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The study of left ventricular relaxation and filling abnormalities in acute coronary syndrome by doppler echocardiography

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Abstract
Objectives: To study the left ventricular relaxation and filling abnormalities by doppler echocardiography and prognosis of acute coronary syndrome.
Methods: Fifty patients of acute coronary syndrome were included in the study. The left ventricular diastolic dysfunction was studied using doppler transmitral velocities within the apical 4- chambers view (1st study-on the day of admission and 2nd study- after one week). The various parameters studied were peak E (peak rapid filling velocity), peak A (atrial contraction wave), E/A ratio, E-DT (E- deceleration time), IVRT (isovolumetric relaxation time), S-wave (systolic forward flow wave), D-wave (diastolic forward flow wave) and AR-wave (atrial reversal wave).
Results: Of 50 patients studied 3 had normal, 36 patients had impaired relaxation, 5 patients had pseudo-normalization, 4 patients reversible and 2 patients irreversible restrictive filling on the day of admission (1st study). In the 2nd study (after one week) 16 were normal, 20 patients had impaired relaxation, 5 patients had pseudo-normalization, 6 patients had reversible and 2 patients had irreversible restrictive filling.
Conclusion: Doppler echocardiographic assessment of left ventricular diastolic dysfunction in the setting of acute coronary syndrome helps in the management and provides independent noninvasive prognostic information.

Keywords: Acute coronary syndrome, Diastolic dysfunction, Doppler echocardiography, Myocardial infarction.

INTRODUCTION

Coronary artery disease (CAD) is the most commonly encountered problem in both developed and developing countries around the globe. Acute coronary syndrome (ACS) is the major cause of morbidity and mortality of human beings today despite spectacular progress in the prevention and detection. In the recent years a fall in the mortality has been witnessed in the developed countries due to effectiveness of preventive measures, early detection and management [1,2,3]. In India, particular concern is the early age of affliction compared to the west and the projected risk in the mortality rate in the next 25 years [4].

Myocardial contraction becomes abnormal immediately after the onset of ischemia and is detected by echocardiography, even before the manifestations on electrocardiography.

The recorded flow velocities across the mitral valve and in the pulmonary veins are used to assess the filling patterns and to indirectly estimate left ventricular filling pressures [5]. The initial diastolic event is myocardial relaxation which is an active energy dependent process that causes pressure to decrease rapidly in the left ventricle (LV) after the end of systole and during early diastole.

Acute myocardial infarction (AMI) that leads to ischemia, cell necrosis, microvascular dysfunction, and regional wall motion abnormalities will influence the rate of active relaxation. In addition, interstitial edema, fibrocellular infiltration, and scar formation will directly affect left ventricular chamber stiffness.

The present study aims to study the relaxation and filling abnormalities in acute coronary syndrome by using color doppler echocardiography and also to assess the management and prognosis of acute coronary syndrome.

MATERIAL AND METHODS

The present study was undertaken in patients admitted with acute coronary syndrome in ICCU of a teaching hospital. Fifty patients of acute coronary syndrome were included in the study. Fifty healthy individuals were used as controls. All patients admitted with acute coronary syndrome within 24 hours of onset of chest pain (unstable angina, non ST -elevation and ST- elevation MI with normal left ventricular systolic function with ejection fraction ≥40%) were included.

Patients with abnormal left ventricular systolic function (Ejection fraction ≤40%) and acute left ventricular failure were excluded. The investigations included serial electrocardiography for diagnosis of acute coronary syndrome, cardiac enzymes (CPKMB, Cardiac Troponin T and SGOT) and colour doppler

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echocardiography (1st study -on the day of admission and 2nd study- after one week) obtained on ATL-ultramark-6 machine.

Systolic function was determined by 2D Echo, M-mode and colour doppler study. Wall motion abnormalities and any complications such as pericardial effusion, left ventricular thrombus, mitral regurgitation secondary to papillary muscle dysfunction were also observed for during the study.

The left ventricular relaxation and filling abnormalities were studied using doppler transmitral velocities within the apical 4-chamber view. The colour M-mode doppler technique, performed in the apical 4-chamber view reflects the distribution of blood velocities along a vertical line from the mitral plane to the apex of the LV. It therefore provides spatiotemporal information on the propagation of blood into the LV [6].

All pulse wave doppler measurements of transmitral flow were made within the same sample volume in the same position in a given patient. The various parameters used were as follows: [7, 8].

1. Peak rapid filling velocity (peak E) normal=71±13cm/sec: This result from the rapid filling phase.
2. Atrial contraction wave (peak A normal=57±13 cm/sec): An important index of LV diastolic function and occurs during atrial contraction.
3. E Deceleration time (E-DT) normal=181±19 msec: Represents the time interval between the peak E and the point on the baseline intercepted by the deceleration waveform.
4. Isovolumetric relaxation time (IVRT) normal=74±7 msec: Measured by positioning the sample volume of the pulse wave (PW) doppler half way between the anterior or mitral leaflet and the ventricular out flow tract. The time interval between the end of the left ventricular outflow velocity waveform and the onset of the mitral inflow velocity waveform represent IVRT.
5. E/A Ratio (normal= 1.28±0.25): Ratio of peak E and A velocity.
6. Systolic forward flow waves:-S wave (normal=49±8 cm/sec): (Pulmonary venous velocities) occurs during the systole of the heart.
7. Diastolic forward flow wave :-D wave (41±8 cm/sec): Occurs when mitral valve is open and produces open conduit between pulmonary vein, left atrium and left ventricle.
8. Atrial reversal wave:- AR wave (23±3cm/sec): Due to reversal of flow at atrial contraction.

The four basic transmitral inflow patterns present a parabolic distribution with respect to the E/A ratio [9]. That is, as the disease progresses from normal to severe diastolic dysfunction, the E to A relationship changes. These were compared with the readings from Mayo Clinic Echocardiography manual and classified as follows [7]:

1. Normal (E>A)
2. Impaired relaxation (IRP)- E/A<1, prolonged IVRT; prolonged DT
3. Pseudo-normalization pattern (PNP)- E>A
4. Reversible restrictive filling pattern (RRFP)- E>>A
5. Irreversible restrictive filling pattern. (IRFP)- E>>A

RESULTS

The maximum incidence of coronary artery disease was in the 40-60 yrs age group (56%) and males (72%) were affected more commonly than females (28%) (Table.1). In the symptom analysis of 50 patients it was found that chest pain (96%) was the predominant symptom following sweating (72%) (Table.2). Smoking was the predominant risk factor (52%) followed by sedentary life style (46%) (Table.3).

Maximum number of patients (33, 66%) were of ST-elevation MI, followed by unstable angina (12, 24%) and non-ST elevation MI (5, 10%) (Table.4). Among the 33 ST- elevation MI patients, 13 patients were inferior wall MI, 8 patients were anterior wall MI and 7 patients were of antero-septal MI (Table.5). 21 patients out of the 33 ST- elevation MI were thrombolysed and 12 not thrombolysed due to contraindications (Table.6).

Of 50 patients studied 3 had normal, 36 patients had impaired relaxation, 5 patients had had pseudo-normalization, 4 patients reversible and 2 patients irreversible restrictive filling on the day of admission (1st study). In the 2nd study (after one week) 16 were normal, 20 patients had impaired relaxation, 5 patients had pseudo-normalization, 6 patients had reversible and 2 patients had irreversible restrictive filling.

Table 1. Age and sex distribution

Age (years)	Male	Female	Total	Percentage (%)
21-30	2	-	2	4
31-40	4	2	6	12
41-50	12	3	15	30
51-60	10	3	13	26
61-70	7	2	9	18
≥71	1	4	5	10
Total	36	14	50	100

Table 2. Symptomatology

Symptoms	No. of cases	(%)
Chest pain	49	98
Sweating	36	72
Giddiness	9	18
Breathlessness	10	20
Vomiting	14	28
unconsciousness	-	-
Palpitation	4	8

Table 3. Risk factors

Risk factors	No. of cases	%
Smoking	26	52
Tobacco chewing	2	4
Hypertension	8	16
Diabetes mellitus	2	4
Family history of coronary artery disease	2	4
Past history of ischemic heart disease	-	-
Sedentary life style	23	46

Table 4. Type of ST-elevation MI.

Type of MI	ST- elevation MI	Non ST- elevation MI
Extensive anterior wall MI	8	2
Antero-septal MI	7	2
Inferior wall MI	13	1
Inferior wall with RVMI	--	--
Antero-septal with lateral extensive MI	--	--
Infero-lateral MI	2	--
Antero-lateral MI	3	--
Total	33	5

Echo doppler study done on admission in 33 patients with ST-elevation MI, 2 patients were normal, 23 patients had impaired relaxation, 6 patients had pseudo-normalization, one patient had reversible and one patient had irreversible restrictive filling pattern.

In those patients with prolonged IVRT, reversal of E/A, increased E-DT were indicating impaired relaxation pattern. Decreased E-DT and changes in pulmonary venous S- wave, D-wave and AR wave detected restrictive filling pattern of diastolic dysfunction.

Out of the 33 MI patients, 21 patients (63.66%) were thrombolysed and 12 patients (36.36%) were not thrombolysed. Among the 21 thrombolysed, 9 patients (42.85%) showed normal left ventricular relaxation and filling in the 2nd study. None of the non-thrombolysed patients showed normal pattern.

Differences in the A, E/A ratio, E-DT, IVRT and pulmonary venous S- wave compared to 1st and 2nd study were statistically significant ($p<0.05$) and hence they are important markers of diastolic dysfunction (Table.8).

During the hospital stay five patients had developed complications in the form of supraventricular tachycardia, left bundle branch block, right bundle branch block, Mitral regurgitation and pulmonary edema. One patient who was admitted with left bundle branch block in irreversible restrictive filling pattern died on the third day of admission after going to ventricular tachycardia.

Table 5. Type of STEMI in different stages of diastolic dysfunction .

Type of MI	Type of diastolic dysfunction				
	Normal	IRP	PNP	RRFP	IRFP
Extensive anterior wall MI (n=8)					
First study (n=8)	--	2	1	4	1
Second study (n=7)	--	4	--	2	1
Anteroseptal MI (n=7)					
First study	--	5	2	--	--
Second study	3	4	--	--	--
Inferior wall MI (n=13)					
First study	1	11	1	--	--
Second study	5	4	3	1	--
Others					
First study	1	3	--	--	1
Second study	1	3	--	--	1

Table 6. Diastolic dysfunction and thrombolytic therapy

Diastolic dysfunction	*Thrombolysed (n=21)*		*Non-thrombolysed (n=12)*	
	1st study	2nd study	1st study	2nd study
Normal	--	9	1	--
IRP	15	10	7	5
PNP	3	1	1	2
RRFP	3	1	1	2
IRFP	--	--	2	2
Result $\chi^2=7.07$, $p<0.01$	Improved-9 Not improved-12		Improved-0 Not improved-12	

Table 7. Different type of relaxation and filling abnormalities in comparison with the first and second study

Type of relaxation	First study		Second study		Controls	
	No.	%	No.	%	No.	%
Normal	3	6	16	32.65	46	92
IRP	36	72	20	40.82	4	8
PNP	5	10	5	10.2	--	--
RRFP	4	8	6	12.24	--	--
IRFP	2	4	2	4.08	--	--
Total	50	100	49	100	50	100

Table 8. Comparison of individual parameters of left ventricular diastolic function (Data presented as mean ± SD;)

	1st study (on admission)	2nd study (after 1 week)	Control	1st study Vs 2nd study		1st study Vs control		2nd study Vs control	
				t' value	p' value	t' value	p' value	t' value	p' value
E	0.55±0.152	0.587±0.136	0.72±0.16	1.25	>0.05	5.67	<0.01	4.67	<0.01
A	0.65±0.144	0.55±0.1176	0.525±0.10	3.33	<0.05	4.17	<0.01	1.5	>0.05
E/A	0.96±0.483	1.14±0.4018	1.43±0.296	2.04	<0.05	5.22	<0.01	16.12	<0.01
E-DT	217.18±43.64	195.86±43.91	177.6±12.06	2.46	<0.05	5.05	<0.01	2.34	<0.05
IVRT	98.76±20.93	85.18±13.12	82.56±6.06	3.88	<0.01	4.26	<0.01	1.06	>0.05
S-WAVE	64.66±20.23	48.04±19.94	47.73±5.98	4.13	<0.01	4.60	<0.01	0.08	>0.05
D-WAVE	41.86±14.49	36.96±15.6	37.4±3.83	1.63	>0.05	8.58	<0.01	0.16	>0.05
AR- WAVE	28.84±12.94	25.57±9.65	22.3±2.07	1.29	>0.05	1.90	<0.05	2.06	<0.05

DISCUSSION

Doppler echocardiography is a non invasive technique that has been used to evaluate left ventricular relaxation and filling. Left ventricular relaxation is an energy dependent process. Prolonged relaxation is the earliest abnormality in left ventricular dysfunction and is preceded by filling abnormality.

A mitral inflow pattern of abnormal relaxation (E<A; prolonged IVRT; prolonged E-DT) is commonly associated with coronary artery disease. As relaxation becomes further delayed, it impinges on the early filling phase, resulting in an increase in left atrial pressure (LAP). This increased LAP causes the filling pattern to appear normal as E/A becomes >1. This transition zone between abnormal relaxation and restrictive filling is termed pseudo-normalization and it is characterized by normal diastolic filling values [5]. In order to differentiate between normal and "pseudo-normal", evaluation of the transmitral flow at peak valsalva (or any maneuver that reduces preload such as reverse Trendelenburg or nitroglycerin) and/or evaluation of pulmonary venous flow is advocated.

If the pseudo-normal pattern is due to abnormal relaxation with elevated filling pressures, the pulmonary venous atrial flow reversal (PVAR) wave will be greater than 0.35 cm/s and the transmitral E/A ratio during the valsalva maneuver will be less than 1. Incidentally, a valsalva maneuver performed with a normal transmitral pattern will show proportional reductions in both E and A velocities and the E/A ratio will remain greater than 1. A valsalva maneuver superimposed on a restrictive pattern (E>>A) may or may not "pseudo-normalize" (E>A). That is, if diastolic dysfunction is at the far end of severity and it is irreversible, there will be no change with the valsalva.

It was found that many patients in the impaired relaxation state (72%) on the first study may become normal (32%) on the 2nd study and some patients went into restrictive filling pattern indicates impaired relaxation is an early stage of left ventricular dysfunction.

During the initial phase of impaired relaxation on 1st study, patients had low E- wave, high A-wave and hence a low E/A ratio as well as prolonged E-DT. On the 2nd study patients went into restrictive filling pattern, had high E and low A in conjunction with short deceleration time of E- wave indicating increased chamber stiffness and high ventricular filling pressure. Low, delayed E wave and an accentuated A wave, is generally indicative of delayed relaxation provided that left atrial pressure is normal or increased. [10].

It was observed that impaired relaxation was highest in the first study and in the 2nd study many patients have improved during a period of 1 week.

Voller H *et al.,* studied serial echocardiography in 78 patients of MI on admission and on days 2, 4 and 6, to discover the temporal course of any early myocardial adaptation. They concluded that serial measurement of left-ventricular filling by doppler echocardiography in the first post-infarction week can identify patients with impaired left-ventricular function through differences in flow pattern. Drug or interventional treatment can then be started early to prevent further left-ventricular dilatation and in this way improve prognosis [11].

Williamson BD *et al.,* studied 60 patients within 24 hours of AMI by doppler echo. Of 54 patients who also underwent catheterization, 45 (83%) were successfully reperfused. A subgroup of 17 patients underwent a follow-up Doppler examination at 7 days after infarction, whereas 15 patients with stable exertional angina served as control subjects. The final recovery values at 7 days were not significantly different from those of the coronary artery disease group [12].

Bonow *et al.,* studied left ventricular (LV) diastolic filling at rest in patients with coronary artery disease (CAD), by high-resolution time-activity curves (10-20 msec/frame) obtained from gated radionuclide angiograms in 231 patients. They observed that LV diastolic filling is abnormal in a high percentage of patients with CAD at rest independent of LV systolic function or previous myocardial infarction [13].

Chenzbraun A *et al.,* studied LV filling patterns with Doppler echocardiography in 15 healthy subjects and 38 patients with recent acute myocardial infarction. LV end-diastolic pressures were low to normal in patients with an E/A ratio less than 1 and were usually greater than 15 mm Hg in those with normal or abnormally increased (greater than 2) E/A ratios. Thus, an apparently normal E/A ratio in patients after myocardial infarction may identify those with more severe LV diastolic dysfunction and increased LV filling pressure [14].

Temesvari A *et al.,* studied 52 patients with acute myocardial infarction by Doppler echocardiography within the first 48 hours and one week later. Systolic function was defined by left ventricular outflow velocity measurements; diastolic function was characterized by mitral inflow parameters and patterns. Diastolic function improved in 18 cases and impaired in 9 pts, systolic function improved only in 11 cases and decreased in 28 pts by the time of the second examination. Worsening of diastolic function was always accompanied by worsening of systolic function. Despite improving diastolic function, worsening in systolic function could be observed in 8 cases. Monitoring of patients with acute myocardial infarction by Doppler echocardiography offers a possibility to select high risk patients with worsening left ventricular function for further closer follow-up [15].

Moller JE *et al.,* studied echocardiography within 24 h, five days and one and three months after MI in 125 unselected consecutive patients. They concluded that pseudonormal or restrictive filling patterns are related to progressive LV dilation and predict cardiac death after a first MI [16].

CONCLUSION

Increased IVRT, reversal of E/A ratio and increased E-DT are early and significant indicators of impaired relaxation phase of diastolic dysfunction. Decreased IVRT and E-DT, normal E/A ratio and pulmonary venous study showing S-wave less than D-wave with increased AR-wave are significant indicators of restrictive filling pattern of diastolic dysfunction.

So this study helps in early diagnosis of left ventricular filling and relaxation abnormalities and their severity. It also helps in monitoring of patients, early detection of complications, management and prognosis.

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