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Serum Calprotectin as a Biomarker for Acute Coronary Syndrome: Comparative Analysis with Troponin and C-Reactive Protein

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Annotation: Background: Inflammatory biomarkers are widely used in cardiovascular risk assessment; however, their diagnostic and predictive performance varies. This study aimed to compare calprotectin with C-reactive protein (CRP) and troponin regarding their association with clinical outcome and angiographic severity.

Methods: Seventy-eight patients were included and categorized into patients (n = 50) and controls (n = 28). According to the results of 37 patients, PCI was noted as positive if the coronary artery lesion was total, subtotal, or significant (70%-90% occlusion). Lesions not meeting these criteria were noted as negative for 13 patients. Serum calprotectin, CRP, and troponin levels were analysed. Normality was assessed using Kolmogorov–Smirnov and Shapiro–Wilk tests. Group comparisons were conducted using the Mann–Whitney U or independent-samples t-test where appropriate. Associations were evaluated using chi-square tests and Spearman correlation. Diagnostic performance was assessed by receiver operating characteristic (ROC) analysis.

Results: All biomarkers showed non-normal distributions ($p < 0.05$). Calprotectin levels were significantly higher in the positive outcome group compared with the negative group (45.15 ± 33.62 vs 14.29 ± 24.42, $p < 0.001$). CRP and troponin showed no significant

differences between outcome groups. Age was significantly associated with angiographic severity (p = 0.005). ROC analysis demonstrated excellent diagnostic accuracy for calprotectin (AUC = 0.809), while CRP and troponin showed poor discrimination.

Conclusion: Calprotectin outperforms CRP and troponin as a predictive and discriminatory biomarker, reflecting neutrophil-driven inflammation and plaque instability rather than systemic inflammation or late myocardial injury.

Keywords: Calprotectin, CRP, Troponin, Inflammation, ROC curve, Cardiovascular biomarker.

1. Introduction

In the recent years the evaluation of chest pain was subjected to many new advances in the sensitivity and availability of cardiac enzyme assays, emerging of new biomarkers, development and easy reached imaging modalities, with building of suitable logarithm mixing both clinical and laboratory results [1]. This fact give the power to physicians to take the decision of and exclusion of acute coronary syndrome in short time of patient presentation in emergency department which facilitate rapid medical intervention, treatments, or exclusion of alternative diagnoses for chest pain, or discharge, and facilitate better administration for healthcare resources [2]. Studies show that three of four patients evaluation depending on reading of high sensitivity troponin level in blood on admission and after one hour after admission to emergency department they were discharge. Those with uncertainty or inconclusive clinical or laboratory evaluation should stay in hospital for rechecking, depending in serial checking of enzymes and serial ECG, specially for old age patients aged 65 years due to an increased risk of a false negative result. Many inflammatory markers had been evaluated and investigated to obtain its correlation with the diagnosis or the prognosis of acute coronary syndrome, for example for these biomarkers (serum troponins leukocytosis, neutrophilia, erythrocytes sedimentation rate, C reactive protein(CRP), fibrinogen and serum calprotectin level) [3].

CRP is an acute-phase reactant substance used widely for many years for detection and evaluation of acute inflammation and stratification and this may have related to availability and the low cost for this assay, monitoring. CRP is has been used widely in last years in evaluation of acute coronary syndrome for the same reasons (in acute myocardial infarction CRP show to be elevated at 4–6 h from the starting of symptoms and reaches the highest concentration after 2–4 days, and its values are return to normal levels after 7–10 days), this delay in releasing and reaching the peak concentration with low specificity, may decrease its usefulness for usage in acute situation when we need fast decision for diagnosis and follow up in acute coronary syndrome [4].

Calprotectin is another acute inflammatory marker (a non-covalently linked dimer of the S100A8 and S100A9 calcium-binding proteins and can also exist in a tetrameric form) [5]. Calprotectin is mainly come from different types of immune cells like(neutrophils, monocytes, and platelets) that play important rule in acute inflammation which play important rule in atherosclerotic occurrence [6]. Calprotectin previously assessed as a biomarker in multiple inflammatory diseases (for example in inflammatory bowel disease) with significant diagnostic and prognostic

significance.in regarding to acute and coronary syndrome, serum level of calprotectin has been shown to be significantly high, this fact noted to the possibility of important role calprotectin in the pathophysiology of atherosclerotic events that accrue in acute coronary syndrome.

Despite of the standard protocols in which serum troponin was the marker of choice for both the diagnosis and prognosis of acute coronary syndrome, its negatively pointing to exact injured area, calprotectin is heavily localized in the cytosol of inflammatory cells in coronary arteries.

Calprotectin levels in atherosclerotic plaques has been noticed to be very high which may be pointing to remarkable cardiac cell death in those presenting with acute coronary syndrome. In addition, in patients with ACS and had other chronic diseases like diabetes, high levels of serum calprotectin correlated with a high chance for severity and complication. The serum level calprotectin is significantly high in ACS patients high number of lesion the coronary branches. Also calprotectin was shown to associated with platelet activation which may play important role in no-reflow in patients with acute coronary syndrome [7]. In chronic stable coronary diseases calprotectin levels has weak but important correlation with platelet aggregation [8]. Calprotectin levels, measured at admission in acute coronary syndrome patients may predict mortality during the next 12 months, which may make calprotectin a new promising prognostic marker in acute coronary syndrome [8]. also some studies show the direct correlation of calprotectin development of left ventricular systolic dysfunction and the increased chance of arrhythmia [9].

This study evaluates the utility of calprotectin compared with CRP and troponin in acute coronary syndrome, the result compares the statistical difference between serum calprotectin, serum troponin and CRP in setting of acute coronary syndrome patients for providing a comprehensive understanding of the clinical usefulness and utility of this biomarker.

2. Methods

2.1 Study design

Seventy-eight patients were included and categorized into patients (n = 50) and controls (n = 28) According to result of 37 patients PCI noted as (positive if the coronary artery lesion was total, subtotal and significant (70%-90%) occlusion) lesions not met these criteria noted as negative of 13 patients.) Demographic variables included age and gender. A subgroup of 37 patients underwent coronary angiography patients were admitted to coronary care unit of AL Imam Al-Sadiq Hospital in Hila with typical ischemic chest pain and typical ECG changes of acute coronary syndrome (ST segment elevation or sub endocardial infarction), in period 2 months from November 2025 to December 2025. In whom the cardiologist decided to refer to PCI, taking informed concern for the participation in the study. We exclude from this study any patient unfits for PCI, those who refused doing PCI and those with collection difficulties in samples collection.

2.2 Study sampling & materials

5 mm of venous blood from the participant, then blood Samples placed in laboratory tube (gel tubes) and leaving them standard time for coagulation (around 30 minutes). Serum calprotectin level then measured using the Enzyme-Linked Immune Sorbent Assay (ELISA) technique taking in account the manufacture guidelines. Then we maintain samples at -20°C until use in analysis (Mybiosource, USA). Then the ELISA reader evaluated the optical density of each well at 450 nm, and the results of the interpolation of the Serum calprotectin concentration from the standard curve were determined. For the serum troponin was tested using a MAGLUMI 800 fully-auto chemiluminescence immunoassay analyzer (China, Shenzhen, Snibe Diagnostic). CRP Analysis on Dimension Xpand Plus The determination of C-Reactive Protein (CRP) on dimension Xpand plus (siemins, USA) used serum samples this system generally follows the Particle-Enhanced Turbidimetric Inhibition Immunoassay (PETINIA) or standard Immunoturbidimetric principle. Calculating Concentration Proportionality: The amount of CRP in the patient's sample is closely correlated with the rise in turbidity (and hence, the shift in light absorbance). Calibration: To get

the final numerical result in mg/dL, the device compares the observed absorbance to a predefined calibration curve that is recorded in its software.

2.3 Statistical Analysis

Normality was assessed using Kolmogorov–Smirnov and Shapiro–Wilk tests. Non-parametric tests (Mann–Whitney U, Spearman correlation) were used for skewed data. Chi-square tests evaluated associations between categorical variables. ROC curves assessed diagnostic accuracy. Statistical significance was set at $p < 0.05$.

2.4 Ethical approval

Informed consent was achieved from each patient. The study protocol, the subject information, and the consent form were reviewed and approved by the University of Babylon-Hammurabi College of Medicine ethical committee (Issue no. 44 dated 10th-Jun-2025).

Results

Among 50 cases ,37 angiographies were positive showing a strong and significant correlation with elevated calprotectin levels suggesting calprotectin as an early and sensitive inflammatory biomarker associated acute coronary syndrome.

2.5 Distribution normality

All biomarkers showed significant deviation from normal distribution ($p < 0.001$), justifying the use of non-parametric analyses (Table 1).

Table-1: Normal distributions of study biomarker

Tests of Normality							
	Outcome	Kolmogorov-Smirnov[a]			Shapiro-Wilk		
		Statistic	df	Sig.	Statistic	df	Sig.
Calprotectin	P	0.147	50	0.009	0.900	50	0.000
	C	0.300	28	0.000	0.642	28	0.000
CRP	P	0.325	50	0.000	0.526	50	0.000
	C	0.354	28	0.000	0.645	28	0.000
Troponin	P	0.262	50	0.000	0.791	50	0.000
	C	0.357	28	0.000	0.680	28	0.000

2.6 Age, gender, and clinical outcome

There was no significant association was found between age and outcome using Pearson chi-square ($p = 0.080$); however, the likelihood ratio test indicated significance ($p = 0.048$). Gender distribution was not associated with age ($p = 0.878$). (Table 2)

Table-2: Age and gender cross tabulation

			Gender		Total
			Male	Female	
Age	< 30	N	2	2	4
		%	4.0%	7.1%	5.1%
	31-40	N	5	3	8
		%	10.0%	10.7%	10.3%
	41-50	N	12	5	17
		%	24.0%	17.9%	21.8%
	> 50	N	31	18	49
		%	62.0%	64.3%	62.8%
Total		N	50	28	78
		%	100.0%	100.0%	100.0%
Chi square: p = 0.87					

2.7 Age and Angiographic Severity

A strong association was observed between increasing age and angiographic severity (Pearson chi-square = 12.747, p = 0.005), with a significant linear trend (p = 0.011) as in table 3.

Table-3: Age and angiographic severity association

			Angiography		Total
			1	2	
Age	< 30	N	3	0	3
		%	37.5%	0.0%	8.1%
	31-40	N	1	3	4
		%	12.5%	10.3%	10.8%
	41-50	N	0	5	5
		%	0.0%	17.2%	13.5%
	> 50	N	4	21	25
		%	50.0%	72.4%	67.6%
Total		N	8	29	37
		%	100.0%	100.0%	100.0%
Chi-Square Tests		**Value**	**df**	**P value**	
Pearson Chi-Square		12.747a	3	0.005	
Likelihood Ratio		12.152	3	0.007	
Linear-by-Linear Association		6.409	1	0.011	

2.8 Biomarker Comparison

Calprotectin levels were significantly higher in the positive outcome group (p < 0.001) (Table 4). In contrast, CRP (p = 0.963) and troponin (p = 0.538) showed no significant differences.

Table-4: Calprotectin, troponin and CRP correlation with patients and control groups

	Levene's Test for Equality of Variances		t-test for Equality of Means	
	F	Sig.	t	df
Calprotectin	11.589	0.001	4.263	76
		CRP	**Troponin**	
Mann-Whitney U		695.500	641.000	
Wilcoxon W		1101.500	1047.000	
Z		-.047-	-.616-	
Asymp. Sig. (2-tailed)		.963	.538	

2.9 Biomarkers and Angiography

Neither CRP nor troponin levels differed significantly according to angiographic severity

Table-5: Correlation between Troponin, CRP with angiographic severity

	CRP	Troponin
Mann-Whitney U	76.000	89.000
Wilcoxon W	511.000	524.000
Z	-1.478-	-0.996-
Asymp. Sig.	0.139	0.319

2.10Correlation Analysis

Spearman analysis revealed a weak but significant correlation between CRP and troponin (r =

0.226, p = 0.047). Calprotectin showed no significant correlation with either marker, suggesting an independent inflammatory pathway. See table 6

Table-6: Correlation of study biomarkers

			Calprotectin	CRP	Troponin
Spearman's rho	Calprotectin	R		0.033	-0.080-
		P		0.775	0.487
		N		78	78
	CRP	R	0.033		0.226*
		P	0.775		0.047
		N	78		78
	Troponin	R	-0.080-	0.226*	
		P	0.487	0.047	
		N	78	78	

2.11ROC Curve Analysis

Calprotectin demonstrated excellent diagnostic accuracy (AUC = 0.809, 95% CI: 0.704–0.914, p < 0.001). CRP (AUC = 0.503) and troponin (AUC = 0.542) showed no meaningful discrimination.

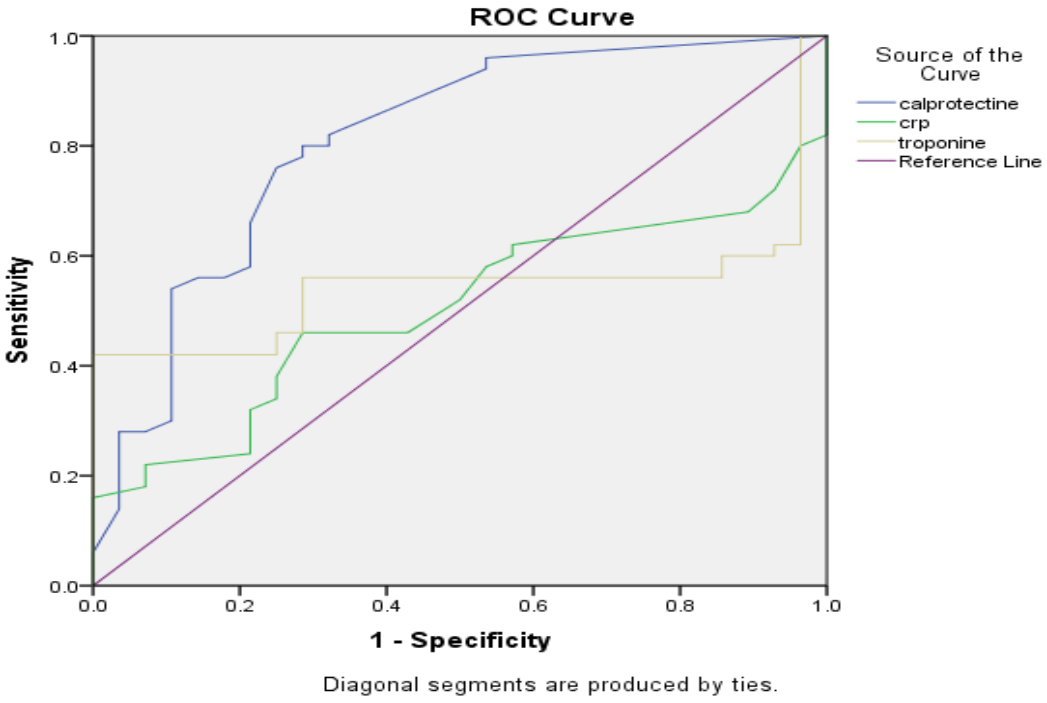

Figure-1: ROC Curve Analysis

Table-7: ROC Curve Analysis

Test Result Variable (s)	Area	Std. Error	Asymptotic Sig.	Asymptotic 95% CI	
				Lower Bound	Upper Bound
Calprotectin	0.809	0.054	0.000	0.704	0.914
CRP	0.503	0.065	0.963	0.376	0.630
Troponin	0.542	0.067	0.539	0.411	0.673

3. Discussion

This study demonstrates as in table 4,6 and 7 that calprotectin is a superior biomarker for

outcome prediction compared with CRP and troponin. Unlike CRP [10], which reflects systemic inflammation, and troponin, which indicates established myocardial injury, calprotectin reflects neutrophil activation and plaque-level inflammation. The strong association between age and angiographic severity as in table 3 supports the role of chronic immune activation and immunosenescence in vascular disease progression. The high AUC value for calprotectin underscores its potential clinical utility in early risk stratification. Correlation between serum troponin and CRP with angiographic severity show weak correlation as in table 5. This can be explained by the nature of their biological kinetics and clinical context of patient management [11]. The increasing availability of specialized cardiac centers and the rapid implementation of coronary catheterization procedures significantly shorten the time interval between symptom onset and clinical intervention [12]. Troponin, as a marker of myocardial necrosis, requires a relatively longer period to rise to detectable levels following myocardial injury [11]. In contrast, calprotectin is an early inflammatory biomarker released rapidly from activated neutrophils and monocytes in response to acute inflammatory and ischemic processes [13]. Therefore, calprotectin may increase earlier in the disease course, even before troponin levels reach their diagnostic threshold.

4. Conclusion

Calprotectin represents a promising inflammatory biomarker with superior diagnostic and predictive performance compared with CRP and Troponin. Its incorporation into clinical algorithms may enhance early detection of high-risk patients.

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