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Impact of percutaneous coronary intervention on critical proximal lesion of left anterior descending artery on left ventricular function by echocardiography and tissue doppler

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***Abstract*---**Introduction: lesions in the proximal segment of the LAD coronary artery present a high-risk lesion, as this important anatomical location of atherosclerotic plaques is associated with increased mortality. Patients with chronic ischemic LV dysfunction but viable myocardium will have better LV geometry after revascularization, which in turn will enhance long-term outcome. Objective: to assess the impact of PCI on critical proximal lesion of LAD artery on LV functions by echocardiography and tissue doppler study. Materials and methods: We included 50 patients older than 18 years old with critical proximal LAD lesion who were undergoing elective PCI in cardiology unit, faculty of medicine, Al-Azhar University, Assiut from April 2021 to November 2021. Results: For E/A ratio, we found that the reduction in this ratio was significantly higher among those with preserved EF compared to others. The increase in IVRT and DT over 1 month period was statistically higher among those with preserved EF when compared with others. For E/A

ratio, we found that the reduction in this ratio was significantly higher among those with preserved EF compared to others. Also, we found that average E/′E ratio was significantly reduced among those with preserved EF when compared to others. The increase in IVRT and DT over 6 months period was statistically higher among those with preserved EF when compared with others. Conclusions: There was significant improvement in cardiac function of patients with critical proximal lesion of LAD artery on left ventricular functions after PCI.

***Keywords*---**coronary artery disease, left ventricular function, percutaneous coronary intervention.

Introduction

Coronary artery disease (CAD) is a major cause of death and disability in developed countries. Although CAD mortality rates worldwide have declined over the past four decades, CAD remains responsible for about one-third or more of all deaths in individuals over age 35 (Farid, Ibraheem, & Ahmed, 2019). CAD is a group of diseases that includes stable angina, unstable angina, myocardial infarction (MI), and sudden cardiac death. It is the most commonly occurring type of cardiovascular diseases (CVDs). Risk factors for CAD include hypertension, diabetes mellitus (DM), smoking, alcohol ingestion, obesity, dyslipidemia, sedentary life, and family history. The underlying mechanism involves atherosclerosis of the arteries of the heart (Helfand et al., 2009).

Lesions in the proximal segment of the left anterior descending (LAD) coronary artery present a high-risk lesion, as this important anatomical location of atherosclerotic plaques is associated with increased mortality (Toutouzas et al., 2011). Indeed, the LAD supplies 40-50% of the total left ventricular (LV) myocardium. Therefore, obstruction at this site causes ischemia in a large portion of the myocardium (Versaci et al., 1997). Percutaneous coronary intervention (PCI) is a procedure performed to relieve ischemic symptoms in patients with CAD. The application of this method to prevent heart failure (HF) can be as effective and efficient as coronary artery bypass grafting (CABG). Coronary artery stenosis (CAS) can result in a HF and consequently systolic and diastolic HF, in case it is disregarded. New angioplasty techniques have led to higher success rates of PCI, and drug-eluting stents (DESs) have decreased the rate of restenosis and re-obstruction (Parsaee, Nabati, Saffar, & Taghavi, 2015).

Echo Doppler studies have reported that patients with asymptomatic LV diastolic dysfunction have a higher incidence of all-cause mortality. Mild diastolic dysfunction and moderate to severe dysfunction were associated with 8.3-fold and 10.2-fold increased risks of mortality, respectively. The overall mortalities of symptomatic patients with diastolic or systolic HF are very similar (Nabati, 2016).
The American Society of Echocardiography (ASE) recommends measurement of LV dimensions with the M-mode line perpendicular to the long axis of the heart and immediately distal to the tips of the mitral valve (MV) leaflets in the parasternal long axis view. Measurements are taken at end-diastole (d) defined as the beginning of the QRS complex but preferably using the widest LV cavity

diameter, and at end systole (s) using the narrowest LV cavity diameter. The leading-edge convention of the ASE is the recommended method of measurement (Ghanem et al., 2020).

The diastolic measurements obtained are the interventricular septal wall thickness, the LV internal diameter at end diastole (LVIDd) and posterior wall thickness. In systole, the LV systolic diameter (LVIDs) is measured. Calculations of other indices of LV systolic function, e.g., LV ejection fraction (EF), volumes, and mass can then be performed. Tissue Doppler imaging (TDI) is a technique used to assess myocardial motion, which is a sensitive index of ventricular relaxation; it is less dependent on the loading condition and is therefore a more reliable diastolic function index. At present, the early diastolic mitral inflow velocity to early diastolic mitral annulus velocity (E/E') ratio is used to evaluate LV filling pressure, and it has been used as a marker for the diagnosis of diastolic heart failure (Huang, Lin, Chen, & Yu, 2019). This study aimed to assess the impact of PCI on critical proximal lesion of LAD artery on LV functions by Echocardiography and tissue Doppler study.

Materials and Methods

A prospective study was conducted on 50 patients with critical proximal LAD lesion with stable cardiac condition underwent elective PCI.

Inclusion criteria

Patients older than 18 years' old who were diagnosed as CAD with critical proximal LAD stenosis, underwent elective PCI at Assiut Azhar University during the period between 15 April 2021 to 15 January 2022. PCI with DESs were performed for all the patients. These patients underwent TTE within 24 h before and 6 months after PCI, and alterations in the LV functions were evaluated.

Exclusion criteria

Patients with multi-vessel disease not candidate for PCI. Patients with a poor echo window. Mild and moderate LAD lesions. Sever renal impairment. Sever hepatic impairment.

Patients in this study were divided into 2 groups;

- Group A (n= 30): Includes 30 patients with preserved EF (50%-60%).
- Group B (n=20): Includes 20 patients with mildly reduced EF (EF between 40% - 50%).

Methods

Each patient was subjected to: Full history taking: including age, sex, smoking, hypertension, DM, cerebrovascular stroke, cardiac history, peripheral artery disease and family history. General and local examination: Hypertension was defined as a systolic BP of 140 millimeters mercury (mmHg), a diastolic BP of 90 millimeters mercury (mmHg), or the need for antihypertensive medication. DM

was defined using the American Diabetes Association's criteria or by the requirement for insulin or oral hypoglycemic medications. A first-degree relative with a history of MI, coronary revascularization, or sudden death was defined as having a family history of CAD. A face-to-face questionnaire was used to determine smoking history. Total lab assessment CBC, PTT, INR, kidney function, Liver function, hepatitis marker, plasma glucose, total cholesterol (T-chol), high density lipoprotein (HDL)-chol, low density lipoprotein (LDL)-chol, and TG levels were determined during fasting. Twelve-lead ECG.

Trans-Thoracic Echocardiography

TTE was performed at baseline within 24 h before PCI and was repeated 6 months after PCI for all patients by a Vivid S5 (GE Healthcare, Wauwatosa, WI, USA), 1–3 MHz transducer. All the measurements represent the average of three consecutive beats between normal HR ranges, 60–100 beat per minute (Nagueh et al., 2016). The results were confirmed by an echocardiographer who is blind to the patient's information, to measure diastolic early filling velocity (E) wave, late diastolic velocity (A) wave, and Pulsed wave TDI was obtained after placement of the sample volume at the level of the septal and lateral mitral annuli. From these recordings, myocardial systolic (Sa), early diastolic (Ea), late diastolic velocities (Aa), and E/Ea ratio were measured and averaged and EF was recorded by M-mode according to the guidelines of American Echocardiography Association. Estimates of the LV systolic and diastolic parameters was assessed according to the guidelines of American Echocardiography Association (Nagueh et al., 2016).

The LV outflow pattern was recorded from the apical 5-chamber view with the pulsed wave Doppler positioned just below the aortic valve. Doppler time intervals of Myocardial Performance Index (MPI) were measured from mitral inflow and LV outflow velocity as described below: The IVRT was measured from closure of the aortic valve to opening of the MV. The isovolumic contraction time (IVCT) was measured from closure of the MV to opening of the aortic valve. Ejection time (ET) was measured from the opening to the closure of the aortic valve on the LV outflow velocity profile. The Mitral Valve Closure Opening Time (MCOT) was defined as IVCT + ET + IVRT. The MPI or Tei index was calculated as

$$\text{LV MPI} = \frac{\text{IVCT} + \text{IVRT}}{\text{LVET}} = \frac{\text{MCOT} - \text{LVET}}{\text{LVET}}$$

Pulsed-wave tissue Doppler echocardiography was done before PCI, as well as 6 months after intervention. Myocardial tissue Doppler velocities were measured S` average (cm/s). (Figure I).

Coronary angiography and PCI

Coronary angiography was performed for all the patients using a cardiac angiography system (Philips Aulura, Italy), and they all underwent PCI. Procedural success was defined as the successful deployment of the stent and residual stenosis of less than 30%. Procedural anticoagulation was achieved with UFH; GPIIb/IIIa inhibitors were used whenever needed. A 600 mg oral dose of

clopidogrel was recommended before the procedure. Thereafter, 81 or 150 mg of aspirin and 75 mg of clopidogrel was prescribed daily. Other standard drugs (angiotensin converting enzyme inhibitors, beta blockers, statins, and oral hypoglycemic agents) were remained unchanged during the study to minimize the effects of alterations on the echocardiographic variables.

Ethical considerations

The study was conducted in full conformance with principles of the "Declaration of Helsinki", Good Clinical Practice (GCP) and within the laws and regulations of Egypt. Approvals from concerned authorities (The board of Cardiology department at Al Azhar University Hospital). Dealing with data and data dissemination was confidential for research purposes only. Informed consent: this document contains rights of the study participants (including the right to withdraw at any stage of the trial), main facts about the study, purpose, required procedures, expected risks and benefits (and the likelihood or probability of their occurrence). All patients signed an informed written consent before recruitment in the study.

Statistical analysis

All data was analyzed using SPSS software Chicago, IL, USA, version 25. Data were statistically described in terms of mean ± standard deviation (±SD, frequencies (number of cases) and relative frequencies (percentages) when appropriate. For comparing paired data (pre and post-operative) Wilcoxon sign rank test was used because the data were not normally distributed. For comparing categorical data, Chi square (x2) test was performed. Exact test was used instead when the expected frequency is less than 5. P-value is always 2 tailed test significant at 0.05 level.

Results

At the start of this study, we found that among the preserved EF group, EF was significantly higher and E/A ratio was significantly lower when compared to the mildly reduced EF group. While we found non -significant difference in E/A, IVRT and DT between the preserved EF group and the mildly reduced EF group at the start of the study. After 1 month, the EF managed to increase in both groups but still was significantly higher among those with preserved EF when compared with others. For E/A ratio, we found that the reduction in this ratio was significantly higher among those with preserved EF compared to others. However, we found that average E/′E ratio was reduced among those with preserved EF when compared to others. on the other hand, the increase in IVRT and DT over 1 month period was statistically higher among those with preserved EF when compared with others. After 6 months, the EF showed more increase in both groups but still was significantly higher among those with preserved EF when compared with others. For E/A ratio, we found that the reduction in this ratio was significantly higher among those with preserved EF compared to others. Also, we found that average E/′E ratio was significantly reduced among those with preserved EF when compared to others. On the other hand, the increase in IVRT and DT over 6 months period was statistically higher among those with preserved EF when compared with others (Table I – Table V).

Discussions

Left ventricular systolic function (LVSF) is a major predictor of long-term survival in patients with CAD, evaluation of regional and global subclinical LVSD could be a good strategy to identify myocardial regions with impaired coronary artery flow and reduced myocardial perfusion (Lloyd-Jones et al., 2009). Tissue Doppler echocardiography has emerged as a sensitive and quantitative measure of both systolic and diastolic longitudinal myocardial function. It is non-invasive, highly available and has minimal risk profile. It may thus serve as a more suitable index to detect early changes in myocardial function in patients with ischemic heart disease (Al Khashab, Ragab, & Agiz, 2020).

Lesions in the proximal segment of the LAD coronary artery present a high-risk lesion, as this important anatomical location of atherosclerotic plaques is associated with increased mortality. PCI in patients with preserved LV function and on optimal medical therapy doesn't reduce the cardiac death and MI, but it also decreases the need for other procedure and the degree of angina (Ioannidis & Katritsis, 2007).

This study aimed to assess the impact of PCI on critical proximal lesion of LAD artery on LV functions by echocardiography and tissue doppler study. To obtain this aim, we included 50 patients older than 18 years old with critical proximal LAD lesion who were undergoing elective PCI in cardiology unit, faculty of medicine, Al-Azhar University, Assiut. Patients with multivessel disease, poor echo window, mild and moderate LAD lesions, severe renal or hepatic impairment, or dilated cardiomyopathy (DCM) were excluded from the study.

TTE was performed at baseline within 24 h before PCI and was repeated 1 month and 6 months after PCI for all. According to EF, patients in this study were divided into 2 groups;

- Group A (n= 30): Includes 30 patients with preserved EF (50%-60%).
- Group B (n=20): Includes 20 patients with mildly reduced EF (EF between 40% - 50%).

The mean age of this study population was 57.49 ± 7.5 years old. Fourty six percent of them (23 participants) were males Twenty-seven patients (54 %) were females. 66% of them (33 participants) were diabetic. And 28 (56%) patients were hypertensive. their mean cholesterol level was 235.9 ± 24.2 mg/dl. The average LDL levels among whole study population were 155.7 ± 16.98 mg/dl. While their average HDL was 35.8 ± 5.75 mg/dl.

Similarly, patient age in El Khashab study was between 39- and 65-year-old with mean ±SD equals 55.5±4.99 years. Gender distribution was: 87 (87%) were males and 13(13%) were females (Al Khashab et al., 2020). Also in El Shafey study, risk factors for CAD including hypertension, DM, and dyslipidemia, were reported (El Shafey et al., 2015). Fifty two percent of patients in the current study (26 patients) were active smokers. That was in concordance with El Khashab who studied associated risk factors in patients with totally occluded coronary arteries.

Smokers were 80% of cases (Al Khashab et al., 2020). Also, in El Shafey study, smoking was reported as a risk factor for CAD (El Shafey et al., 2015).

Among the whole study population, there was a significant increase in EF after 1 month of treatment and even after 6 months by the end of follow up (P<0.001 for both). In El Khashab study, the only affected parameter was EF with statistically significant improvement after intervention (p <0.001). El Khashab study was to evaluate the effect of elective Chronic Total Occlusion Percutaneous Coronary Intervention (CTO PCI) on LV functions, using conventional echocardiography. In El Khashab study, 100 patients with a chronic total occlusion artery selected and global LV systolic and diastolic functions examined by echo and TDI, before PCI and within one month after PCI. Their findings suggested a survival benefit of successful CTO PCI Procedural success was associated with an improvement in LVSF (Al Khashab et al., 2020).

Also similar to our finding, improvement of LVEF by CTO-PCI were observed at up to 3 and 6 months in Wang study which was conducted on 43 patients with CTO using two-dimensional speckle tracking echocardiography (Wang et al., 2019). Also, El Shafey and colleagues studied a total of 37 CTO lesions (in 40 patients) were targeted, EF showed a significant improvement 3 months after successful PCI group (El Shafey et al., 2015).

Similarly, Maryam and colleagues assessed the effects of PCI on LVEF and WMA in 40 patients who presented with ischemic cardiac chest pain, an EF less than 40%, and significant coronary occlusion (70%). Echocardiography was performed at baseline and one month after the procedure. Left ventricular EF increased from 0.33 ± 0.064 at baseline to 0.44 ± 0.072 after the angioplasty. This change in left ventricular EF was statistically significant and the mean of it was 0.11 ± 0.036 (P-value = 0.000). All of the patients (100%) had wall motion abnormality at the baseline that decreases to 90.5% of them (Maryam, Masoud, & Shahrzad, 2008).
We also found a significant improvement in each E/A ratio, and E/e ratio after 6 months. While the improvement after 1 month was not significant. There was also a significant increase in each IVRT and DT after 6 months. While the improvement after 1 month was not significant.

In Salehi study, 51 patients with CAD who were scheduled for elective PCI were investigated provided that their EF was > 30%. Echocardiography was carried out before and three months after PCI. They reported a significant decline for E/E indices which as in line with our findings (Salehi et al., 2015). In Hashemi study that included 30 patients, echocardiography was done for patients 3 months after PCI. None of the left ventricular diastolic parameters showed significant difference before and after elective PCI (3 months after PCI), except for mitral E/A ratio (0.94 ± 0.15 before treatment versus 1.05 ± 0.18 3 months after treatment) (p value ≤ 0.053), which improved significantly 3 months after PCI (p=0.04) (Hashemi et al., 2010). The difference between our result and Hashemi can be attributed to the difference in sample sizes between both studies.

At the start of this study, we found that the preserved EF group had significantly higher EF and IVRT and lower E/A ratio. While we found non-significant difference in DT or E/′E ratio between the preserved EF group and the mildly

reduced EF group at the start of the study. It is well known that restrictive filling (E/A ratio ≥ 1.5) is a powerful predictor of HF. E/A ratio has significant prognostic value in patients with CAD (Mishra, Devereux, Cohen, Whooley, & Schiller, 2011). E/A ratio could be a first step echocardiographic risk stratification, which could precede and indicate the need for more advanced diagnostic and prognostic considerations in high-risk acute MI and HF patients (Rigolli et al., 2015).

For E/A ratio after 1 month, we found that the reduction in this ratio was significantly higher among those with preserved EF compared to others ($p < 0.001$). However, we found that average E/′E ratio was reduced among those with preserved EF when compared to others ($p=0.038$). on the other hand, the increase in IVRT and DT over 1 month period was statistically higher among those with preserved EF when compared with others ($p=0.04$, $p=0.045$) respectively. In Maryam study, that studied 21 patients with angina pectoris and chronic coronary occlusion with a successfully recanalized coronary artery occlusion by angioplasty and stenting, the improvement of EF in patients with significant stenosis of the LAD was higher than in patients without LAD lesions ($p = 0.008$) (Maryam et al., 2008).

Megaly and colleagues in their meta-analysis of 34 studies with 2804 patients demonstrates that successful CTO PCI is associated with statistically significant increase in mean LVEF by 3.8% during a mean follow-up duration of 7.9 months (Megaly et al., 2018). Further studies have attempted to more precisely predict functional myocardial recovery using contrast enhanced MRI, dobutamine stress echocardiography, wall thickness or a combination of these different modalities. Infarction of<25% of the myocardial wall thickness strongly predicts recovery, >75% predicts no recovery, and between these values lies a grey zone (Safley et al., 2011).

Chimura and colleagues studied a total of 70 CTO lesions (in 70 patients) were targeted, and 60 lesions were effectively revascularized with PCI, and 10 lesions were unsuccessful Echocardiographic measurement showed a considerable recovery 9 months after successful PCI group), whereas that did not alter significantly after failed PCI group (Chimura, Yamada, Yasaka, & Kawai, 2019). However, another study found no difference in in-hospital mortality between successful and unsuccessful cases. A number of potential mechanisms by which revascularization of CTOs might improve prognosis have been proposed. These include prevention of adverse LV remodelling, prevention of sudden cardiac death through improved electrical stability, and greater tolerance of any subsequent ACS events (Jones et al., 2012).

Similar to our finding, Nozari et al. examined 115 patients with CAD who underwent elective PCI. They did not put a limit to EF and they excluded patients with a normal echo study. All patients had TDI and conventional echo done before, one day after PCI and 3-6 months later. They demonstrated that EF significantly increased during the 3 stages of measurements ($P < 0.0001$). However, in contrary to our findings, diastolic dysfunction significantly improved the day after PCI ($p < 0.0001$), but no further changes were seen in the results 3-6 months later (Nozari, Oskouei, & Khazaeipour, 2012).

Conclusions

There was significant improvement in cardiac function of patients with critical proximal lesion of LAD artery on left ventricular functions after PCI.

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Tables

Table (I): Showing the sociodemographic characteristics of all participants (n=50)

Variable	Value
Group Preserved EF (>=50%) Mildly reduced EF (40%-50%)	 30 (60) 20 (40)
Age	57.49 ± 7.5*
Gender Female Male	 23 (46) 27 (54)
HTN	28 (56)
Dm IDDM NIDDM	 17 (34) 16 (32)
Smoking	26 (52)
Cholesterol	235.9 ± 24.2*
LDL	155.76 ± 16.98*
HDL	35.8 ± 5.75*

* mean ± SD. LDL: low-density lipoprotein. HDL: high-density lipoprotein

Table (II): showing the baseline echocardiographic parameters for all participants (n=50)

Parameter	Mean ± SD
EF	51.16 ± 5.33
E/A ratio	1.8 ± 0.34
Average E/′E ratio	13.26 ± 0.42
IVRT	87.29 ± 4.14
DT	183.74 ± 17.21

EF: ejection fraction. E/A: the ratio of peak velocity blood flow from left ventricular relaxation in early diastole (the E wave) to peak velocity flow in late diastole caused by atrial contraction (the A wave). E/′E: the ratio between early mitral inflow velocity and mitral annular early diastolic velocity. IVRT: isovolumic relaxation time. DT: deceleration time

Table (III): Showing the difference in echocardiographic parameters over time for all patients (n=50)

	1m	P value	6m	P value
EF	52.62 ± 5.64	<0.001	54.98 ± 5.5	<0.001
E/A	1.49 ± 0.4	0.034	0.75 ± 0.05	<0.001
Average E/′E ratio	12.59 ± 0.44	0.004	9.53 ± 0.68	<0.001
IVRT	95.63 ± 3.72	0.04	114.78 ± 3.75	<0.001
DT	190.3 ± 16.28	0.034	211.08 ± 15.62	<0.001

EF: ejection fraction. E/A: the ratio of peak velocity blood flow from left ventricular relaxation in early diastole (the E wave) to peak velocity flow in late diastole caused by atrial contraction (the A wave). E/′E: the ratio between early mitral inflow velocity and mitral annular early diastolic velocity. IVRT: isovolumic relaxation time. DT: deceleration time

Table (IV): showing the difference between study groups concerning 1 month follow up echocardiographic parameters (n=50)

Parameter	preserved EF	Mildly reduced EF	P value
EF	56.33 ± 3.41	47.05 ± 3.13	<0.001
E/A	1.43 ± 0.03	1.85 ± 0.2	<0.001
Average E/′E ratio	11.32 ± 0.44	12.97 ± 0.45	0.038
IVRT	99.92± 4.3	88.51 ± 2.78	0.04
DT	195.7 ± 15.6	184.6 ± 17.57	0.045

EF: ejection fraction. E/A: the ratio of peak velocity blood flow from left ventricular relaxation in early diastole (the E wave) to peak velocity flow in late diastole caused by atrial contraction (the A wave). E/′E: the ratio between early mitral inflow velocity and mitral annular early diastolic velocity. IVRT: isovolumic relaxation time. DT: deceleration time

Table (V): Showing the difference between study groups concerning 6 month follow up echocardiographic parameters (n=50)

Parameter	Preserved EF	Mildly reduced EF	P value
EF	58.53 ± 3.44	49.65 ± 3.2	<0.001
E/A	0.69 ± 0.04	0.79 ± 0.06	<0.001
Average E/′E ratio	8.43 ± 0.67	9.53 ± 0.42	<0.001
IVRT	115.75 ± 4.7	102.1 ± 3.05	<0.001
DT	208.43 ± 15.04	201.5 ± 16.8	0.031

EF: ejection fraction. E/A: the ratio of peak velocity blood flow from left ventricular relaxation in early diastole (the E wave) to peak velocity flow in late diastole caused by atrial contraction (the A wave). E/′E: the ratio between early mitral inflow velocity and mitral annular early diastolic velocity. IVRT: isovolumic relaxation time. DT: deceleration time

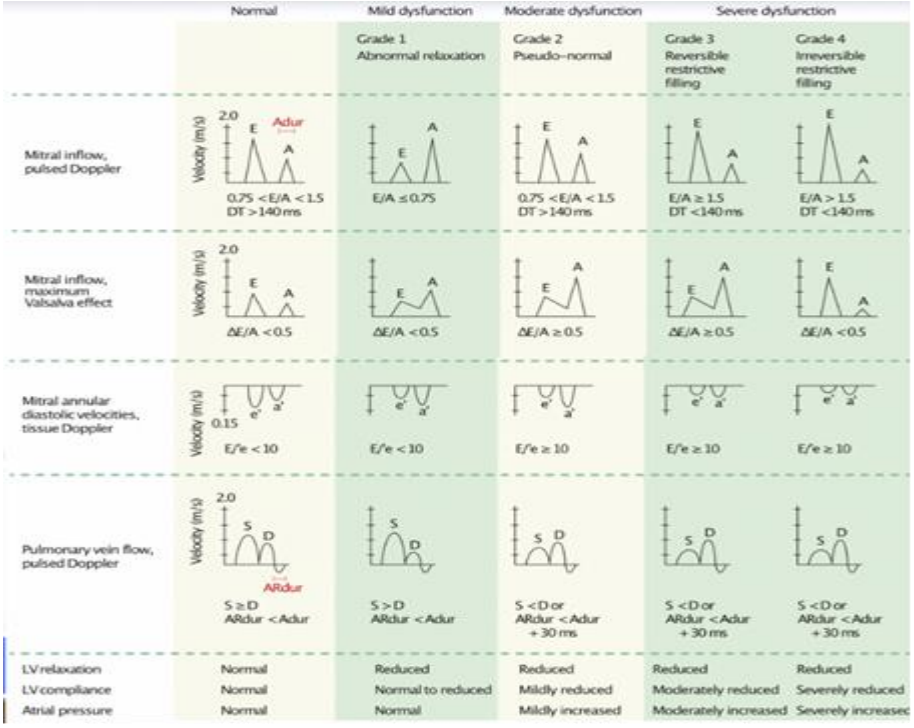

Figure (I): Diastolic dysfunction grades (Natarajan et al., 2013)