ORIGINAL ARTICLE

Association between mean HbA1c, HbA1c variability, and severity of coronary artery disease using SYNTAX score in patients with type 2 diabetes

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Background: Coronary artery disease (CAD) is a significant complication of type 2 diabetes mellitus (T2DM). The relationship between long-term glycemic variability (GV) and CAD severity remains uncertain. This study aimed to investigate the association between long-term GV and the extent of CAD in individuals with T2DM. **Materials and Methods:** This retrospective cohort study included patients with T2DM who underwent coronary angiography. Mean-HbA1c was calculated for each patient. GV was assessed by measuring the standard deviation (SD) and coefficient of variation (CV) of HbA1c measurements. The severity of coronary artery lesions was evaluated using the SYNTAX scoring system. Linear regression analyses were performed to assess the differences in SYNTAX scores among different mean-HbA1c groups, as well as SD-HbA1c and CV-HbA1c quartiles. **Results:** A total of 115 diabetic patients were included in the study. The mean-HbA1c cutoff value of 7.5 was derived from the receiver-operating characteristic curve. Fifty-six patients had a mean-HbA1c of 7.5 or lower, whereas 59 patients had a mean-HbA1c above 7.5. Univariate analysis revealed that patients with mean-HbA1c above 7.5 had significantly higher SYNTAX scores compared to those with lower mean-HbA1c levels (12.79 vs. 7.33, $P < 0.05$). There was no significant correlation observed between SD-HbA1c, CV-HbA1c, and SYNTAX scores in both univariate and multivariate analyses. **Conclusion:** This study suggests that higher mean-HbA1c levels are associated with increased severity of CAD in individuals with T2DM. However, long-term HbA1c variability, as measured by SD-HbA1c and CV-HbA1c, does not appear to have a significant impact on the severity of CAD.

Key words: Coronary angiography, coronary artery disease, diabetes mellitus, glycated hemoglobin

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INTRODUCTION

Diabetes mellitus (DM) has been known as a major traditional risk factor for coronary artery disease (CAD) for a long time.[1] Approximately 32.2% of those with DM are reported to have cardiovascular disease, which plays a critical role in mortality, leading to nearly 50% of total deaths.[2] Three main components of dysglycemia that are responsible for DM complications are chronic hyperglycemia, hypoglycemia, and glycemic variability (GV).[3] Hyperglycemia and GV can affect the cardiovascular system by impairment of the endothelium, vascular inflammation, and increasing oxidative stress. On the other hand, hemodynamic changes associated with hypoglycemia (e.g., increase in heart rate and peripheral systolic blood pressure) increase cardiac stress.[4-6] In recent years, there has been growing interest in understanding the role of GV as a novel risk factor for CAD.[7] It was a result of reviews on certain studies indicating that achieving HbA1c levels in the suggested range does not necessarily improve the entire outcomes of type 2 DM. Therefore, discussions

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centered on whether glycemic metrics (i.e. GV) other than HbA1c exist that could help explain the complications associated with DM.[8] GV indicates the fluctuations in blood glucose levels over time, including both short-term fluctuations within a day and variations measured by HbA1c over a longer period (HbA1c variability).[9] Several studies have investigated the association between GV and CAD, reporting mixed findings, with some demonstrating a significant association between GV and CAD, while others have found no significant correlation.[10-12] Some studies have indicated that even individuals with normal blood glucose levels can experience cardiovascular complications due to HbA1c variability, because of the independent effect of the GV than other glycemic metrics on the cardiovascular system. It has been shown in different studies that HbA1c variability can be an independent risk factor for CAD; however, there remains a scarcity of definitive evidence regarding the hard clinical outcomes of HbA1c variability on the cardiovascular system.[13,14]

Several cardiovascular imaging tests are available to assess the severity of CAD, including intravascular ultrasonography, coronary computed tomography (CT) angiography, and invasive coronary angiography.[15] Among these, invasive coronary angiography is considered the gold standard for diagnosing and quantifying the extent of CAD.[16] While some studies have explored the relationship between long-term GV and coronary plaque progression using coronary CT angiography, the understanding of the link between long-term GV and CAD severity using invasive coronary angiography remains limited.[11] This limitation is due to the focus of the previous studies on non-invasive methods because of limitations in the data access. Nevertheless, invasive angiography provides more definitive and high-quality imaging results, and therefore, it remains the gold standard method for determining the severity of CAD.[17]

The SYNTAX score is one of the most common angiographic tools that aids in grading the severity of CAD and enables comparison of CAD severity among patients.[18,19] In addition, it aids in risk stratification by categorizing patients based on the complexity of their coronary lesions, which influences treatment decisions and selecting appropriate revascularization strategies.[20]

There is a gap in research concerning the association between long-term GV and CAD severity assessed by invasive coronary angiography, despite short-term GV, and so we focused on HbA1c variability. In this study, we aimed to investigate the association between mean HbA1c, long-term GV (Hb1c variability), and the extent of coronary artery lesions, as assessed by the SYNTAX scoring system, in individuals with DM.

MATERIALS AND METHODS

Study design and patient selection

This retrospective cohort study included patients with established type 2 diabetes mellitus (T2DM) who underwent coronary angiography at Afshar and Shahid Sadoughi Hospital in Yazd, Iran, between January 2015 and March 2022. The study was approved by the Ethical Committee of the Shahid Sadoughi University of Medical Science, Yazd, Iran (approval code: IR.SSU.MEDICINE.REC.1400.353).

The inclusion criteria encompassed patients with T2DM who had a minimum of three HbA1c measurements documented in their medical records at the Diabetes Research and Clinical Practice Centre in Yazd. Assessment of HbA1c levels was conducted prior to the angiographic procedures and the time interval between HbA1c records was 3–6 months. Patients with a history of coronary artery bypass graft, incomplete angiographic data, heart failure, diabetes duration of <2 years, and <3 HbA1c measurements were excluded from the study.

Data collection and variables

Demographic and laboratory data were collected from the patient's medical records. The collected variables included age, sex, body mass index (BMI), hypertension, diabetes duration, HbA1c measurements, fasting blood sugar (FBS), creatinine, total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG). Variables other than HbA1c were measured at a single time point.

HbA1c variability

HbA1c variability was assessed by calculating the standard deviation (SD) and coefficient of variation (CV) of all HbA1c measurements for each patient. The CV-HbA1c was determined by dividing the SD-HbA1c by the Mean-HbA1c and multiplying by 100. The mean-HbA1c was calculated as the average of all HbA1c measurements for each patient. There are different statistical metrics to assess GV, but none of them are known to be the gold standard. However, SD and CV are the most common and accurate measurements, and therefore, we used them in this study.[18]

SYNTAX score and angiographic analysis

The severity of coronary artery lesions was assessed using the SYNTAX scoring system, based on each patient's coronary angiogram. The SYNTAX score was calculated using an online SYNTAX calculator (version 2.28), which takes into account parameters such as right/left dominancy, lesion location, the presence of total occlusion, bi/trifurcation, aorto-ostial lesion, severe tortuosity, lesion length >20 mm, heavy calcification, thrombus, and small vessels/diffuse disease.[21] It should also be noted that, all

angiograms were reviewed by a same expert interventional cardiologist.

Statistical analysis

Continuous variables were presented as mean ± SD, whereas categorical variables were presented as numbers and percentages. One-way analysis of variance test and Pearson Chi-square test were used to compare continuous and categorical variables between groups, respectively. Univariate linear regression analysis was performed to evaluate the correlation between baseline variables (i.e., age, FBS, and diabetes duration) and SYNTAX score separately. Receiver-operating characteristic (ROC) curve analysis was used to determine the cutoff value for Mean-HbA1c. A SYNTAX score >22 was used as the threshold for CAD severity in the ROC analysis. This is an established cutoff value for the SYNTAX score that guides clinicians in selecting appropriate revascularization strategies.[22] Univariate and multivariate linear regression analyses were conducted to assess the significant differences in SYNTAX score among Mean-HbA1c groups and CV-HbA1c and SD-HbA1c quartiles. Multivariate analysis was adjusted for different groups of variables. $P < 0.05$ was considered statistically significant. Statistical analysis was performed using IBM SPSS for Windows, version 26.0 (Armonk, NY, USA: IBM Corp).

RESULTS

Baseline characteristics

A total of 115 diabetic patients were enrolled in this study. We compared the baseline characteristics of the patients between the mean-HbA1c groups and CV-HbA1c quartiles separately [Table 1]. Patients were divided into two groups based on the mean-HbA1c cutoff value of 7.5, which was calculated in this study. We found that the duration of diabetes, FBS, SD-HbA1c, and CV-HbA1c were significantly higher in patients with mean-HbA1c >7.5 ($P < 0.05$ for all). The SYNTAX score was also significantly higher in the mean-HbA1c >7.5 group (12.79 vs. 7.33, $P < 0.05$, effect size = 0.08). Comparing the CV-HbA1c quartiles showed that higher mean-HbA1c values were significantly associated with higher CV-HbA1c levels. However, the SYNTAX score did not show any significant differences between the CV-HbA1c quartiles (9.56, 11.07, 10.71, and 9.16 in Q1-Q4, respectively, $P = 0.873$). There were no significant differences in other variables between the Mean-HbA1c groups and CV-HbA1c quartiles.

Univariate linear regression analysis

Univariate linear regression analysis identified a significant correlation between age, FBS, and SYNTAX score individually, unlike the other variables listed in Table 1. Specifically, age had an odds ratio (OR) of 0.262 ($P = 0.005$), and FBS had an OR of 0.281 ($P = 0.002$). However SD-HbA1c and CV-HbA1c did not show a significant correlation with the SYNTAX score [Figure 1].

Determining the cutoff value for mean-HbA1c and linear regression analysis for evaluating the correlation between mean-HbA1c groups and SYNTAX score

A mean-HbA1c cutoff value of 7.5 was determined through ROC curve analysis based on a SYNTAX score >22 (with a sensitivity of 0.800 and specificity of 0.500; AUC [area under the curve] = 0.55) [Figure 2].

Univariate linear regression analysis revealed that the SYNTAX score was significantly higher in patients with mean-HbA1c >7.5. Multivariate linear regression analysis was performed to evaluate the correlation between mean-HbA1c and SYNTAX score using two models. Model 1 was adjusted for age, sex, BMI, diabetes duration, total cholesterol, LDL-C, HDL-C, and TG; and model 2 was adjusted for variables in model 1 plus FBS and CV-HbA1c. In both models, the SYNTAX score remained consistently higher in the mean-HbA1c >7.5 group (model 1: OR = 0.316, $P = 0.001$; model 2: OR = 0.300, $P = 0.003$) [Table 2].

Linear regression analysis evaluating the correlation between HbA1c variability and SYNTAX score

When comparing SD-HbA1c quartiles, the univariate linear regression analysis did not show a significant correlation between the SYNTAX score and SD-HbA1c (Q1: reference; Q2: OR = 0.026, $P = 0.819$; Q3: OR = 0.116, $P = 0.318$; Q4: OR = 0.017, $P = 0.885$). Similarly, the univariate linear regression analysis did not show a significant correlation between the SYNTAX score and CV-HbA1c quartiles (Q1: reference; Q2: OR = 0.065, $P = 0.573$; Q3: OR = 0.051, $P = 0.661$; Q4: OR = −0.018, $P = 0.878$).

Multivariate linear regression analysis, adjusted for age, sex, BMI, and dyslipidemia, showed no significant correlation between the SYNTAX score and SD-HbA1c (Q1: reference; Q2: OR = 0.014, $P = 0.905$; Q3: OR = 0.176, $P = 0.128$; Q4: OR = 0.035, $P = 0.761$). Furthermore, there was no correlation between the SYNTAX score and CV-HbA1c quartiles in this multivariate linear regression analysis (Q1: reference; Q2: OR = −0.018, $P = 0.879$; Q3: OR = 0.032, $P = 0.779$; Q4: OR = −0.044, $P = 0.705$) [Table 3].

DISCUSSION

Overall findings

The present study investigated the relationship between glycemic control, as measured by mean-HbA1c and its variability, and the severity of CAD assessed by the SYNTAX score in diabetic patients. Our study showed that Mean-HbA1c, despite HbA1c variability, measured

Table 1: Baseline characteristics of patients according to mean-glycated hemoglobin groups and coefficient of variation – glycated hemoglobin quartiles

Variables	Total (*n*=115)	Mean-HbA1c		*P*	CV-HbA1c				*P*
		≥7.5 (*n*=56)	>7.5 (*n*=59)		Q1 (<6.20) (*n*=29)	Q2 (6.21–10.73) (*n*=28)	Q3 (10.74–14.41) (*n*=30)	Q4 (>14.42) (*n*=28)	
Age (years)	62.79±8.15	62.21±7.49	62.33±8.76	0.462	61.86±8.71	63.9±9.47	62.93±6.84	62.53±7.81	0.820
Male, *n* (%)	55 (47.8)	29 (51.8)	26 (44.1)	0.408	16 (55.2)	12 (42.9)	16 (53.3)	11 (39.3)	0.554
BMI (kg/m^2)	29.91±4.74	30.48±4.69	29.36±4.76	0.199	30.94±4.07	28.32±4.14	30.60±4.99	29.77±5.41	0.141
Dyslipidemia, *n* (%)[a]	95 (82.6)	45 (80.4)	50 (84.7)	0.535	24 (82.8)	21 (75)	24 (80)	26 (92.9)	0.345
Hypertension, *n* (%)	82 (71.3)	39 (69.6)	43 (72.9)	0.701	19 (65.5)	20 (71.4)	21 (70)	22 (78.6)	0.748
Diabetes duration (years)	10.44±6.33	8.88±5.98	11.95±6.34	0.007	8.96±6.62	11.2±7.00	11.43±5.11	10.16±6.43	0.420
eGFR (ml/min/1.73 m^2)	83.11±35.47	84.84±46.86	81.53±20.48	0.625	81.22±20.25	86.72± 14.59	75.80±21.92	89.02±62.57	0.514
Cr (mg/dl)	0.97±0.35	0.99±0.32	0.96±0.38	0.714	0.98±0.30	0.87±0.16	1.05±0.36	1.00±0.51	0.286
FBS (mg/dl)	161.74±60.16	141.30±48.46	181.85±64.03	<0.001	151.16±60.12	152.63±49.21	175.31±61.32	168.33±68.02	0.330
TC (mg/dl)	163.53±42.47	161.78±39.00	165.18±45.79	0.667	162.30±37.15	176.06±46.49	154.17±33.81	161.36±49.35	0.265
LDL-C (mg/dl)	87.03±36.55	87.35±37.65	86.72±35.77	0.925	84.07±32.76	96.80±4.72	83.62±30.18	83.34±38.61	0.415
HDL-C (mg/dl)	43.74± 12.68	41.66±11.10	45.76± 13.84	0.081	43.50±12.13	44.86± 13.77	41.43± 13.36	45.13±11.60	0.675
TG (mg/dl)	169.30±71.32	163.18±64.47	175.31±77.54	0.355	170.13±71.83	147.7±63.01	166.37±72.31	192.90±73.83	0.106
Mean-HbA1c	7.65± 1.33	6.59±0.53	8.67± 1.04	<0.001	6.84± 1.09	7.45±1.20	8.14± 1.27	8.17± 1.33	<0.001
CV-HbA1c	11.54±7.50	8.88±5.51	14.11±8.29	<0.001	4.02± 1.67	8.14±1.37	12.48±1.15	21.52±7.13	<0.001
SD-HbA1c	0.91±0.67	0.59±0.39	1.22±0.74	<0.001	0.27±0.12	0.60±0.14	1.01±0.16	1.77±0.70	<0.001
Syntax score	10.13±9.93	7.33±8.39	12.79± 10.60	0.002	9.56± 10.24	11.07±9.54	10.71± 10.54	9.16±9.73	0.873

[a]Dyslipidemia was defined as: TC ≥190 or LDL-C≥115 or HDL-C<40 or TG≥150. Data are presented as mean±SD or as number and percentage. HbA1c=Glycated hemoglobin; Mean-HbA1c=Intra-individual mean of HbA1c; CV-HbA1c=Intra-individual coefficient of variation of HbA1c; BMI=Body mass index; eGFR=Estimated glomerular filtration rate; Cr=Plasma creatinine; FBS=Fasting blood sugar; TC=Total cholesterol; LDL-C=Low density lipoprotein cholesterol; HDL-C=High-density lipoprotein cholesterol; TG=Triglycerides; SD-HbA1c=Intra-individual standard deviation of HbA1c; SD=Standard deviation

Table 2: Linear regression analysis evaluating correlation between mean-glycated hemoglobin and syntax score

Variables[a]	Univariate[b]			Multivariate model 1[c]			Multivariate model 2[d]		
	OR	95% CI	*P*	OR	95% CI	*P*	OR	95% CI	*P*
Mean-HbA1c >7.5[e]	0.276	1.921–9.011	0.003	0.316	2.495–9.825	0.001	0.300	2.003–9.718	0.003
Sex (male)	0.167	−0.325–6.952	0.074	0.202	0.159–7.747	0.041	0.190	0.094–7.326	0.044
Age	0.262	0.098–0.550	0.005	0.332	0.184–0.630	<0.001	0.365	0.234–0.661	<0.001
FBS	0.281	0.017–0.076	0.002	-	-	-	0.270	0.014–0.072	0.004

[a]The variables which got a level of *P*<0.05 in the univariate analysis or multivariate models was presented in this table; [b]Univariate regression analysis was not adjusted for any variables; [c]Multivariate regression analysis (model 1) was adjusted for age, sex, BMI, diabetes duration, total cholesterol, LDL-C, HDL-C, TG; [d]Multivariate regression analysis (model 2) was adjusted for variables in model 1 plus FBS, CV.HbA1c; [e]Mean-HbA1c was divided into two groups according to mean-HbA1c cutoff (7.5). HbA1c=Glycated hemoglobin; Mean-HbA1c=Intraindividual mean of HbA1c; OR=Odds ratio; CI=Confidence interval; FBS=Fasting blood sugar; BMI=Body mass index; LDL-C=Low-density lipoprotein cholesterol; HDL-C=High-density lipoprotein cholesterol; TG=Triglycerides; CV-HbA1c=Intra-individual coefficient of variation of HbA1c

Table 3: Linear regression analysis evaluating correlation between glycated hemoglobin variability and syntax score

Variability index	Univariate[a]			Multivariate[b]		
	OR	95% CI	*P*	OR	95% CI	*P*
SD-HbA1c quartiles						
Q1 (<0.428)	Reference			Reference		
Q2 (0.429–0.841)	0.026	−4.608–5.814	0.819	0.014	−4.898–5.528	0.905
Q3 (0.842–1.188)	0.116	−2.573–7.849	0.318	0.176	−1.137–8.870	0.128
Q4 (>1.189)	0.017	−4.874–5.640	0.885	0.035	−4.632–5.947	0.761
CV-HbA1c quartiles						
Q1 (<6.20)	Reference			Reference		
Q2 (6.21–10.73)	0.065	−3.767–6.772	0.573	−0.018	−5.822–4.987	0.879
Q3 (10.74–14.41)	0.051	−4.031–6.327	0.661	0.032	−4.232–5.632	0.779
Q4 (>14.42)	−0.018	−5.677–4.861	0.878	−0.044	−6.094–4.137	0.705

[a]Univariate regression analysis was not adjusted for any variables; [b]Multivariate regression analysis was adjusted for age, sex, BMI, dyslipidemia. SD-HbA1c=Intraindividual standard deviation of HbA1c; CV-HbA1c=Intra-individual coefficient of variation of HbA1c; OR=Odds ratio; CI=Confidence interval, BMI=Body mass index, HbA1c=Glycated hemoglobin

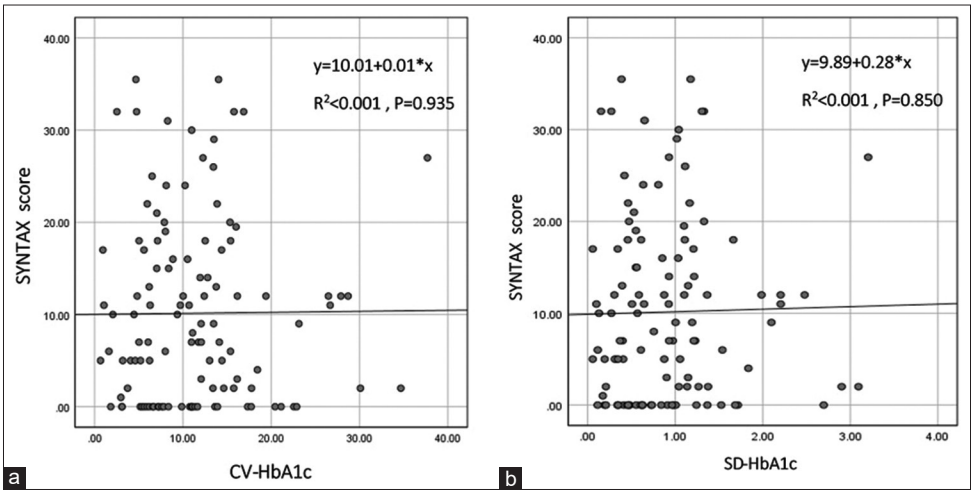

Figure 1: Correlation between CV-HbA1c (a), SD-HbA1c (b) and SYNTAX score

by SD-HbA1c and CV-HbA1c, is a predictor of the severity of CAD.

Mean-HbA1c, a predictor of the severity of coronary artery disease and its cutoff value

The SYNTAX score, a measure of the severity of CAD, was significantly higher in patients with mean-HbA1c >7.5. In the univariate analysis, FBS was also in association with the SYNTAX score, unlike the duration of DM. It can reflect that uncontrolled glycemic states bear more cardiovascular complications than longer durations of diabetes in a normoglycemic state. To further evaluation of the relationship between mean-HbA1c and CAD severity, multivariate linear regression analyses were performed, adjusting for various confounding factors. In all models, the SYNTAX score remained consistently higher in the mean-HbA1c >7.5 group. Higher mean-HbA1c levels reflect uncontrolled glycemic states that are responsible for higher SYNTAX score. These findings align with many other studies, which have revealed the association between mean-HbA1c levels and the cardiovascular outcomes of DM.[10,23,24] This can be concluded that higher mean-HbA1c

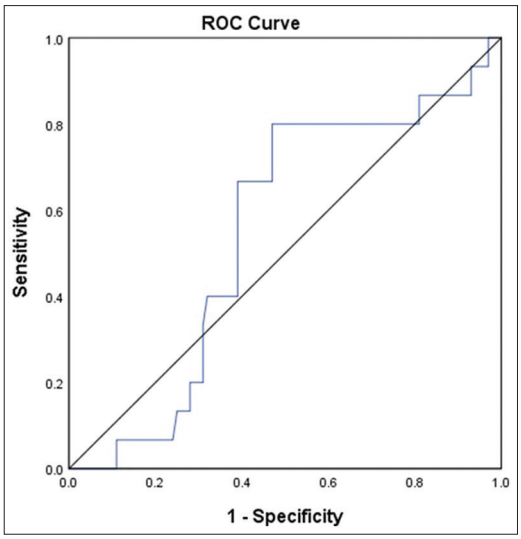

Figure 2: Receiver operating curve analysis determining Mean-HbA1c cut-off value related to SYNTAX score

levels can be a potential predictor of CAD severity. Therefore, regular monitoring of blood glucose levels and maintaining optimal glycemic control, as shown by lower mean-HbA1c levels, may be crucial for reducing the severity of CAD in diabetic patients.

Through ROC curve analysis, we determined that a cutoff value of 7.5 for mean-HbA1c levels exhibited the highest sensitivity and specificity in predicting CAD severity. It is worth noting that recent guidelines recommend maintaining HbA1c levels at or below 7 to prevent the progression of CAD in individuals with diabetes.[25,26] Furthermore, a 10-year cohort study found that HbA1c levels equal to or >6.5 during the 1st year following a diabetes diagnosis were associated with an elevated risk of macrovascular events. However, for durations longer than 1 year, HbA1c levels exceeding 8 were linked to an increased risk of diabetes complications.[27] While this previous study focused on the incidence of CAD, our current study specifically aimed to determine the cutoff value for mean-HbA1c levels based on the severity of CAD, measured by SYNTAX score. This can somewhat explain the differences in results; furthermore, discrepancy in the study design and sample size is notable. Additional prospective studies based on CAD severity can be helpful to confirm the findings of this study, and if so, a cutoff value of 7.5 for mean-HbA1c levels can be valuable for physicians in diagnosing patients at higher risk for severe CAD and implementing appropriate management strategies to mitigate complications.

Glycemic variability and severity of coronary artery disease

The analysis of HbA1c variability, represented by SD-HbA1c and CV-HbA1c, did not show a significant correlation with the SYNTAX score in this study. It can be due to the medical treatment and minimization of the HbA1c level to the normal range during visits. For further explanation, we document an elevated HbA1c level for patient in the first visit but after treatment, the third HbA1c level decreases to the normal range. Therefore, HbA1c variability is high because of the difference between visits, but glycemic states have been controlled during follow-up that can reduce cardiovascular complications. Another reason for this insignificance may be that HbA1c shows mean blood glucose in approximately 3 months. The fluctuations of the blood glucose levels over these 3 months cannot be measured by the HbA1c level, and as a result, they can be dismissed. This reflects that the short-term GV can be more reliable for the real variability in the glycemic levels than HbA1c variability.

During recent years, numerous studies investigated the association between short term and long term GV, and cardiovascular complications of DM. Short term GV has been established as a risk factor for the development of CAD, and some studies have demonstrated its association with SYNTAX score.[28,29] In the other hand, long-term GV has been put under consideration in the past decade. Several studies investigated the association between HbA1c variability and cardiovascular events in diabetic patients. Some of them showed that HbA1c variability significantly increases cardiovascular events and mortality.[13,23,30] Nevertheless, some other studies found that HbA1c variability does not have a correlation with cardiovascular complications.[10] These studies focused on the incidence of cardiovascular events to investigate the cardiovascular complications of HbA1c variability, but just a few other studies attempted to determine the impact of HbA1c variability on the severity of CAD based on the cardiovascular imaging tests. Suhua Li *et al.* demonstrated a significant correlation between HbA1c variability, measured by CV-HbA1c, and coronary atherosclerosis progression, based on the coronary CT angiography.[11] However, to the best of our knowledge, the present study is the first investigation about association between HbA1c variability and severity of CAD based on invasive coronary angiography and SYNTAX score. In contrast with some of the previous studies, we did not find a significant correlation between HbA1c variability and cardiovascular disease. It can be due to different methods for the determination of cardiovascular complications. Many of previous studies used incidence of cardiovascular disease or mortality to describe cardiovascular complications, but in this study, we utilized invasive coronary angiography, as the gold standard imaging test for determination of the severity of CAD and SYNTAX scoring system. Another reason for this discrepancy may be differences in study design (retrospective and prospective). The differences in the sample size, which is a limitation of this study, are noteworthy. Overall, we suggest additional prospective

studies with a larger sample size to determine the association between HbA1c variability and the severity of CAD based on invasive coronary angiography.

Limitations

It is important to consider some limitations of this study. In this study, there was not any baseline angiography for patients to compare with the secondary angiography and to attribute progression of the CAD severity to the HbA1c variability. If so, the results could be more reliable. On the other hand, the study design was retrospective, which prevents explaining a definite relationship between glycemic control and severity of CAD. Moreover, there were data limitations on a number of the known confounding factors, such as medication use (e.g. GLP1 agonists and SGLT2 inhibitors) and concurrent comorbidities that may have significantly influence the study's outcomes. Other factors, including lifestyle choices, ethnic backgrounds, measurement variability, psychosocial influences, follow-up periods, and the clinical setting, could further complicate the interpretation of the results. Therefore, the potential effects of these confounding variables must be considered when evaluating the observed associations.

On the other hand, the findings of this study may not be generalizable to other populations, primarily due to the modest sample size and the specific characteristics of the study cohort. The limited diversity within the sample may not accurately reflect the broader population. Consequently, further prospective studies with larger sample sizes should be conducted to confirm these findings.

CONCLUSION

This study provides evidence supporting the association between glycemic control, as measured by mean-HbA1c, and the severity of CAD in diabetic patients. Higher mean-HbA1c levels were associated with increased severity of CAD, independent of other clinical factors. However, HbA1c variability did not show a significant correlation with CAD severity. These findings underscore the importance of attainment suitable glycemic control in diabetic patients to reduce the burden of CAD.

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Conflicts of interest

There are no conflicts of interest.

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