ORIGINAL RESEARCH PAPER

Cardiology

KEY WORDS: Non ST Elevation ACS, unstable angina, non ST elevation MI, Diastolic Dysfunction.

DIASTOLIC DYSFUNCTION IN NON ST ELEVATION ACS PATIENTS

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ABSTRACT

Background: Patient without persistent ST elevation in two or more contiguous leads but with biomarker evidence of myocardial necrosis are classified as having non ST elevation MI where as in patients without such evidence of myocardial necrosis, unstable angina is diagnosed. Diastolic dysfunction as a cause of left heart failure and its importance as a powerful predictor of cardiovascular events is now well established. Among patients with symptoms, an assessment of diastolic dysfunction should be part of every comprehensive adult echocardiographic examination. The main causes of diastolic dysfunction are the same as that results in systolic dysfunction. Hypertension, coronary disease and valvular heart disease are common causes of both the conditions. Acute coronary syndrome is one of the leading causes of morbidity and mortality in both younger and older age groups. In this study we will evaluate diastolic dysfunction in patients with unstable angina and Non ST Elevation MI.

Aims and Objectives: To Study Diastolic dysfunction in patients of Non ST elevation ACS and to Study Tissue Doppler Echocardiographic Profile in Patients of Non ST elevation Acute Coronary Syndrome.

Materials and Methods: It will be a prospective, one year study in the department of cardiology, CMC Ludhiana from 1/04/2016 to 31/03/2017. Patients enrolled in the study and will be subjected to 12 Lead ECG and complete Echoca rdio graphy to assess Diastolic dysfunction.

INTRODUCTION

Coronary Artery Disease is reaching epidemic proportions in developing countries like India. AHA/ACC 2007 guidelines states that the first step in assessing chest discomfort and other symptoms suggestive of Acute Coronary Syndrome (ACS) is determining the likelihood that symptoms are indeed secondary to obstructive Coronary Artery Disease.[1]

Second step is determining the short term risk of adverse clinical outcomes for patients with intermediate and high likelihood of Acute Coronary Syndrome. This is achieved by history, physical examination, ECG and cardiac biomarkers.[1]

According to European Society of Cardiology Guidelines Non ST Elevation Acute Coronary Syndrome is defined as:
Patients with acute chest pain but without persistent ST-segment elevation. They have rather persistent or transient ST-segment depression or T-wave inversion, flat T–wave, pseudonormalization of T-waves, or no ECG changes at presentation. The initial strategy in these patients is to alleviate ischemic symptoms, to monitor the patient with serial ECGs, and to repeat measurements of markers of myocardial necrosis. At presentation, the working diagnosis of Non-ST Elevation-Acute Coronary Syndrome (Non STEACS), based on the measurement of troponins, will be further qualified into Non-ST elevation Myocardial Infarction (NSTEMI) or unstable angina. The therapeutic management is guided by the final diagnosis.[2]

During Experimental induction or spontaneous ischemia, reduced perfusion is ofcourse the first event. ECG changes followed by chest pain are relatively late events. Regional wall motion abnormalities occur earlier to these. However, the first event after reduced perfusion, even before development of regional wall motion abnormalities is diastolic left ventricular dysfunction.[3]

Diastolic dysfunction refers to decline in performance of one or both ventricles during diastole in the cardiac cycle. Diastolic dysfunction as a cause of left heart failure and as a powerful predictor of cardiovascular events is now well established. Diastolic dysfunction is present in over 25% of adults over 40 years of age and is the primary cause of approximately 50% of heart failure cases. Among patients with symptoms, Doppler combined with two dimensional echocardiography is the best method to ascertain whether or not diastolic dysfunction is present and is the likely cause of these symptoms.[4]

Diastolic dysfunction should be a part of every compreh ensive adult echocardiographic examination. The main causes of diastolic dysfunction are the same conditions that results in systolic dysfunction. Hypertension, coronary disease and valvular heart disease are common causes of both the conditions. It is helpful to consider diastolic dysfunction as a continuum of disease that progress from mild to more advanced stages.[4]

Stages of Diastolic dysfunction
Grade 1 –Impaired relaxation
Grade 2 –Pseudonormalization
Grade 3 –Restrictive filling (reversible)
Grade 4 – Restrictive filling (Irreversible).

Echo-Doppler Parameters of Diastolic Function.

1) Mitral inflow

An Accurate measurement of the mitral inflow velocity is the most important parameter for the assessment of diastolic function. The primary measurements for assessment of mitral inflow include the peak early filling velocity (E wave), peak filling velocity in atrial systole (A wave), the E/A ratio and the deceleration time of the early filling velocity.[4]

2)Tissue Doppler imaging

In Tissue Doppler imaging the Doppler principles are used to quantify the higher amplitude, lower velocity signals of myocardial tissue motion[5].

Pulsed wave TDI is used to measure peak myocardial velocities and is particularly well suited to the measurement of long axis ventricular motion because the longitudinally oriented endocardial fibers are most parallel to the ultrasound beam in the apical views. Because the apex remains relatively stationary throughout the cardiac cycle, mitral annular motion is a good surrogate measure of overall longitudinal left ventricular (LV) contraction and relaxation.[6]

MATERIAL AND METHODS

The study was a prospective cohort study that was conducted in the department of Cardiology, Christian Medical College and Hospital Ludhiana. This study included all new patients presenting to ICCU with Non ST Elevation ACS from 1/4/2016 to 31/03/2017. Patients were enrolled in the study after satisfying the inclusion and exclusion criteria. Detailed informed consent was taken from the patients enrolled in the study.

Type of study: Prospective Cohort Study

Inclusion criteria

1. All patients of 18 years of age and above, with sign and symptoms of ACS without evidence of ST Elevation were included in the study.

Exclusion criteria.

1. Patients who did not give consent for the study.

In all selected patients history and physical examination were noted and each patient was subjected to 12 lead ECG (PHILIPS PAGEWRITERTC 30 CARDIOGRAPH), Echocardiography (PHILIPS HD 11 XE) and tissue Doppler myocardial imaging. To obtain a baseline hemodynamic status, subjects were made to rest in the Supine position for 10 minutes before undergoing the imaging examination. Patients underwent imaging in the left lateral decubitus position using the above system equipped with a 3.5 MHz transducer. Two dimensional gray scale, pulsed, continuous, and color Doppler data were acquired in parasternal and apical views. For tissue Doppler imaging, the sector was adjusted to obtain a frame rate of atleast 115 frames/second.

Diastolic dysfunction was studied with the above parameters recorded on Echocardiography.

The following parameters were noted at presentation and discharge:

1) LV size measurements
   LVIDD
   LVIDS
2) LA size
3) LVEF
4) PW at MITRAL VALVE annulus (E, A, E/A ratio)
5) Tissue Doppler Imaging at mitral valve annulus

The following parameters was noted

a) Early diastolic filling velocity (e') was checked at septal and lateral wall.
b) Systolic myocardial velocity (s') was checked at septal and lateral wall.
c) Ratio of transmitral blood flow velocity to tissue Doppler velocity (E/e')

In case of mortality after admission, the echocardiography findings for assessment of diastolic function at time of admission were considered for the study.

Diastolic dysfunction was interpreted by two important parameters:

1) Reduction in the e'. (Normal septal e' is 8.6 cm/s and normal lateral is 12.2 cm/s)
2) E/e' ratio: Ratio more than 15 using septal e' or more than 12 using lateral e'.

STATISTICAL ANALYSIS

Categorical variables were presented in number and percentage (%) and continuous variables were presented as mean ± SD and median. Normality of data was tested by Kolmogorov-Smirnov test. If the normality was rejected then non parametric test was used.

Statistical tests were applied as follows-

1. Quantitative variables were compared using ANOVA/ Kruskal Wallis test between three groups and ANOVA was used for comparison between groups after adjusting for confounding factors.
2. Qualitative variables were correlated using Chi-Square test.

A p value of <0.05 was considered statistically significant.

The data was entered in MS EXCEL spreadsheet and analysis was done using Statistical Package for Social Sciences (SPSS) version 21.0.

RESULT AND ANALYSIS

Table 1

Subject Distribution of Unstable Angina Vs NSTEMI Vs Control in study population

Study population (Total)	Unstable Angina	Non ST Elevation Myocardial Infarction	Controls
488	266	178	44

Figure-1

Subject Distribution of Unstable Angina Vs NSTEMI Vs Control in study population

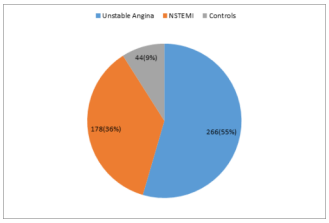


Table 2

Sex distribution of study population

Sex	Figures
Males	308(63%)
Females	180(37%)

Figure 2

Sex distribution of study population

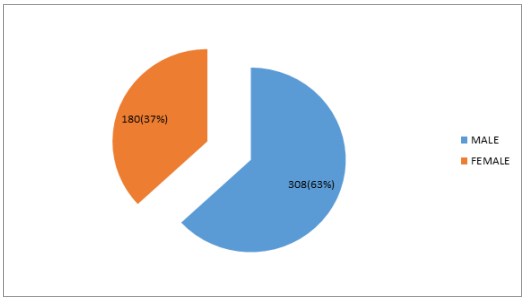


Table 3

Mean Age amongst Control Vs Untable Angina Vs NSTEMI

Age	Control	UA	NSTEMI	P value
Sample size	44	266	178	0.0002
Mean ± ST	55.32 ± 17.59	62.29 ± 11.8	65.14 ± 11.22	

Fig.3 : Mean Age amongst Control Vs Unstable Angina Vs NSTEMI

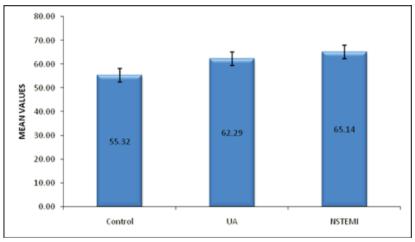
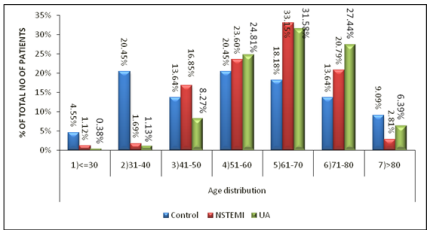


Table 4 Age distribution versus Control /UA/ NSTEMI

		N/UA/ NSTEMI			Total	P value
		Control	NSTEMI	UA		
Age distribution	1)≤30	2 (4.55%)	2 (1.12%)	1 (0.38%)	5 (1.02%)	<.0001
	2)31-40	9 (20.45%)	3 (1.69%)	13 (1.13%)	15 (3.07%)	
	3)41-50	6 (13.64%)	10 (16.85%)	84(8.27%)	58 (11.89%)	
	4)51-60	9 (20.45%)	42 (23.60%)	86 (24.81%)	117 (23.98%)	
	5)61-70	8 (18.18%)	31 (33.15%)	22 (31.58%)	151 (30.94%)	
	6)71-80	6 (13.64%)	57 (20.79%)	53 (27.44%)	116 (23.77%)	
	7)>80	4 (9.09%)	25 (2.81%)	7 (6.39%)	26 (5.33%)	
Total		44 (100.00%)	178 (100.00%)	266 (100.00%)	488 (100.00%)	

Figure 4 :Age distribution Vs. Control/Unstable Angina/ NSTEMI



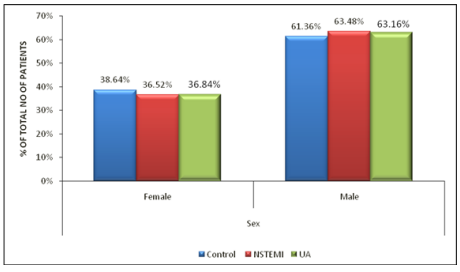
UA=Unstable Angina
NSTEMI = Non ST Elevation Myocardial Infarction

There is significant difference in age between control, Non ST Elevation Myocardial Infarction and UA. Maximum incidence of NSTE ACS was seen in the age group 61- 70 years. More age significantly increases the chances of Non ST Elevation Myocardial Infarction in the patients.

Table 5
Sex Distribution in Controls versus Unstable Angina versus NSTEMI

		Control/UA/ NSTEMI			Total	P value
		Control	NSTEMI	UA		
Sex	Female	17 (38.64%)	65 (36.52%)	98 (36.84%)	180 (36.89%)	0.966
	Male	27 (61.36%)	113 (63.48%)	168 (63.16%)	308 (63.11%)	
Total		44 (100.00%)	178(100.00%)	266(100.00%)	488(100.00%)	

Figure 5: Sex Distribution in Controls versus Unstable Angina versus NSTEMI



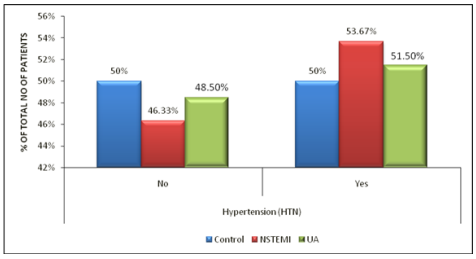
UA=Unstable Angina
NSTEMI = Non ST Elevation Myocardial Infarction

Incidence of NSTEMI and unstable angina was more in males(63.48% and 63.16% respectively). Between NSTEMI and unstable angina the sex distribution was not significant (p value 0.966).

Table 6
Hypertensive subjects in study population amongstControlversus Unstable Angina versus NSTEMI

		Control/UA/ NSTEMI			Total	P value
		Control	NSTEMI	UA		
HTN	No	22 (50.00%)	82 (46.33%)	129 (48.50%)	233 (47.84%)	0.865
	Yes	22 (50.00%)	96 (53.67%)	137 (51.50%)	255(52.16 %)	
Total		44 (100.00%)	178 (100.00%)	266 (100.00%)	488 (100.00%)	

Figure 6: Hypertensive subjects in study population amongst Control versus Unstable Angina versus NSTEMI



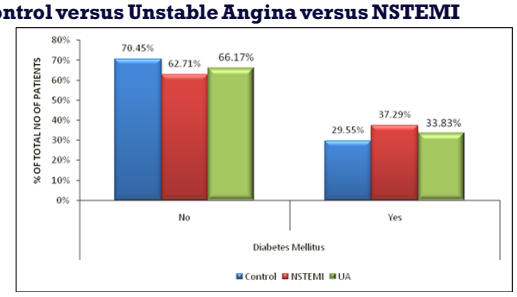
UA=Unstable Angina
NSTEMI = Non ST Elevation Myocardial Infarction

Distribution of hypertension in control, Non ST Elevation Myocardial Infarction and unstable angina are comparable (50%, 53.67% and 51.5% respectively), with p value 0.865.

Table 7
Diabetic subjects in study population amongst Control versus Unstable Angina versus NSTEMI

		Control/UA/ NSTEMI			Total	P value
		Control	NSTEMI	UA		
Diabetes Mellitus	No	31 (70.45%)	111 (62.71%)	176 (66.17%)	318 (65.30%)	0.569
	Yes	13 (29.55%)	67 (37.29%)	90 (33.83%)	169 (34.70%)	
Total		44 (100.00 %)	178 (100.00%)	266 (100.00%)	488(100.00%)	

Figure 7: Diabetic subjects in study population amongst Control versus Unstable Angina versus NSTEMI



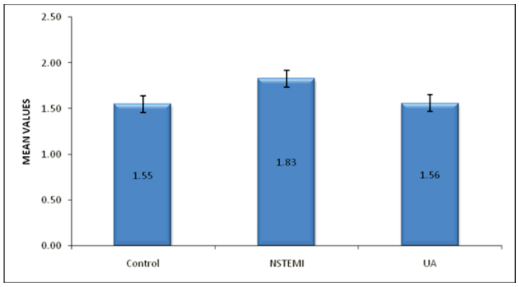
UA=Unstable Angina
NSTEMI = Non ST Elevation Myocardial Infarction

Figure 7 showing distribution of diabetes mellitus in control, Non ST Elevation Myocardial Infarction and unstable angina is comparable with p value .569.

Table 8
E/A ratio on admission amongst Control /UA/ NSTEMI

on ad(E/A)	Control	NSTEMI	UA	Control vs NSTEMI	Control vs UA	NSTEMI vs UA
Sample size	44	178	266	0.586	0.461	0.523
Mean ± ST	0.65 ± 0.18	0.73 ± 0.35	0.66 ± 0.21			

Figure 8 : E/A ratio on admission amongst Control /UA/ NSTEMI

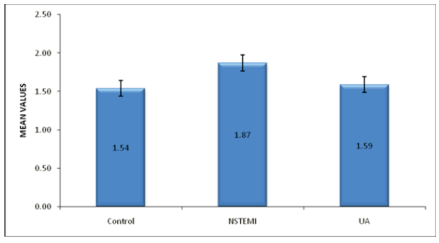


UA=Unstable Angina
NSTEMI = Non ST Elevation Myocardial Infarction
E/A mean value is higher in NSTEMI group as compared to control and unstable angina but there was no statistical significance as evidence by p value >0.05.

Table 9
E/A ratio on discharge amongst Control /UA/ NSTEMI

on d/c(E/A)	Control	NSTEMI	UA	Control vs NSTEMI	Control vs UA	NSTEMI vs UA
Sample size	44	178	266	<.0001	<.083	<.0001
Mean ± ST	0.64 ± 0.17	0.77 ± 0.3	0.69 ± 0.19			

Fig. 9 : E/A ratio on discharge amongst Control/ UA/ NSTEMI

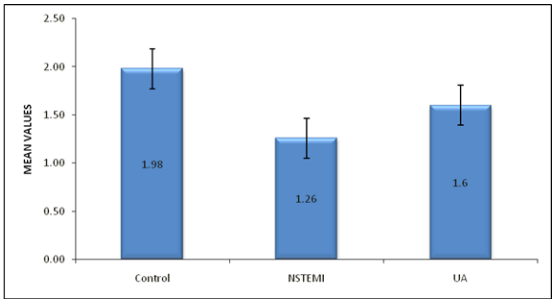


UA=Unstable Angina
NSTEMI = Non ST Elevation Myocardial Infarction
E/A mean value is higher in Non ST Elevation Myocardial Infarction as compared to control and unstable angina

Table 10
e'/a' ratio On admission amongst Control /UA/ NSTEMI

on ad(e'/a')	Control	NSTEMI	UA	Control vs NSTEMI	Control vs UA	NSTEMI vs UA
Sample size	44	178	266	0.662	0.965	0.749
Mean ± ST	2.98 ± 0.53	2.26 ± 0.31	2.6 ± 0.39			

Figure10 : e'/a' ratio On admission amongst Control /UA/ NSTEMI

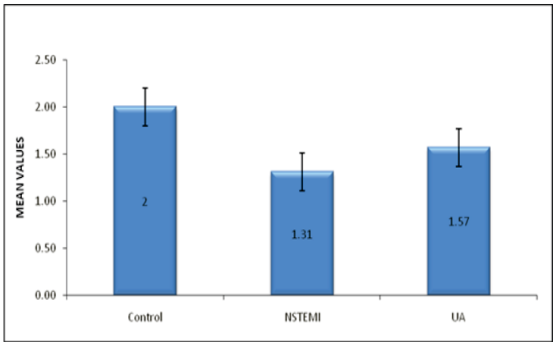


UA=Unstable Angina
NSTEMI = Non ST Elevation Myocardial Infarction
Lower e'/a' mean values are in Non ST Elevation Myocardial Infarction, and higher values are in control group. However the result is not statistically significant.

Table 11
e'/a' ratio On discharge amongst Control /UA/ NSTEMI

on d/c(e'/a')	Control	NSTEMI	UA	Control vs NSTEMI	Control vs UA	NSTEMI vs UA
Sample size	44	178	266	<.0001	<.0001	<.0001
Mean ± ST	3 ± 0.58	2.31 ± 0.84	2.57 ± 0.9			

Figure11 : e'/a' ratio On discharge amongstControl /UA/ NSTEMI



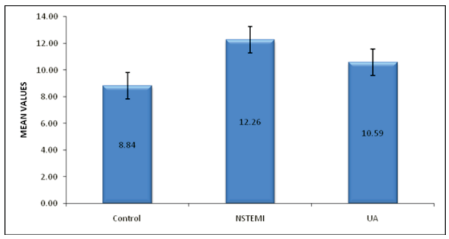
UA=Unstable Angina
NSTEMI = Non ST Elevation Myocardial Infarction

e'/a' mean value is significantly different in Non ST Elevation Myocardial Infarction, control and unstable angina. Lower e'/a' mean values are in Non ST Elevation Myocardial Infarction, and higher values are in control group.

Table 12
E/e' ratio on admission amongstControl /UA/ NSTEMI

on ad(E/e')	Control	NSTEMI	UA	P value	Control vs NSTEMI	Control vs UA	NSTEMI vs UA
Sample size	44	178	266	<0.001	<0.001	<0.02	<0.04
Mean ± ST	8.84 ± 2.28	12.26 ± 3.57	10.59 ± 3.73				

Figure 12 : E/e' ratio on admission amongst Control /UA/ NSTEMI



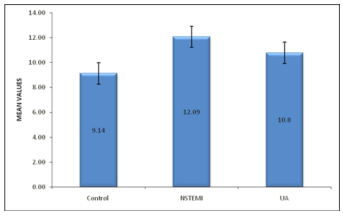
UA=Unstable Angina
NSTEMI = Non ST Elevation Myocardial Infarction

E/e' mean value is significantly different in Non ST Elevation Myocardial Infarction, control and unstable angina(12.26 ± 3.57vs8.84 ± 2.28 vs10.59 ± 3.73). Higher E/e' mean values are in Non ST Elevation Myocardial Infarction, and lower values are in control group.

Table 13
E/e' ratio on discharge amongst Control /UA/ NSTEMI

on d/c(E/e')	Control	NSTEMI	UA	P value	Control vs NSTEMI	Control vs UA	NSTEMI vs UA
Sample size	44	178	266	<0.001	<0.001	<0.03	<0.02
Mean ± ST	9.14 ± 2.07	12.09 ± 3.42	10.8 ± 3.78				

Figure 13 :E/e' ratio on discharge amongst Control /UA/ NSTEMI

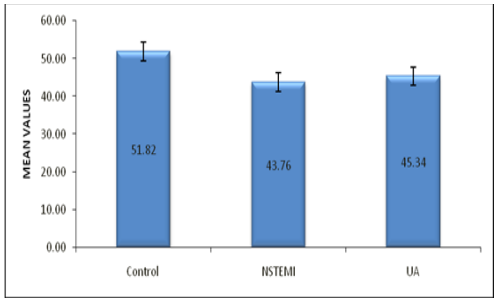


UA=Unstable Angina
NSTEMI = Non ST Elevation Myocardial Infarction
E/e' mean value is significantly different in Non ST Elevation Myocardial Infarction, control and unstable angina. Higher E/e' mean values are in Non ST Elevation Myocardial Infarction, and lower values are in control group.

Table14
Ejection fraction amongst study population in Control vs. UA vs. NSTEMI

EF(in %)	Control	NSTEMI	UA	P value
Sample size	44	178	266	<0.05
Mean ± ST	51.82 ± 6.2	43.76 ± 8.17	45.34 ± 10.88	

Figure 14 : Ejection fraction amongst study population in Control vs. UA vs. NSTEMI

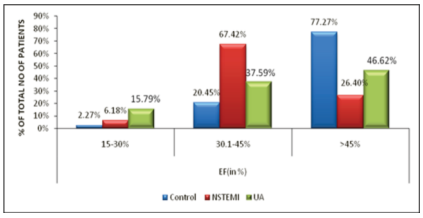


UA=Unstable Angina
NSTEMI = Non ST Elevation Myocardial Infarction
There is significant difference in EF between control, Non ST Elevation Myocardial Infarction and unstable angina with higher EF(51.82 ± 6.2%)in control, followed by unstable angina (45.34 ± 10.88%) and lowest EF(43.76 ± 8.17%) in Non ST Elevation Myocardial Infarction. Lower EF significantly increases the chances of Non ST Elevation Myocardial Infarction in the patients.

Table 15
Distribution of Ejection fraction amongst study popula tion in Control vs. UA vs. NSTEMI

		N/UA/ NSTEMI			Total	P value
		Control	NSTEMI	UA		
EF(%)	15-30%	1 (2.27%)	11 (6.18%)	42 (15.79%)	54 (11.07%)	<.0001
	30-45%	9 (20.45%)	120 (67.42%)	100 (37.59%)	229 (46.93%)	
	>45%	34 (77.27%)	47 (26.40%)	124 (46.62%)	205 (42.01%)	
Total		44(100.00%)	178(100.00%)	266(100.00%)	488(100.00%)	

Figure 15 : Distribution of Ejection fraction amongst study population in Control vs. UA vs. NSTEMI



UA=Unstable Angina

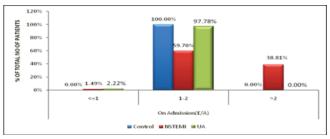
NSTEMI = Non ST Elevation Myocardial Infarction

There is significant difference in EF between control, Non ST Elevation Myocardial Infarction and unstable angina. Lower EF significantly increases the chances of Non ST Elevation Myocardial Infarction in the patients (p value <0.001). 67.42% patients in NSTEMI group had EF between 30.1- 45% while 46.62% patients in unstable angina group had EF >45%.

Table 16
On admission (E/A) versus Control /UA/ NSTEMI in Diabetic patients

		Control/UA/ NSTEMI			Total	P value
		Control	NSTEMI	UA		
on ad(E/A)	1)≤1	4 (30.7%)	11 (16.41%)	22 (24.44%)	37 (21.76%)	0.705
	2)1-2	3 (23.07%)	40 (59.70%)	48 (53.33%)	91 (53.52%)	
	3)>2	6 (46.15%)	16 (23.88%)	20 (22.22%)	42 (24.70%)	
Total		13 (100.00%)	67 (100.00%)	90 (100.00%)	170 (100.00%)	

Figure 16 :On Admission (E/A) Vs. Control/UA/ NSTEMI in Diabetic patients



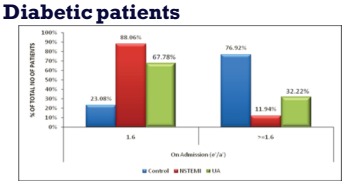
UA=Unstable Angina
NSTEMI = Non ST Elevation Myocardial Infarction

Mild diastolic dysfunction was higher in NSTEMI patients with diabetes whereas severe diastolic dysfunction was observed more in patients with unstable angina. But the results were not statistically significant.

Table 17
On admission (e'/a') versus Control /UA/ NSTEMI in Diabetic patients

		Control/UA/ NSTEMI			Total	P value
		Control	NSTEMI	UA		
on ad(e'/a')	1)<1.6	6 (46.15%)	39 (58.20%)	41 (45.55%)	86 (50.58%)	0.789
	2)≥1.6	7(53.84%)	28 (41.79%)	49 (54.44%)	84 (49.41%)	
Total		13(100.00%)	67(100.00%)	90(100.00%)	170(100.00%)	

Figure 17 :On admission (e'/a') versus Control /UA/ NSTEMI in Diabetic patients



UA=Unstable Angina
NSTEMI = Non ST Elevation Myocardial Infarction

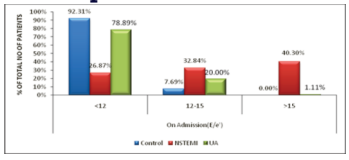
e'/a' is lower in Non ST Elevation Myocardial Infarction as compared to unstable angina and control signifying diastolic dysfunction in diabetics. However, the results are not statistically significant (p value – 0.789)

Table 18 (A)
On admission (E/e') versus Control /UA/ NSTEMI in Diabetic patients

		Control/UA/ NSTEMI			Total	P value
		Control	NSTEMI	UA		
on ad(E/e')	1)<12	12 (92.31%)	18 (26.87%)	71 (78.89%)	101 (59.41%)	<.0001
	2)12-15	1 (7.69%)	22 (32.84%)	18 (20.00%)	41 (24.12%)	
	3)>15	0 (0.00%)	27 (40.30%)	1 (1.11%)	28 (16.47%)	
Total		13 (100.00%)	67 (100.00%)	90 (100.00%)	170 (100.00%)	

In NSTEMI group E/e' was greater than 15 in 40.30% subjects. Diastolic dysfunction thus was significantly higher in Non ST Elevation Myocardial Infarction with p value <.0001.

Figure 18 :On Admission (E/e') versus Control /UA/ NSTEMI in Diabetic patients



UA=Unstable Angina
NSTEMI = Non ST Elevation Myocardial Infarction

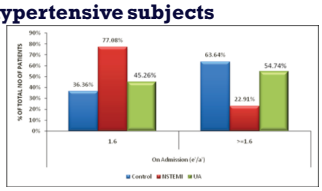
Table 18 (B)

	Control vs NSTEMI	Control vs UA	NSTEMI vs UA
1)<12	<.0001	0.454	<.0001
2)12-15	0.095	0.453	0.101
3)>15	0.003	1	<.0001

Table 19
On admission (e'/a') versus Control/UA/ NSTEMI in hypertensive subjects

		Control/UA/ NSTEMI			Total	P value
		Control	NSTEMI	UA		
on ad(e'/a')	1)<1.6	8 (36.36%)	74 (77.08%)	62 (45.26%)	136 (53.33%)	0.543
	2)≥1.6	14 (63.64%)	22 (22.91%)	75 (54.74%)	97 (38.03%)	
Total		22 (100.00%)	96(100.00%)	137(100.00%)	255 (100.00%)	

Figure 19 : On admission (e'/a') versus Control/UA/ NSTEMI in hypertensive subjects



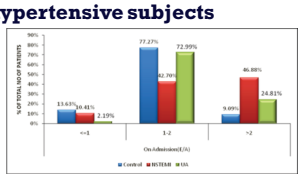
UA=Unstable Angina
NSTEMI = Non ST Elevation Myocardial Infarction

Abnormal e'/a'(<1.6) is higher in Non ST Elevation Myocardial Infarction as compared to UA and control but was statistically not significant with p value 0.543.

Table 20
On admission (E/A) versus Control/UA/ NSTEMI in hypertensive subjects

		Control/UA/ NSTEMI			Total	P value
		Control	NSTEMI	UA		
on ad(E/A)	1)≤1	3(13.63%)	10 (10.41%)	3 (2.19%)	16 (6.28%)	<0.05
	2)1-2	17 (77.27%)	41 (42.70%)	100 (72.99%)	158 (61.96%)	
	3)>2	2 (9.09%)	45 (46.88%)	34 (24.81%)	81 (31.76%)	
Total		22 (100.00%)	96(100.00%)	137(100.00%)	255(100.00%)	

Figure 20 : On admission (E/A) versus Control/UA/ NSTEMI in hypertensive subjects



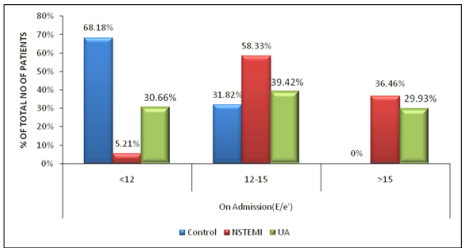
UA=Unstable Angina
NSTEMI = Non ST Elevation Myocardial Infarction
Mild diastolic dysfunction is significantly higher in UA and control whereas severe diastolic dysfunction is higher in Non ST Elevation Myocardial Infarction.

Table 21 (A)
On admission (E/e') versus Control/UA/ NSTEMI in hypertensive subjects

E/e' on admission		Control/UA/ NSTEMI			Total	P value
		Control	NSTEMI	UA		
	1)<12	15 (68.18%)	5 (5.21%)	42 (30.66%)	62 (24.31%)	<0.05
	2)12-15	7 (31.82%)	56 (58.33%)	54 (39.42%)	117 (45.88%)	
	3)>15	0 (0.00%)	35 (36.46%)	41 (29.93%)	76 (29.80%)	
Total		22 (100.00%)	96(100.00%)	137(100.00%)	255 (100.00%)	

E/e' diastolic dysfunction is significantly higher in Non ST Elevation Myocardial Infarction with p value <0.05.

Figure 21 :On admission (E/e') versus Control/UA/ NSTEMI in hypertensive subjects



UA=Unstable Angina
NSTEMI = Non ST Elevation Myocardial Infarction

Table 21(B)

E/e' on admission	Control vs NSTEMI	Control vs UA	NSTEMI vs UA
1)<12	<.0001	0.001	<.0001
2)12-15	0.044	0.657	0.007
3)>15	0.0002	0.001	0.366

DISCUSSION

Diastolic dysfunction (DD) of the heart refers to an increased stiffness and abnormal relaxation of the left ventricle leading to impaired filling during diastole. Despite this simple definition, truly understanding the cause of DD and its interrelationship with myocardial ischemia and hypertension is extremely complex. DD and coronary artery disease (CAD) are intertwined. Myocardial ischemia plays a role in the pathophysiology of DD. DD has been shown to alter the clinical course in CAD patients, and CAD presents a therapeutic target for DD for which no currently available treatments are known to affect outcome. It has been recognized, however, that some patients with DD have no symptoms while others with similar abnormalities present with overt heart failure. The trigger that tips DD patients into the symptomatic phase is unknown. Since there is a heavy load (significant burden) of patients in the OPDs with DD and coronary artery disease (CAD), we aimed to investigate the status of DD in advanced CAD patients.

In our study, total of 488 subjects were taken out of which 178 had NSTEMI, 266 had UA and 44 subjects were taken as controls **(table 1 and figure 1)**. Out of 488 subjects 180(36.89%) were females and 308(63.11%) were males **(table 2 and figure 2)**.

Mean age of patients in NSTEMI group was 65.14 ± 11.22 years, in UA group was 62.29 ± 11.8 years and control group was 55.32 ± 17.59 years**(table 3 and figure 3)**. There was significant different in age between control, NSTEMI and UA groups with higher age in NSTEMI than UA and lowest age in control group**(table 4 and figure 4)**.The results of age-group variation are consistent with study (Chaowalit et al).[7]where as patients in NSTEMI and UA had mean age of 69.1 ± 10.6years and 67.8 ± 12.4 years respectively. More age significantly increases the chances of NSTEMI in the patients. This finding is consistent with the study by**(Kyto V et al)**[8] where it was observed that incidence rate of NSTEMI increases by an estimated 61% per 5 years increase in age. However there was no statistical significant in sex distribution in the study population (p value – 0.966) **(table 5 and figure 5)**.

In our study approximately 52% of patients had hypertension and 34.70% of patients had diabetes. Distribution of hypertension in control **(table 6 and figure 6),** NSTEMI and UA were compared with p value of 0.865 and so was the distribution of diabetics with p value – 0.569**(table 7 and figure 7)**. There was no statistical significance of presence of hypertension in NSTEMI vs. UA. The same has been observed in another study **(Dumaine R et al)**[9] where hypertension was associated more in patients with UA than NSTEMI.

In our study about 47% of patients had moderate LV dysfunction (LVEF – 30 – 45%) and 11% of patients had severe LV dysfunction (LVEF < 30%). There was found to the significant difference in EF between control, NSTEMI and UA. Lower EF was found significantly more amongst patients with NSTEMI.

Diastolic dysfunction was measured using tissue Doppler on 2-D Echocardiography. The variables which were studied included E/A ratio, E/e' and e'/a' on admission as well as at the time of discharge. Mean value of E/A amongst control, NSTEMI and UA at time of admission were 0.65 ± 0.18, 0.73 ± 0.35 and 0.66 ± 0.21 respectively**(table 8 and figure 8)**.There was no statistical significant difference amongst the study group. As seen in **table 9 and figure 9,** mean value of E/A amongst control, NSTEMI and UA at time of discharge were 0.64 ± 0.17, 0.77 ± 0.3 and 0.69 ± 0.19 respectively. The results were statistically non-significant. Similar results were observed by another study **(Sharp et al).**[10]

As seen in table 10 and figure 10 e'/a' value amongst control, NSTEMI and UA groups at time of admission were 2.98 ± 0.53, 2.26 ± 0.31 and 2.6 ± 0.39 respectively. Lower e'/a' mean values were observed in NSTEMI group as compared to control and UA. The results were statistically found to be non-significant. As seen in **table 11 and figure 11,** e'/a' values amongst the same groups at the time of discharge were 3.0 ± 0.58, 2.31 ± 0.84 and 2.57 ± 0.90 respectively. The results were not found to be statistically significant.

In our study, we also calculated E/e' ratio amongst the study groups at the time of admission as well as on discharge. As seen in **table 12 and figure 12,** E/e' ratio at the time of admission amongst control, NSTEMI and UA groups was 8.84 ± 2.28, 12.26 ± 3.57 and 10.59 ± 3.73. Higher E/e' values were observed in NSTEMI group when compared to UA and

control. There was high statistical significance in the results observed, signifying high prevalence of diastolic dysfunction amongst NSTEMI group.

As seen in **table 13 and figure 13**E/e' ratio at the time of discharge amongst the same groups were 9.14 ± 2.07, 12.09 ± 3.42 and 10.8 ± 3.78 respectively.

There was slight improvement in E/e' ratio at the time of discharge, however the results were not statistically significant.

The results observed in our study in identifying diastolic dysfunction using E/e' ratio in tissue Doppler echocardio graphy revealed statistically significant results. Similar results were observed in another study **(Sharp et al)**[10]in which diastolic dysfunction was compared to other indices. One possible explanation is that when coronary artery disease causes regional hibernation of myocardium, the e' velocity drops. This velocity has been shown to rise again after percutaneous coronary intervention **(Diller GP et al).**[11]

An alternative hypothesis is that the cumulative burden of hypertension per patient is proportionate to the degree of diastolic dysfunction. This measure may therefore be acting as a surrogate for the overall effect which may in turn predict outcomes.

In our study as seen in **table 14 and figure 14,** we also observed difference in left ventricular ejection fraction amongst the study groups. Mean values of LVEF (in%) amongst control, NSTEMI and UA were 51.82 ± 6.2, 43.76 ± 8.17 and 45.34 ± 10.88 respectively. There was significant difference in LVEF between the study groups with higher LVEF in control than mean LVEF in UA and lower LVEF in NSTEMI ($p<0.05$). Similar findings were observed in a study which found that LV systolic dysfunction was more prevalent in patients with NSTEMI than in those with UA. Patient's with NSTEMI had statistically significant lower LVEF than those with UA (51.8 ± 1.4.9% vs. 60.2 ± 12.9%, $p=0.002$).

Losses of myocardial contractile function / tissue and changes in ventricular geometry have been described in the setting of acute coronary syndrome. These abnormalities can modify LV systolic and diastolic function and furthermore, affect the clinical course. LV systolic dysfunction contributes to impaired LV pump function and leads to mortality and morbidity after acute myocardial infarction. Several previous studies showed that LV systolic dysfunction strongly predicted adverse clinical outcomes such as mortality and heart failure after acute myocardial infarction **(Hellermann JP, Velazquez EJ, Nicod P, White HD, Weir RA et al)**[12-16] most of which were conducted in patients with acute myocardial infarction and the majority was from patients with NSTEMI. As seen in **table 15 and figure 15,** information from the present study is unique in that it was obtained specifically from patients with NSTEACS which includes both underlying pathology of myocardial infarction, represented by patients with NSTEMI and myocardial ischemia represented by patients with UA. The results shows that LV systolic dysfunction and the more advanced LV diastolic dysfunction were more prevalent in patients with NSTEMI than those with UA which may reflect the severity of underlying acute coronary pathology and extent of myocardial injury.

Our study included 34.70% diabetics. **Table 16 and figure 16 depicts** E/A ratio on admission in diabetics amongst control, NSTEMI and UA. E/A ratio was ≤ 1 in 30.7%, 16.41% and 24.44% respectively, 1-2 in 23.07%, 59.70% and 53.33% respectively and >2 in 46.15%, 23.88%, 22.22% respectively. The results inferred that mild diastolic function is higher in NSTEMI but the results were not statistically significant.

e'/a' ratio on admission in diabetics was lower in NSTEMI (58.02%) as compared to UA (45.55%) and control (46.15%); **(Table 17 and Figure 17)** signifying diastolic dysfunction in diabetics. However, the results were not statistically significant as evidenced by a value of 0.789.

E/e' ratio however on the other side revealed significant correction between presence of diastolic dysfunction amongst diabetic sub-group. E/e' on admission amongst NSTEMI, control and UA in diabetics was >15 in 40.30%, 0%, 1% respectively; 12-15 in 32.84%, 7.69 and 20.0% respectively. **(Table 18A and Figure 18).** The results improved that diastolic dysfunction in significantly higher in NSTEMI (p value <0.0001) in diabetics as compared to UA and control.

Diabetes mellitus is one of the major risk factors for diastolic heart failure. Diastolic dysfunction is observed in 40% of patients with diabetes mellitus and correlates with poor glycemic control **(Tsujino T et al).**[17] Suggested mechanism for diastolic dysfunction in the diabetic heart are: (i) abnormalities in high-energy phosphate metabolism; (ii) impaired calcium transport; (iii) interstitial accumulation of advanced glycosylation end products; (iv) imbalance in collagen synthesis and degradation; (v) abnormal microvascular function ; (vi) activated cardiac rennin angiotensin system; (vii) decreased adiponectin levels; (viii) alteration in the metabolism of free fatty acid and glucose. Poor glycemic control is associated with high incidence of heart failure in diabetic patients, but the preferable anti-hyperglycemic regimen for diastolic heart failure in patients with diabetes mellitus needs to be determined in further studies.

e'/a' ratio amongst hypertensive in control, NSTEMI and UA on admission was <1.6 in 36.36%, 77.08% and 45.26% respectively**(Table 19 and Figure 19).** Abnormal e'/a' was higher in NSTEMI as compared to UA and control. The results were however not statistically significant.

E/A ratio amongst hypertensive in control, NSTEMI and UA on admission was ≤1 in 13.63%, 10.41% and 2.19%, 1-2 in 77.27%, 42.70% and 72.99%; >2 in 9.09%, 46.88% and 24.81% respectively**(Table 20 and Figure 20).** Mild diastolic dysfunction is significantly higher in UA and control whereas severe diastolic dysfunction is higher in NSTEMI.

E/e' ratio in hypertensive was <12 in 68.18%, 5.21%, 30.66%; 12-15 in 31.82%, 58.33%, 39.42% and >15 in 0%, 36.46% and 29.93% amongst normal, NSTEMI and UA patients respectively**(Table 21A and Figure 21).** E/e' diastolic dysfunction is significantly higher in NSTEMI with p value <0.05.

Diastolic dysfunction is common in hypertension. Hypertension induces a compensatory thickening of the ventricular wall in an attempt to normalize wall stress, which results in concentric hypertrophy of LV, which in turn decreases LV compliance and LV diastolic filling. There is an abnormal accumulation of fibrillar collagen accompanying the hypertension – induced LV hypertrophy, which is also associated with decreased compliance and LV diastolic dysfunction. Most patients have elevated end diastolic pressure or delayed relaxation, many with normal or reduced diastolic chamber volumes (i.e. lower compliances) **(Zile MR et al).**[18]However accurate analysis of chamber volume based on the basis of 3-D imaging methods such as MRI or echocardiography remains scant. The majority of data are based on non-invasive parameters that indirectly index diastolic properties often determined under stable resting conditions. Furthermore many of these indexes are abnormal in elderly hypertensive individuals (Like E/A ratio, e'/a' ratio)**(Kitzman DW et al).**[19]In another study conducted on left ventricular diastolic dysfunction in adolescents with arterial

hypertension,**(Aleksandra Morka et al)**[20] It was found that the values for isovolumetric relaxation time (IVRT), PV-D (peak anterograde diastolic velocity) and E/e' ratio using lateral insertion do not change. However, significantly higher values were recorded for the speed of the A-MITRAL VALVE wave at the time of inflow through the initial value as well as the speed of myocardium movement (wave a'). Analysis of the structural matrix showed that the strongest features differentiating the groups were septal e'/a' ratio, septal e' and a' whereas the weakest links were lateral e' and a', A-MITRAL VALVE and IVRT.

CONCLUSION

We studied most frequently used parameters of diastolic LV dysfunction on echocardiography in ACS patients i.e. transmitral E/A, mitral valve annular e'/a' and E/e'.

We found that transmitral E/A and mitral valve annular e'/a' were not significantly abnormal in ACS patients as compared to controls. These parameters anyway have proven to be of less value in assessing diastolic LV dysfunction accurately at present day in cardiology.

As expected only E/e' was significantly increased in ACS patients relative to control when cut off values of either mild (12-15) or severe (>15) abnormality were used for comparison of two groups. There was no statistically significant difference in two groups when cut off values of <12 were used.

This proves our pre-study hypothesis that diastolic dysfunction occurs early in ACS patients and as a group it differentiates ACS patients from controls. Thus it is especially true when E/e' is taken as a parameter of diastolic LV dysfunction. However, this applies to patients groups and it may not applicable in all individual patients taken separately. E/A and e'/a' were not significantly different in ACS patients as a group when compared to controls.

However when only hypertensive patients were taken separately in all groups from non-hypertensive, even non ACS hypertensive had significantly increased E/A as compared non ACS, non hypertensive. When the values were taken for comparison, p remained <0.05 when hypertensive UA patients were compared with non ACS hypertensive or hypertensive NSTEMI were compared with hypertensive UA. This means that hypertension as a group increased E/A ratio in all groups .

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