C-reactive Protein Levels in Acute Myocardial Infarction and Their Association with Heart Failure: Analysis of 118 Cases

ABSTRACT

Introduction: Inflammation plays a key role in the initiation and progression of atherosclerosis. A few inflammatory biomarkers have been associated with cardiovascular outcomes, both in healthy individuals and in patients with established coronary heart disease and high-sensitivity C-reactive protein (hsCRP) has been identified as a more important prognostic biomarker than low-density lipoprotein (LDL) cholesterol.
Aims: The study aimed to investigate whether variations in inflammatory markers at the time of an Acute Coronary Syndrome (ACS) event are linked to patient prognosis.
Materials and methods: An observational prospective study was conducted with 118 patients diagnosed with ACS, admitted to the intensive care unit at ERRAZI hospital from January 2024 to June 2024 . The inclusion criteria were: patients between 41 and 84 years old, with confirmed ACS (unstable angina, ST-segment elevation myocardial infarction (STEMI), or non–ST-segment elevation myocardial infarction patients (NSTEMI)), and who provided informed consents. The outcome measure was the development of heart failure during follow-up. Statistical analyses were performed using Microsoft Excel and IBM SPSS software, with significance set at $p < 0.05$.
Results: The study involved 118 patients, with a median age of 61.5 years. The majority were male (94 men, sex ratio of 3.91). 94 patients had MI and 24 had unstable angina. Common risk factors included smoking (64 patients), hypertension (46 patients), and diabetes (58 patients). The study found the following outcomes:50% of patients experienced pump failure. 22% had thrombolysis, with 9% experiencing failure.84 patients received PCI, 15 had CABG, and 19 were treated medically due to complex coronary anatomy. Short-term cardiovascular mortality (<29 days) was 16%, with causes including cardiogenic shock, uncontrolled arrhythmias, and severe metabolic disorders. Platelet counts ranged from 54,000 to 710,000 but this was not significantly linked to ACS outcomes. However, hs-CRP levels were significantly elevated (median: 45.04), and elevated hs-CRP, white blood cell count, and serum cholesterol were associated with a higher probability of adverse cardiac outcomes.

Discussion: Cardiovascular disease (CVD), particularly coronary heart disease (CHD), is the leading cause of death globally. Inflammation plays a crucial role in the onset and progression of CHD, with CRP being a key inflammatory biomarker. Studies have shown that elevated hs-CRP levels at the time of an ACS event are associated with both short-term and long-term mortality, and CRP is an important predictor of adverse cardiovascular outcomes. Additionally, blood cell profiles (such as neutrophils and monocytes) have been shown to predict mortality.

While hs-CRP is linked to the severity of ACS events, its predictive power is modest, and its addition to traditional risk factors (age, smoking, cholesterol) provides only slight improvements in risk assessment.

Those results suggest that anti-inflammatory therapies might reduce ischemic events after

myocardial infarction.

Conclusion: CRP, particularly hs-CRP, has proven to be an important biomarker in ACS, with elevated levels correlating to a higher risk of heart failure both in the short and long term. While hs-CRP is not specific to heart failure, it provides valuable prognostic information and can help guide clinical decision-making. However, further research is needed to fully understand the role of CRP in post-myocardial infarction heart failure and to explore the potential benefits of CRP-targeted therapies in improving long-term cardiovascular outcomes.

Keywords: Acute coronary syndrome; new markers ; inflammation ; hs-CRP ; heart failure

1. INTRODUCTION :

Atherosclerosis is a slowly progressing condition that typically involves a prolonged, asymptomatic phase, which can eventually lead to acute coronary syndrome (ACS), presenting as either myocardial infarction (MI) or unstable angina (UA). ACS often represents a late-stage complication and is frequently the first clinical manifestation of underlying atherosclerotic disease.

A chronic, low-grade inflammatory process is widely recognized as a key factor in the development and progression of atherosclerosis, as well as in the acute thrombotic events that characterize ACS. Numerous studies have demonstrated a strong association between blood cell profiles, the level of inflammation at the time of admission, and the outcomes of ACS. These findings highlight the ability to differentiate between MI and UA outcomes and suggest that anti-inflammatory therapies may offer potential benefits in reducing ischemic events following myocardial infarction. C-reactive protein (CRP), an acute-phase protein indicative of early inflammatory responses, has become a valuable and straightforward tool for assessing the risk of coronary events in the general population (Zhang et al., 2021; Danesh et al., 2004; Pai et al., 2004; Ridkar et al., 1997). In this context, CRP levels may indicate localized inflammation within the coronary arteries or the exacerbation of focal inflammatory processes that destabilize vulnerable plaques (Zhang et al., 2021; Hansson, 2005). Growing evidence also underscores the significance of CRP concentrations in clinical risk stratification for patients with ACS or those who have survived stable myocardial infarction (Zhang et al., 2021; Stumpf et al., 2017; Lim et al., 2013; Makrygiannis et al., 2013; Urbano-Moral et al., 2012; Schiele et al., 2010).

The present study aimed to investigate whether variations in inflammatory markers at the time of an ACS event are linked to patient prognosis.

2. MATERIALS AND METHODS :

We performed an observational prospective study including 118 patients diagnosed with an ACS admitted to the intensive care unit with acute chest pain at ERRAZI Hospital from January 2024 to June 2024

Inclusion criteria:

1. Patients above 18 years of age: between 41 and 84 years old.

2. All patients gave their informed consent before taking part.

3. Having ACS including unstable angina, STEMI, NSTEMI enrolled as per ESC definition of MI 2023.

Exclusion criteria:

1. Not confirmed diagnosis of ACS.
2. Subjects are not willing to give consent.
3. Patients suffering from CKD and cancer.
4. Patients lost in follow-up.

The development of heart failure during the follow-up period was our outcome measure.

The patients/participants provided their written informed consent to participate in this study. This study was performed in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Harbin Medical University.

Statistical analysis:

Statistical analysis was performed using the software Microsoft Excel Office 2016 and IBM SPSS software for IOS version 22. The categorical variables were compared by Chi-square test.

Continuous variables were presented as mean (±SD) and were compared by unpaired test.

A probability value of <0.05 at 95% Confidence Interval (CI) was considered significant.

3. RESULTS AND DISCUSSION

RESULTS:

Results:

The study population comprised 118 patients with ACS. The age varies between 41 and 84 years old with a median of 61.50 y.o +/- 8.89. 94 men were included in our study with a sex ratio= 391.94 who were diagnosed with myocardial infarction and 24 with unstable angina. With regard to the distribution of risk factors, smoking history was noted in 64 patients, hypertension in 46 patients, and diabetes mellitus in 58 patients (Table 1).

Table 1: Clinical characteristics of patients at inclusion

Total (n=118)	HF (n=60)	Non HF(n=58)	P value
Age (years)>61 yo	42	28	0.016
Male	49	45	0.582

Myocardial infarction	56	45	
Unstable angina	4	13	0.015
Hypertension	24	26	0.596
Diabetes mellitus	33	25	0.196
Smoking (current)	36	29	0.275

In our study, the incidence of adverse events was observed as follows:

- **Pump failure:** 50 % of patients experienced pump failure.
- **Failed thrombolysis:** 22% of patients had thrombolysis of whom 09% had thrombolysis failure.
- 84 patients beneficed from PCI, 15 beneficed of CABG and 19 patients were referred to only medical treatment for several causes which the complexity of coronary's anatomy was the leading cause with a rate of 78%
- **Short-term mortality (<29 days) due to cardiovascular causes:** 16% of patients died due to cardiovascular-related complications.

Short-term total mortality was primarily due to cardiac disease mortality:10 patients due to cardiogenic shock, 6 patients due to arrythmias non controlled and 3 patients due to severe metabolic disorders.

The platelet count variates between 54000 and 710000 with a median of 241000+/-104121. After analyzing the data on platelet, we found that platelet count was not significantly different between groups.

It was observed that hs-CRP level was significantly elevated among ACS cases. The Hs-CRP variates between 0.4 and 276 with a median of 45.04+/-65.76.

The median of serum cholesterol level is 1.58. The white cells count variates between a min 3340 and a max of 30110 with a median of 11350 +/-4758

Further doing multiple logistic regression analysis it was observed that probability of adverse cardiac outcome increases with increase in hs-CRP level, white blood cells count and high serum cholesterol.

Table 2: blood characteristics of patients at inclusion

TOTAL (N=118)	HF (N=60)	NON HF (N=58)	P VALUE
SERUM CHOLESTEROL >1.58	40	27	0.027
HS CRP>45.04	29	7	0.0001

PQ >241000	38	31	0.276
LEUCO >11350	31	15	0.004

Discussion:

Cardiovascular disease (CVD) is the leading cause of death globally, with coronary atherosclerotic heart disease (CHD) being the primary contributor to these fatalities. Research has increasingly highlighted the significant role of inflammation in the onset and progression of CHD. In particular, C-reactive protein (CRP), a key biomarker of inflammation, has drawn considerable interest for its association with atherosclerosis (AS), CHD, and inflammatory processes.[1]

Many studies were realized :

In an observational cohort sub-study CHAPS [2], which included a 10-year follow-up using registry data, we found that plasma inflammatory biomarkers (such as hsCRP, SAA, and fibrinogen) measured during the acute event were independently associated with long-term mortality, regardless of the initial ACS diagnosis. Additionally, blood cell profiles (e.g., neutrophils, monocytes) at the time of the acute event were predictive of both short- and long-term mortality. We also observed that recently identified inflammatory composite biomarkers (such as NLR and MLR) were linked to long-term mortality. These findings suggest that standard blood biomarkers of inflammation measured during the acute event can provide valuable prognostic information for assessing future risk.

An other study, [3] proved that patients with high SYNTAX scores had significantly higher levels of age, glucose, fibrinogen, monocyte, and total cholesterol LDL, and lower levels of albumin and total protein. We found that FAR and monocyte levels were independent predictors of the high SYNTAX score.

Finally, a study published on JIMA[4], showed that the increase in hs-CRP levels is significantly higher in ACS patients, and it is strongly associated with an elevated risk of developing ACS events. Furthermore, it was observed that hs-CRP levels were directly correlated with the severity of the adverse outcome of ACS events otherwise the platelet count was not significant as a prognostic indicator of combined ACS events.

Zhang et al. (2021) identified a significant correlation between hs-CRP levels and the occurrence of in-hospital heart failure (HF) as well as HF after discharge. Additionally, hs-CRP emerged as a prognostic marker for all-cause mortality in acute myocardial infarction (AMI) patients, independent of traditional risk factors.

The relationship of Hs CRP levels to future vascular risk is not a new relation revealed. In the 1930s, CRP gained attention among cardiovascular researchers following reports in the mid-1990s that increased levels are associated with unstable angina and acute coronary ischemia.[5]

High-sensitivity CRP relates more closely to the risks of plaque rupture and vascular thrombosis than to the extent of underlying atherosclerotic burden. In terms of cardio-vascular event-free survival, the risks associated with hsCRP are comparable with and independent of LDL-C. [6]

However, these effects are modest; the addition of hsCRP testing to traditional factors, such as age, smoking, and blood pressure, has only a modest impact on the C-statistic (a measure of discrimination) and indexes of reclassification. Analyses from the Framingham Heart Study, Women's Health Study, EPIC-Norfolk, and MESA (Multi Ethnic Study of Atherosclerosis), reported net reclassification index values of 8% to 12%, but smaller effects were seen elsewhere [7].

The interpretation of hsCRP levels is relatively straightforward. Levels below 1 mg/L are considered optimal, indicating a low systemic inflammatory state and a lower risk of atherosclerosis. Levels ranging from 1 to 3 mg/L suggest a moderate vascular risk, while

levels above 3 mg/L are associated with a higher vascular risk, especially when considered alongside other risk factors. If hsCRP levels exceed 10 mg/L, this may indicate a transient infectious process or an acute-phase response, in which case the test should be repeated after 2 to 3 weeks. For risk prediction, the lower value from repeated tests, rather than the average, should be used. Persistently elevated hsCRP levels, however, are not necessarily false positives and may indicate a significantly increased vascular risk[8–10].

To move forward, and propose interventions to reduce cardiovascular event rates; Initial interventions for patients with elevated hsCRP levels should focus on lifestyle changes, including a healthy diet, regular exercise, and smoking cessation. Additionally, evidence-based use of statins and aspirin can be considered for primary prevention in individuals with elevated hsCRP. However, it is important to note that while aspirin primarily exerts antiplatelet effects and statins primarily lower lipid levels, the available data do not directly support the notion that reducing inflammation alone will necessarily lead to a reduction in cardiovascular event rates[11,12].

Alternative anti-inflammatory strategies are also under investigation for chronic atherosclerosis or acute coronary syndrome. These include agents such as colchicine (commonly given for pericarditis), for which the nonblinded LoDoCo trial provided provocative preliminary data) [13]; salsalate (an anti-inflammatory agent shown to have efficacy in diabetes) [14]; anakinra (an IL-1 receptor antagonist) [15]; and mitogen-activated protein kinase inhibitors (under investigation in the ongoing TIMI-60 trial of acute ischemia) [16]. Careful assessment of risks for infection are needed in anti-inflammatory trials, and it is important to recognize that prior studies of non-steroidal anti-inflammatory agents and tumor necrosis factor inhibitors have not shown vascular protection.

4.LIMITATIONS :

Our study has several limitations. First of all, the sample size was relatively small, which limits the statistical power and makes it difficult to draw definitive conclusions. Then , as an observational study, the strength of our findings may be subject to potential biases and limitations inherent in this design. This is a single-centre study, therefore the findings should be extrapolated cautiously to other populations with different genetic backgrounds.

5.CONCLUSION

In conclusion, C-reactive protein (CRP) has emerged as an important biomarker in the context of acute coronary syndrome (ACS), with growing evidence linking elevated CRP levels to the development and progression of heart failure.

CRP, as a marker of systemic inflammation, reflects the underlying inflammatory processes that contribute to myocardial injury, tissue damage, and subsequent adverse cardiac remodeling. Elevated CRP levels in ACS patients are associated with an increased risk of heart failure, both in the short and long term, making it a valuable prognostic tool. Although CRP is not specific to heart failure, its measurement can help identify patients at higher risk for poor outcomes, guide clinical decision-making, and potentially inform the development of targeted therapies aimed at reducing inflammation.

However, further research is needed to fully elucidate the role of CRP in the pathophysiology of heart failure following AMI and to determine whether CRP-targeted interventions can improve long-term cardiovascular outcomes.

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