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Severity of Coronary Artery Disease by Coronary CT Angiography in Relation to Left Ventricular Diastolic Function

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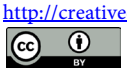

Abstract

Objectives: The aim of this study is to evaluate the relationship between severity of CAD by coronary mutlislice computed tomography scan and the degree of diastolic function Methods: The study consisted of 80 patients who underwent both coronary CTA and TTE within 1 year with no identifiable intervening cardiovascular event in National Heart Institute and Menoufia University Hospitals. All patients were subjected to detailed medical history, physical examination, full electrocardiography study including tissue Doppler imaging on mitral annulus, MSCT coronary angiography and different laboratory investigation as CBC, creatinine, lipid profile. Results: From 80 patients who have done both echocardiography examination and MSCT coronary angiography, the CT scan results were 38 patients with non-obstructive coronary artery disease and 42 patients with obstructive CAD, higher number of patients with diastolic dysfunction with higher values of E/E', medial e', lateral e', LAVI (left atrial volume index) and TRV (tricuspid regurge velocity) were found in the group with obstructive coronary artery disease. Conclusion: Our study showed that diastolic dysfunction is more prevalent in patients with obstructive coronary artery disease with higher grade of diastolic dysfunction.

Keywords

Coronary Artery Disease, Diastolic Dysfunction, MSCT Coronary Angiography

1. Introduction

Diastolic dysfunction (DD) is an important cause of heart failure (HF) with preserved ejection fraction (pEF) and a major public health issue. Epidemiological

studies indicate that varying severities of DD are present in the community. DD is predictive of developing overt HF and all-cause mortality [1].

With advancing age and acquired cardiac conditions, such as hypertensive heart disease or coronary artery disease (CAD), LV relaxation may worsen and LA pressures increase, and despite preservation of LV systolic function, the clinical syndrome of diastolic heart failure (HF), otherwise known as HF with preserved ejection fraction (HFpEF), may develop [1].

Abnormal diastolic function of the left ventricle (LV) detected by transthoracic echocardiography (TTE), is associated with worse prognosis [2]. Diastolic function (DD) is the first cardiac function to be impaired in ischemic heart disease [3].

Early detection of LV diastolic dysfunction has important diagnostic and prognostic and therapeutic implications. Echocardiography is the most important feasible noninvasive method to evaluate LV DD, because of the inaccuracy of conventional pulsed wave mitral inflow Doppler analysis and having multiple limits and the inconclusive findings to diagnose DD. Tissue Doppler imaging is significantly sensitive and conclusive modality to get the velocity of the longitudinal motion of the mitral valve annulus and has the ability to early detect and confirm the diagnosis of left ventricular diastolic dysfunction [4].

Ischemic heart disease is one of the utmost causes of mortality and disability in the world, although coronary heart disease mortality rates have declined worldwide over the past decades, it remains the cause of for about one third or more of all-cause mortality in individuals above 40 years old [5].

MSCT angiography is a noninvasive scanning modality that permits the diagnosis of coronary arteries atherosclerosis. Since rapidly evolving technology results in better quality scanning and accurate for the diagnosis of coronary artery disease, despite the fact that MSCT is still less accurate than invasive coronary angiography due to lower resolution, significant satisfactory diagnostic accuracies have been validated for the diagnosis of significant coronary plaque burden [6].

In our study we have investigated the relationship between severity of coronary artery disease and LV diastolic dysfunction and to how extent could the presence of severe diastolic dysfunction predict the presence of obstructive coronary artery disease.

2. Methods

2.1. Study Design

This is a cross sectional observational study conducted during the period from June 2018 to June 2019 on 80 patients who underwent both coronary CTA and TTE within 1 year with no identifiable intervening cardiovascular event in National heart institute and Menoufia university hospitals.

2.2. Study Population

The exclusion criteria were LV ejection fraction (LVEF) < 45%, moderate or se-

vere valvular disease, other primary myocardial pathology (eg, hypertrophic cardiomyopathy, restrictive cardiomyopathy), significant pericardial disease (eg, constriction), congenital heart disease, primary pulmonary hypertension, and atrial or ventricular arrhythmias at the time of imaging, contraindications to coronary CT angiography testing.

All patients were subjected to informed consent and evaluated as regards to: Full clinical assessment (Detailed medical history such as Age, gender, smoking, hypertension, diabetes, hypercholesterolemia), Physical Examination, 12 lead surface ECG, Laboratory investigation as creatinine, lipid Profile, CBC parameters, echocardiography examination including tissue Doppler imaging on mitral annulus and MSCT coronary angiography, the CT scan results were classified into non obstructive coronary artery disease (with maximum degree of stenosis in the coronaries <50% in any major vessel) and (obstructive CAD with maximal degree of stenosis > 50%)

According to the results our study included two groups:

Group I: included patients with non-obstructive coronary artery disease.

Group II: included patients with obstructive coronary artery disease.

2.3. Statistical Analysis

Data were analyzed using Statistical Program for Social Science (SPSS) version 25.0 for windows (SPSS Inc., Chicago, IL, USA) and NCSS 12.0 for windows (NCSS LCC., Kaysville, UT, USA).

Quantitative data of normal distribution were expressed as mean ± standard deviation (SD). Median and inter-quartile range (IQR) were also calculated for quantitative data with abnormal distribution. Qualitative data were expressed as frequency and percentage.

The following tests were done:

Independent-samples t-test of significance was used when comparing between two means of normally distributed data.

Mann Whitney U test is used to compare differences between two independent groups when the dependent variable is continuous, but not normally distributed.

Chi-square (X2) test also called Pearson's chi-square test or the chi-square test of association is used to discover if there is a relationship between two categorical variables.

Fisher Exact test is a test of significance that is used in the place of chi square test in 2 by 2 tables, especially in cases of small samples.

The "Linear-by-Linear" test is for ordinal (ordered) categories and assumes equal and ordered intervals. The Linear-by-Linear Association test is a test for trends in a larger than 2 × 2 table.

Multivariate regression analysis is used when we want to predict the value of a variable based on the value of two or more other variables. The variable we want to predict is called the dependent variable (or sometimes, the outcome, target or

criterion variable). The variables we are using to predict the value of the dependent variable are called the independent variables (or sometimes, the predictor, explanatory or regressor variables). Results were represented in tables. The level of significance was considered statistically significant if (P value is <0.05) and was high statistically signification if (P-value is <0.01), While P value > 0.05 was considered non-significant.

3. Results

The 80 patients were classified into two groups:

Group one: patients with non-obstructive coronary artery disease (n = 38).

Group two: patients with obstructive coronary artery disease (n = 42).

3.1. Regarding Risk Factors and Laboratory Data

From 80 patients, 41 (51.2%) of the patients were male, and mean age of patients was 55.9 ± 8.0 years, 35 (43.8%) patients were hypertensive, 36 (45%) patients were diabetic and 24 (30%) patients were smokers. Regarding Age, patients in obstructive coronary artery disease group were significantly older compared to those in controls (p = 0.028) [Table 1]. The proportion of male patients were higher in obstructive group 27 (64.3%) than non-obstructive group 14 (36.8%), (P = 0.014) [Figure 1]. Diabetic cases also were higher in obstructive CAD patients 24 (57.1%) than non-obstructive CAD 12 (31.6%), also hypertension was more prevalent in obstructive CAD than non-obstructive 23 (54.8%) and 12 (31.6%) respectively. On the other hand, there was no significant relationship between study groups and smoking, dyslipidemia and family history (P = 0.241, p = 0.181, p = 0.768 respectively) [Table 1].

3.2. Regarding Assessment of Diastolic Dysfunction

The relation between the degree of CAD either obstructive or non-obstructive assessed by MSCT coronary angiography and diastolic dysfunction detected by tissue Doppler assessment of mitral annular velocities. There are statistically significant relationship between septal e', lateral e', E/E', E/A, LAVI and TR velocity and the degree of CAD, with higher values of those parameters in patients with obstructive CAD than patients with non-obstructive CAD (p ≤ 0.001, 0.017, 0.005, 0.029, <0.001, 0.034) respectively [Table 2].

In the other hand, the ejection fraction was significantly lower in patients with obstructive coronary artery disease group compared to non-obstructive CAD (p = 0.027). DT (deceleration time) and IVRT (isovolumetric relaxation time) were also found to be significantly lower in the obstructive CAD group (p ≤ 0.001, 0.004) respectively [Table 3].

The number of patients with diastolic dysfunction was significantly higher in the obstructive CAD group (n = 35) in comparison to non-obstructive group (n = 19) (p value = 0.001) with higher number of patients with advanced grades of diastolic dysfunction (grade 2 and 3) in the obstructive group [Table 4].

Table 1. Comparison between the studied groups regarding the baseline characteristics.

Baseline characteristics	Non-obstructive CAD	Obstructive CAD	P-value (Sig.)
Count	38	42	
	Age (years)		
Mean ± SD	53.9 ± 7.8	57.8 ± 7.8	0.028 (S)
	BMI (kg/m²)		
Mean ± SD	26.9 ± 3.3	27.1 ± 2.9	0.728 (NS)
	Risk factors		
Male gender	14 (36.8%)	27 (64.3%)	0.014 (S)
DM	12 (31.6%)	24 (57.1%)	0.022 (S)
HTN	12 (31.6%)	23 (54.8%)	0.037 (S)
Smoking	9 (23.7%)	15 (35.7%)	0.241 (NS)
Dyslipidemia	10 (26.3%)	17 (40.5%)	0.181 (NS)
Family history	8 (21.1%)	10 (23.8%)	0.768 (NS)

Table 2. Comparison between the studied groups regarding the mitral annular velocities using tissue Doppler echocardiography E/A ratio, TR velocity and LAVI.

Echocardiographic data	Non-obstructive CAD	Obstructive CAD	P-value (Sig.)
Count	38	42	
	Septal e' (m/s)		
Mean ± SD	0.09 ± 0.02	0.07 ± 0.02	<0.001 (HS)
	Lateral e' (m/s)		
Mean ± SD	0.14 ± 0.11	0.10 ± 0.02	0.017 (S)
	E/e'		
Mean ± SD	8.1 ± 2.8	10.6 ± 4.6	0.005 (S)
	E/A		
Mean ± SD	1.26 ± 0.55	1.64 ± 0.91	0.029 (S)
	LAVI (mL/m²)		
Mean ± SD	30.6 ± 4.5	35.9 ± 8.4	<0.001 (HS)
	TR velocity (m/s)		
Mean ± SD	1.7 ± 0.9	2.1 ± 1.1	0.034 (S)

Table 3. Comparison between the studied groups regarding the other echocardiographic data.

Echocardiographic data	Non-obstructive CAD	Obstructive CAD	P-value (Sig.)
Count	38	42	
	EF (%)		
Mean ± SD	61.8 ± 8.3	57.6 ± 8.4	0.027 (S)
	DT (ms)		
Mean ± SD	215 ± 53	165 ± 47	<0.001 (HS)
	IVRT (ms)		
Mean ± SD	117 ± 27	100 ± 24	0.004 (S)
	LVH		
	11 (28.9%)	18 (42.9%)	0.196 (NS)

Table 4. Comparison between the 2 groups regarding diastolic dysfunction grading.

Echocardiographic data	Non-obstructive CAD	Obstructive CAD	P-value (Sig.)
Count	38	42	
Diastolic dysfunction			
No DD	19 (50%)	7 (16.7%)	0.001 (S)
Grade 1	8 (21.1%)	10 (23.8%)	
Grade 2	8 (21.1%)	13 (31%)	
Grade 3	3 (7.8%)	12 (28.6%)	

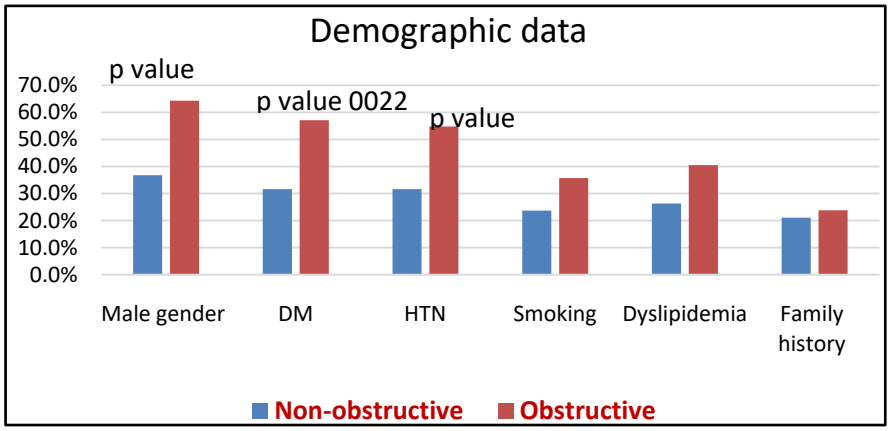

Figure 1. Comparison of the obstructive and non-obstructive CAD according to demographic data.

In the univariate analysis across the study, age, DM, HTN and male sex as risk factors were found to be statistically significant with degree of CAD Obstruction, as well as E/E', EF, LAVI and TR velocity by echocardiography, After multivariable adjustment that considered age, CAD risk factors an independent association was found between obstructive CAD and the presence of diastolic dysfunction with higher parameters E/E' and LAVI [**Figure 2**]. Tricuspid regurge velocity (TRV) and ejection fraction (EF) weren't found to have significant relationship with severity of CAD obstruction [**Table 5**, **Table 6**].

4. Discussion

In our study we have investigated the relationship between severity of coronary artery disease and LV diastolic dysfunction and to how extent could the presence of severe diastolic dysfunction predict the presence of obstructive coronary artery disease.

We divided the study into two groups based on the MSCT coronary angiography finding as 2 groups, first group is patients with non-obstructive coronary artery disease (maximum degree of stenosis in coronaries < 50%), and second group is patients with obstructive coronary artery disease (maximum degree of stenosis > 50%) and we compared both groups regarding risk factors of coronary artery disease and diastolic dysfunction, echocardiographic parameters to diagnosis

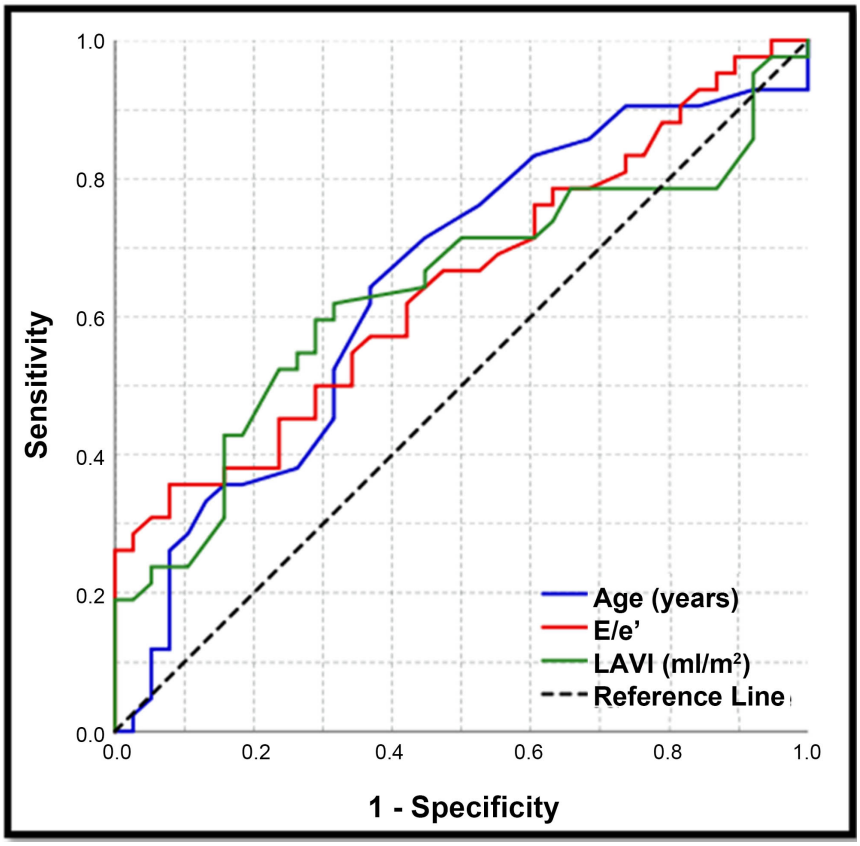

Figure 2. ROC curve analysis for the independent predictors of obstructive CAD.

Table 5. Univariate regression analysis for incidence of obstructive CAD.

Variable	Unadjusted OR	95% Confidence Interval for OR		P-value (Sig.)
		Lower Bound	Upper Bound	
Age (years)	1.067	1.006	1.132	0.032
Male gender	3.086	1.239	7.686	0.016
DM	2.889	1.154	7.229	0.023
HTN	2.623	1.051	6.548	0.039
EF (%)	0.939	0.887	0.995	0.033
E/e'	1.197	1.047	1.367	0.008
LAVI (mL/m²)	1.091	1.015	1.172	0.018
TR velocity (m/s)	1.595	1.049	2.425	0.029

and classify diastolic dysfunction. Our study shows highly significance correlation between diastolic dysfunction degree and presence of obstructive coronary artery disease [Figure 3], according to diastolic dysfunction parameters, we found tissue Doppler imaging of mitral annular velocities data such as septal e', lateral e', and E/E' were significantly higher in the obstructive CAD group than non-obstructive CAD [Table 2] also IVRT, and deceleration time are significantly lower in the same group [Table 3].

Table 6. Multivariate regression analysis for incidence of obstructive CAD.

Variable	Unadjusted OR	95% Confidence Interval for OR		P-value (Sig.)
		Lower Bound	Upper Bound	
Age (years)	1.095	1.010	1.186	0.027
Male gender	6.340	1.505	26.699	0.012
DM	10.401	2.027	53.356	0.005
HTN	5.062	1.118	22.919	0.035
EF (%)	0.956	0.880	1.038	0.286
E/e'	1.395	1.078	1.805	0.011
LAVI (mL/m^2)	1.132	1.003	1.277	0.044
TR velocity (m/s)	1.067	0.426	2.675	0.890

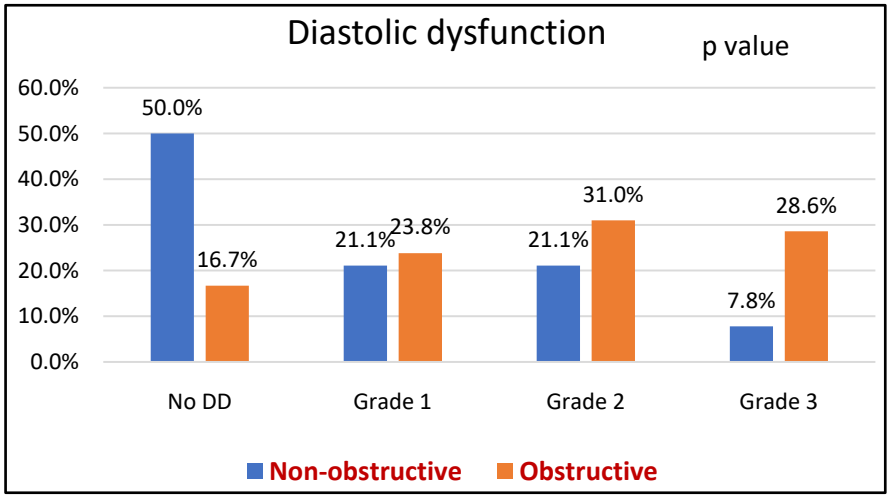

Figure 3. Comparison between obstructive and non-obstructive CAD regarding diastolic dysfunction degree.

Left atrial volume index (LAVI) and tricuspid regurge velocity (TRV) are two important factors in the diagnosis of diastolic dysfunction according to latest guidelines. The present study compared both groups regarding those factors and LAVI and TRV are found to be high in the obstructive group with statistical significance [Table 2].

Estimation of cardiac systolic function of LV has also been compared between the groups and we found ejection fraction to be significantly lower in the obstructive group. According to risk factors of coronary artery disease, we found that hypertension, diabetes, and male sex are more common in patients with obstructive coronary artery disease with statistical significance.

These result are in agreement with the results of many studies like fay Y *et al.*, the study observed a direct relationship between DD degree and LVEDP and the extent and severity of noninvasively assessed CAD burden by the presence of obstructive coronary artery disease as well as number of coronary vessels with obstructive CAD. There were significantly higher values of septal e', lateral e'

and E/E' in patients with higher burden of coronary artery disease. Lower values of IVRT and Deceleration time were also found among patients were more severe obstructive CAD [7].

Abhayaratna *et al.* is a study to detect significance of CAD and presence of preclinical diastolic they found increase incidence of diastolic dysfunction among patients with coronary artery disease and myocardial infarction. There were highly significant correlation between CAD and preclinical diastolic dysfunction [8].

In agreement with our study the result of Ren *et al.* who found that CAD is considered an independent risk factor for developing diastolic dysfunction [9].

Vlasseros, I. *et al.* investigated the combined effects of hypertension and coronary artery disease (CAD) on left ventricular (LV) diastolic function. The study participants were divided into two groups according to the presence of CAD by coronary angiography. Patients with CAD exhibited lower ejection fraction. The main finding of this study was that severely depressed LV diastolic function, as suggested by various echocardiographic indices, is indicative of CAD coexistence in patients with uncomplicated essential hypertension., In hypertensive, the early recognition of LV diastolic performance alteration may be associated with the presence of significant CAD [10].

Prior studies assessing the association between DD and CAD came to conflicting conclusions. Garcia *et al.* demonstrated that early stage of subclinical atherosclerotic disease is negatively associated with DD parameters [11]. Only 48 subjects included in the study, no tissue Doppler assessment of mitral annular velocity was done, and carotid intima-media thickness was used as a surrogate for subclinical atherosclerosis instead of presence of coronary artery disease by MSCT.

Eleid *et al.* did not find consistent relation between coronary artery plaque burden as assessed by coronary calcium score and echocardiographic grade of LV DD [12]. Their study population had lower risk factor profile than our study: Only 6% are diabetic and 36% hypertensive furthermore the study only assessed coronary artery disease by calcium score without angiographic evidence of luminal narrowing.

In the other hand Abdelrahman J., *et al.* is another cross sectional study. the study suggests that CACS, as well as CAD by CCTA, are not independently associated with measures of DD on echocardiography [13].

The difference of the result could be explained by more than half of the former study subjects have prevalent CAD in the form of angina, previous myocardial infarction, or previous coronary artery bypass surgery, on the contrary our study excluded subjects with previous MI or CABG.

Study Limitations

Although the number of patients enrolled in our study is relatively small, the results are quite comparable to larger studies.

5. Conclusion

Our study showed that obstructive coronary artery disease has major implications on diastolic function of the heart and the extent and severity of CAD by coronary CTA which is associated with worsening diastolic function.

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Conflicts of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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