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A Correlative Study of Cardiac Enzymes and Diastolic Dysfunction in Patients with Acute Coronary Syndrome

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Abstract: ***Background**: Acute Coronary Syndrome (ACS) is a leading cause of global morbidity and mortality. While systolic function is routinely assessed, the role of diastolic dysfunction (DD) and its correlation with the extent of myocardial injury, as indicated by cardiac enzymes, is increasingly recognized. This study aimed to evaluate the prevalence of DD in ACS patients and examine its relationship with Creatine Kinase-MB (CK-MB) levels. **Methods**: A cross-sectional study was conducted on 150 patients admitted with ACS. Diastolic function was assessed via 2D Echocardiography and classified as normal, impaired LV relaxation (Grade 1), or pseudonormal/restrictive (Grade 2/3/4). CK-MB levels were measured upon admission. Statistical analysis was performed using SPSS. **Results**: The mean age was 49.87 years with a near-equal gender distribution. A highly significant positive correlation was found between CK-MB levels and the severity of DD (Spearman's rho = 0.854, p<0.001). Mean CK-MB levels were 6.34 ng/mL, 34.97 ng/mL, and 70.37 ng/mL for normal, Grade 1, and Grade 2/3/4 DD, respectively. A significant association was found between smoking status and DD grades (p=0.019), though with an unexpected inverse relationship. Trends suggested worse DD with higher BMI and comorbidities like diabetes, though not statistically significant. **Conclusion**: There is a strong correlation between the severity of diastolic dysfunction and elevated CK-MB levels in ACS patients. Early echocardiographic assessment of diastolic function, alongside cardiac enzyme monitoring, is crucial for risk stratification and guiding management, emphasizing lifestyle interventions like weight management and smoking cessation.*

Keywords: Diastolic Dysfunction, CK-MB, Acute Coronary Syndrome, Comorbidities, Echocardiography.

1. Introduction

Acute Coronary Syndrome (ACS) represents a critical spectrum of coronary artery disease and is a leading cause of death worldwide. It encompasses conditions including ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI), and unstable angina (UA), all characterized by an acute imbalance between myocardial oxygen supply and demand[1]. The cornerstone of myocardial injury in ACS is necrosis, the extent of which is reliably indicated by cardiac biomarkers like troponins and Creatine Kinase-MB (CK-MB).

Traditionally, management has focused on systolic function. However, diastolic dysfunction impaired ventricular relaxation and filling is now recognized as a significant and often earlier manifestation of ischemic injury. DD is prevalent in ACS patients and is an independent predictor of adverse outcomes, including heart failure and mortality. The pathophysiological link between myocardial necrosis (reflected by elevated cardiac enzymes) and the development of DD involves mechanisms like ischemia-induced stiffness, fibrosis, and adverse ventricular remodeling[2]. This study explores the relationship between cardiac enzymes (CK-MB) and diastolic dysfunction in patients presenting with ACS.

2. Aim and Objectives

a) To evaluate the prevalence of diastolic dysfunction in patients with acute coronary syndrome.
b) To examine the relationship between cardiac enzymes (CK-MB) and diastolic dysfunction in patients with acute coronary syndrome.

3. Review of Literature

Acute Coronary Syndrome represents a state of acute myocardial ischemia, primarily triggered by the rupture or erosion of an atherosclerotic plaque, leading to platelet activation and thrombus formation, which partially or completely occludes a coronary artery[10]. Other mechanisms include coronary vasospasm and microvascular dysfunction[10]. The diagnosis and risk stratification of ACS rely heavily on clinical presentation, electrocardiographic (ECG) changes, and cardiac biomarkers.

Cardiac biomarkers are substances released into the bloodstream upon myocardial injury. Cardiac troponins (I and T) are the gold-standard biomarkers due to their high cardiac specificity. They rise within 3-6 hours of injury, peak at 12-24 hours, and can remain elevated for up to two weeks, making them crucial for both early and late diagnosis[11]. Creatine Kinase-MB (CK-MB), though less specific than troponin, remains a valuable marker. It elevates within 4-6 hours, peaks around 24 hours, and normalizes in 2-3 days, making it particularly useful for detecting reinfarction[11]. Natriuretic peptides like BNP and NT-proBNP, indicative of myocardial wall stress, are elevated in ACS complicated by heart failure and carry prognostic significance[11].

Diastolic dysfunction refers to an impairment in the ventricle's ability to relax and fill at normal pressures during diastole. Its pathophysiology in ACS is multifactorial. Myocardial ischemia disrupts energy-dependent processes like calcium reuptake into the sarcoplasmic reticulum, leading to impaired active relaxation[11]. Chronic ischemia can also promote myocardial fibrosis and remodeling, increasing ventricular stiffness and reducing compliance[12]. Echocardiography is the primary tool for assessing DD,

utilizing parameters such as the E/A ratio (early to late diastolic filling velocity), E/e' ratio (a marker of filling pressure), deceleration time (DT), and left atrial volume index (LAVI).

The interplay between cardiac enzymes and DD is rooted in their shared pathophysiological origin. The extent of myocardial necrosis, quantified by elevated troponins and CK-MB, directly correlates with the degree of systolic and diastolic impairment. Studies have consistently demonstrated this relationship. Gupta et al. found a positive correlation between elevated cardiac troponin T levels and the presence of left ventricular DD in ACS patients, with this combination predicting worse clinical outcomes[5]. Similarly, Smith et al. demonstrated that DD was an independent predictor of major adverse cardiac events (MACE) in NSTE-ACS patients with elevated cardiac enzymes[6].

Thompson et al. further highlighted the role of natriuretic peptides, showing that BNP and NT-proBNP levels were significantly higher in ACS patients with DD and were positively associated with its severity[7]. Johnson et al. reinforced the clinical impact, finding that DD in ACS patients with elevated enzymes was associated with higher in-hospital mortality and heart failure rates[8]. Lee et al. and Martinez et al. corroborated these findings in AMI and unstable angina populations, respectively, establishing a strong link between biomarker elevation and DD severity[9]. This body of evidence underscores the importance of an integrated assessment that combines biochemical markers with functional echocardiographic evaluation for comprehensive risk stratification in ACS.

4. Materials and Methods

Study Design and Setting: A hospital-based, cross-sectional observational study was conducted in the General Medicine wards and ICU of a tertiary care institution over 18 months.

Study Population: 150 patients diagnosed with ACS (STEMI, NSTEMI, or Unstable Angina) were enrolled via convenient sampling after obtaining written informed consent.

Inclusion Criteria: Patients of both sexes, aged over 18 years, with a diagnosis of ACS were included.

Exclusion Criteria: Patients with a past history of MI, complete heart block, atrial fibrillation, heart failure, valvular heart disease, or cardiomyopathies were excluded.

Study Procedure: A pre-designed proforma was used to collect demographic and clinical data. All patients underwent 2D Echocardiography to assess diastolic function, which was classified into three grades: Normal, Impaired LV relaxation (Grade 1), and Pseudonormal/Restrictive profile (Grade 2/3/4). CK-MB levels were measured from blood samples obtained at admission.

Statistical Analysis: Data were analyzed using SPSS version 26.0. Descriptive statistics, Chi-square tests, ANOVA, and Spearman's correlation were used as appropriate. A p-value of <0.05 was considered statistically significant.

5. Results (Including Observations)

Table 1: Baseline Demographic and Clinical Characteristics (N=150)

Characteristic	Category	Frequency (n)	Percentage (%)
Age Group (years)	33-47	66	44
	48-62	70	46.7
	63-78	14	9.3
Gender	Male	79	52.7
	Female	71	47.3
BMI Category	Underweight	24	16
	Normal	66	44
	Overweight/Obese	60	40
Comorbidities	Diabetes Mellitus	108	72
	Hypertension	89	59.3
	Dyslipidemia	116	77.3
Lifestyle Factors	Smoking	80	53.3
	Alcohol Use	63	42

Table 2: Distribution of ACS Type and Diastolic Dysfunction

Variable	Category	Frequency (n)	Percentage (%)
Type of ACS	STEMI	60	40
	NSTEMI	61	40.7
	Unstable Angina	29	19.3
Diastolic Dysfunction Grade	Normal	50	33.3
	Grade 1	50	33.3
	Grade 2/3/4	50	33.3

Table 3: Descriptive Statistics of Key Continuous Variables

Variable	N	Mean	Std. Deviation	Minimum	Maximum
Age (years)	150	49.87	8.49	33	78
CK-MB (ng/mL)	150	37.23	33.08	1	146.6

Table 4: Association between Comorbidities and Diastolic Dysfunction Grade

Comorbidity	Status	Number of Patients (n)	Diastolic Dysfunction Grade, n (%)			P value
			Normal	Grade 1	Grade 2/3/4	
Diabetes Mellitus	Present	108	31 (28.7%)	37 (34.3%)	40 (37.0%)	0.125
	Absent	42	19 (45.2%)	13 (31.0%)	10 (23.8%)	
Hypertension	Present	89	29 (32.6%)	30 (33.7%)	30 (33.7%)	0.973
	Absent	61	21 (34.4%)	20 (32.8%)	20 (32.8%)	
Dyslipidemia	Present	116	37 (31.9%)	38 (32.8%)	41 (35.3%)	0.610
	Absent	34	13 (38.2%)	12 (35.3%)	9 (26.5%)	
Any Comorbidity	Present	143	45 (31.5%)	49 (34.3%)	49 (34.3%)	0.091
	Absent	7	5 (71.4%)	1 (14.3%)	1 (14.3%)	

Table 5: Mean CK-MB Levels across Diastolic Dysfunction Grades

Diastolic Dysfunction Grade	N	Mean CK-MB (ng/mL)	Std. Deviation
Normal	50	6.34	2.78
Grade 1 (Impaired Relaxation)	50	34.97	13.91
Grade 2/3/4 Pseudonormal/ Restrictive)	50	70.37	32.05
Overall	150	37.23	33.08

ANOVA Result: F=125.623, p<0.001, Eta Squared=0.631

Table 6: Correlation between CK-MB and Diastolic Dysfunction Grade

Correlation	Spearman's Rho (ρ)	p-value
CK-MB & Diastolic Dysfunction Grade	0.854	<0.001

The cohort was relatively young (mean age ~50 years) with a high burden of comorbidities, particularly diabetes (72%) and dyslipidemia (77.3%). A statistically significant association was found between hypertension and ACS type, with hypertensive patients more likely to present with NSTEMI (p=0.046). A highly significant, strong positive correlation was observed between CK-MB levels and the severity of diastolic dysfunction (p<0.001), with Grade 2/3/4 DD showing mean CK-MB levels over ten times higher than the normal group. A significant association was found between smoking and DD grades (p=0.019), with a counterintuitive finding of a higher proportion of normal diastolic function among smokers (42.5%) compared to non-smokers (22.9%).

6. Discussion

This study confirms a robust correlation between the extent of myocardial injury, as reflected by CK-MB levels, and the severity of diastolic dysfunction in ACS patients. The stepwise increase in mean CK-MB from normal to restrictive physiology underscores that greater necrotic burden severely impairs ventricular relaxation and compliance. This aligns with previous research by Garg et al. and Okuda et al., who linked elevated troponins to adverse ventricular remodeling and DD[13].

The cohort's demographic profile was notable for a younger mean age and a high prevalence of cardiometabolic risk factors compared to global registries. The significant association between hypertension and NSTEMI presentation may be explained by hypertension-induced concentric LV hypertrophy, predisposing to subendocardial ischemia, which typically manifests as NSTEMI rather than STEMI[3].

While the association between BMI and DD was not statistically significant, a clear trend was observed, with overweight/obese patients having a lower proportion of normal diastolic function. This is consistent with population studies like CARDIA and MESA, which link obesity to worse diastolic function through mechanisms like increased preload and inflammation[5,6].

The unexpected finding of a higher prevalence of normal DD among smokers warrants careful interpretation. This may be due to confounding factors, such as differences in comorbidity profiles or the acute, transient autonomic effects of smoking that can temporarily alter filling dynamics, as suggested by Al-Safi et al. It should not be misconstrued as a protective effect of smoking.

7. Summary and Conclusion

7.1 Summary

This cross-sectional study of 150 ACS patients demonstrated a very strong positive correlation between CK-MB levels and the severity of diastolic dysfunction. The cohort was characterized by a young age and a high prevalence of diabetes and dyslipidemia. Hypertension was significantly associated with a presentation of NSTEMI.

7.2 Conclusion

The severity of diastolic dysfunction in ACS is strongly correlated with the magnitude of myocardial necrosis, as indicated by CK-MB. Early echocardiographic assessment of diastolic function, combined with cardiac biomarker evaluation, is essential for comprehensive risk stratification. Lifestyle modifications targeting weight management and smoking cessation are crucial components of secondary prevention to mitigate the progression of diastolic dysfunction.

Limitations: The cross-sectional design precludes causal inference. The sample size and single-center setting may limit generalizability. Unmeasured confounding factors (e.g., duration of smoking) may have influenced the results.

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