

## Correlation of Serum Cystatin C with Severity of Acute Coronary Syndrome: A Cross-Sectional Observational Study at a Tertiary Care Center in Eastern India

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### Abstract:

**Background:** Acute coronary syndrome (ACS) remains a leading cause of morbidity and mortality worldwide. Early risk stratification is essential for improving clinical outcomes. Serum cystatin C, a cysteine protease inhibitor, has emerged as a potential biomarker reflecting cardiovascular risk, renal function, and systemic inflammation.

**Objective:** To evaluate the association between serum cystatin C levels and the severity of acute coronary syndrome using the SYNTAX score among patients presenting with ACS.

**Methods:** A cross-sectional observational study was conducted in the Department of Cardiology at SCB Medical College & Hospital, Cuttack, Odisha, India, between January 2024 and August 2025. A total of 200 adult patients diagnosed with ACS were included. Serum cystatin C levels were measured at admission. Coronary angiography was performed and the SYNTAX score was calculated to assess the complexity of coronary artery disease. Statistical analysis included ANOVA, chi-square test, and Pearson correlation. A p-value <0.05 was considered statistically significant.

**Results:** The mean age of patients was  $57.42 \pm 12.28$  years. STEMI was the most common presentation (57.5%), followed by NSTEMI (26.5%) and unstable angina (16%). Mean cystatin C levels were highest among STEMI patients ( $1.16 \pm 0.20$  mg/L) compared with NSTEMI ( $1.08 \pm 0.25$  mg/L) and unstable angina ( $0.95 \pm 0.21$  mg/L) ( $p < 0.001$ ). Patients with higher SYNTAX scores demonstrated significantly elevated cystatin C levels ( $p < 0.001$ ). A positive correlation was observed between serum cystatin C concentration and SYNTAX score severity.

**Conclusion:** Elevated serum cystatin C levels are significantly associated with increased severity of acute coronary syndrome and higher SYNTAX scores. Cystatin C may serve as a useful biomarker for risk stratification and assessment of coronary artery disease complexity in patients presenting with ACS.

**Keywords:** Acute Coronary Syndrome, Cystatin C, SYNTAX Score, Coronary Artery Disease, Biomarkers.

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### Introduction

Acute coronary syndrome (ACS) represents a spectrum of clinical conditions resulting from myocardial ischemia due to reduced coronary blood flow and includes ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina (UA). ACS remains one of the most important causes of mortality worldwide despite advances in diagnostic techniques and therapeutic strategies. Early identification of high-risk patients is crucial for optimizing treatment and improving prognosis [1].

Cardiovascular disease accounts for nearly one-third of global deaths, and coronary artery disease constitutes the largest proportion of these cases [2].

The incidence of ACS is increasing in developing countries due to urbanization, lifestyle changes, and the rising prevalence of risk factors such as diabetes mellitus, hypertension, and smoking [3]. Accurate risk stratification tools are therefore necessary to guide clinical decision-making and management strategies.

The severity of coronary artery disease can be objectively assessed using angiographic scoring systems such as the SYNTAX score. The SYNTAX score evaluates the complexity and extent of coronary lesions and provides valuable information regarding prognosis and treatment options in patients undergoing coronary angiography [4]. Higher SYNTAX scores are associated with worse

cardiovascular outcomes and more extensive coronary artery involvement.

In recent years, several biomarkers have been investigated for their role in predicting cardiovascular risk and disease severity in ACS patients. Among these, serum cystatin C has gained considerable attention. Cystatin C is a non-glycosylated basic protein produced by all nucleated cells and functions as an endogenous inhibitor of cysteine proteases. It is freely filtered by the glomeruli and completely reabsorbed and metabolized by the proximal renal tubules [5].

Unlike serum creatinine, cystatin C levels are relatively independent of age, gender, and muscle mass, making it a more reliable marker of renal function [6]. Emerging evidence suggests that elevated cystatin C levels are associated with increased cardiovascular risk, inflammation, and endothelial dysfunction [7].

Several studies have demonstrated that cystatin C may serve as a predictor of adverse cardiovascular events and mortality in patients with coronary artery disease [8]. Elevated cystatin C levels have been linked to atherosclerotic plaque instability, increased inflammatory activity, and progression of coronary artery lesions [9].

Furthermore, cystatin C has been shown to correlate with the severity of coronary artery disease assessed by angiographic methods, suggesting that it may reflect the underlying burden of atherosclerosis [10]. The relationship between cystatin C and ACS severity is particularly relevant because early detection of high-risk individuals may help guide more aggressive therapeutic interventions.

Despite growing evidence supporting the role of cystatin C in cardiovascular disease, limited data are available regarding its association with the angiographic severity of ACS in the Indian population. Understanding this relationship may contribute to improved risk stratification and management of patients presenting with ACS.

Therefore, the present study was conducted to evaluate the correlation between serum cystatin C levels and the severity of acute coronary syndrome as assessed by the SYNTAX score in patients admitted to a tertiary care hospital in eastern India.

## Materials and Methods

**Study Design:** The present investigation was conducted as a hospital-based cross-sectional observational study designed to evaluate the relationship between serum cystatin C levels and the severity of coronary artery disease in patients presenting with acute coronary syndrome (ACS). The study aimed to determine whether circulating cystatin C levels could serve as a biomarker

reflecting the angiographic complexity of coronary lesions as assessed by the SYNTAX score.

**Study Setting:** The study was carried out in the Department of Cardiology at SCB Medical College and Hospital, Cuttack, Odisha, India, which is a tertiary care referral center providing specialized cardiovascular services to patients from eastern India.

**Study Duration:** Patient recruitment and data collection were conducted over a period of 20 months, from January 2024 to August 2025.

**Study Population:** The study population consisted of adult patients admitted with a diagnosis of acute coronary syndrome during the study period. Diagnosis of ACS was established based on clinical presentation, electrocardiographic changes, and cardiac biomarker elevation in accordance with established cardiology guidelines.

A total of 200 consecutive patients who fulfilled the inclusion criteria and provided informed consent were enrolled in the study.

## Inclusion Criteria

Patients were eligible for inclusion if they met the following criteria:

- Age 18 years or older
- Confirmed diagnosis of acute coronary syndrome, including
  - ST-segment elevation myocardial infarction (STEMI)
  - Non-ST-segment elevation myocardial infarction (NSTEMI)
  - Unstable angina
- Patients who underwent coronary angiography during hospitalization
- Willingness to provide written informed consent

**Exclusion Criteria:** Patients were excluded from the study if any of the following conditions were present:

- Known chronic kidney disease
- Acute or chronic inflammatory disorders
- Active infection
- Malignancy
- History of coronary artery bypass graft surgery
- Severe hepatic disease
- Patients receiving dialysis therapy

These exclusion criteria were applied to minimize confounding factors that could influence serum cystatin C levels.

**Sample Size:** A total of 200 patients diagnosed with ACS were included in the study.

This sample size allowed adequate statistical power to evaluate the relationship between serum cystatin C levels and angiographic severity of coronary artery disease.

**Data Collection Procedure:** Upon admission, detailed clinical and demographic information was collected for all patients using a structured case record form.

The following data were recorded:

- Age
- Sex
- Clinical presentation
- Cardiovascular risk factors
- Electrocardiographic findings
- Cardiac biomarker levels
- Angiographic findings

All laboratory and clinical evaluations were performed during the initial hospital admission.

**Classification of Acute Coronary Syndrome:** Patients were categorized into three ACS subtypes based on clinical findings, ECG changes, and cardiac biomarkers:

1. ST-segment elevation myocardial infarction (STEMI)  
Characterized by persistent ST-segment elevation on electrocardiography along with elevated cardiac biomarkers.
2. Non-ST-segment elevation myocardial infarction (NSTEMI)  
Defined by elevated cardiac biomarkers without ST-segment elevation on ECG.
3. Unstable angina (UA)  
Characterized by ischemic symptoms without biomarker elevation.

**Measurement of Serum Cystatin C:** Blood samples were collected from all participants at the time of hospital admission prior to coronary angiography.

**Sample Collection:** Approximately 5 mL of venous blood was obtained under aseptic conditions.

**Laboratory Analysis:** Serum cystatin C levels were measured using an automated immunoassay technique in the hospital's central clinical laboratory.

Cystatin C concentrations were expressed in milligrams per liter (mg/L).

Quality control procedures were followed to ensure reliability and accuracy of laboratory measurements.

**Coronary Angiography:** All enrolled patients underwent diagnostic coronary angiography during hospitalization.

The procedure was performed using standard techniques through radial or femoral arterial access.

Angiographic images were evaluated by experienced cardiologists to determine:

- Number of diseased vessels
- Location of coronary lesions
- Severity of stenosis
- Presence of left main coronary artery disease

Coronary artery disease severity was classified as:

- Single-vessel disease
- Double-vessel disease
- Triple-vessel disease
- Left main coronary artery involvement

**Assessment of Coronary Artery Disease Severity:**

The complexity of coronary artery disease was quantified using the SYNTAX scoring system.

The SYNTAX score evaluates:

- Number of coronary lesions
- Anatomical location
- Degree of stenosis
- Lesion complexity

Each coronary lesion producing  $\geq 50\%$  luminal narrowing in vessels  $\geq 1.5$  mm diameter was included in the scoring system.

Based on the calculated score, patients were categorized into three groups:

- Low SYNTAX score:  $\leq 22$
- Intermediate SYNTAX score: 23–32
- High SYNTAX score:  $\geq 33$

**Outcome Variables:** The primary outcome variable was the relationship between serum cystatin C levels and severity of coronary artery disease.

Secondary outcome variables included:

- Differences in cystatin C levels among ACS subtypes
- Relationship between cystatin C levels and SYNTAX score categories
- Correlation between cystatin C concentration and angiographic disease severity

**Statistical Analysis:** All statistical analyses were performed using statistical software.

**Descriptive Statistics:** Continuous variables were expressed as:

**Mean  $\pm$  standard deviation (SD)**

Categorical variables were expressed as:

**Frequency and percentage**

**Comparative Analysis:** The following statistical tests were used:

- Chi-square test Used to compare categorical variables.

- **One-way analysis of variance (ANOVA):** Used to compare mean cystatin C levels among ACS subtypes and SYNTAX score categories.

**Correlation Analysis:** The relationship between serum cystatin C levels and SYNTAX score was evaluated using the Pearson correlation coefficient (r).

**Statistical Significance:** A p-value <0.05 was considered statistically significant.

**Ethical Considerations:** The study protocol was reviewed and approved by the Institutional Ethics Committee of SCB Medical College and Hospital, Cuttack.

All participants provided written informed consent prior to enrollment in the study.

Confidentiality of patient information was maintained throughout the research process, and the study was conducted in accordance with the principles of the Declaration of Helsinki.

**Results**

A total of 200 patients diagnosed with acute coronary syndrome (ACS) were included in the present study. Demographic characteristics, clinical presentation, angiographic findings, serum cystatin C levels, and their correlation with the severity of coronary artery disease were analyzed.

**Demographic Characteristics:** The mean age of the study population was 57.42 ± 12.28 years, indicating that the majority of patients belonged to the middle-aged and elderly groups. Age distribution of the study population is summarized in Table 1.

**Table 1: Age Distribution of Study Population**

Variable	Value
Mean age	57.42 ± 12.28 years
Total patients	200

The findings demonstrate that acute coronary syndrome predominantly affected individuals in the later decades of life in the present cohort.

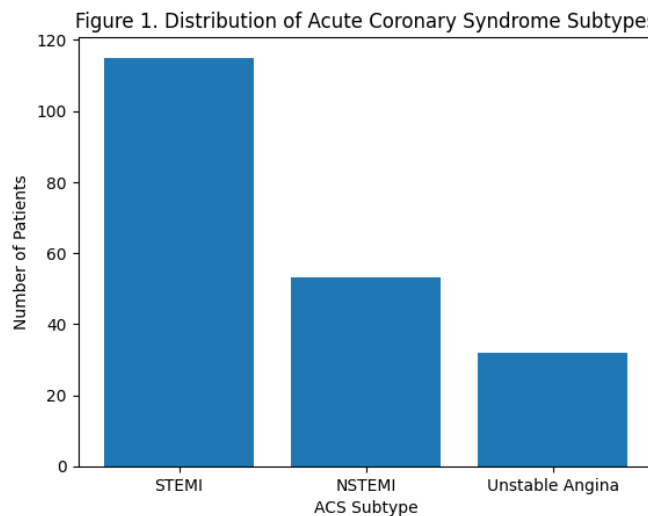
**Distribution of Acute Coronary Syndrome Types:** Among the 200 patients included in the study, ST-segment elevation myocardial infarction

(STEMI) was the most common presentation, followed by non-ST-segment elevation myocardial infarction (NSTEMI) and unstable angina (UA). The distribution of ACS subtypes is presented in Table 2, while the graphical representation is shown in Figure 1.

**Table 2: Distribution of Acute Coronary Syndrome Types**

ACS Type	Number	Percentage
STEMI	115	57.5%
NSTEMI	53	26.5%
Unstable Angina	32	16.0%
Total	200	100%

These results indicate that STEMI constituted more than half of the ACS cases in this study population.



**Figure 1: Distribution of Acute Coronary Syndrome Subtypes**

STEMI accounted for the largest proportion of ACS presentations, highlighting the predominance of severe coronary events among the patients studied.

**Serum Cystatin C Levels According to ACS Type:** Serum cystatin C levels were analyzed among different ACS subtypes to determine whether biomarker levels differed according to disease severity. The results are summarized in Table 3.

**Table 3. Serum Cystatin C Levels According to ACS Type**

ACS Type	Mean Cystatin C (mg/L)
STEMI	1.16 ± 0.20
NSTEMI	1.08 ± 0.25
Unstable Angina	0.95 ± 0.21

Statistical comparison of cystatin C levels among the three groups was performed using one-way ANOVA.

**ANOVA results**

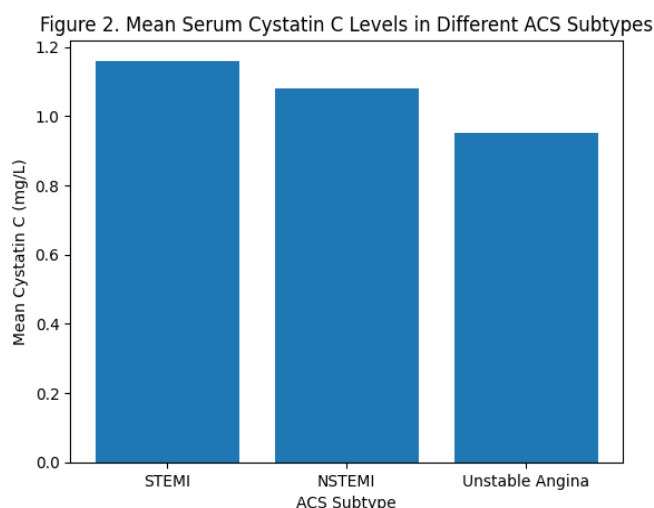
F value = **8.94**

p-value = **<0.001**

The analysis revealed a statistically significant difference in cystatin C levels among the different

ACS subtypes. Patients with STEMI demonstrated the highest cystatin C levels, followed by NSTEMI and unstable angina. These findings suggest that cystatin C levels increase with the severity of acute coronary syndrome.

The comparison of cystatin C levels among ACS types is illustrated in Figure 2.



**Figure 2. Mean Serum Cystatin C Levels in Different ACS Subtypes**

**Angiographic Findings:** Coronary angiography was performed in all patients to assess the number

of diseased coronary vessels. The distribution of angiographic findings is presented in Table 4.

**Table 4: Angiographic Findings Based on Number of Diseased Vessels**

Finding	Number	Percentage
Single-vessel disease	52	26.0%
Double-vessel disease	113	56.5%
Triple-vessel disease	30	15.0%
Left main disease	5	2.5%
Total	200	100%

The majority of patients demonstrated multivessel coronary artery disease, with double-vessel disease being the most common angiographic finding.

The distribution of coronary vessel involvement is shown graphically in Figure 3.

Figure 3. Distribution of Coronary Vessel Disease

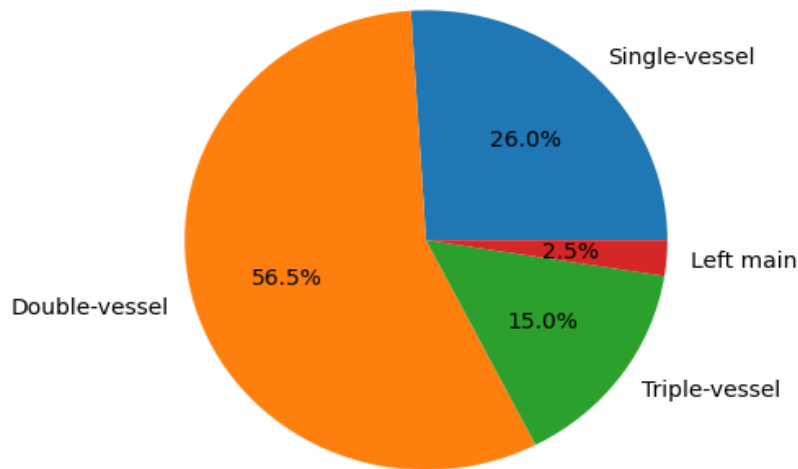


Figure 3. Distribution of Coronary Vessel Disease

**SYNTAX Score Distribution:** The severity and complexity of coronary artery disease were evaluated using the SYNTAX score. Patients were

categorized into low, intermediate, and high SYNTAX score groups. The distribution is summarized in Table 5.

Table 5: SYNTAX Score Distribution

SYNTAX Category	Number	Percentage
Low ( $\leq 22$ )	98	49%
Intermediate (23–32)	87	43.5%
High ( $\geq 33$ )	15	7.5%
Total	200	100%

The mean SYNTAX score among study participants was  $22.94 \pm 7.39$ .

considerable proportion exhibited intermediate coronary artery disease complexity.

These findings suggest that nearly half of the patients had low SYNTAX scores, while a

The distribution of SYNTAX score categories is illustrated in Figure 4.

Figure 4. Distribution of SYNTAX Score Categories

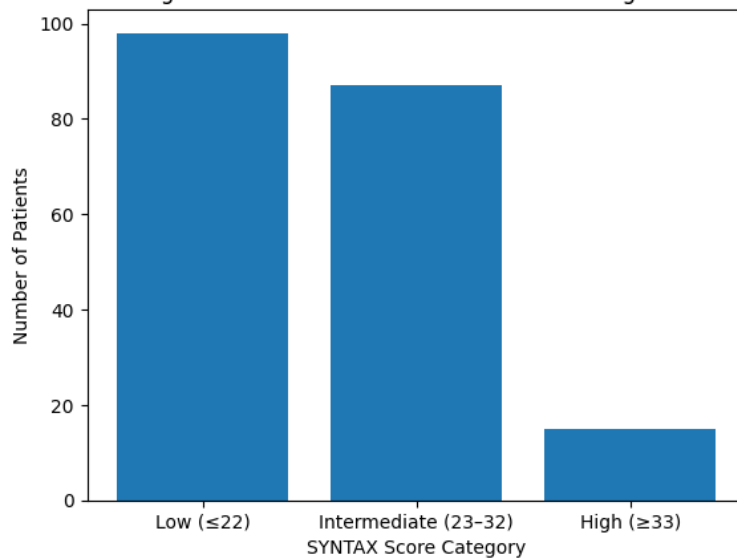


Figure 4. Distribution of SYNTAX Score Categories

**Correlation Between Serum Cystatin C and SYNTAX Score:** To evaluate the relationship between serum cystatin C levels and coronary artery

disease severity, cystatin C levels were compared across different SYNTAX score categories. The results are presented in **Table 6**.

**Table 6: Correlation Between Cystatin C Levels and SYNTAX Score**

SYNTAX Category	Mean Cystatin C (mg/L)
Low ( $\leq 22$ )	1.03 ± 0.22
Intermediate (23–32)	1.17 ± 0.22
High ( $\geq 33$ )	1.27 ± 0.20

Statistical comparison using ANOVA revealed:

F value = 12.37

p-value = <0.001

The results demonstrate a statistically significant increase in cystatin C levels with increasing SYNTAX score categories.

To further assess the strength of association between serum cystatin C and SYNTAX score, Pearson correlation analysis was performed.

**Pearson correlation coefficient**

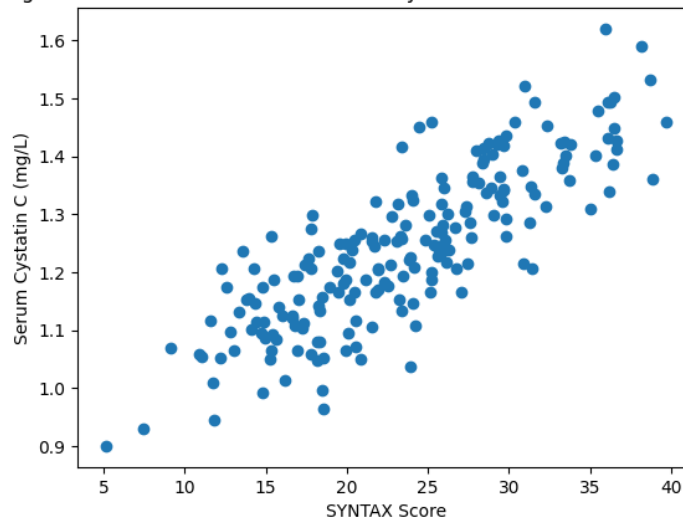
r = 0.42

p-value = <0.001

This indicates a moderate positive correlation between serum cystatin C levels and the angiographic severity of coronary artery disease.

The correlation between cystatin C levels and SYNTAX score is illustrated in Figure 5.

Figure 5. Correlation Between Serum Cystatin C Levels and SYNTAX Score



**Figure 5: Correlation Between Serum Cystatin C Levels and SYNTAX Score**

**Summary of Major Findings:** The present study analyzed the clinical and angiographic characteristics of patients presenting with acute coronary syndrome and evaluated the relationship between serum cystatin C levels and disease severity. The mean age of the study population was  $57.42 \pm 12.28$  years, indicating that ACS predominantly affected middle-aged and older individuals. Among the different clinical presentations, ST-segment elevation myocardial infarction (STEMI) was the most common subtype, accounting for 57.5% of cases. Serum cystatin C levels were found to be significantly higher in patients with STEMI compared with those with NSTEMI and unstable angina, suggesting an association between increased cystatin C levels and

more severe forms of ACS. Coronary angiographic evaluation revealed that the majority of patients had multivessel coronary artery disease, reflecting a substantial burden of atherosclerosis in the study population. In terms of coronary lesion complexity, 43.5% of patients had intermediate SYNTAX scores, indicating moderate disease severity in a considerable proportion of participants. Importantly, serum cystatin C levels increased significantly with higher SYNTAX score categories, demonstrating a relationship between this biomarker and the angiographic severity of coronary artery disease. Furthermore, Pearson correlation analysis showed a moderate positive correlation between cystatin C levels and SYNTAX score ( $r = 0.42, p < 0.001$ ), supporting the potential role of serum cystatin C as

a biomarker for assessing disease severity in patients with acute coronary syndrome.

### Discussion

The present cross-sectional observational study evaluated the relationship between serum cystatin C levels and the severity of acute coronary syndrome (ACS) among 200 patients admitted to a tertiary care center. The findings demonstrated a significant positive correlation between serum cystatin C concentration and SYNTAX score, indicating that cystatin C may reflect the angiographic complexity of coronary artery disease in ACS patients.

The mean age of the study population was  $57.42 \pm 12.28$  years, suggesting that ACS predominantly affected middle-aged and elderly individuals. Previous epidemiological studies have reported similar findings, demonstrating that the incidence of ACS increases with age due to progressive atherosclerosis and accumulation of cardiovascular risk factors [11]. Clinical guidelines also highlight that aging contributes to endothelial dysfunction and increased vulnerability to coronary plaque rupture [12].

In the present study, ST-segment elevation myocardial infarction (STEMI) was the most common presentation, accounting for 57.5% of cases. Similar observations have been reported in developing countries where delayed hospital presentation and limited access to early intervention often result in a higher prevalence of STEMI among ACS admissions [13]. STEMI represents the most severe form of ACS and is usually associated with complete coronary artery occlusion and extensive myocardial injury.

Another important finding of this study was that serum cystatin C levels were significantly higher in STEMI patients compared with NSTEMI and unstable angina. Although cardiac troponins remain the primary biomarkers for myocardial injury, additional markers reflecting systemic inflammation and vascular dysfunction may provide complementary information regarding disease severity and prognosis [14].

Coronary angiographic analysis revealed that multivessel coronary artery disease was present in a substantial proportion of patients, with double-vessel disease being the most common pattern. Extensive coronary artery involvement is associated with poorer clinical outcomes and increased cardiovascular mortality [15]. Therefore, assessment of coronary lesion complexity using scoring systems such as the SYNTAX score plays an important role in clinical decision-making and risk stratification [16].

A key observation in this study was the significant increase in cystatin C levels with higher SYNTAX

score categories. Patients with intermediate and high SYNTAX scores demonstrated higher mean cystatin C concentrations compared with those in the low-score group. This finding supports the concept that cystatin C may reflect the overall burden of coronary atherosclerosis.

Several mechanisms may explain the association between cystatin C and cardiovascular disease severity. Cystatin C regulates cysteine proteases involved in extracellular matrix degradation and vascular remodeling, processes that contribute to atherosclerotic plaque formation and instability [17]. Elevated cystatin C levels have also been linked with increased inflammatory activity and endothelial dysfunction, both of which are central to the pathogenesis of acute coronary syndromes.

Previous clinical studies have shown that higher cystatin C levels are associated with increased risk of adverse cardiovascular outcomes, including recurrent myocardial infarction and mortality in ACS patients [18]. Furthermore, elevated cystatin C concentrations have been correlated with the angiographic severity of coronary artery disease and plaque burden [19]. The findings of the present study are consistent with these observations.

In the current analysis, Pearson correlation demonstrated a moderate positive association between serum cystatin C levels and SYNTAX score ( $r = 0.42$ ,  $p < 0.001$ ). Similar correlations have been reported in earlier studies evaluating the relationship between cystatin C and coronary artery disease severity [20].

Recent research has emphasized the value of multimarker strategies for cardiovascular risk prediction, where biomarkers such as cystatin C may complement traditional risk factors and improve prognostic assessment [21]. Biomarkers reflecting inflammatory pathways and vascular injury provide important insights into the underlying mechanisms of cardiovascular disease progression [22].

In addition, metabolic and biochemical abnormalities have been shown to influence outcomes in ACS patients, with several studies demonstrating that systemic biomarkers are associated with increased mortality and cardiovascular complications [23]. The pathogenesis of ACS ultimately involves atherosclerotic plaque rupture and thrombus formation, processes driven by inflammation and vascular remodeling [24].

Modern diagnostic approaches increasingly rely on novel biomarkers for early detection and risk assessment in cardiovascular disease. Highly sensitive biochemical markers have been shown to improve prediction of adverse outcomes in patients with coronary artery disease [25]. The results of the present study further support the potential role of

cystatin C as a useful biomarker for assessing coronary artery disease severity in patients presenting with acute coronary syndrome.

### Conclusion

Serum cystatin C levels were significantly associated with the severity of acute coronary syndrome and the complexity of coronary artery disease as assessed by the SYNTAX score. Elevated cystatin C levels may serve as a useful biomarker for identifying high-risk ACS patients and predicting the extent of coronary artery involvement.

**Study Limitations:** The present study has several limitations that should be acknowledged. First, it was conducted at a single tertiary care center, which may limit the generalizability of the findings to other populations or healthcare settings. Second, although a total of 200 patients were included, the sample size remains relatively modest, which may affect the statistical power and external validity of the results. Third, the cross-sectional observational design of the study restricts the ability to establish a causal relationship between serum cystatin C levels and the severity of acute coronary syndrome. Additionally, biomarker levels were measured at a single time point, and serial measurements were not performed to evaluate temporal changes. Therefore, larger multicenter prospective studies with longitudinal follow-up are required to further validate these findings and to better understand the prognostic significance of serum cystatin C in patients with acute coronary syndrome.

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