and ischaemia, yet BNP was insufficiently sensitive to detect it [10]. This discrepancy may reflect differences in the target phenotype: tissue-velocity abnormalities can occur without enough wall stress to raise BNP, whereas MPI integrates global systolic and diastolic intervals and may align more closely with NT-proBNP in a cohort enriched for obesity and poor glycaemic control. Pham et al. found left ventricular hypertrophy, dilatation, hypokinesia or systolic dysfunction among asymptomatic T2DM patients without hypertension or coronary disease [13], while Loncarevic et al. demonstrated additional abnormalities using speckle-tracking echocardiography [16]. These observations reinforce that preserved LVEF does not exclude diabetic myocardial involvement.

Age-related correlation deserves caution. McGrady et al. showed that NT-proBNP tracked both systolic and moderate-to-severe diastolic dysfunction in high-risk asymptomatic adults, but its interpretation was intertwined with age and comorbidity [17]. In a real-world T2DM screening programme, Zhou et al. found increasing NT-proBNP prevalence with age and chronic kidney disease, and 45% of patients with elevated NT-proBNP had LVEF below 50% [18]. Al-Daydamony et al. also showed that MPI >=0.60 predicted silent ischaemia with 85.9% sensitivity and 90% specificity [15], indicating that markedly abnormal MPI may reflect occult coronary disease rather than diabetes-specific cardiomyopathy alone. Finally, von Scholten et al. demonstrated that NT-proBNP added long-term prognostic information for cardiovascular events and mortality [14], supporting clinical relevance beyond cross-sectional detection.

The study has limitations. It was single-centre, cross-sectional and relatively small, without a non-diabetic control group or longitudinal outcomes. The ROC threshold was not externally validated. The available variables did not permit adjustment for renal function, sex, BMI, diabetes duration, medications or occult coronary disease, all of which may influence NT-proBNP or MPI. Assay platform, echocardiographic reproducibility and observer blinding were not available for analysis. Accordingly, the findings establish a strong association, not causal independence. Prospective multicentre studies should validate the 66 pg/mL threshold, compare MPI with tissue Doppler and strain, and determine whether biomarker-guided echocardiography improves treatment or prevents heart failure.

CONCLUSION

Asymptomatic adults with T2DM frequently exhibited impaired global myocardial performance and diastolic dysfunction despite preserved LVEF. MPI increased in parallel with serum NT-proBNP and showed strong relationships with HbA1c, age and diastolic dysfunction, while correlating inversely with LVEF. An NT-proBNP threshold of 66 pg/mL demonstrated excellent internal discrimination for abnormal MPI, suggesting that a low-cost biomarker followed by targeted Doppler echocardiography could support earlier recognition of diabetic cardiac involvement. Because the study was small, cross-sectional and unadjusted for important confounders, the threshold should not yet be adopted as a universal screening criterion. External validation and longitudinal outcome studies are essential.

Declarations

Ethics Approval: Approved by the Institutional Ethics Committee of The Oxford Medical College Hospital and Research Centre

Consent to Participate: Written informed consent was obtained according to the approved study protocol.

Funding: The authors received no external funding for this study.

Conflicts of Interest: The authors declare that they have no competing interests.

Data Availability: The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request, subject to approval by the Institutional Ethics Committee and institutional policies.

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19. *Abbreviations: AUC, area under the receiver operating characteristic curve; BMI, body mass index; HbA1c, glycated haemoglobin; LVEF, left ventricular ejection fraction; MPI, myocardial performance index; NT-proBNP, N-terminal pro-B-type natriuretic peptide; ROC, receiver operating characteristic.*