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Research Article

Prognostic Value of Fibrinogen in Acute Coronary Syndrome: A Meta-Analysis

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Abstract:

Background: Acute coronary syndrome (ACS) is one of the leading causes of cardiovascular mortality worldwide. Fibrinogen, a key mediator of coagulation and inflammation, remains controversial in its prognostic value. This meta-analysis aims to evaluate the predictive role of fibrinogen in ACS patient outcomes.

Methods: Following PRISMA guidelines, we systematically searched PubMed, Embase, and other databases (from inception to November 2024) for cohort or case-control studies assessing the association between fibrinogen and ACS outcomes (all-cause mortality/major adverse cardiovascular events [1]). Study quality was evaluated using the Newcastle-Ottawa Scale (NOS), and pooled effect sizes were calculated using random- or fixed-effects models. Subgroup and sensitivity analyses were performed.

Results: Nine studies (12,714 patients) were included. Elevated fibrinogen levels significantly increased the risk of all-cause mortality (HR = 1.51, 95% CI: 1.27-1.81, $p < 0.001$), but no significant association was found with MACE (HR = 3.00, 95% CI: 0.96-9.39, $p > 0.05$). Subgroup analysis suggested regional differences as a source of heterogeneity.

Conclusion: Fibrinogen may serve as an independent predictor of all-cause mortality in ACS patients, but its prognostic value for MACE requires further investigation. Future studies should explore its potential in clinical risk stratification.

Key words: fibrinogen; acute coronary syndrome; all-cause mortality; major adverse cardiovascular events

Introduction

Acute coronary syndrome (ACS) is a major global cause of cardiovascular Mmorbidity and mortality [1], particularly in high-risk populations such as patients with diabetes or dyslipidemia, where the risk of adverse outcomes is significantly elevated. Despite advances in percutaneous coronary intervention (PCI) and antithrombotic therapies, some patients still experience recurrent events and long-term cardiovascular mortality [2], highlighting the need for more precise prognostic tools. NF Zibrinogen, a critical mediator in both coagulation and inflammatory pathways [3], has garnered increasing attention for its role in ACS pathophysiology [4]. Elevated fibrinogen levels are associated with plaque instability and may directly influence clinical outcomes by promoting thrombosis and microvascular dysfunction [5]. Although existing studies have demonstrated the prognostic significance of fibrinogen, its role in ACS remains debated. For instance, a meta-analysis of acute myocardial infarction (AMI) patients found that elevated fibrinogen levels (HR = 1.218, 95% CI: 1.027-1.444, p= 0.02) independently predicted long-term cardiac mortality, with each 1 g/L increase associated with a 21.8% higher risk of death. The AUC for predicting AMI-related mortality was 0.684 ($p< 0.001$), with a specificity of 84.3%. However, the study did not evaluate other MACE endpoints, underscoring the need for further research to validate its stratification value across ACS subtypes [6]. While current research has provided preliminary evidence linking fibrinogen levels to poor ACS outcomes, significant challenges remain in establishing its broad clinical utility. First, studies have yielded inconsistent conclusions about fibrinogen's prognostic value - while it shows clear association with all-cause mortality, its ability to predict MACE remains uncertain [7, 8]. Second, most available evidence comes from small-scale or single-center studies characterized by population heterogeneity (variations in ACS subtypes and comorbidities) and methodological variations (differences in measurement protocols and follow-up durations) [4-6, 9-14]. Moreover, conventional risk assessment tools like the GRACE score have not yet incorporated emerging biomarkers such as fibrinogen, potentially resulting in underestimated risk for high-risk patients [15]. These limitations highlight the importance of conducting systematic reviews and meta-analyses to synthesize existing evidence on fibrinogen's role in ACS

prognosis, and examine its varying effects across different clinical contexts (particularly in STEMI versus NSTEMI cases and patients with diabetes) [16]. Such investigations would provide crucial evidence for refining personalized treatment approaches.

Methods

This study adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [17]. The protocol was registered on PROSPERO (CRD42024621282).

Search strategy

We conducted comprehensive searches in PubMed, Embase, Cochrane Library, and Web of Science databases. The search timeframe spanned from each database's inception to November 25, 2024, with results limited to English-language publications. Our search methodology employed a combination of Medical Subject Headings (MeSH) and free-text terms, with the primary search terms being "Fibrinogen" and "Acute Coronary Syndrome. "To ensure thorough literature coverage, we additionally: Manually examined reference lists of relevant articles; Searched grey literature sources; Performed backward citation tracking. The complete search strategy, including all specific search terms and syntax variations for each database, is provided in Appendix 1. Inclusion/Exclusion Criteria Studies were included if they: (1) enrolled ACS patients, (2) measured baseline fibrinogen levels, (3) were cohort or case-control designs, and (4) reported all-cause mortality. Exclusions: animal/cell studies, case reports, reviews, editorials, conference abstracts, duplicate publications, or studies with missing/unavailable data.

Data Extraction

Two reviewers independently screened titles/abstracts and full texts using EndNote. Discrepancies were resolved via discussion or consultation with a third reviewer. Data on study characteristics, patient demographics, outcomes, and treatments were extracted using a standardized form. Quality Assessment NStudy quality was evaluated using the NOS (0-9 scale). Scores ≥6 indicated high quality. N Statistical Analysis STATA 15.1 was used to pool hazard ratios (HRs) with 95% CIs. I Heterogeneity was assessed via ²and Cochran's Qtests (I^2> 50% or p< 0.10 indicated significant heterogeneity, warranting random-effects models). Sensitivity, subgroup (by region/study design), and meta-regression analyses were performed. Publication bias was evaluated via funnel plots and Egger's test (p< 0.05 indicated bias).

Results

Study Selection From 12,670 records, 9 studies [4-6, 9-14] (12,714 patients) were included after screening (Figure 1).

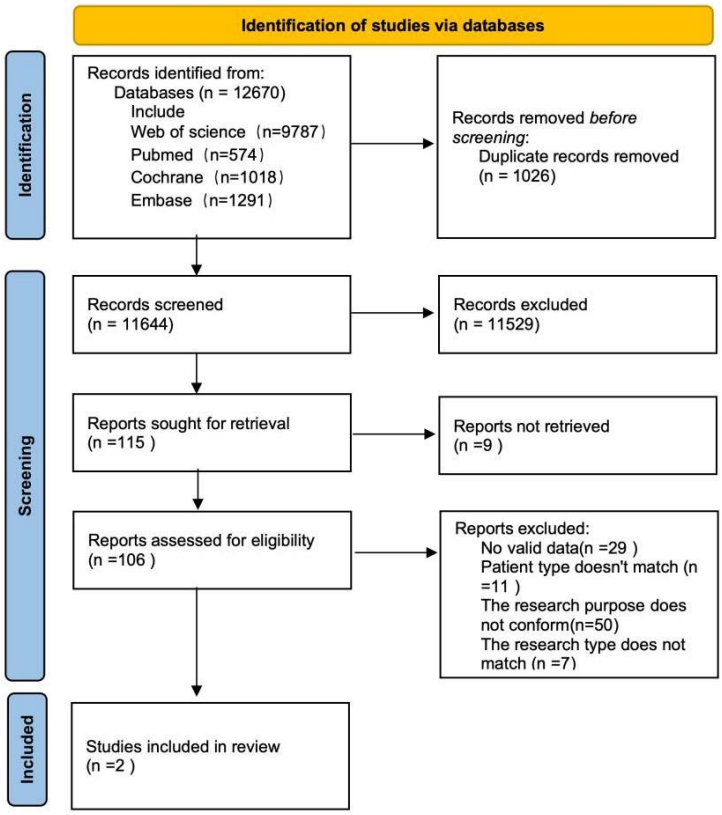


Figure 1: PRISMA fowchart of literature search and study selection

Baseline Characteristics

The studies [4-6, 9-14] spanned three countries (China, Spain, Greece), with 8,219 male and 2,987 female patients (mean age: 61.3 ± 10.2 years). All studies had NOS scores ≥6 (Table 1).

author	year	Study Design	country	Sample size	Gender(M/F)	Age (year) Median (range)	outcome indicator	Human Disease Model	NOS score
Zhen-Fa Zhou	2024	case-control	china	232	180/52	72.6712(4.1319)	MI-related death	AMI	7
Enmin Xie	2024	cohort	china	1079	789/290	62.1 (10.4)	All-cause Mortality (Cardiovascular Mortality)	ESRD and ACS	8
Jia Song	2020	cohort	china	1211	814/397	62.6257(10.6892)	death or death/nonfatal reinfarction	NSTE-ACS	8
Ping Jiang	2019	cohort	china	6293	4489/1804	58.3348(8.3783)	All-cause Mortality (Cardiovascular Mortality)	ACS	8
Juan Carlos Kaski	2010	cohort	Spain	610	449/61	64.739(11.2826)	All-cause Mortality (Cardiovascular Mortality)	UA and NSTEMI	7
Michael N. Zairis	2007	cohort	Greece	458	354/104	60.1 (11.5)	Cardiovascular death	STEMI	8
		cohort	Greece	476	313/163	70.2 (7.9)	Cardiovascular death	NSTE-ACS	
P L Sanchez	2004	case-control	Spain	83	57/26	71	All-cause Mortality	non-ST elevation acute coronary syndrome	6
M. A. Arnau Vives	2002	cohort	Spain	325	235/90	65 (11)	death	ACS	9
Yi ming Li	2024	cohort	china	2405		64.3 (11.1)	all-cause mortality	ACS	7

Table 1: Basic characteristics of included studies in this meta-analysis Meta- Analysis Findings

1. All-Cause Mortality

Nine studies involving 12,714 patients were included in the analysis of this outcome. Heterogeneity assessment revealed significant variation across studies (I^2 = 68%, P = 0.002), prompting the use of a random-effects model. The pooled results demonstrated that patients with elevated fibrinogen levels had significantly higher risk of all-cause mortality compared to controls (HR = 1.51, 95% CI: 1.27-1.81, p < 0.001). Forest plot visualization showed consistent direction of effect across most studies (Figure 2).

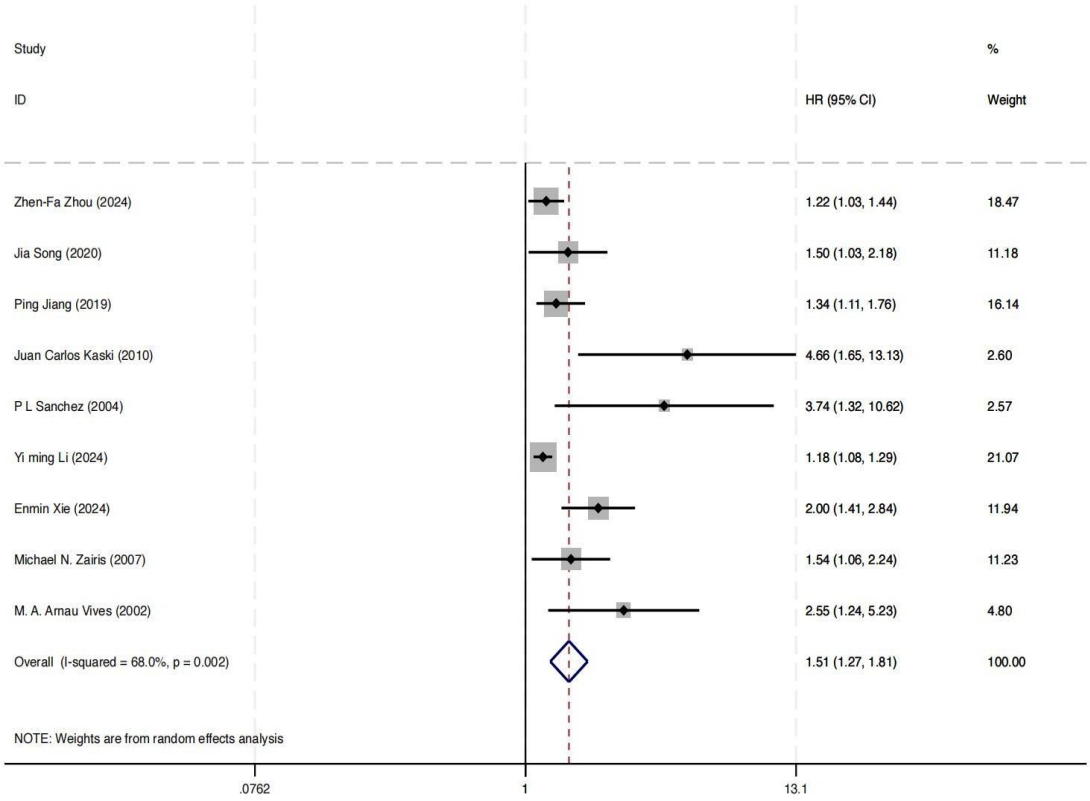


Figure 2: forest plots of association between all-cause mortality and fibrinogen in patients with acs

Subgroup Analysis:

Regional subgroup analysis revealed differential effects between Asian and European populations (Figure 3). The European subgroup showed more pronounced fibrinogen elevation (fibrinogen = 0.69, 95% CI: 0.39 to 0.99) compared to the Asian subgroup. Notably, within-group heterogeneity was reduced in both Asian (P = 0.044, I^2 = 59.1%) and European (P = 0.100, I^2 = 52.0%) subgroups, suggesting regional differences contribute substantially to overall heterogeneity.

Analysis by study design (cohort vs. case-control) showed no significant differences between groups (Figure 4). The case-control subgroup demonstrated an effect size of HR = 0.23 (95% CI: 0.06 to 0.39) while cohort studies showed HR = 0.24 (95% CI: 0.1 to 0.32), indicating study design was not a major source of heterogeneity.

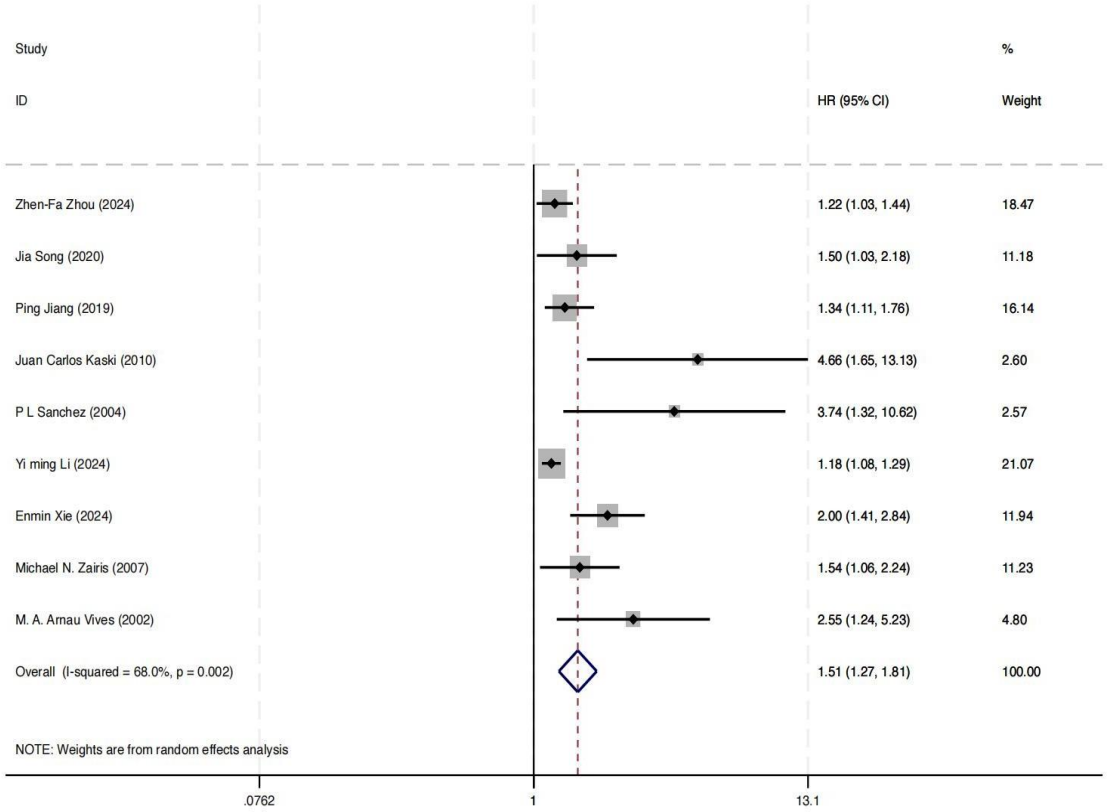


Figure 4: Forest plots of association between all-cause mortality and fibrinogen in patients with ACS.

2、Sensitivity Analysis

To evaluate result robustness, we conducted leave-one-out sensitivity analysis (Figure 5). Sequentially excluding each study and recalculating the pooled effect size revealed stable estimates throughout, with all recalculated HRs remaining within the 95% CI of the primary analysis (range: 1.47-1.54). This consistency confirms our findings are not disproportionately influenced by any single study.

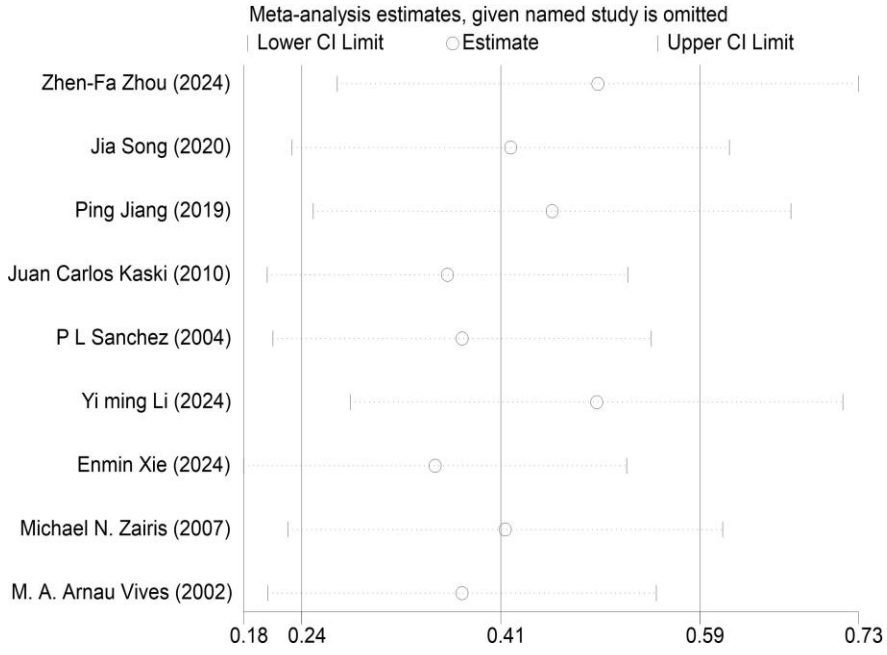
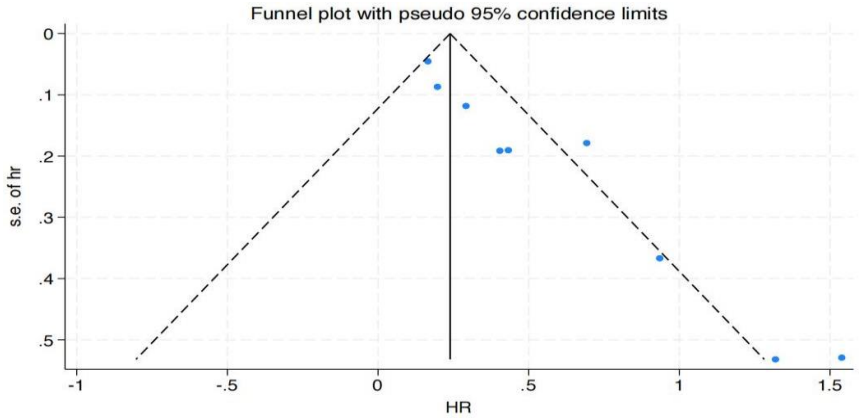


Figure 5: Sensitivity analysis.

3、Publication Bias



For outcomes with ≥9 studies (all-cause mortality), we assessed publication bias using funnel plot symmetry and Egger's test (Figure 6). Visual inspection of the funnel plot revealed mild asymmetry, with smaller studies showing more positive effects. This was confirmed quantitatively by Egger's test ($p < 0.05$), suggesting possible publication bias or small-study effects.

Figure 6: Publication bias tests for OS and PFS

4 MACE Outcomes

Only two studies (n = 771 patients) reported data on major adverse cardiovascular events. Considerable heterogeneity was observed (I^2 = 89.6%, P = 0.002), necessitating a random-effects model. The pooled analysis showed no statistically significant association between fibrinogen levels and MACE risk (HR = 3.00, 95% CI: 0.96-9.39, p > 0.05) (Figure 7). The wide confidence interval reflects substantial uncertainty in this estimate.

5 Meta-Regression

For outcomes with significant heterogeneity (I^2 > 50%) and adequate study numbers (n ≥ 9), we performed meta-regression to explore potential moderators. Neither sample size (coefficient = 0.0001, p = 0.89) nor gender distribution (coefficient = -0.012, p = 0.76) showed significant associations with effect size magnitude, suggesting these factors do not explain the observed heterogeneity.

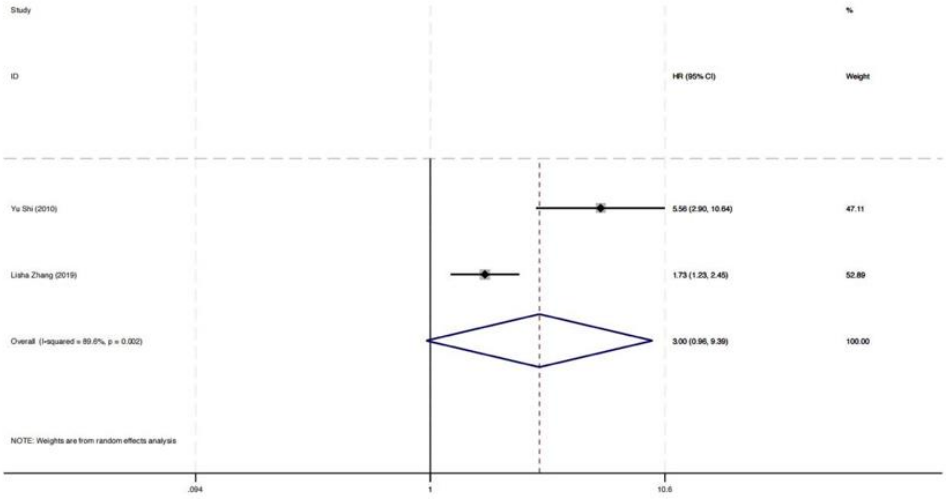


Figure 7: Forest plot of association between MACE and fibrinogen in patients with ACS

Conclusion and Discussion

This meta-analysis, incorporating 9 high-quality studies involving 12,714 patients, demonstrated a significant association between elevated fibrinogen levels and increased risk of all-cause mortality in ACS patients (HR=1.51, 95%CI: 1.27–1.81), supporting its role as an independent prognostic factor. However, the predictive value of fibrinogen for MACE did not reach statistical significance (HR=3.00, 95%CI: 0.96–9.39), which may be attributed to the limited number of included studies or heterogeneity in MACE definitions [18, 19]. The prognostic significance of fibrinogen likely stems from its dual pathophysiological mechanisms. As a key mediator in the coagulation cascade, elevated fibrinogen promotes platelet aggregation and thrombus formation [20-22], exacerbating coronary microcirculatory dysfunction. Additionally, through leukocyte and endothelial cell activation, fibrinogen contributes to plaque destabilization and myocardial reperfusion injury[23, 24]. Subgroup analysis further suggested potential regional variations (Europe vs. Asia) in the fibrinogen-outcome relationship, warranting further investigation into population-specific factors such as genetic background and treatment differences. Our findings provide evidence-based support for incorporating fibrinogen into ACS risk stratification. Baseline fibrinogen levels may serve as an early warning indicator for all-cause mortality, particularly offering supplementary value for intermediate-risk

patients classified by traditional scoring systems [4-6]. Patients with elevated fibrinogen might benefit from intensified antithrombotic and anti-inflammatory therapies [25, 26], though optimal treatment strategies require validation through prospective studies. Several limitations should be acknowledged. First, the predominance of observational studies introduces potential residual confounding. Second, the lack of standardized fibrinogen assays and cutoff values may contribute to heterogeneity. Third, conclusions regarding MACE remain tentative due to the limited number of relevant studies. Finally, the analysis did not thoroughly explore potential effect modifications by ACS subtypes (e.g., STEMI vs. NSTEMI) or comorbidities (e.g., diabetes).

Future research should focus on multicenter prospective studies to clarify fibrinogen's role in MACE prediction. Investigating the dynamic changes in fibrinogen levels rather than relying solely on baseline measurements may yield additional prognostic insights. Furthermore, integrating fibrinogen with established risk scores (e.g., GRACE) could enhance the precision of risk prediction tools in ACS management.

Abbreviations

- ACS Acute coronary syndrome
- PCI Percutaneous Coronary Intervention NOS
- Newcastle-Ottawa Scale
- AMI acute myocardial infarction
- PRISMA Preferred Reporting Items for Systematic Reviews and Meta-Analyses MACE Major
- Adverse Cardiovascular Events STEMI Stsegment Elevation Myocardial Infarction
- NSTEMI Non stsegment Elevation Myocardial Infarction

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Reference:

1. Bergmark, B.A., et al., Acute coronary syndromes. Lancet, 2022. 399(10332): p. 1347-1358.
2. Rao, S.V., et al., 2025 ACC/AHA/ACEP/NAEMSP/SCAI Guideline for the Management of Patients With Acute Coronary Syndromes: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation, 2025. 151(13): p. e771-e862.
3. Wolberg, A.S., Fibrinogen and fibrin: synthesis, structure, and function in health and disease. J Thromb Haemost, 2023. 21(11): p. 3005-3015.
4. Li, Y.M., et al., U-Shaped Relationship Between Fibrinogen Level and 10-year Mortality in Patients With Acute Coronary Syndrome: Prospective Cohort Study. JMIR Public Health Surveill, 2024. 10: p. e54485.
5. Xie, E., et al., High Fibrinogen Levels with Diabetes Mellitus are Associated with
6. All-Cause and Cardiovascular Mortality in Patients with End-Stage Renal Disease and Acute Coronary Syndrome. J Inflamm Res, 2024. 17: p. 7409-7422.
7. Zhou, Z.F., et al., The predictive value of serum fibrinogen and platelet distribution width for long-term cardiac death in acute myocardial infarction patients. Journal of Thoracic Disease, 2024. 16(8): p. 5073-5085.
8. Khorasani, N., et al., Understanding Myocardial Infarction with Non-Obstructive Coronary Arteries (MINOCA): a comprehensive meta-analysis of clinical characteristics, management, and prognosis compared to MI with the Obstructive Coronary Artery (MIOCA). BMC Cardiovasc Disord, 2025. 25(1): p. 143.
9. Wang, L., et al., Prognostic performance of multiple biomarkers in patients with acute coronary syndrome without standard cardiovascular risk factors. Front Cardiovasc Med, 2022. 9: p. 916085.
10. Arnau Vives, M.A., et al., Prognostic value of fibrinogen in patients admitted with suspected unstable angina and non-Q-wave myocardial infarction. Revista Espanola de Cardiologia, 2002. 55(6): p. 622-630.
11. Jiang, P., et al., Relationship between fibrinogen levels and cardiovascular events in patients receiving percutaneous coronary intervention: a large single-center study. Chin Med J (Engl), 2019. 132(8): p. 914-921.
12. Sanchez, P.L., et al., Prognostic relations between inflammatory markers and mortality in diabetic patients with non-ST elevation acute coronary syndrome. Heart, 2004. 90(3): p. 264-9.
13. Shi, Y., et al., Predictive value of plasma fibrinogen levels in patients admitted for acute coronary syndrome. Tex Heart Inst J, 2010. 37(2): p. 178-83.
14. Song, J., et al., Comparison of prognostic significance between serum fibrinogen and Global Registry of Acute Coronary Events score for prognosis of patients with
15. non-ST-elevation acute coronary syndromes undergoing percutaneous coronary intervention. Coron Artery Dis, 2020. 31(2): p. 124-129.
16. Zairis, M.N., et al., The impact of hs C-reactive protein and other inflammatory biomarkers on long-term cardiovascular mortality in patients with acute coronary syndromes. Atherosclerosis, 2007. 194(2): p. 397-402.
17. Schiele, F. and N. Meneveau, NSTEMI management: a fall from GRACE? Eur Heart J, 2022. 43(24): p. 2300-2302
18. Paolisso, P., et al., Impact of admission hyperglycemia on short and long-term prognosis in acute myocardial infarction: MINOCA versus MIOCA. Cardiovasc Diabetol, 2021. 20(1): p. 192.
19. Page, M.J., et al., The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Bmj, 2021. 372: p. n71.
20. Bosco, E., et al., Major adverse cardiovascular event definitions used in observational analysis of administrative databases: a systematic review. BMC Med Res Methodol, 2021. 21(1): p. 241.
21. Melo, M., et al., Heterogeneity amongst GLP-1 RA cardiovascular outcome trials results: can definition of established cardiovascular disease be the missing link? Diabetol Metab Syndr, 2021. 13(1): p. 81.
22. Donkin, R., Y.L. Fung, and I. Singh, Fibrinogen, Coagulation, and Ageing. Subcell Biochem, 2023. 102: p. 313-342.
23. Liu, D., et al., GRSF1 antagonizes age-associated hypercoagulability via modulation of fibrinogen mRNA stability. Cell Death Dis, 2023. 14(11): p. 717.
24. Nencini, F., et al., Post-translational modifications of fibrinogen: implications for clotting, fibrin structure and degradation. Mol Biomed, 2024. 5(1): p. 45.
25. Lorenzo-Almorós, A., et al., Atrial Fibrillation and Diabetes Mellitus: Dangerous Liaisons or Innocent Bystanders? J Clin Med, 2023. 12(8).

26. Xia, K.R., et al., Network pharmacology analysis and experimental verification of the antithrombotic active compounds of trichosanthis pericarpium (Gualoupi) in treating coronary heart disease. J Ethnopharmacol, 2024. 329: p. 118158.
27. Ryu, J.K., et al., Fibrin drives thromboinflammation and neuropathology in COVID-19. Nature, 2024. 633(8031): p. 905-913.
28. Ząbczyk, M., R.A.S. Ariëns, and A. Undas, Fibrin clot properties in cardiovascular disease: from basic mechanisms to clinical practice. Cardiovasc Res, 2023. 119(1): p. 94-111.

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