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Original Article

The Relationship between Left Ventricular Diastolic Function Parameters and Coronary Artery Disease Severity

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Abstract

Background: The relationship between diastolic function parameters and the severity of coronary artery disease (CAD) is controversial. This study aimed to determine the relationship between left ventricular diastolic function and the severity of CAD.

Methods: This cross-sectional study included 63 patients with Ischemic heart disease (IHD) or those suspected of having IHD, who underwent angiography. The study was conducted in Shafa Hospital, Kerman, Iran, from 2021 to 2022. Two-dimensional (2D) strain echocardiography was used to assess left ventricular (LV) function parameters, followed by coronary angiography. Based on the severity of the disease, patients with significant CAD were placed in the case group, and patients with insignificant CAD were placed in the control group. The correlation between the CAD severity and the severity of LV diastolic dysfunction was computed. Descriptive tests, independent *t* tests, and Spearman correlation coefficients were used. P<0.05 was considered statistically significant.

Results: The results indicated that there was no correlation between E/e′ (P=0.103), left atrial volume index (LAVI) (P=0.168), tricuspid regurgitation velocity (TRV) (P=0.217), myocardial performance index (MPI) (P=0.106), E wave deceleration time (dt) (P=0.644), and late diastolic strain rate (P=0.502) with CAD severity based on SYNTAX score. However, there was a correlation between left atrial (LA) strain (P=0.017), global longitudinal strain (GLS) (P<0.001), early diastolic strain rate (P<0.001), and systolic strain rate (P=0.047) with SYNTAX score. Besides, there was a correlation between LA strain (P=0.017), GLS (P<0.001), early diastolic strain rate (P<0.001), and late diastolic strain rate (P=0.035) with numbers of epicardial coronary arteries with significant lesions.

Conclusion: In contrast with 2D strain echocardiography, this study showed that conventional echocardiography parameters had no significant relationship with CAD severity. GLS had the strongest correlation with CAD severity, and diastolic strain rates had a weaker correlation with CAD severity.

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Keywords ● Ventricular dysfunction, left ● Coronary angiography ● Global longitudinal strain ● Echocardiography

What's Known

- Patients with ischemic heart disease frequently experience diastolic dysfunction.
- Several studies investigated the relationship between conventional echocardiographic diastolic parameters with coronary artery disease, and the results were conflicting.

What's New

- Modern echocardiography methods, such as 2-dimensional speckle tracking echocardiogram, are beneficial in assessing coronary artery disease. The present study evaluated the association between the severity of coronary artery disease and diastolic parameters using strain echocardiography.
- There was a correlation between left atrial strain, global longitudinal strain, early diastolic strain rate, and late diastolic strain rate with numbers of epicardial coronary arteries with significant lesions.

Introduction

Ischemic heart disease (IHD) is a developing global pandemic. World Health Organization (WHO) reports indicated that about 17.9 million died in 2019, accounting for 32% of all global deaths.[1]

Considering the great burden of coronary artery disease (CAD), it seems necessary to develop methods for early diagnosis and treatment. Non-invasive imaging tests such as coronary computed tomography angiography (CTA), radionuclide imaging, stress echocardiography, and exercise tolerance test (ETT) can aid in the evaluation and detection of CAD.[2, 3]

Echocardiography, which measures left ventricular (LV) diastolic function, is a low-cost, noninvasive method for assessing CAD. LV diastolic dysfunction is defined as abnormalities in LV relaxation, left atrium emptying, and LV filling that cause the failure to increase cardiac output with exercise and an increase in pulmonary pressure, resulting in a variety of symptoms.[4] Diastolic dysfunction increases the risk of mortality and hospitalization, as well as the development of heart failure.[5]

Assessing LV diastolic function has diagnostic, therapeutic, and prognostic advantages. Elevated left ventricular filling pressure (LVFP) is a major factor in dyspnea in patients with a variety of cardiac diseases. While issues such as anemia and lung diseases can also cause shortness of breath, biomarkers aid in detecting LV wall stress. However, their interpretation is influenced by factors such as age and sex. On the other hand, cardiovascular imaging, particularly echocardiography, directly examines heart functions, valve health, and pulmonary pressures, providing a comprehensive diagnostic image. Accurate diagnosis is essential for successful treatment. Echocardiography plays a pivotal role in accomplishing this goal by providing accurate insights into cardiac structure and function, thereby guiding optimal treatment strategies. Recent data suggested that the potential of LV diastolic strain rate and LA strain in predicting outcomes was gaining recognition among patients dealing with acute myocardial infarction and atrial fibrillation.[6]

The relationship between conventional echocardiographic diastolic parameters and CAD has been investigated in several studies, where some confirmed the usefulness of these parameters such as transmitral flow velocities (peak early diastolic mitral inflow velocity - E, mitral annulus early diastolic velocity e′, E/e′ ratio) and tissue Doppler imaging (TDI),[7, 8] while others arguing against the reliability of these parameters for assessing patients with CAD.[9] In recent years, modern echocardiography methods, such as two-dimensional (2D) speckle tracking echocardiography (2DSTE), have received a lot of attention and have shown promising benefits in terms of assessing CAD. This study aimed to examine the relationship between LV diastolic function parameters and the severity of CAD in symptomatic patients. Thus, it can be utilized in planning better diagnostic options and selecting the patients who require invasive procedures.

Patients and Methods

The study was approved by the Ethical Committee of Kerman University of Medical Sciences (code: IR.KMU.REC.1400.176). The participants were informed about the goals of the research, and written informed consent was obtained from the patients before participation.

This cross-sectional study included 63 patients with IHD or those who were suspicious of having IHD, and underwent coronary angiography at Shafa Hospital, Kerman, Iran, between 2021 to 2022. The inclusion criteria were patients with stable angina with preserved LV systolic function. On the other hand, patients with ST-segment elevation myocardial infarction (STEMI) or Non-ST segment elevation myocardial infarction (NSTEMI) or unstable angina, LV Ejection Fraction (EF)<50%, congenital heart disease, history of coronary artery bypass graft (CABG) or percutaneous coronary intervention (PCI), left ventricular hypertrophy (LVH), valvular heart disease and arrhythmia were excluded from the study.

All participants underwent echocardiography using the Philips affinity-50 machine, and the parameters related to left ventricular diastolic function (myocardial performance index (MPI), E wave deceleration time (E dt), left Atrial volume Index (LAVI), tricuspid regurgitation (TR) velocity, E/e′), as well as myocardial deformation indices including global longitudinal strain (GLS), early diastolic strain rate, late diastolic strain rate, systolic strain rate and left atrial (LA) strain were studied. Subsequently, all patients underwent coronary angiography. Based on the disease severity, patients with severe CAD comprised the case group, while those with mild CAD formed the control group. Demographic characteristics and cardiovascular risk factors, including age, sex, weight, height, and history of diabetes, hypertension, and smoking were assessed through patient survey.

Conventional Echocardiography

The conventional echocardiography parameters such as LV end-diastolic dimensions (including interventricular septum wall thickness, LV internal dimension, and LV posterior wall thickness) were obtained from the parasternal long-axis view at the mitral valve leaflet tips. The parameters presented were LV mass index (LVMI), E dt, and LAVI, where E denotes the peak velocity of early diastolic filling, and dt denotes the deceleration time of the E wave. The LVMI was estimated by dividing the LV mass by the body surface area where LV mass=0.8{1.0 4[([LVEDD+IVSd+PWd]^3−LVEDD^3)]}+0.6, where LVEDD is the LV end-diastolic diameter, IVSd is the interventricular septum thickness, and PWd is the posterior wall diameter.

The LA volume index was calculated by first estimating the LA volume using the area-length method and then dividing it by the body surface area. In addition, E/e′ was reported, where e′ denoted the peak longitudinal early diastolic velocity. To this end, pulsed-wave TDI tracings were obtained with the range gate placed at the septal and lateral mitral annular segments in the 4-chamber view. The peak longitudinal early diastolic velocity (e′) was measured, and the average was calculated using the lateral and septal velocities.

Two-dimensional Strain Echocardiography

Two-dimensional strain Echocardiography (2DSE) plays a vital role in this study. In brief, 2DSE was performed from the apical 4-chamber, 2-chamber, and apical long-axis view. The endocardial border was traced in the end systole via speckle tracking. The global longitudinal peak systolic strain (GLS) was computed by averaging over 18 segments of regional longitudinal peak systolic strain (RLS). These segments included six basal, six mid-ventricular, and six apical, which were measured in all views between the opening and closure of the aortic valve. In each segment, peak longitudinal systolic strain rate (SR), peak longitudinal early diastolic SR, and peak longitudinal late diastolic SR were measured and averaged to provide global estimates. Left atrial reservoir strain was measured using speckle tracking.

Coronary Angiography

Coronary angiography was used to diagnose CAD. For this purpose, the standard Judkins technique was used.[10] It involved visualization of coronary arteries in left and right oblique planes with cranial and caudal angles at a speed of 30 frames per second by manual injection of 6-10 mL of contrast agent at each position. The severity and the number of stenotic coronary arteries were determined by a trained cardiologist. Coronary artery stenosis greater than or equal to 70% was considered serious. In addition, an online calculator (https://syntaxscore.org/calculator/syntaxscore/frameset.htm) was used to determine the synergy between percutaneous coronary intervention with taxus and coronary artery bypass surgery (SYNTAX) score for each patient.

Statistical Analysis

All the statistical analyses were performed using IBM Statistics SPSS software for Windows (version 20.0, Armonk, NY: IBM Corp). The relationship between the CAD severity and the severity of LV diastolic dysfunction was calculated. A descriptive test, independent *t* test, and Spearman correlation coefficients were employed for the analysis. $P<0.05$ was considered statistically significant.

Results

The study included 63 patients, with 34 patients in the control group and 29 patients in the case group. In addition, 27 individuals (42%) of the participants were women, and 36 (58%) were men. A summary of the demographic information of the patients, including age, family history of cardiovascular diseases, smoking, opium addiction, history of diabetes, hypertension, hyperlipidemia, and BMI average is shown in table 1. Table 2 shows the angiographic results of patients based on the number of vessels with severe stenosis. Table 3 demonstrates the average echocardiographic parameters for each group with and without severe coronary artery stenosis, including late diastolic strain rate, early diastolic strain rate, systolic strain rate, E dt, GLS, LA strain, MPI, TRV, LAVI, and E/e′.

As illustrated in figure 1, there was no correlation between the SYNTAX score and

Table 1: Demographic information of the participating patients

Groups	Age (mean±SD)	Family history of CAD	Smoking	Diabetes	Hypertension	Hyperlipidemia	BMI (Kg/m^2)
Case	59.14±8.8	6 (20.6%)	7 (24.1%)	8 (27.6%)	16 (55.2%)	3 (10.3%)	25.8
Control	51.44±8.7	5 (14.7%))	9 (26.5%)	7 (20.6%)	14 (41.2%)	2 (5.9%)	24.8
Total	56.63±8.8	11 (17.5%)	16 (25.4%)	15 (23.8%)	30 (47.6%)	5 (7.9%)	25.2

BMI: Body mass index; CAD: Coronary artery disease

Table 2: Angiography results and number of patients in each group		
Groups	**Angiography results**	**Number of patients**
Significant CAD (Case)	3VD	5 (17.4%)
	2VD	14 (48.2%)
	SVD	10 (34.4%)
Nonsignificant CAD (Control)	Normal or non-significant CAD	20 (58.8 %)
	Slow flow	14 (41.2 %)

3VD: Three vessel disease; 2VD: Two vessel disease; SVD: Single vessel disease

Table 3: Comparison of echocardiographic parameters between two groups			
Echocardiographic parameters	**Case**	**Control**	**P value**
SSR	-1.54	-1.7	0.066
E dt	168.5	167.7	0.285
Late DSR	1.8	1.99	0.035
Early DSR	1.4	1.7	0.001<
GLS	-18.4	-20.1	0.001<
LAS	28.3	30.5	0.017
MPI	0.58	0.50	0.051
TRV	2.36	2.29	0.272
LAVI	19.6	18.3	0.092
E/e′	12.5	10.7	0.078

SSR: Systolic strain rate; Late DSR: Late diastolic strain rate; Early DSR: Early diastolic strain rate; LAS: Left atrial strain; LAVI: Left atrial volume index; P<0.05 was considered statistically significant.

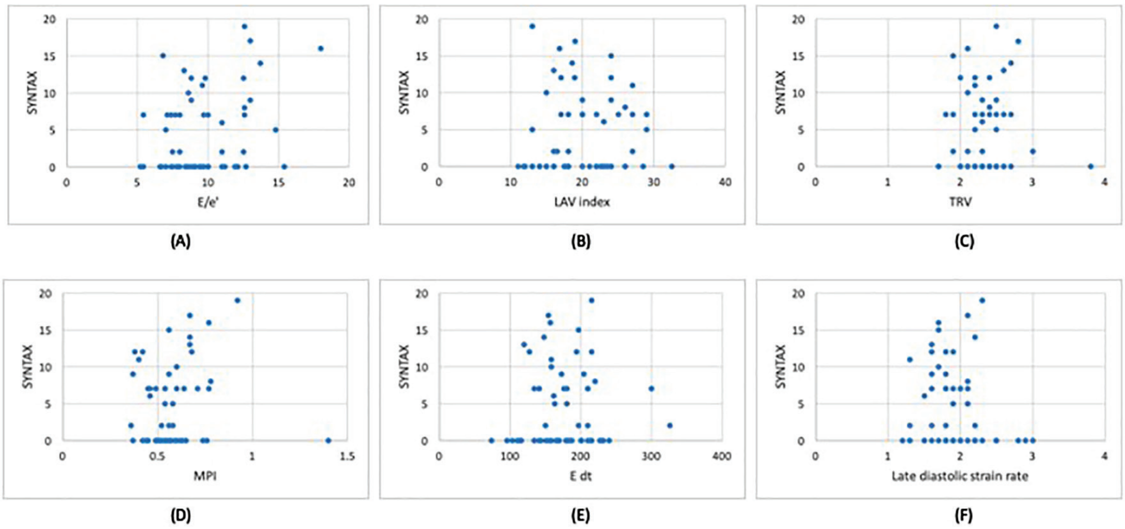

Figure 1: The graphs show the correlation between E/e′, LAV index, TRV, MPI, E dt, and late diastolic strain rate with the SYNTAX score. LAV: Left Atrial Volume; TRV: Tricuspid Regurgitation Velocity; MPI: Myocardial Performance Index; dt: deceleration time

E/e′ (P=0.103), LA volume index (P=0.168), TR velocity (P=0.217), MPI (P=0.106), E dt (P=0.644) and late diastolic strain rate (P=0.502). In other words, while these factors increased, the SYNTAX score did not change. On the contrary, there was a significant correlation between the SYNTAX score and LA strain (P=0.017), GLS (P<0.001), early diastolic strain rate (P<0.001), and systolic strain rate (P=0.047, figure 2). In fact, figure 2 shows a negative relationship between the LA strain and early diastolic strain rate with the SYNTAX score, R=-0.301 and R=-0.461, respectively. Furthermore, there was a positive correlation between GLS and the SYNTAX score (R=0.696) and between the systolic strain rate and the syntax score (R=0.251).

Furthermore, as shown in figure 3, there was no correlation between CAD and E/e′ (P=0.078), LAV index (P=0.092), TRV (P=0.272), MPI (P=0.051), E dt (P=0.285) and systolic strain rate (P=0.066) based on the number of stenotic coronary arteries, indicating no positive or negative correlation between these parameters and the CAD severity based on the number of stenotic coronary arteries. On the other hand, there was a correlation between parameters, such as LA strain (P=0.017), GLS (P=0.00), early diastolic strain rate (P=0.00), late diastolic strain rate (P=0.035), and the severity of CAD based on the number of coronary arteries involved.

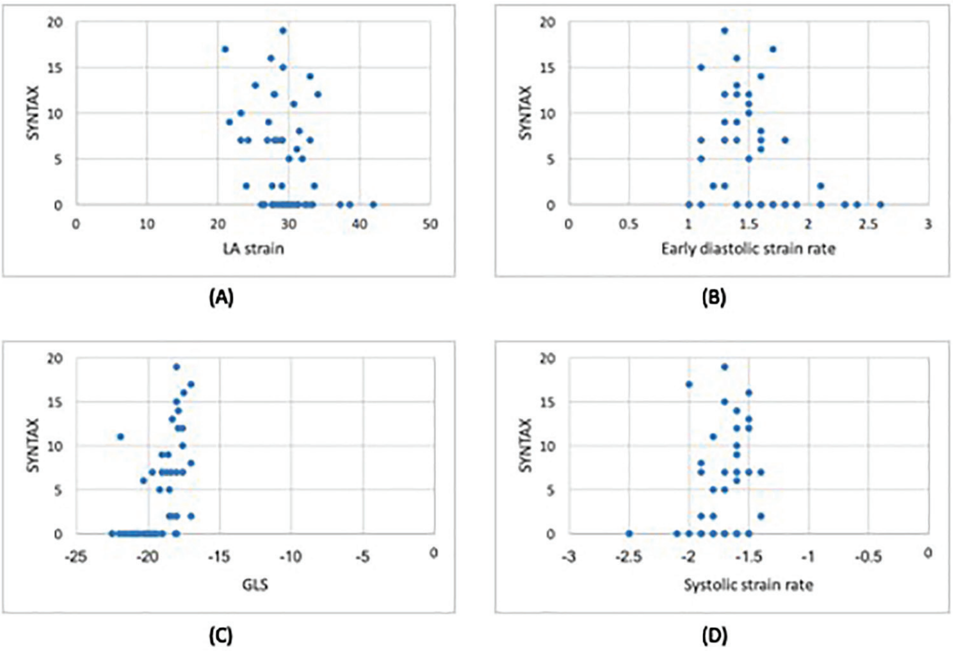

Figure 2: The graphs show the correlation between LA strain, GLS, early diastolic strain rate, and systolic strain rate with the SYNTAX score. GLS: Global Longitudinal Strain; LA: Left Atrial

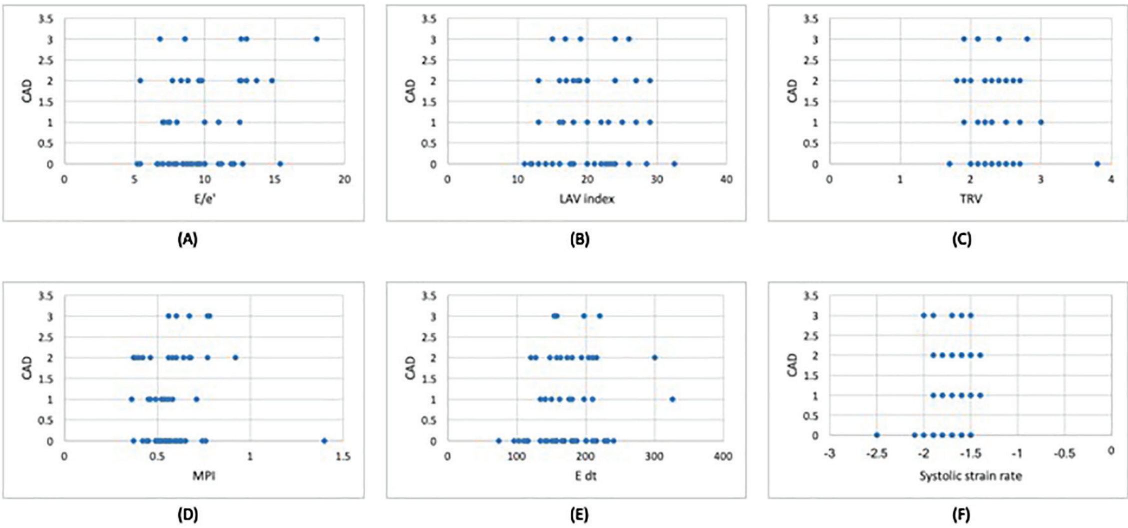

Figure 3: These graphs illustrate the correlation between E/e′, LAV index, TRV, MPI, E dt, and systolic strain rate with the severity of CAD based on the number of coronary stenotic coronary arteries. LAV: Left Atrial Volume; TRV: Tricuspid Regurgitation Velocity; MPI: Myocardial Performance Index; dt: deceleration time

Figure 4 demonstrates that there was a negative correlation between LA strain, early diastolic strain rate, late diastolic strain rate, and CAD severity based on the number of stenotic coronary arteries, R=-0.30, R=-0.48, and R=-0.267, respectively. Moreover, there was a positive correlation between GLS and CAD severity based on the number of stenotic coronary arteries with R=0.698.

Finally, the findings indicated that there was no significant difference between patients with slow-flow coronary arteries (SCF) and the control group in terms of the diastolic function indices, including E/e′, LAVI, TRV, MPI, E dt, late diastolic strain rate, early diastolic strain rate, systolic strain rate, and LA strain.

Discussion

The findings of the present study highlighted an important aspect of assessing CAD severity. Remarkably, parameters such as E/e′, LAV index, TR velocity, MPI, and E dt had no significant relationship with the severity of CAD. In contrast, the present study found that GLS, early diastolic strain rate, and LA strain were directly associated with both the SYNTAX score and the number of diseased arteries. These parameters consistently decreased as the severity of CAD increased. Besides, a higher SYNTAX score decreased the systolic strain rate, and as the number of damaged coronary arteries increased,

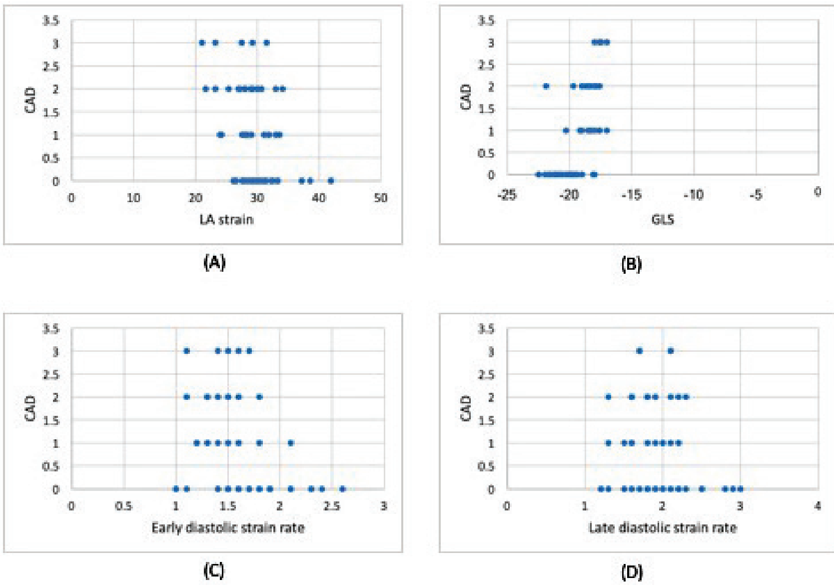

Figure 4: These graphs show the correlation between LA strain, GLS, early diastolic strain rate, and late diastolic strain rate with the severity of CAD based on the number of stenotic coronary arteries. LA: Left Atrium; GLS: Global Longitudinal Strain

the late diastolic strain rate decreased.

The observed decline in GLS, LA strain, and early diastolic strain rate supported the hypothesis that chronic myocardial ischemia caused by obstructive CAD could lead to impaired myocardial relaxation and subsequent LV diastolic dysfunction.[11, 12] Although previous studies investigated this association, the present study provided new insights by demonstrating a clear relationship with the severity of CAD, as measured by both the SYNTAX score and the number of affected vessels.

Comparisons with previous studies revealed nuanced differences in findings. For instance, Lin and colleagues reported that the extent and severity of obstructive and non-obstructive CAD by coronary CT angiography were associated with increased LV end Diastolic Pressure (LVEDP), E/e', and measures of diastolic dysfunction (LV mass and relative wall thickness).[13] However, their study group was different from those of the present study in terms of CAD risk factors prevalence, and also they used CT angiography for evaluating CAD severity.

In another study, Nakajima and others reported that the development of symptoms and myocardial ischemia during dobutamine stress echocardiography (DSE) were both associated with an increase in E/e′.[14]

Maragiannis and others found that left ventricular diastolic dysfunction (E/A, E/e′, E dt) was associated with an abnormal CAD score even after adjusting for Framingham Risk Score or clinical risk factors.[15] However, some other studies reported that there was no relationship between CAD and LV diastolic dysfunction in patients with normal EF.

In a study, Jamiel and others found that CAD diagnosed by CT angiography was not associated with diastolic function measures (E/e′,) on echocardiography.[16] Besides, Abali and others reported that in individuals with stable CAD undergoing coronary angiography, the diastolic function (LA volume index, mitral inflow E/e′) indicated no impairment based on CAD severity.[17] Despite the effect of atherosclerosis on LV function and shared risk factors, the present study found no correlation between the severity of CAD and conventional echocardiography parameters. This finding suggested that these risk factors could affect atherosclerosis and myocardial function in different ways. On the other hand, evaluating the coronary arteries only by anatomical means is not a comprehensive method to assess the severity of CAD, which might impair myocardial function.

Recently, 2D speckle tracking accompanied by conventional echocardiography has provided improved techniques for evaluating LV function. The longitudinally oriented myocardial fibers in the subendocardium were particularly vulnerable to ischemia. Therefore, measuring the longitudinal motion and deformation might be a sensitive marker of CAD using TDI or 2DSTE.[18]

Several studies investigated the 2DSTE and CAD relationship. For instance, Biering and others found that global longitudinal peak systolic strain (assessed at rest) in patients with stable angina was an independent predictor of significant CAD and could identify high-risk patients.[18]

Moreover, Radwan and others demonstrated that measurement of global longitudinal strain, using 2D speckle tracking echocardiography, was a sensitive and accurate way of predicting severe CAD.[19] Said and others reported that left atrial deformation investigation using 2DSTE was a predictor of the severity of CAD in patients with stable CAD.[20] Similarly, the present study showed that GLS, early diastolic strain rate, and LA strain were all related to the severity of CAD. This means that when CAD severity increased, the value of LA strain, the absolute value of GLS, and the early diastolic strain rate all decreased. These findings could indicate that 2DSTE parameters were more sensitive predictors for assessing LV diastolic function and CAD than conventional echocardiography.

Nevertheless, a limitation of the present study was the exclusive reliance on coronary angiography to assess CAD severity. Recognizing the anatomical focus of this method, future investigations should explore a combined approach incorporating both anatomical and functional tests to gain a more comprehensive knowledge of the relationship between CAD severity and echocardiographic parameters.

Conclusion

In contrast with 2DSTE, the present study found no significant relationship between conventional echocardiography parameters and CAD severity. In strain echocardiography, GLS had the strongest correlation with CAD severity, and diastolic strain rates had a weaker correlation with CAD severity. Further studies with larger study groups and functional CAD evaluation in combination with anatomical studies, could be helpful in evaluating the usefulness of 2DSTE in CAD patients.

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Authors' Contribution

All authors contributed to the conception and design of the work; acquisition, analysis, or interpretation of data for the work; and contributed to the drafting of the paper and reviewing it for important intellectual content; and final approval of the version to be published; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conflict of Interest: None declared.

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