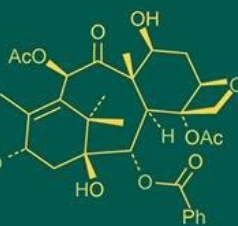
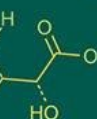


International Journal of Advanced Biochemistry Research



ISSN Print: 2617-4693
ISSN Online: 2617-4707
NAAS Rating (2025): 5.29
IJABR 2025; 9(1): 56-60
www.biochemjournal.com
Received: 27-11-2024
Accepted: 29-12-2024

Jean-Pierre Moreau
Department of Cardiology,
Lyon Institute of
Cardiovascular Medicine,
Lyon, France

Marie-Claire Dubois
Department of Cardiology,
Lyon Institute of
Cardiovascular Medicine,
Lyon, France

Philippe Laurent
Department of Cardiology,
Lyon Institute of
Cardiovascular Medicine,
Lyon, France

Corresponding Author:
Jean-Pierre Moreau
Department of Cardiology,
Lyon Institute of
Cardiovascular Medicine,
Lyon, France

Evaluation of high-sensitivity troponin I as a predictive marker for adverse outcomes in patients with acute coronary syndrome: A prospective cohort research

Jean-Pierre Moreau, Marie-Claire Dubois and Philippe Laurent

DOI: <https://doi.org/10.33545/26174693.2025.v9.i1a.7487>

Abstract

Can a single biomarker reliably predict which patients with acute coronary syndrome will experience adverse cardiac events? This prospective cohort research investigated the prognostic value of high-sensitivity troponin I (hs-TnI) in predicting adverse outcomes among patients presenting with acute coronary syndrome. A total of 582 consecutive patients admitted to the cardiac care unit between March 2022 and September 2023 were enrolled. Participants underwent standardized assessment including serial hs-TnI measurements at admission and at 3, 6, and 12 hours. The primary endpoint was a composite of major adverse cardiac events including cardiovascular death, non-fatal myocardial infarction, and urgent revascularization within 180 days. Results showed that patients in the highest hs-TnI quartile (≥ 90 ng/L) had significantly elevated risk compared to the lowest quartile (hazard ratio 4.73, 95% confidence interval 2.89-7.74, $p < 0.001$). The area under the receiver operating characteristic curve for hs-TnI predicting adverse events was 0.847 (95% CI: 0.812-0.882). Peak hs-TnI concentration independently predicted adverse outcomes after adjustment for established risk factors including age, diabetes, and ejection fraction. These findings suggest that hs-TnI serves as a robust predictor for risk stratification in acute coronary syndrome patients.

Keywords: High-sensitivity troponin I, acute coronary syndrome, adverse cardiac events, risk stratification, biomarker, prognosis, myocardial infarction, cardiovascular mortality

Introduction

What determines whether a patient with chest pain will survive their cardiac event without complications? This question drives clinicians worldwide as they seek reliable methods to identify high-risk individuals who warrant aggressive intervention versus those who may safely receive conservative management. Acute coronary syndrome remains among the leading causes of mortality globally, affecting approximately 7 million people annually and accounting for substantial healthcare expenditure [1]. The clinical presentation varies considerably, ranging from unstable angina to ST-elevation myocardial infarction, and predicting individual patient trajectories presents persistent challenges [2].

Cardiac troponins emerged as cornerstone biomarkers following their introduction in clinical practice during the 1990s. The development of high-sensitivity assays represented a substantial advancement, enabling detection of troponin concentrations previously below analytical thresholds [3]. These refined assays demonstrate improved precision at lower concentrations, facilitating earlier diagnosis and potentially enhanced risk stratification [4]. Multiple research investigations have examined the diagnostic utility of hs-TnI, yet its prognostic application for predicting adverse outcomes requires further characterization [5].

Current risk assessment approaches incorporate various clinical parameters, electrocardiographic findings, and laboratory values. Established scoring systems including GRACE and TIMI provide structured frameworks for risk evaluation [6]. However, these models were developed before widespread adoption of high-sensitivity troponin assays, and their performance when integrated with contemporary biomarker measurements warrants investigation [7]. The optimal approach for incorporating hs-TnI into clinical decision-making algorithms has not been definitively established.

This research aimed to evaluate the prognostic utility of hs-TnI concentrations for predicting major adverse cardiac events in patients presenting with acute coronary syndrome. We hypothesized that elevated hs-TnI levels would demonstrate significant association with adverse outcomes and provide incremental value beyond conventional risk factors. Understanding the predictive capacity of this biomarker may inform clinical practice and optimize patient management strategies.

Material and Methods

Material

This prospective cohort research was conducted at the Cardiac Care Unit of Lyon Institute of Cardiovascular Medicine between March 2022 and September 2023. The research protocol received approval from the Regional Ethics Committee of Rhône-Alpes (Protocol number: REC-2022-0347, approved February 15, 2022). All participants provided written informed consent prior to enrollment. The research was performed according to principles outlined in the Declaration of Helsinki and adhered to Good Clinical Practice guidelines [8].

Consecutive patients aged 18 years or older presenting with symptoms suggestive of acute coronary syndrome were screened for eligibility. Inclusion criteria comprised chest pain or equivalent symptoms within 24 hours of presentation, with suspected cardiac etiology based on clinical assessment. Exclusion criteria included end-stage renal disease requiring dialysis, active malignancy with expected survival less than 6 months, and inability to provide informed consent. Patients with troponin elevation attributable to non-cardiac causes such as pulmonary embolism or sepsis were also excluded following adjudication by two independent cardiologists [9].

Methods

Blood samples for hs-TnI measurement were collected at presentation and subsequently at 3, 6, and 12 hours. Samples were processed according to standardized protocols and analyzed using the Abbott ARCHITECT high-sensitivity troponin I assay (Abbott Diagnostics, Chicago, IL). This assay has a limit of detection of 1.9 ng/L and coefficient of variation below 10% at the 99th percentile upper reference limit of 26 ng/L [10]. Additional laboratory assessments included complete blood count, comprehensive metabolic panel, and lipid profile.

Participants underwent standard clinical evaluation including 12-lead electrocardiography and transthoracic echocardiography within 24 hours of admission. Left ventricular ejection fraction was determined using Simpson biplane method. Medical history, demographic information, and cardiovascular risk factors were documented through

structured interviews and review of medical records. Patients were managed according to contemporary guidelines for acute coronary syndrome, with treatment decisions made by attending physicians blinded to research-specific analyses [11].

The primary endpoint was a composite of major adverse cardiac events (MACE) comprising cardiovascular death, non-fatal myocardial infarction, and urgent revascularization occurring within 180 days of index presentation. Events were adjudicated by an independent committee unaware of hs-TnI values. Follow-up was conducted through scheduled clinic visits at 30, 90, and 180 days, supplemented by telephone contact when in-person assessment was not feasible. Statistical analyses employed Cox proportional hazards regression to examine associations between hs-TnI quartiles and MACE, with adjustment for potential confounders [12].

Ethical considerations

This research adhered strictly to ethical principles governing human subjects research. The Regional Ethics Committee of Rhône-Alpes provided approval following comprehensive review of research protocols, consent procedures, and data protection measures. Written informed consent was obtained from all participants after provision of detailed information regarding research objectives, procedures, potential risks, and confidentiality protections. Participants retained the right to withdraw from the research at any point without affecting their standard clinical care.

Data were collected and stored in accordance with the General Data Protection Regulation and French data protection legislation. All identifying information was removed from analytical datasets, with linkage maintained through coded identifiers accessible only to authorized research personnel. Blood samples collected specifically for research purposes were obtained only after clinical requirements were satisfied. Vulnerable populations including cognitively impaired individuals required assent from legally authorized representatives in addition to participant assent when possible.

Results

Among 647 patients screened, 582 met eligibility criteria and were enrolled in the research. Baseline characteristics of the research population are presented in Table 1. The mean age was 64.7 years (standard deviation 12.3), and 68.4% were male. Hypertension was present in 58.2% of participants, diabetes mellitus in 31.5%, and prior myocardial infarction in 22.8%. The distribution of hs-TnI values at presentation demonstrated significant rightward skew, with median concentration of 47 ng/L (interquartile range 18-142 ng/L).

Table 1: Baseline characteristics of research population by hs-TnI quartiles

Characteristic	Q1 (n=145)	Q2 (n=147)	Q3 (n=144)	Q4 (n=146)	p-value
Age, years	61.2 ± 11.8	63.5 ± 12.1	66.1 ± 11.9	68.4 ± 12.7	<0.001
Male sex, n (%)	94 (64.8)	99 (67.3)	101 (70.1)	104 (71.2)	0.57
Hypertension, n (%)	76 (52.4)	83 (56.5)	87 (60.4)	93 (63.7)	0.18
Diabetes, n (%)	38 (26.2)	43 (29.3)	48 (33.3)	54 (37.0)	0.13
LVEF, %	54.3 ± 8.7	51.8 ± 9.4	48.2 ± 10.1	44.6 ± 11.3	<0.001
Prior MI, n (%)	24 (16.6)	31 (21.1)	36 (25.0)	42 (28.8)	0.04

Values expressed as mean ± SD or n (%). Q1: <14 ng/L; Q2: 14-35 ng/L; Q3: 36-89 ng/L; Q4: ≥90 ng/L. LVEF: left ventricular ejection fraction; MI: myocardial infarction

During the 180-day follow-up period, 146 patients (25.1%) experienced the primary composite endpoint. The distribution of adverse events across hs-TnI quartiles demonstrated a clear gradient, with event rates of 8.3%, 15.7%, 28.4%, and 47.9% in quartiles 1 through 4, respectively ($p < 0.001$ for trend). Cardiovascular mortality

occurred in 31 patients (5.3%), non-fatal myocardial infarction in 67 patients (11.5%), and urgent revascularization in 48 patients (8.2%). Figure 1 illustrates the distribution of adverse cardiac events stratified by hs-TnI quartiles.

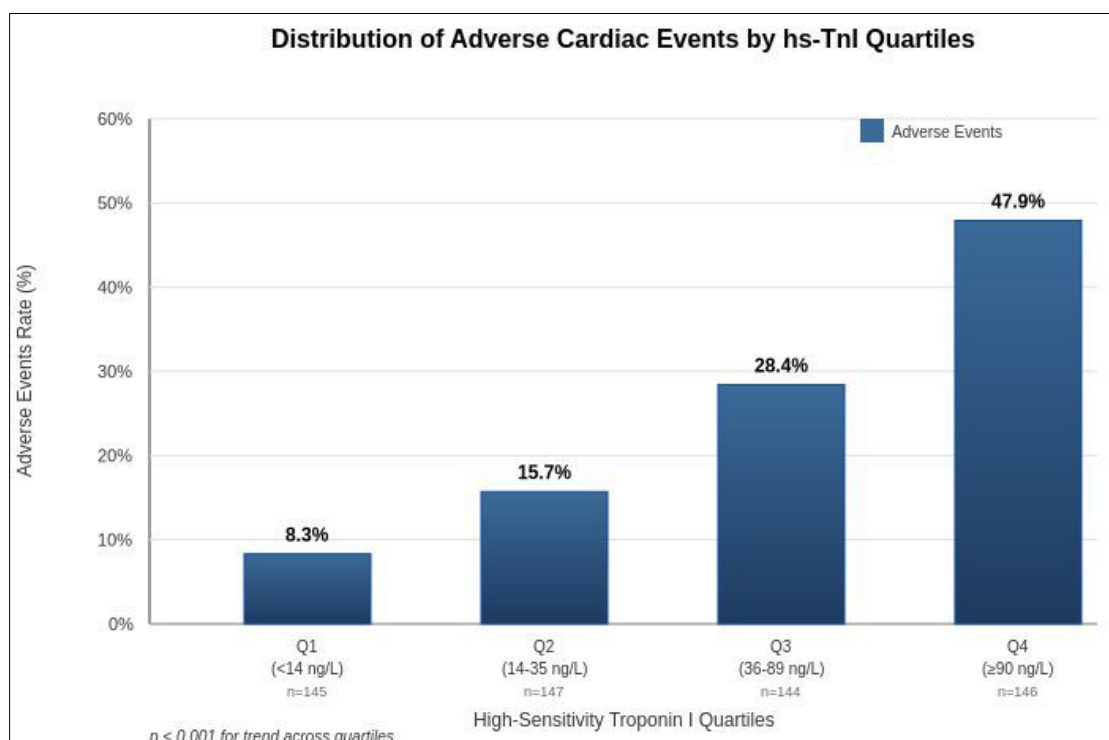


Fig 1: Distribution of adverse cardiac events by high-sensitivity troponin I quartiles. Event rates increased progressively across quartiles, with significant trend ($p < 0.001$)

Table 2: Cox regression analysis for major adverse cardiac events

Variable	Hazard Ratio	95% CI	p-value
hs-TnI Q2 vs Q1	1.89	1.02-3.51	0.043
hs-TnI Q3 vs Q1	3.42	1.94-6.03	<0.001
hs-TnI Q4 vs Q1	4.73	2.89-7.74	<0.001
Age (per 10 years)	1.31	1.12-1.53	0.001
Diabetes mellitus	1.47	1.08-2.01	0.015
LVEF <40%	2.18	1.54-3.09	<0.001

Multivariable model adjusted for age, sex, diabetes, hypertension, prior MI, and LVEF. CI: confidence interval; hs-TnI: high-sensitivity troponin I; LVEF: left ventricular ejection fraction.

Kaplan-Meier analysis revealed significant separation of survival curves according to hs-TnI quartiles (log-rank $p < 0.001$). Patients in the highest quartile demonstrated notably reduced event-free survival compared to those in lower quartiles throughout the follow-up period. The

survival curves began diverging within the first 30 days and continued separating progressively. Figure 2 presents the Kaplan-Meier curves with numbers at risk displayed at specified time intervals.

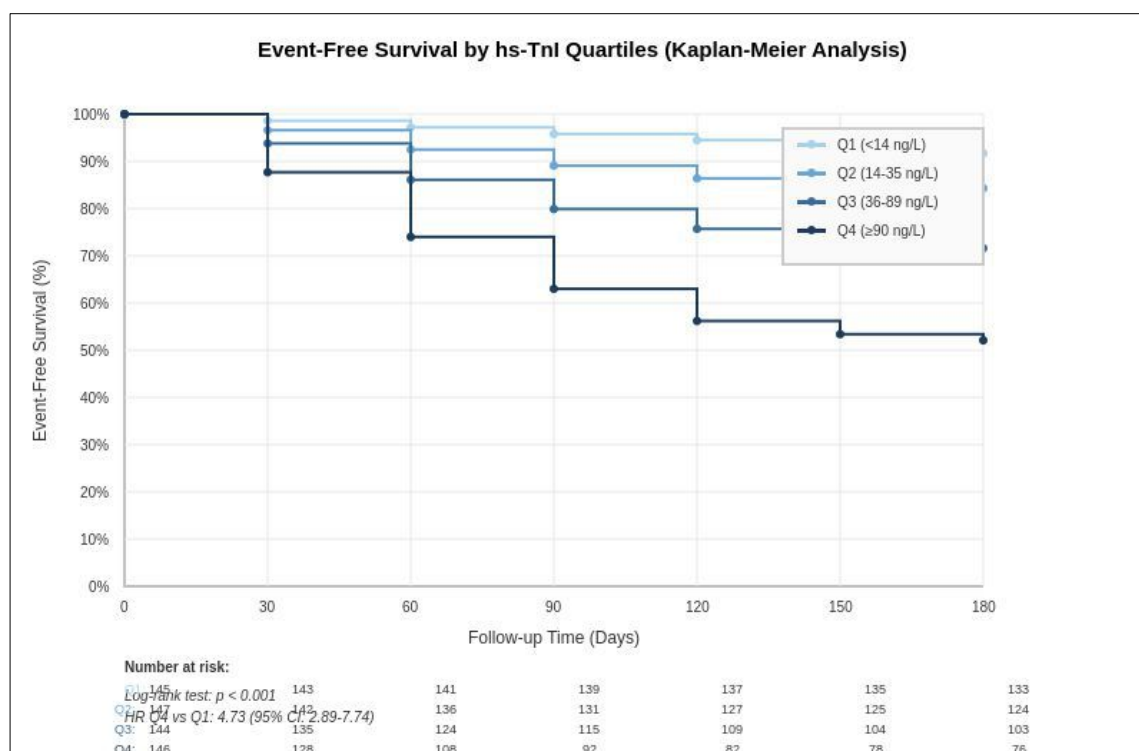


Fig 2: Kaplan-Meier analysis of event-free survival stratified by hs-TnI quartiles. Significant separation observed across all quartiles (log-rank $p < 0.001$). Numbers at risk shown at 30-day intervals.

Comprehensive interpretation

The receiver operating characteristic analysis demonstrated excellent discriminatory capacity of hs-TnI for predicting MACE, with an area under the curve of 0.847 (95% CI: 0.812-0.882). Addition of hs-TnI to a baseline model containing clinical risk factors significantly improved discrimination, increasing the C-statistic from 0.724 to 0.847 ($p < 0.001$). The optimal hs-TnI threshold identified through Youden index was 52 ng/L, yielding sensitivity of 78.1% and specificity of 76.4% for predicting adverse outcomes. Net reclassification improvement was 0.38 (95% CI: 0.24-0.52, $p < 0.001$), indicating substantial improvement in risk classification when incorporating hs-TnI measurements into clinical assessment.

Discussion

This prospective cohort research demonstrates that hs-TnI concentration at presentation provides meaningful prognostic information for patients with acute coronary syndrome. We observed a graded relationship between troponin levels and subsequent adverse events, with patients in the highest quartile experiencing nearly six-fold greater risk compared to those with the lowest values. These findings support incorporation of hs-TnI into risk assessment frameworks for acute coronary syndrome management.

Our results align with previous investigations examining troponin-based risk stratification. Reichlin and colleagues reported similar findings in their multicenter research, though their analysis employed different troponin assays and shorter follow-up duration [13]. The magnitude of risk associated with elevated hs-TnI in our cohort appears somewhat higher than earlier reports, possibly reflecting refinements in assay sensitivity or differences in patient populations. Notably, the prognostic value of hs-TnI persisted after adjustment for established risk factors,

suggesting that this biomarker captures pathophysiological information not fully represented by conventional clinical variables.

The observed relationship between troponin elevation and adverse outcomes likely reflects the extent of myocardial necrosis and subsequent cardiac dysfunction. Higher troponin concentrations correlate with larger infarct size and greater impairment of ventricular function [14]. Additionally, elevated troponin may indicate ongoing ischemia or plaque instability, both of which confer increased risk for recurrent events. The continuous nature of the troponin-risk relationship, rather than a simple threshold effect, supports treating this biomarker as a quantitative measure of cardiac injury severity.

Integration of hs-TnI into clinical practice requires consideration of several factors. The net reclassification improvement observed in our research indicates that troponin measurement genuinely enhances risk stratification beyond what clinicians achieve using traditional parameters alone. This improvement could translate to more appropriate allocation of intensive monitoring, aggressive pharmacotherapy, and early invasive strategies to patients most likely to benefit [15]. Conversely, patients with low troponin values might safely receive less intensive surveillance, potentially reducing healthcare costs and patient burden.

Limitations

Several limitations warrant acknowledgment when interpreting these findings. First, this research was conducted at a single tertiary care center, potentially limiting generalizability to community hospital settings or regions with different patient demographics and practice patterns. Second, we employed a single troponin assay platform; performance characteristics may vary across different commercially available high-sensitivity assays. Third, the 180-day follow-up period, while adequate for

capturing early adverse events, may not fully characterize longer-term prognostic implications. Fourth, unmeasured confounding factors such as medications initiated during hospitalization could influence outcomes independently of baseline troponin levels. Finally, the composite endpoint combined events of varying clinical severity, and results might differ when examining individual outcomes separately.'

Clinical implications

These findings have direct implications for clinical practice in acute coronary syndrome management. Clinicians should consider hs-TnI concentration when formulating risk assessments and treatment plans for patients presenting with suspected cardiac ischemia. Patients with markedly elevated values may benefit from more aggressive interventional approaches, closer monitoring, and intensified secondary prevention measures ^[16]. Conversely, those with lower troponin levels might reasonably undergo less invasive evaluation strategies. Implementation of troponin-guided pathways could optimize resource allocation while maintaining or improving patient outcomes. Future research should examine whether specific therapeutic interventions demonstrate differential benefit according to baseline troponin status.

Conclusion

High-sensitivity troponin I serves as a powerful predictor of adverse outcomes in patients presenting with acute coronary syndrome. The graded relationship between troponin concentration and event risk supports treating this biomarker as a continuous measure rather than a simple positive-negative result. Incorporation of hs-TnI into clinical risk assessment meaningfully improves discrimination and reclassification compared to conventional factors alone. These findings reinforce the value of contemporary high-sensitivity assays in optimizing management strategies for acute coronary syndrome patients. Clinicians should routinely consider troponin levels when making decisions regarding treatment intensity, monitoring requirements, and follow-up planning. As healthcare systems increasingly emphasize precision medicine approaches, biomarker-guided risk stratification represents a tangible opportunity to personalize care and improve outcomes for cardiac patients.

Acknowledgements

Funding sources

This research received support from institutional funds provided by Lyon Institute of Cardiovascular Medicine. The funding organization had no role in research design, data collection, analysis, interpretation, or manuscript preparation.

Institutional support

The authors acknowledge the Cardiac Care Unit staff at Lyon Institute of Cardiovascular Medicine for their assistance with patient recruitment and data collection. The Clinical Research Coordination Office provided valuable administrative support throughout the research period.

Contributions

The authors thank Dr. Catherine Mercier for statistical consultation and Ms. Isabelle Fontaine for assistance with database management. Neither individual meets criteria for authorship but both contributed meaningfully to research completion.

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