Left ventricular diastolic dysfunction as a predictor of coronary artery disease and its severity in diabetic patients

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ABSTRACT

Background: Over 366 million individuals throughout the world have diabetes mellitus (DM), and by 2030, that number is projected to increase to 522 million. Diabetes' macrovascular consequences raise the risk of illness and death. Systolic and diastolic dysfunction are caused by ischemic heart disease, although diastolic function appears to be more vulnerable to ischemia than systolic function. We thus look into the connection between coronary artery disease severity and left ventricular (LV) diastolic performance in diabetic individuals presenting with symptoms similar to angina.

Objective: to assess the connection between 2D echocardiography and the SYNTAX score, as well as the amount and severity of left ventricular diastolic dysfunction in diabetic individuals.

Patients and methods: one hundred patients undergoing elective angiography of coronaries were enrolled in the research with assessment for LV diastolic and systolic function by transthoracic echocardiography before coronary angiography. This study was carried out at cardiovascular department Azhar-Assiut university hospital and Sohag Cardiac Specialized center, from December 2020 to December2021.

Results: SYNTAX score and (E/A & E/e' & LA volume index), which are various determinants of diastolic dysfunction, were significantly correlated. Additionally, there was a highly significant positive correlation between the grade of Left Ventricular Diastolic Dysfunction and the severity of CAD as determined by SYNTAX score. (P below than 0.001)

Conclusion: Patients with CAD frequently had LV diastolic dysfunction, and there is a significant positive correlation between the grade of diastolic dysfunction and the severity of CAD as determined by the SYNTAX score, supporting the need to take this into account when risk-stratifying diabetic patients.

Key words: SYNTAX score, diabetes mellitus, coronary artery disease, and diastolic dysfunction.

INTRODUCTION

The biggest cause of mortality globally is coronary artery disease (CAD). According to the Global Burden of Disease data collection, CAD is thought to afflict 126 million people (1,655 per 100,000), and it causes close to 10 million deaths annually. The global prevalence of CAD is increasing due to population ageing, and rates are anticipated to approach 1,845 per 100,000 by 2030, with greater medical and economic impact, even though age-adjusted prevalence rates show a positive decline[1].

It is well recognized that left ventricular (LV) systolic and diastolic dysfunction will result from ischemia or infarction brought on by coronary artery disease (CAD). Previous research has shown that chronic CAD patients experience diastolic dysfunction that is unrelated to LV systolic functioning[1].

Diastolic function is the first cardiac function to be impaired in ischemic heart disease[2]. It has been demonstrated that diastolic dysfunction can help predict the onset of heart failure and overall mortality[3].

The most often used clinical method for assessing left ventricular (LV) diastolic function is echocardiography, a non-invasive procedure. Tissue Doppler imaging (TDI) can measure early mitral filling peak blood flow velocity (E) and early diastolic mitral annular velocity (e') during routine echocardiograms, and the ratio of these values (E/e') is widely regarded as a non-invasive substitute for LV diastolic function[4].

The examination of the coronary arteries still relies heavily on coronary angiography, which is used to diagnose coronary artery disease (CAD) and gauge its severity. These data are then combined with additional clinical data to determine therapy choices[5]**.**

In diabetic individuals with symptoms similar to angina, the goal of this study is to assess diastolic dysfunction as a predictor of coronary artery disease (CAD) and its severity discovered by coronary angiography.

PATIENTS AND METHODS

The present research includes 100 patients admitted to cardiovascular department Azhar-Assiut university hospital and Sohag Cardiac Specialized center, from December 2020 to December 2021. for elective **CA**

- **Inclusion criteria:**
  - Age: 18-80 years .
  - Sex: both male and female included.
  - Diabetic patients with chest pain or angina equivalent.
  - Normal resting 12 leads ECG
  - Normal LV systolic function with No resting RWMA

- **Exclusion criteria:**
  - Congenital heart disease
  - Cardiomyopathy EF<50%
  - Valvular heart disease

- Post CABG status
- Post PCI status
- • A heart rhythm disorder such as frequent ventricular ectopic, fluttering of the atrium, or fibrillation of the atrium.

- **EthicalAspects:**
- Following an explanation of the technique to each patient, consent was acquired. The study was authorized by the medical research and ethics council.
- **Data collection:** The data collection included:

1- Every patient had a complete medical history obtained, including name, age, sex, employment, family history, and risk factors for coronary artery disease (CAD), such as smoking, high blood pressure, diabetes mellitus, dyslipidemia, and sedentary behavior.

2-Full clinical examination and local cardiac examination.

3- A complete blood count (CBC), international normalized ratio (INR), random blood glucose (RBG) level, serum creatinine level, lipid profile (total cholesterol (TC), LDL, HDL, and triglyceride (TG), as well as serology (HBsAg, HCVAb, and HIV) are all examples of laboratory tests.

4-Electrocardiogram (ECG): Resting 12-leads ECG was done by **ECG Fukuda Cardimaxdevice.** Evaluation of all electrocardiographs was done to diagnose each type of coronary artery disease.

5-Echocardiography (ECHO) was done using **Vivid GE S5**, Two Dimensions echocardiogram using 3-5 MHz transducer TTE will be done for every patient in the study for evaluation of Systolic and diastolic activity of the left ventricle.

The following parameters will be measured:

- **Systolic function:**

  For the objective of quantifying LVEF% and FS, the LV end-diastolic diameter (LVDd) and LV end-systolic diameter (LVDs) have been measured using M-mode echocardiography.

- **Diastolic function:**

- **The following parameters will be evaluated while using pulsed wave Doppler:** Peak Speed of early mitral diastole filling (E)Peak There was a documented late (atrial) filling velocity (A).E/A (the ratio of E to A) was evaluated.IVRT, or isovolumteric relaxation time ,Deceleration time of the E wave(DT)
- **TDI**: The apical 4-chamber image was used to calculate the myocardial tissue Doppler velocities at the septal and lateral mitral annuli.

  The mean E/e' () ratio as well as the early diastolic and late diastolic mitral annular velocities (e' and a') were measured.
- **TR jet maximum velocity** by continuous wave (CW)Doppler
- **Left atrial volume index.**

6-Coronary angiography (CA) was done by using **Siemens Artis zee 20×20** for assessment of the severity and distribution of coronary affection by SYNTAX score.

Statistical analysis:

Version 20.0 of the Statistical Package for the Social Sciences (SPSS) was used to analyze the data. The mean and standard deviation (SD) were used to convey quantitative data. Frequency and percentage were used to convey qualitative data.

Independent T-test to contrast among two independent means, Statistical analysis for non-normal distributed data was performed by Kruskal-Wallis followed by Mann-Whitney Test for pairwise contrasting between groups.

Pearson In order to compare proportions between two subjective variables, the Chi-square (X2) test of significance was carried out, along with the correlation coefficient test (r), which was used to corroborate the findings. P-values lower than 0.05 were deemed noteworthy.

RESULTS

In our study, the mean **age** of the patients was 48.63 ± 7.95, 66 patients (66%) were **males** and 34 (34%) were **females**, 49 patients (49%) were **hypertensive**, 49 (49%) were current **smokers.** 54 (54%) patients were **dyslipidemic,** 49 patients (49%) have a verified ischemic heart disease family history. **(Table 1)**.

Table (1): Demographic data and clinically risk factors of the study population:

Sociodemographic characteristics and clinical data	Study sample (No=100)	
	No	**%**
Male	66	66
Female	34	34
Age (Years) Mean± SD	48.63 ± 7.95	
	Positive No	**%**
Smoking	49	49
HTN	49	49
Dyslipidemia	54	54
Family history of IHD	49	49

Echocardiographic descriptive data of the patients shows mean **EF** was (60.8±6.91), mean **IVRT** was (93.04±19.48) , mean **TR Velocity** was (2.35±0.5) , mean **LA Volume index** was (20.81±7.52) , mean **E wave** velocity was (67.89±20.55) , mean **A wave** velocity was (66.05±17.3), mean **E/A ratio** was (1.14±0.62) , mean **E wave DT** was (193.79±44.2) , mean **e wave** velocity was (8.48±3.14) , mean **a wave** velocity was (8.41±2.15) and mean **E/e ratio** was (9.48±5.52). **(Table 2)**

Table (2): Descriptive data on the patients' cardiac echocardiograms

Echocardiograms of theheart	Mean ± SD
IVRT (msec.)	93.04±19.48
EF (%)	60.8±6.91
TR Velocity (m/s)	2.35±0.5
LA Volume index (ml/m2)	20.81±7.52
E wave (cm/sec.)	67.89±20.55
A wave (cm/sec.)	66.05±17.3
E/A ratio	1.14±0.62
E wave DT (msec.)	193.79±44.2
e` (cm/sec.)	8.48±3.14
a` (cm/sec.)	8.42±2.16
E/e ratio	9.48±5.52

Distribution of diastolic function state among the study group shows that 40% of the study group are Normal (have no diastolic dysfunction) , 10% of the examined group has Grade III diastolic disorders, 20% have Grade II, and 30% have Grade I disorder. (table 3)

Table (3): Distribution of grades of diastolic dysfunction among the study group:

Diastolic Dysfunction Grade	No.	Percentage
No Diastolic Dysfunction	40	40%
Diastolic Dysfunction Grade I	30	30%
Diastolic Dysfunction Grade II	20	20%
Diastolic Dysfunction Grade III	10	10%
Total	100	100.0%

Comparing SYNTAX score with clinical characteristics data shows SYNTAX score and smoking history (P-Value = 0.014), dyslipidemia (P-Value = 0.042), family history (P-Value = 0.035), and HTN (P-Value = 0.033) were significantly distinct. **(Table 4).**

Table (4): comparing the SYNTAX with clinical characteristicsdata.

Risk factors	SYNTAX Score		P-Value**
	Yes	No	Yes Vs. No
Smoking	12.55±14.36	6.49±11.51	0.022[S]
Family history	12.20±14.77	6.82±11.17	0.044[S]
HTN	12.40±15.37	6.52±10.10	0.026[S]
Dyslipidemia	12.09±11.63	6.36±10.63	0.027[S]

- ** S significant: independent T-test (p-value <0.05)

- Comparing the diastolic function with demographic and clinical characteristic, ANOVA and Independent T- test test shows, Between four groups of diastolic function with demographic and medical characteristics, there was no statistically significant variation. (table 5)

Table (5): comparing diastolic function with demographic and clinical characteristics data (Mean ±SD (mean rank)).

- Clinical traits and Demographic information *	Grade of Diastolic Dysfunction				
	Normal	**Grade I**	**Grade II**	**Grade III**	**P value**
Age	48.1+ 9.14	52.7+6.5	48.1+9.8	50.5+5.3	0.104 NS*
BMI	29.4+7.5	27.4+7.8	29.5+7.2	31.04+5.1	0.508 NS*
SEX					
Male	19 (47.5%)	12 (40%)	10(50%)	8(80%)	0.186 NS**
Female	21 (52.5%)	18 (60%)	10(50%)	2(20%)	
Family history					
Yes	19 (47.5%)	12 (40%)	10(50%)	8(80%)	0.186 NS**
No	21 (52.5%)	18 (60%)	10(50%)	2(20%)	
Smoking					
Yes	14 (35%)	20 (66.7%)	10 (50%)	5(50%)	0.075 NS**
No	26 (65%)	10 (33.3%)	10 (50%)	5(50%)	
HTN					
Yes	18 (45%)	14 (46.7%)	9 (45%)	9(90%)	0.068 NS**
No	22 (55%)	16 (53.3%)	11 (55%)	1(10)	
Dyslipidemia					
Yes	16 (40%)	17 (56.7%)	13 (65%)	8(80%)	0.074 NS**
No	24 (60%)	13 (43.3%)	7 (35%)	2(20)	

Multivariate regression analysis shows that diastolic dysfunction was statistically significantly associated with significant CAD and non-significant CAD (OR= 2.33, CI95%= [1.50-3.60], p value <0.001 & 0.041 respectively) while normal function was statistically significantly associated with normal coronary angiography p value= 0.041 (table 6)

Taple (6): comparing significance and prescience of CAD according to diastolic function.

Coronary angiography	Diastolic function		Total	P value
	Normal function	Diastolic dysfunction		
Normal	23	4	27	<0.001[hs]
Non-significant CAD	1	9	10	0.041[s]
Significant CAD	16	47	63	<0.001[hs]
Total Count	40	60	100	

Comparison between the four groups of Diastolic function & dysfunction Grades according to SYNTAX score shows that Patients with normal diastolic function mean SYNTAX score is **2.57±6.50(34.55)c** and Patients with grade I diastolic dysfunction mean SYNTAX score is **11.06±13.02(55.60)b** and Patients with grade II diastolic dysfunction mean SYNTAX score is **9.90±11.84(64.23)b** and Patients with grade III diastolic dysfunction mean SYNTAX score is**31.30±12.61(84.55)a**.

comparing the four groups according to diastolic function with syntax score, Kruskal-Wallis test shows there were a highly statistically significant differences between the four groups (Normal, Grade I, Grade II, and Grade III) in the mean ranks of syntax score (P-value
> 0.001).

From Mann-Whitney test for inter-group comparisons (pairwise) between groups we can conclude the following results:

According to the syntax score, there was no statistically significant difference between Grade I and Grade II (the means have the same superscript letters (b)), but there was a statistically significant difference between Normal and (Grade I, Grade II, and Grade III), as well as between Grade I and Grade III and between Grade II and Grade III. (table 7)

Table (7): Comparison between the four groups of diastolic function according to SYNTAX score

Echocardiographic parameters	Diastolic & Dysfunction Grades				p
	Normal	Grade I	Grade II	Grade III	
SYNTAX score	2.57±6.50 (34.55)[c]	11.06±13.02 (55.60)[b]	9.90±11.84 (64.23)[b]	31.30±12.61 (84.55)[a]	>0.001[HS]

- Small letters for inter-group comparison (Mann-Whitney test) and the means with different superscripts are
statistically significant at P≤ 0.05
-** Kruskal-Wallis testP-value
- Highly significant, with a p-value of<0.001.
- S = significant (<0.05p-value)

Based on the Pearson correlation test, the echocardiographic parameters and syntactic score (Table4) we can conclude the following:

Diastolic dysfunction grade and SYNTAX score showed a favorable connection that was statistically highly significant. (P < 0.001).

Between the SYNTAX score and EF, there was a substantial negative connection. (P < 0.05).

SYNTAX score and LA Volume index exhibited a positive connection that was statistically significant. (P < 0.05).

Between the SYNTAX score and the E Wave, there was a substantial positive association (P < 0.05).

SYNTAX score and E/A ratio exhibited a positive connection that was statistically highly significant (P < 0.001).

There was a statistically very significant negative connection between the SYNTAX score and e' (P < 0.001).

SYNTAX score and E/e ratio correlated favorably, and this connection was quite significant. (P < 0.001).)

There was a substantial negative association between the SYNTAX score and the E wave DT. (P < 0.05). **(Table 8)**.

Table (8): Relationship between SYNTAX score and echocardiographic data

Parameters	SYNTAX Score	
	r	p-value
Diastolic Dysfunction Grade	.546**	**<0.001^{HS}**
IVRT (msec.)	-0.181	0.071^{NS}
EF (%)	-.233*	**0.002^{S}**
TR Velocity (m/s)	.341**	**<0.001^{Hs}**
LA Volume index (ml/m2)	.221**	**0.027^{S}**
E wave (cm/sec.)	.165*	**0.007^{S}**
A wave (cm/sec.)	-0.070	0.101^{NS}
E/A ratio	.367**	**<0.001^{HS}**
E wave DT (msec.)	-0.222*	**0.027^{S}**
e` (cm/sec.)	-.381**	**<0.001^{HS}**
a` (cm/sec.)	-0.327**	**<0.001^{HS}**
E/e ratio	.437**	**<0.001^{HS}**

r: Pearson Correlation Coefficient *Correlation is significant at the 0.05 level, **Correlation is significant at the 0.001 level. S stands for "significant," HS for "highly significant," and NS for "non-significant," all of which have p-values below 0.05.

Discussion

Globally, the incidence of coronary artery disease (CAD) is growing along with patient morbidity and death rates.

Diastolic dysfunction can be recognized non-invasively by TTE in the initial phases of ischemic heart disease (IHD) prior overt systolic dysfunction emerges. These distinctive echocardiographic attributes could provide predictive information on CAD load in a patient grouping with stable angina and ACS prior to invasive cardiac catheterization can be carried out [6].

In the current study, we observed a favorable link between diastolic dysfunction grade and CAD load as assessed by the SYNTAX score (P <0.001).

It is concordant with a study by Mishra. According to the study, diastolic dysfunction in individuals with higher SYNTAX scores is more severe [7].

Furthermore, it coincides with the study conducted by El-Sayed et al. a summary of the study, diastolic dysfunction in those with higher SYNTAX scores is more profound[8].

It conflicts with a research by Abali that found no association between angiographic CAD severity as assessed by the SYNTAX score and Gensini score and diastolic dysfunction.[9]

Our study also demonstrated that In multivariate analysis, diastolic dysfunction was statistically significantly associated with significant CAD p value <0.001, while normal function was statistically significantly associated with normal coronary angiography p value 0.041.

It is concordant with a study by Foudad et al. study. The study demonstrated that patients with diastolic dysfunction have significant CAD than normal diastolic function patients .[10]

In accordance with the mean SYNTAX score, our study additionally indicated that there was a statistically significant variance between those who had normal diastolic function and patients with grades (I&II&III), Grade I and Grade III, and Grade II and Grade III diastolic dysfunctions.

likewise it agrees with a research by El-Sayed et al. In accordance with the study, diastolic dysfunction among those with higher SYNTAX scores is more serious .[8].

Our investigation also revealed that there was substantial negative connection between SYNTAX score and EF (p-value= 0.02) .

According to a research by Liu et al. that looked at systolic and diastolic echocardiographic characteristics, this outcome is consistent. As stated in the study, those with greater SYNTAX scores had lower EF .[6].

Based on SYNTAX score, E/A ratio, and E wave velocity, our study established a highly substantial beneficial link between CAD burden and these variables (P < 0.001).

The result in question is consistent with research conducted by Liu et al. which, after multivariate analysis, proved that, in a mixed patient group, a higher E/A ratio was indicative of an increased CAD burden based on the SYNTAX score Liu et al.[6].

A higher E/A ratio has been shown to be a predictor of a greater CAD burden based on the SYNTAX score after multivariate analysis in a research by Shuangbo Liu et al. which involved ACS and stable CAD individuals with diabetes.[6].

It conflicts with a research by Hoffmann et al. that measured diastolic function, including TDI, in patients with suspected angina pectoris who had intact LVEF and no cardiac history prior to coronary angiography. In contrast to age-matched controls, they reported that the E/A ratio was not substantially changed in CAD patients. Hoffmann et al. measured the E/A ratio in CAD patients and the control group, but they did not measure how severe the CAD load was .[12].

In this investigation, we observed a strong negative relationship among DT and CAD burden based on SYNTAX score (P = 0.027)

It coincides with the research by Liu et al. They noticed that among individuals with an increased burden of CAD, DT reduced. DT was a variable that predicted a higher SYNTAX score after multivariate analysis (P= 0.001).[6].

Contrary to Hoffmann et al.'s study, which obtained that DT was not substantially different from control population (mean age 65 .9 years) in 82 patients (mean age 66. 8 years) with probable angina pectoris and intact

LVEF. Although the research encompassed individuals with one, two, and three vascular diseases, they did not distinguish if DT altered as the burden of CAD .**[11]**.

Moreover, we identified a highly significant positive conjunction between the CAD burden estimated using SYNTAX score and E/e ratio in our study ($P < 0.001$).

It correlates with the work of Ma,li et al.[12] They recognized that the E/e' ratio is a straightforward and useful predictor of CAD, and their findings demonstrate how the E/e' ratio may be used as a stand-alone risk factor for diagnosing CAD..**[13]**.

LIMITATIONS

The primary drawback of our study was the lack of a randomized controlled comparison. Using the information at hand for this analysis. The insufficient number of samples of our study further increased its overall limits. But the outcome would be more meaningful if a large number of patients were included (likely from numerous centers). Invasive methods to assess the markers of diastolic dysfunction were not used in our investigation.

CONCLUSION

Patients with CAD often included LV diastolic dysfunction, and there is a significant positive correlation between the grade of diastolic dysfunction and the severity of CAD based on by the SYNTAX score, supporting the need to take this into account when risk-stratifying diabetic patients

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