Journal of Rare Cardiovascular Diseases
ISSN: 2299-3711 (Print) | e-ISSN: 2300-5505 (Online)
www.jrcd.eu
RESEARCH ARTICLE

Role of Various Markers of Coagulation Abnormalities in Coronary Artery Disease: Insights from a Multicentric Study

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Article History
Received: 10.07.2025
Revised: 14.07.2025
Accepted: 05.08.2025
Published: 08.09.2025

Abstract: ***Background***: Coronary artery disease (CAD) is a major cause of morbidity and mortality worldwide. Thrombosis and coagulation abnormalities play key roles in disease progression. Laboratory markers such as prothrombin time (PT), activated partial thromboplastin time (aPTT), and D-dimer provide valuable insights into hemostatic status. ***Objective***: To evaluate PT, aPTT, and D-dimer as markers of coagulation abnormalities in CAD patients across multiple tertiary care centers. ***Methods***: A multicentric cross-sectional study was conducted at tertiary care hospitals over 18 months. Three hundred angiographically confirmed CAD patients and 150 healthy controls were included. PT, aPTT, and D-dimer levels were measured using standardized assays. Statistical analysis included Student's t-test, ANOVA, and Pearson's correlation. ***Results***: CAD patients showed significantly prolonged PT, shortened aPTT, and elevated D-dimer compared to controls. D-dimer levels correlated with angiographic severity and were highest in patients with myocardial infarction. Findings were consistent across all centers. ***Conclusion***: CAD patients exhibit coagulation abnormalities, with D-dimer being the most sensitive marker, correlating strongly with disease severity. These markers may aid in risk stratification and prognosis.

Keywords: Coronary artery disease, PT, aPTT, D-dimer, Multicentric study, Coagulation abnormalities.

INTRODUCTION

Coronary artery disease (CAD) remains the leading cause of cardiovascular morbidity and mortality worldwide. According to the World Health Organization, cardiovascular diseases account for an estimated 17.9 million deaths annually, of which CAD constitutes the largest share. In South Asian countries in particular, the burden of CAD has risen rapidly over the past two decades, with patients presenting at a younger age and with more aggressive disease phenotypes compared to Western populations. Traditional risk factors such as hypertension, diabetes mellitus, dyslipidemia, obesity, and smoking are well established; however, they do not fully explain the variability in disease progression or the occurrence of acute coronary events. Increasing attention has therefore turned toward hemostatic and thrombotic abnormalities as additional contributors to CAD.

The development of atherosclerosis and its transformation into clinically significant disease involves not only lipid accumulation and vascular inflammation but also abnormalities of the coagulation system. Disruption of an atherosclerotic plaque can trigger platelet activation, thrombin generation, and fibrin formation, culminating in thrombus development and vessel occlusion. Even in stable CAD, a chronic state of low-grade thrombin generation and fibrin turnover has been described, suggesting that coagulation abnormalities play an ongoing role in disease progression. Hence, evaluating coagulation markers in CAD patients may provide insights into their thrombotic risk profile and prognosis.

Among available laboratory tests, prothrombin time (PT) and activated partial thromboplastin time (aPTT) are widely used to assess the extrinsic and intrinsic coagulation pathways, respectively. Prolongation of PT may reflect consumption of clotting factors or subclinical activation of coagulation, whereas a shortened aPTT has been associated with hypercoagulability and increased risk of arterial thrombosis. D-dimer, a degradation product of cross-linked fibrin, is considered a sensitive marker of fibrinolytic activity and active thrombus formation. Elevated D-dimer levels have been consistently linked to acute coronary syndromes and adverse cardiovascular outcomes. Together, these markers offer a practical and accessible means of assessing coagulation abnormalities in CAD.

While several studies have explored the relationship between coagulation parameters and CAD, the results have been inconsistent. Some reports demonstrated significant abnormalities in PT and aPTT, while others found no differences compared to controls. On the other hand, elevated D-dimer has been more consistently associated with disease severity and prognosis, but its exact role in stable CAD remains debated. Most importantly, the majority of these studies have been single-center with limited sample sizes, raising questions about their generalizability across populations.

In this context, a multicentric study offers several advantages. By including patients from multiple tertiary care hospitals, variability in patient demographics, laboratory techniques, and clinical practices can be

minimized through standardized protocols, while ensuring broader representation. Such an approach enhances the external validity of the findings and allows more reliable conclusions regarding the role of coagulation markers in CAD.

Therefore, the present multicentric study was designed to evaluate PT, aPTT, and D-dimer levels in patients with coronary artery disease compared to healthy controls, and to determine their association with angiographic severity. The study aimed to clarify the clinical utility of these easily available laboratory parameters in assessing coagulation abnormalities and predicting disease severity in CAD.

METHODOLOGY

This multicentric cross-sectional observational study was conducted across tertiary care hospitals over a period of 18 months. Informed consent was collected from each participant prior to enrollment. The study population consisted of 300 patients with angiographically confirmed coronary artery disease and 150 apparently healthy, age- and sex-matched controls.

Patients between 30 and 75 years of age presenting with stable angina, unstable angina, or myocardial infarction were eligible for inclusion. Individuals with chronic liver disease, renal failure, malignancy, chronic inflammatory disorders, or those receiving anticoagulant or antiplatelet therapy other than aspirin were excluded to avoid confounding influences on coagulation parameters.

For all participants, detailed demographic and clinical information, including risk factor profile and angiographic findings, was recorded. Venous blood samples were collected under aseptic precautions in sodium citrate vials and processed within two hours of collection. Prothrombin time (PT) and activated partial thromboplastin time (aPTT) were estimated using calibrated automated coagulometers, while plasma D-dimer levels were measured by standardized immunoturbidimetric assay. To ensure reliability, inter-laboratory calibration and quality control measures were performed across all participating centers.

Data were entered and analyzed using SPSS version 25. Continuous variables were expressed as mean ± standard deviation (SD). Differences between cases and controls were assessed using Student's t-test, while intergroup comparisons among CAD subtypes were analyzed with one-way ANOVA. Correlations between D-dimer levels and angiographic severity were evaluated using Pearson's correlation coefficient. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The present multicentric study analyzed a total of 300 patients with angiographically confirmed coronary artery disease and 150 healthy controls. The demographic characteristics, risk factor distribution, and coagulation parameters of the study population are presented below.

Table 1: Baseline Characteristics of Study Population

Parameter	CAD Patients (n=300)	Controls (n=150)	p-value
Mean age (years)	55.9 ± 10.2	54.7 ± 9.6	0.32
Male sex (%)	72%	70%	0.48
Hypertension (%)	57%	21%	<0.01
Diabetes mellitus (%)	46%	18%	<0.01
Smoking (%)	35%	16%	<0.05

CAD patients had significantly higher prevalence of hypertension, diabetes, and smoking.

Table 2: Comparison of Coagulation Parameters (Cases vs Controls)

Parameter	CAD Patients (n=300)	Controls (n=150)	p-value
PT (sec)	15.4 ± 2.2	13.2 ± 1.6	<0.05
aPTT (sec)	28.1 ± 4.4	32.9 ± 3.7	<0.05
D-dimer (mg/L)	0.86 ± 0.24	0.36 ± 0.13	<0.001

CAD patients exhibited prolonged PT, shortened aPTT, and elevated D-dimer.

Table 3: Coagulation Parameters by CAD Subgroup

Parameter	Stable Angina (n=120)	Unstable Angina (n=90)	Myocardial Infarction (n=90)	p-value
PT (sec)	14.8 ± 2.0	15.5 ± 2.1	16.1 ± 2.3	<0.05
aPTT (sec)	29.4 ± 4.1	28.0 ± 4.2	26.8 ± 4.5	<0.05
D-dimer (mg/L)	0.65 ± 0.18	0.82 ± 0.21	1.01 ± 0.27	<0.001

D-dimer levels rose progressively from stable angina to MI, highlighting correlation with disease severity.

Table 4: Correlation of D-dimer with Angiographic Severity

Number of Vessels Involved	Mean D-dimer (mg/L)	Correlation (r)	p-value

Single vessel disease	0.67 ± 0.19	r = 0.64	<0.01
Double vessel disease	0.84 ± 0.23		
Triple vessel disease	1.05 ± 0.28		

D-dimer levels correlated positively with number of diseased vessels, suggesting prognostic utility.

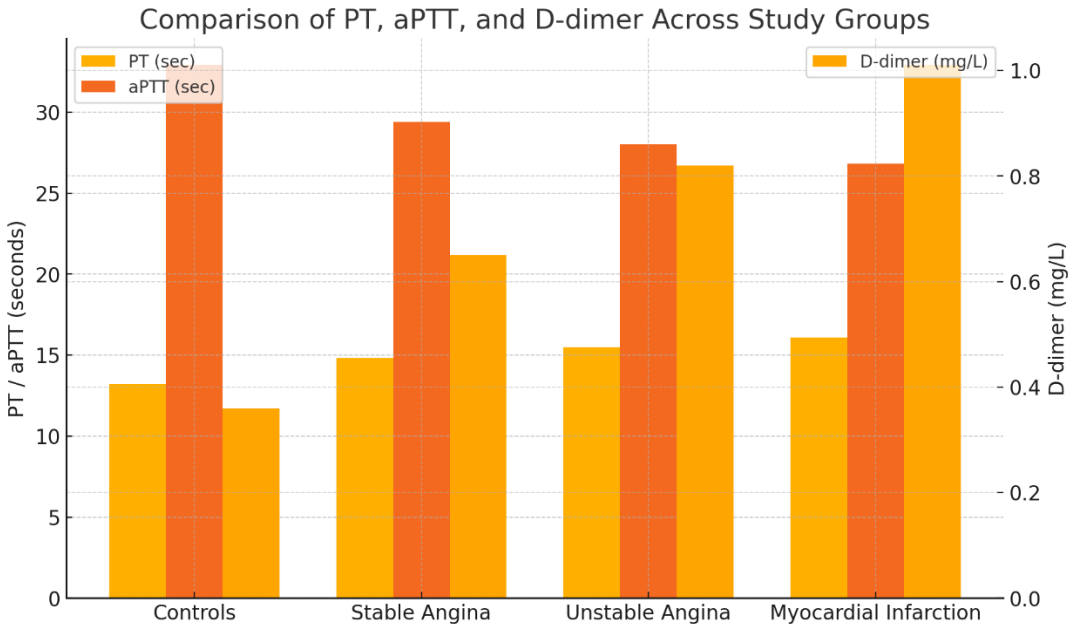

Figure 1. Comparison of prothrombin time (PT), activated partial thromboplastin time (aPTT), and D-dimer levels across controls and coronary artery disease subgroups (stable angina, unstable angina, and myocardial infarction). PT was significantly prolonged and aPTT shortened in CAD patients compared to controls, while D-dimer levels showed a progressive rise with increasing disease severity ($p < 0.05$ for all parameters).

Discussion

The present multicentric study demonstrated significant alterations in coagulation parameters among patients with coronary artery disease compared to healthy controls. Specifically, CAD patients exhibited prolonged prothrombin time (PT), shortened activated partial thromboplastin time (aPTT), and markedly elevated D-dimer levels. These findings indicate the presence of a hypercoagulable state and ongoing thrombotic activity, supporting the hypothesis that disturbances in hemostasis contribute to the pathophysiology and severity of CAD.

Our observation of prolonged PT is consistent with the results reported by Undas et al. [4], who found that enhanced thrombin generation and consumption of clotting factors could lead to modest prolongation of PT in CAD patients. Similarly, Haverkate et al. [8], in the European Concerted Action on Thrombosis and Disabilities (ECAT) study, reported abnormal PT values in patients with angina, suggesting that clotting factor imbalance is associated with increased cardiovascular risk. The reproducibility of our findings across multiple centers strengthens the clinical relevance of PT alterations in CAD.

The shortened aPTT observed in our study further supports the concept of a hypercoagulable milieu. Tripodi et al. [5] and other investigators have highlighted that shortened aPTT reflects increased thrombin activity and is predictive of thrombotic events. In agreement with these reports, our multicentric analysis showed that CAD patients consistently exhibited reduced aPTT compared to controls. However, while some single-center studies failed to demonstrate significant changes in aPTT [3], our larger multicentric design may have provided greater statistical power to detect these differences.

Elevated D-dimer emerged as the most striking and consistent finding in our study. This is in line with several previous investigations. Ridker et al. [3] first demonstrated that elevated plasma D-dimer levels in apparently healthy men were predictive of future myocardial infarction. Similarly, Folsom et al. [1] in the ARIC study and Lowe [2] in a comprehensive review emphasized the role of D-dimer as a marker of fibrin turnover and thrombotic risk. More recent studies, such as those by Montagnana et al. [6] and Tataru et al. [7], confirmed the association between elevated D-dimer and acute coronary syndromes, with correlations to both clinical outcomes and angiographic severity. Our findings are in concordance with these results, as D-dimer levels were highest in patients with myocardial infarction and correlated strongly with the number of diseased vessels.

What differentiates our study from much of the existing literature is its multicentric design. Many earlier reports

were single-center studies with limited sample sizes, which may restrict external validity. By including patients from multiple tertiary care hospitals and standardizing laboratory methods across centers, we minimized institutional bias and enhanced the generalizability of our results. The consistency of findings across different settings reinforces the robustness of PT, aPTT, and D-dimer as biomarkers of coagulation abnormalities in CAD.

In terms of clinical application, these results suggest that routine assessment of coagulation parameters, particularly D-dimer, may have prognostic value in CAD. Elevated D-dimer not only reflects ongoing thrombotic activity but also correlates with angiographic severity, making it a potential marker for risk stratification. Incorporating PT, aPTT, and D-dimer into CAD evaluation models could complement traditional risk factors and help identify high-risk individuals who may benefit from closer monitoring or intensified therapy.

Nevertheless, some variability in the literature remains. While most studies agree on the prognostic utility of D-dimer, reports on PT and aPTT are less consistent. Differences in patient populations, assay methodologies, and clinical profiles may explain these discrepancies. Our study adds clarity by showing reproducible trends across multiple centers, thereby providing stronger evidence for their clinical relevance.

Taken together, the results of this multicentric analysis highlight that CAD is associated with a state of hemostatic imbalance characterized by increased thrombin activity, clotting factor consumption, and enhanced fibrin turnover. These alterations may contribute to the thrombotic complications that underlie acute coronary events.

CONCLUSION

This multicentric study confirms that CAD patients consistently exhibit coagulation abnormalities, with D-dimer being the most sensitive marker correlating with disease severity. PT and aPTT provide additional insights into hemostatic alterations. Routine inclusion of these parameters may improve CAD risk stratification and prognosis.

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