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RESEARCH

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Association between glycated hemoglobin (HbA1c) level and cardiac perfusion and function on gated myocardial perfusion SPECT

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Abstract

Background Glycated hemoglobin (HbA1c) is a recognized biomarker that keeps track of long-term blood sugar levels. Some studies revealed that even a modest elevation of blood glucose levels was linked to a higher chance of developing CAD. In this study we aim to test the impact of HbA1c level on perfusion and function metrics derived from myocardial perfusion gated SPECT (MPGS) imaging.

Results Two hundred patients were recruited in this study (mean age 58.21 ± 11.53 years; 51% males), of whom 132 patients (66%) were diabetic. Diabetic patients had a higher mean HbA1c of 7.92 ± 1.99 versus 6.05 ± 0.99 in non-diabetics ($p < 0.001$). HbA1c% was negatively correlated to LVEF% (r = − 0.262; $p < 0.001$) and HDL (r = − 0.316; $p < 0.001$), though, it was positively correlated to ESV (r = 0.221; $p = 0.002$) and EDV (r = 0.291; $p < 0.001$). Patients with HbA1c% > 6.5 compared to ≤ 6.5%, had lower LVEF% of 53.17 ± 14.55 vs. 57.8 ± 12.61 ($p = 0.017$), lower HDL of 1.046 ± 0.262 vs. 1.196 ± 0.295 ($p < 0.001$), more LVEF < 50% (30% vs. 15.6%; $p = 0.017$), ESV > 44 ml (38.2% vs. 20%; $p = 0.005$), and WMA (24.5% vs. 12.2%; $p = 0.027$), hypertension (77.3% vs. 54.4%; $p = 0.001$) and dyspnea (27.3% vs. 15.6%; p = 0.047), however, with less chest pain (70.9% vs. 83.3%; $p = 0.039$). Diabetic patients with HbA1c% > 7.5 had lower LVEF% (52.0 ± 14.59 vs. 57.6 ± 11.55; $p = 0.018$) and HDL (1.005 ± 0.239 vs 1.148 ± 0.273; $p < 0.002$), more LVEF < 50% (33.3% vs. 14.5%; $p = 0.011$), ESV > 44 ml (41.3% vs. 20.3%; $p = 0.009$), WMA (30.2% vs. 11.6%; $p = 0.008$), and EDV > 100 ml (34.9% vs. 18.8%; $p = 0.037$). No significant relation was found between HbA1c% and perfusion variables.

Conclusions Elevated HbA1c% was associated with multiple abnormal MPGS function parameters including lower LVEF, greater ESV, and more WMA. The same was observed in the diabetic group, together with greater EDV. No significant relation was detected between HbA1c% and perfusion parameters. The effect of impaired glycemic control on cardiac function parameters, even in absence of significant effect on perfusion, could be an alarming sign, while interpreting MPGS studies, both in known diabetic patients and in those with probably insulin resistance but not known to be diabetic. Such findings may be calling for further investigations, to uncover the true mechanisms behind cardiac dysfunction and the possibility of associated microvascular disease.

Keywords HbA1c, Myocardial perfusion gated SPECT, Diabetes mellitus

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Background

Diabetes mellitus is considered a major risk factor for coronary artery disease (CAD) worldwide [1]. The impact of abnormal glucose homeostasis on CAD had previously been discussed in several research studies [2, 3]. Some studies revealed that even a modest elevation of blood glucose levels in non-diabetics was linked to a higher chance of developing CAD [4, 5]. Glycated hemoglobin (HbA1c) is a recognized biomarker that keeps track of long-term blood sugar levels. The link between HbA1c and myocardial perfusion gated SPECT (MPGS) imaging could aid in the early detection of cardiovascular complications related to diabetes or impaired glucose homeostasis.

Diabetic patients are three to four times as likely to die from cardiovascular causes as people who do not have diabetes [6]. Diabetic individuals are more likely to experience silent ischemia, even in the absence of epicardial CAD disease [7]. Early detection of myocardial ischemia and myocardial dysfunction is of great importance in such patients, leading to early management aiming at reduction in morbidity as well as mortality rates. We aimed to test the relationship between HbA1c level and various perfusion and function parameters derived from MPGS imaging.

Methods

Following approval by the local ethical committee and waiving the requirement of informed consent for this retrospective cohort, the medical records and MPGS images of 200 patients were reviewed. The images were retrieved from the PACS system and re-examined by a well-trained nuclear medicine doctor to evaluate both perfusion and function parameters. Perfusion parameters included are; summed rest score (SRS), summed stress score (SSS), and summed difference score (SDS). Function/gated parameters included are; [left ventricular ejection fraction (LVEF), end-diastolic volume (EDV), end-systolic volume (ESV), and wall motion abnormalities (WMA). Data collected from patients' records included demographics, clinical, and laboratory data [hypertension (HTN), smoking, chest pain, dyspnea, diabetes mellitus (DM), HbA1c, total cholesterol, high-density lipoprotein (HDL), and low-density lipoprotein (LDL)].

Acquisition protocol

All patients performed one-day stress–rest myocardial perfusion gated SPECT (MPGS) imaging using ^{99m}Technetium Methoxy Isobutyl Isonitrile (Tc-99 m-MIBI). The patient received a lower administered dose for the rest study first; 8–10 mCi (296–370 MBq) of Tc-99 m MIBI intravenously, while a higher dose of 25–30 mCi (925–1110 MBq) was used for the stress study. Imaging was obtained 30–45 min following intravenous injection of the tracer using a Siemens E.cam; dual-head SPECT/CT gamma camera fitted with low energy high-resolution collimators, an energy window adjusted to 15%, set at 140 keV, and a matrix size of 128 × 128. Patients were imaged while lying flat on their backs with their arms raised. Step and shoot mode for 64 projections (25 s/projection) over 180° arc in a non-circular/elliptical orbit from 45° right anterior oblique (RAO) to 135° left posterior oblique (LPO) were used. ECG gated acquisition was applied with 8 frames per R-R interval. Image reconstruction was done using OSEM (ordered subset expectation maximization) iterative reconstruction with a 0.40/10 Butterworth filter, occasionally adjusted based on image counts.

Stress protocol

Pharmacological stress using dipyridamole was performed in all patients. Dipyridamole was infused intravenously for four minutes at a rate of approximately 0.14 mg/kg (the total dose was 0.56 mg/kg). ^{99m}Tc-MIBI was injected 4 min following dipyridamole infusion. Twelve-lead ECG monitoring was carried out, and blood pressure was recorded at rest, during Dipyridamole administration, and 3 min in recovery. Intravenous aminophylline (100–250 mg) was administered in the recovery period (at least 3 min after ^{99m}Tc-MIBI injection).

Image analysis

Data assessment of myocardial perfusion was based on both visual assessment and quantitative data automatically derived from the standard 17-segment model using Quantitative Perfusion SPECT (QPS) software. As a binary variable, perfusion was considered abnormal if SRS or SSS were > 3. Wall motion abnormalities (WMA), including hypokinesis, akinesis, or dyskinesis, were assessed visually based on myocardial wall excursion and were expressed as either present or absent.

Statistical analysis

Data were analyzed using SPSS version 21 and MedCalc 11.0 software. The Chi-Square test for categorical data was a tool to compare patient groups. The Student T-test was employed to evaluate differences between means of continuous variables. Pearson's correlation was performed to test the magnitude of correlation between continuous variables (degree of correlation was deemed low if r = 0 to 0.25, moderate if r = 0.25 to 75, and high if r = 0.75 to 1.0). Receiver-operator characteristic (ROC) curves were plotted to define the cutoff values for HBA1C%, EDV, and ESV that best identify patients with LVEF < 50%. Analysis was performed to compare perfusion and function variables between documented

diabetic patients and non-diabetic patients based on patient records as well as between patient groups stratified by HbA1c ≤ or > 6.5% (cutoff point for diagnosis of DM according to the American Diabetic Association) for the entire population and HbA1c ≤ or > 7.5 (derived from ROC analysis) for the diabetic group. Frequencies and percentages were used to express qualitative data, whereas mean ± SD was utilized for quantitative data. *P*-values less than 0.05 were considered significant.

Results

Two hundred patients were retrospectively recruited in this study. The mean age is 58.44 ± 10.91 years with 102 (51%) males and 98 (49%) females. Sixty six % (132/200) of patients had documented diabetes mellitus type 2. Prior coronary artery bypass grafting (CABG) was documented in 4 patients (2%), all of whom are diabetics, while 15 patients had prior Percutaneous Coronary Intervention (PCI), 8 (53%) of whom are diabetics.

The patient's demographic and clinical data are illustrated in Table 1. The overall values of perfusion and function parameters expressed as means ± SD or frequencies, and percentages for the entire study population are displayed in Table 2. The mean HbA1c level was considerably greater in the diabetic group of patients (7.92 ± 1.99 compared to 6.05 ± 0.99 in the non-diabetic group, with $p < 0.001$). The diabetic group had a higher mean age than the non-diabetic one (59.6 vs. 56.15 years respectively; $p = 0.033$). Hypertension was more frequent among the diabetic group 102/132 (77.3%) vs. 32/68 (47.1%) in the non-diabetic group ($p < 0.0001$) (Table 3).

Females had lower mean HbA1c of 6.99 ± 1.87 compared to 7.57 ± 1.97 in males ($p = 0.034$). The HBA1C% showed a moderately negative correlation with LVEF% (r = − 0.262; $p < 0.01$) and HDL ($r = -0.316$; $p < 0.01$), while it had a moderate positive correlation with ESV

Table 1 Patients' demographics and clinical data

Variable	Mean ± SD (range) or Frequency (%)
Age (years)	58.44 ± 10.907 (30–92)
Sex (Male)	102 (51%)
Weight (kg)	84.41 ± 16.026 (38–131)
Height (cm)	159.92 ± 9.824 (134–184)
BMI	33.10 ± 6.142 (18.20–53.42)
HR	96.94 ± 27.673 (58–174)
BP (systolic)	144.23 ± 23.525 (93–204)
BP (diastolic)	70.74 ± 12.464 (42–99)
Hypertension	134 (67%)
Diabetes mellitus	132 (66%)
HgA1C (%)	7.284 ± 1.935 (4.4–14.1)
HbA1c ≥ 6.5	110 (55%)
Hyperlipidemia	90 (45%)
Total cholesterol (mmol/L)	4.319 ± 0.915 (2.0–6.7)
HDL (mmol/L)	1.114 ± 0.287 (0.49–2.30)
LDL (mmol/L)	2.42 ± 0.753 (0.78–4.70)
Smoking	16 (8%)
Chest pain	153 (76.5%)
Dyspnea	44 (22%)
Previous CABG	4 (2%)
Previous PCI	15 (53%)

Table 2 Values of perfusion and function parameters for the entire study population

Variable	Mean ± SD or Frequency (%)
SRS	5.14 ± 7.02
SSS	9.79 ± 8.02
SDS	4.50 ± 3.68
Abnormal perfusion	180 (90%)
LVEF (%)	55.26 ± 13.87
LVEF < 50%	47 (23.5%)
EDV (ml)	92.72 ± 41.90
EDV ≥ 100	55 (27.5%)
ESV (ml)	45.49 ± 36.87
ESV ≥ 44	60 (30%)
WMA	38 (19%)

Table 3 Comparison of various parameters for diabetic group versus non-diabetic group

Variable	Diabetic (*n* = 132) Mean ± SD / Frequency (%)	Non-diabetic (*n* = 68) Mean ± SD / Frequency (%)	*P*-value
Age (years)	59.61 ± 10.46	56.15 ± 11.45	0.033*
Sex (Males)	71(53.8%)	31(45.6%)	0.272
BMI	33.42 ± 6.24	32.49 ± 5.94	0.310
Smoking	11 (8.3%)	5 (7.4%)	0.809
Hypertension	102 (77.3%)	32 (47.1%)	< 0.0001*
Dyspnea	34 (25.8%)	10 (14.7%)	0.074
Chest pain	96 (72.7%)	57 (83.8%)	0.080
Hyperlipidemia	63 (47.7%)	27 (39.7%)	0.280
HbA1c %	7.92 ± 1.99	5.8 ± 0.99	< 0.0001*
Abnormal Perfusion	113 (85.6%)	60 (88.2%)	0.606
SRS	4.86 ± 5.79	5.68 ± 8.94	0.498
SSS	9.61 ± 7.38	10.16 ± 9.32	0.646
SDS	4.73 ± 3.864	4.06 ± 3.273	0.224
LVEF %	54.91 ± 13.33	55.92 ± 14.94	0.624
EDV (ml)	93.30 ± 39.90	91.62 ± 45.82	0.789
ESV (ml)	45.48 ± 35.27	45.53 ± 40.07	0.992
WMA	27 (20.5%)	11 (16.2%)	0.465

* $P < 0.05$

(r = 0.221; $p = 0.002$) and EDV (r = 0.291; $p < 0.001$) (Fig. 1).

Based on ROC analysis HbA1c > 7.5% (AUC = 0.620; $p = 0.0132$), EDV > 100 (AUC = 0.873; $p = 0.0001$) and ESV > 44 (AUC = 0.960; $p = 0.0001$) were the optimal cutoff points to predict LVEF of < 50% with sensitivity, specificity, positive predictive value, negative predictive value and accuracy of 51.1%, 70.6%, 34.8%, 82.4% & 66% ($p = 0.011$), 78.7%, 88.25, 67.3%, 93.1% & 86% ($p < 0.037$) and 91.55, 88.95, 71.7%, 97.7% & 89.5 ($p < 0.009$), respectively.

Patients with HbA1c% > 6.5 compared to those with HbA1c% ≤ 6.5, had significantly lower mean LVEF (53.17 ± 14.55 versus 57.80 ± 12.61; $p = 0.019$), higher prevalence of LVEF < 50% (30% compared to 15.6%; $p = 0.017$), WMA (24.5% compared to 12.2%; $p = 0.027$), and ESV > 44 ml (38.2% compared to 20%; $p = 0.005$) (Table 4).

As regards clinical features, patients with HgA1c% > 6.5% compared to HbA1c% ≤ 6.5, exhibited a higher incidence of hypertension [85/110 (77.3%) vs 49/90 (54.4%); ($p = 0.001$)] and dyspnea [30/110 (27.3%) vs. 14/90 (15.6%); ($p = 0.047$)], but a lower incidence of chest pain [78/110 (70.9%) vs. 75/90 (83.3%); ($p = 0.039$)] (Fig. 2), and a lower mean HDL (1.046 ± 0.262 versus 1.1960 ± 0.295; $p < 0.001$).

Again, in the subgroup of diabetic individuals, those with HBA1C% > 7.5% compared to HBA1C% ≤ 7.5%, had a lower mean LVEF% (52.02 ± 14.59 versus 57.55 ± 11.55; $p = 0.017$), more frequency of LVEF < 50% (33.3% versus 14.5%; $p = 0.011$), WMA (30.2% versus 11.6%; $p = 0.008$), ESV > 44 ml (41.3% versus 20.3%; $p = 0.009$), EDV > 100 ml (34.9% versus 18.5%; $p = 0.037$) (Table 5), and a lower mean HDL (1.005 ± 0.239 versus 1.148 ± 0.273; $p = 0.002$). However, no significant association could be detected between HbA1c % and MPGS perfusion parameters including perfusion scores (SRS, SSS, or SDS) (Fig. 3).

Table 4 Comparison of perfusion and function parameters in patients with HBA1C% > 6.5 versus patients with HBA1C% ≤ 6.5

	HBA1C% > 6.5% (*n* = 110) Mean ± SD / Frequency (%)	**HBA1C% ≤ 6.5% (*n* = 90) Mean ± SD / Frequency (%)**	***P*-Value**
LVEF %	53.17 ± 14.55	57.8 ± 12.61	0.019*
LVEF < 50%	33 (30.0%)	14 (15.6%)	0.017*
EDV (ml)	96.80 ± 42.10	87.74 ± 41.34	0.129
EDV > 100 ml	35 (31.8%)	20 (22.2%)	0.131
ESV (ml)	49.10 ± 37.57	41.09 ± 35.71	0.127
ESV > 44 ml	42 (38.2%)	18 (20.0%)	0.005*
WMA	27 (24.5%)	11 (12.2%)	0.027*
SRS	4.94 ± 6.258	5.39 ± 7.889	0.649
SSS	9.55 ± 7.74	10.09 ± 8.49	0.642
SDS	4.70 ± 4.006	4.26 ± 3.241	0.397
Abnormal perfusion	93 (84.5%)	80 (88.9%)	0.371

* $P < 0.05$

Discussion

Diabetes mellitus (DM) is coupled to both microvascular and macrovascular complications. CAD in diabetic patients is usually silent, sophisticated at the first presentation, and consistently related with poor prognosis when compared to the non-diabetics [8].

Diabetic cardiomyopathy is a diabetes-related myopathy that is initially identified by diastolic dysfunction in the left ventricle, and later on by heart failure. It is unaffected by known risk variables such as hypertension or CAD. The risk of heart failure increases two to eightfold in type 2 diabetics. However, diabetic

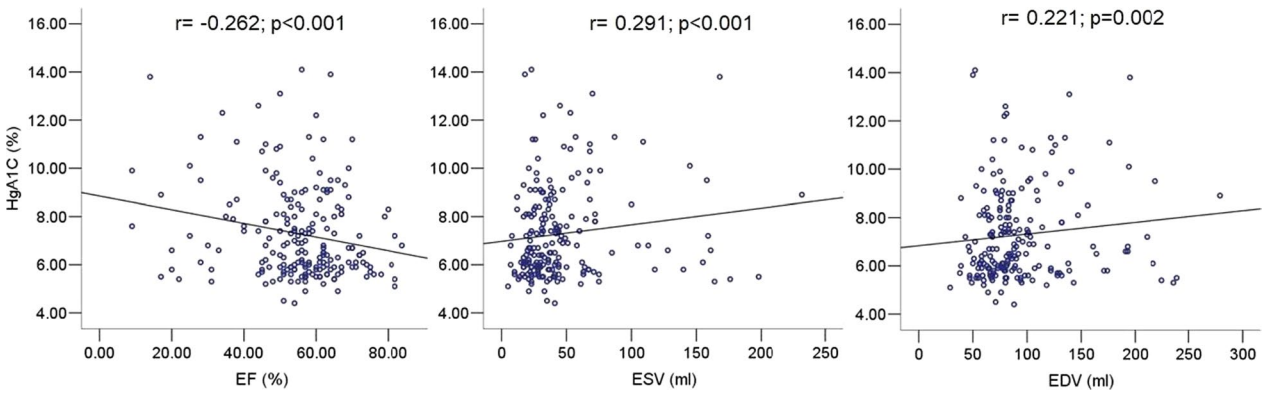

Fig. 1 Scatter plots with HbA1c % negatively correlated with LVEF% (left panel), and positively correlated with EDV (middle panel) and ESV (right panel)

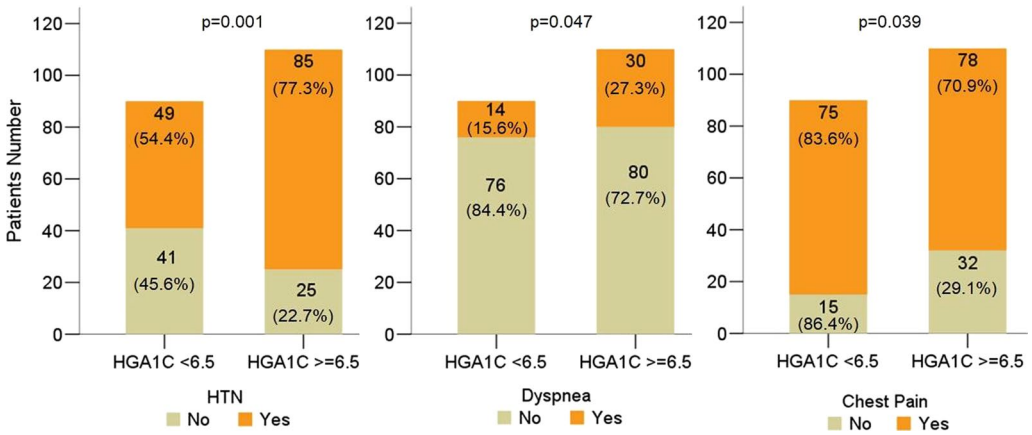

Fig. 2 Patients with an HBA1C% > 6.5 had more frequency of hypertension (left panel), and dyspnea (middle panel) but less frequency of chest pain (right panel)

Table 5 Comparison of perfusion and function parameters of myocardial perfusion gated SPECT in the diabetic subgroup patients with HBA1C% > 7.5 versus HBA1C% ≤ 7.5

	HBA1C% > 7.5 (*n* = 63) Mean ± SD / Frequency (%)	**HBA1C% ≤ 7.5 (*n* = 69) Mean ± SD / Frequency (%)**	**P-Value**
LVEF%	52.0 ± 14.59	57.6 ± 11.55	0.017*
LVEF < 50%	21 (33.3%)	10 (14.5%)	0.011*
EDV (ml)	96.76 ± 43.92	90.13 ± 35.87	0.342
EDV > 100 ml	22 (34.9%)	13 (18.8%)	0.037*
ESV (ml)	50.27 ± 39.68	41.10 ± 30.33	0.136
ESV > 44 ml	26 (41.3%)	14 (20.3%)	0.009*
WMA	19 (30.2%)	8 (11.6%)	0.008*
SRS	4.94 ± 5.34	4.79 ± 6.228	0.889
SSS	9.94 ± 7.12	9.30 ± 7.65	0.625
SDS	5.06 ± 3.99	4.42 ± 3.75	0.341
Abnormal perfusion	55 (87.3%)	58 (84.1%)	0.596

* $P < 0.05$

cardiomyopathy may not have any obvious clinical signs, and left ventricular ejection fraction is not a useful predictor of left ventricular dysfunction in the initial stage of the disease [9].

As a trustworthy indicator of glycated proteins, HbA1c was employed as a surrogate for glucose control and management, additionally various researches have shown its diagnostic and prognostic utility in individuals with and without diabetes. Managing hyperglycemia lowers the incidence of both micro- and macro-vascular disease in diabetic patients, as shown in the United Kingdom Prospective Diabetes Study [10, 11]. HbA1c levels of 6.0–6.5% are considered high-risk for diabetes, necessitating the implementation of effective preventative strategies [12].

We aimed to study the relationship between HbA1c and the perfusion and function metrics derived from MPGS imaging. According to a previous study by Salonen et al., we noticed that diabetic individuals had hypertension much more frequently than non-diabetic patients (77.3% vs. 47.1%; $p < 0.01$). This can be due to the fact that atherosclerosis had been linked to insulin metabolism disruption, with significantly increased incidence of insulin resistance in hypertensive people, even who aren't overweight [13].

Concordant to literature, we found that male patients showed a higher HBA1C % level than female patients (7.57 ± 1.97 vs. 6.99 ± 1.87 respectively; $p = 0.034$) [14].

In our cohort, HBA1C% was moderately negatively correlated with HDL ($p < 0.01$). Compared to LDL, HDLs have been found to stimulate insulin production, decrease beta cell apoptosis, and probably improve skeletal muscle glucose absorption. However, prediabetes and diabetes type 2, which are characterized by a high body mass index and atherogenic lipids, add metabolic stress that hinders the production of HDL, further worsening pancreatic cellular malfunction and insulin resistance. As a result, in those at risk, low HDL levels may impair blood sugar control and precipitate the emergence of type 2 diabetes [15]. The considerable association between total cholesterol and cardiovascular disease, LDL, triglycerides, and HbA1c, had been previously addressed by several authors, whereas others have revealed no significant relationship. Also, some studies, have found a negative correlation between HbA1c and LDL, while others have found the opposite [16–19].

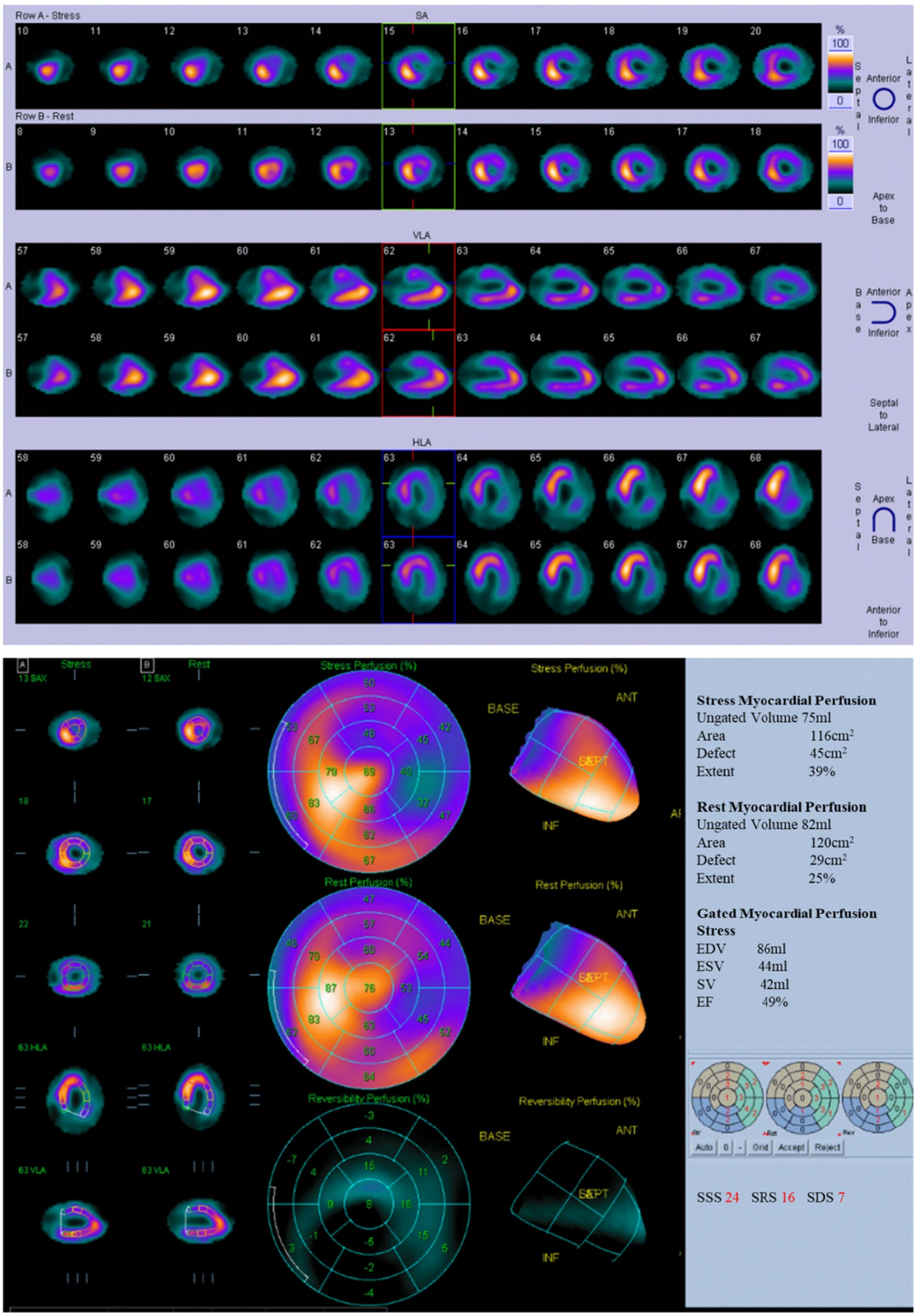

Fig. 3 A 62 years old diabetic female (HbA1c 11.8%), presented with chest pain. Perfusion images (upper panel) revealed severe hypoperfusion of the lateral wall in stress, with partial improvement during rest, denoting mixed non-transmural myocardial infarction with residual ischemia in the distribution of left circumflex. Mild anterior wall soft tissue attenuation is also noted. Quantitation (lower panel) revealed SSS = 24, SRS = 16, SDS = 7, EDV = 86 ml, ESV = 44 ml, & LVEF = 49%

In agreement with several studies we found that HBA1C% was moderately negatively correlated to LVEF ($p < 0.01$) [20–22]. Gu et al. found that HbA1c fluctuation was linked to LV diastolic dysfunction [21]. In our study, we found that HbA1c was moderately positively correlated with ESV and EDV (r = 0.221; $p = 0.002$ and r = 0.291; $p < 0.001$).

Deluca et al. found that among the diabetic patients or those with glucose intolerance, 27 of 54 patients (50%) with HBA1C level of ≥ 7.6% and 39 of 137 patients (28%) with HbA1c level of < 7.6% had silent myocardial ischemia ($p < 0.005$) [23]. Concordantly, we found that patients with HbA1c% > 6.5 exhibited less chest pain (70.9% versus to 83.9%; p = 0.039) but more frequent dyspnea (27.3% versus 15.6%; $p = 0.047$) and hypertension (77.3% versus 54.4%; $p = 0.001$) compared to those with HbA1c% ≤ 6.5.

In a prospective study including 457 diabetic patients and 556 nondiabetic controls, patients with HbA1c > 7.3% showed a significantly higher frequency of both fixed and reversible myocardial perfusion defects, a lower LVEF, and a higher EDV, and ESV when compared to those with HbA1c ≤ 7.3% [24]. In line with these findings, we found that patient group with HbA1c > 6.5% had more proportion of patients with LVEF < 50% (30.0% versus 15.6%; $p = 0.017$), WMA (24.5% versus 12.2%; $p = 0.027$) and ESV > 44 ml (38.2% versus 20%; $p = 0.005$). In addition diabetic cases with HBA1C% > 7.5% had lower mean LVEF% ($p < 0.01$), more frequency of LVEF < 50% ($p = 0.011$), WMA ($p = 0.008$), ESV > 44 ml ($p = 0.009$), and EDV > 100 ml ($p = 0.037$). However, we were not able to detect any statistically significant association between HBA1C level and MPGS perfusion measures, including SRS, SSS, and SDS. This could be attributed to the fact that in diabetic patients, coronary artery compromise is attributed in a large proportion to microvascular dysfunction which is not reflected as perfusion defects on MPGS imaging, but rather as a homogenously reduced perfusion that requires myocardial flow or flow reserve measurement to be detected [25]. Coronary flow reserve (CFR) is often calculated in conjunction with cardiac positron emission tomography (PET), which can measure the absolute myocardial blood flow (ml/min) during pharmacological stress, and at rest [26]. Similar to our findings, Adamikova et al. reported no significant correlation to perfusion parameters except for transient ischemic dilatation (TID), which shows a statistically significant correlation ($p = 0.035$) [27]. Although TID was not one of the included parameters in the current study, it had been linked to either severe CAD with significant ischemia or coronary microvascular dysfunction. Chen, et al. concluded that an increased TID ratio out of proportion to perfusion abnormalities or with normal perfusion (isolated TID) is a marker of underlying coronary microvascular dysfunction [28].

Limitations and recommendations

The relatively small sample size and the heterogeneous study population with mixed diabetics and non-diabetics and a wide range of clinical characteristics are among our study's drawbacks. Additionally, being a retrospective work with a non-randomized population would have introduced a selection bias. The study populations were those referred for myocardial perfusion imaging may tend to have more advanced stages of diabetic complications or an association with more comorbidity, thus results might not be completely applicable to general population.

Conclusions

An elevated HbA1c level was generally associated with multiple abnormal MPGS function parameters, including lower LVEF, greater ESV, and more WMA. The same association was specifically observed in the diabetic group, in addition to greater EDV. However, no significant association was found between the HbA1c% and MPGS perfusion parameters.

The effect of impaired glycemic control measured by HbA1c, on cardiac function parameters, even in absence of significant effect on perfusion, could be an alarming sign, while interpreting myocardial perfusion gated SPECT studies, both in known diabetic patients and in those with probably insulin resistance but not known to be diabetic. Such findings may be calling for further investigations, to uncover the true mechanisms behind cardiac dysfunction in such patients, as well as probably correlation with coronary flow reserve, to rule out the possibility of underlying microvascular disease with or without epicardial disease and to assess its magnitude.

The current results may raise attention, to the need of stricter glycemic threshold, beyond which more aggressive management should be implemented, early enough to prevent or stop further cardiovascular complications.

Abbreviations

BMI	Body mass index
CABAG	Coronary artery bypass graft
CAD	Coronary artery disease
EDV	End diastolic volume
ESV	End systolic volume
HbA1c	Glycated hemoglobin
HDL	High density lipoprotein
HTN	Hypertension
LDL	Low density lipoprotein
LVEF	Left ventricular ejection fraction

MPGS	Myocardial perfusion gated SPECT
PCI	Percutaneous coronary intervention
SDS	Summed difference score
SPECT	Single photon emission tomography
SRS	Summed rest score
SSS	Summed stress score
TID	Transient ischemic dilatation
WMA	Wall motion abnormalities

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Author contributions
HN: Conceptualization, Methodology, Formal analysis, writing (Original draft preparation). HA: Data management, Abstract preparation IS: Data management, Writing, Reviewing and Editing. AA: Writing, Reviewing Editing and validation. NM: Project administration Writing, Reviewing and Editing. All authors have read and approved the manuscript.

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Availability of data and materials
The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Approval for this research was provided by IRB and local ethical committee of Inaya Medical Colleges (# 221/2). The requirement for an informed consent was waived based on the retrospective nature of the study.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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