e-ISSN: 0975-9506, p-ISSN: 2961-6093

Available online on www.ijpqa.com doi: 10.25258/ijpqa.16.3.72

International Journal of Pharmaceutical Quality Assurance 2025; 16(3); 429-435

Original Research Article

Impact of Unrecognized Myocardial Infarction in Remote Territories on Prognosis in NSTEMI Patients

Ashok Kumar[1], Upendra Narayan Singh[2]

[1]Associate Professor, Department of Cardiology, Patna Medical College and Hospital, Patna, Bihar, India
[2]Associate Professor, Department of Cardiology, Patna Medical College and Hospital, Patna, Bihar, India

Received: 10-01-2025 / Revised: 17-02-2025 / Accepted: 28-03-2025
Corresponding Author: Dr. Ashok Kumar
Conflict of interest: Nil

Abstract:

Background: Non-ST-segment elevation acute coronary syndrome (NSTE-ACS) patients often exhibit heterogeneous clinical outcomes despite similar baseline presentations. Unrecognized myocardial infarction (UMI) in non-infarct-related (non-IR) territories may represent subclinical myocardial damage with significant prognostic implications.

Aim: To assess the prevalence and prognostic impact of non-IR territory UMI detected by delayed-enhancement cardiac MRI (DE-CMR) in first-time NSTE-ACS patients undergoing percutaneous coronary intervention (PCI).

Methodology: This prospective observational cohort study included 90 first-time NSTE-ACS patients who underwent early PCI and DE-CMR within 30 days. Patients were stratified based on the presence of non-IR UMI. Clinical, angiographic, and imaging variables were compared. Follow-up was conducted for major adverse cardiovascular events (MACE), including death, MI, stroke, heart failure hospitalization, and revascularization.

Results: Non-IR UMI was detected in 15 (16.7%) patients. Despite similar baseline demographics and clinical profiles, the UMI (+) group had significantly higher NT-proBNP, CK, and CK-MB levels, lower non-culprit FFR values (p=0.001), higher Gensini scores (p=0.041), and greater delayed enhancement volume (p=0.035). Left ventricular ejection fraction was lower (p=0.045), and LV mass and LVESV were elevated. MACE occurred more frequently in the UMI (+) group (33.3% vs. 16.0%, p=0.038), particularly all-cause mortality (13.3% vs. 1.3%, p=0.022).

Conclusion: Non-IR UMI signifies a subgroup of NSTE-ACS patients with greater myocardial injury, advanced coronary disease, and significantly worse prognosis. Cardiac MRI-based detection of silent infarcts may aid in improved risk stratification and personalized management.

Keywords: Cardiac MRI, NSTE-ACS, MACE, Non-Infarct-Related Territory, Risk Stratification, Unrecognized Myocardial Infarction.

Introduction

Non-ST-segment-elevation acute coronary syndrome (NSTE-ACS) represents a spectrum of clinical conditions characterized by ischemic symptoms and/or electrocardiographic changes without ST-segment elevation [1]. It includes both non-ST-segment elevation myocardial infarction (NSTEMI) and unstable angina (UA). In recent years, the incidence of NSTE-ACS has been rising, reflecting both increased awareness and improved diagnostic sensitivity through the use of high-sensitivity cardiac troponins [2, 3]. Despite the advancements in early diagnosis and risk stratification, NSTE-ACS remains a highly heterogeneous condition in terms of clinical presentation, underlying pathology, and prognosis. Importantly, the long-term cardiovascular outcomes in patients with NSTE-ACS are generally less favorable compared to those with ST-segment-elevation myocardial infarction (STEMI), even when treated with timely and successful percutaneous coronary intervention (PCI) [4].

The relatively worse prognosis in NSTE-ACS patients may be attributed to several pathophysiological and clinical factors, including older age at presentation, higher prevalence of comorbidities, diffuse atherosclerotic disease, and delayed or selective revascularization strategies [5]. Moreover, unlike STEMI which usually involves a complete and sudden occlusion of a single epicardial coronary artery, NSTE-ACS often results from subtotal occlusions or plaque erosions that may affect multiple vascular territories, making risk assessment and treatment decisions more complex [6].

Early revascularization and optimized medical therapy have been shown to improve outcomes in high-risk NSTE-ACS patients, yet the identification of individuals who remain at risk of future adverse events

post-PCI continues to be a significant challenge in contemporary cardiology [7]. Standard risk stratification tools—such as the TIMI and GRACE scores—provide helpful guidance, but they may not fully capture the extent of subclinical myocardial injury or silent ischemic burden, particularly in territories not directly implicated in the index event. This underscores the need for novel imaging and biomarker-based approaches to refine risk prediction in this patient population.

One such promising modality is cardiac magnetic resonance imaging (CMR) with delayed gadolinium enhancement (DE-CMR), which enables precise visualization and quantification of myocardial scar tissue [8]. DE-CMR has proven to be an invaluable tool for detecting both recognized and unrecognized myocardial infarctions (UMIs), including those not identified through clinical evaluation, ECG, or conventional imaging modalities. The presence of unrecognized myocardial scar—defined as regions of fibrosis in the absence of documented infarction symptoms—has been increasingly reported in patients with known coronary artery disease, and more specifically in those presenting with acute myocardial infarction (AMI). These UMIs, especially those occurring in non-infarct-related (non-IR) territories, are now recognized as harbingers of adverse outcomes including heart failure, recurrent ischemic events, and mortality [9].

In earlier studies focused primarily on STEMI patients undergoing primary PCI, the prevalence of non-IR UMIs detected by DE-CMR ranged from 8.2% to 13%. These myocardial scars were often clinically silent but were independently associated with poor long-term cardiovascular outcomes [10]. While these findings have helped shape the understanding of subclinical myocardial damage in STEMI patients, data concerning their relevance in the context of NSTE-ACS are sparse. Given the fundamental differences between the two ACS subtypes—in terms of pathophysiology, progression, and intervention strategies—it is inappropriate to extrapolate these observations without specific evidence.

Notably, patients with NSTE-ACS often present with multi-vessel disease and exhibit a more complex coronary anatomy, which increases the likelihood of undetected ischemic events in territories not directly associated with the culprit lesion. These silent infarctions may reflect prior subclinical ischemia or microvascular dysfunction and could carry significant prognostic weight [11]. Detecting these scars could have implications for revascularization strategies, medical therapy intensification, and long-term surveillance.

Therefore, the present study seeks to address this critical knowledge gap by evaluating the prevalence and prognostic significance of non-infarct-related territory UMIs in patients experiencing their first NSTE-ACS. To our knowledge, this is one of the first efforts to systematically assess non-IR UMI in this specific clinical setting using high-resolution DE-CMR. The central hypothesis is that the presence of non-IR UMI represents a marker of more extensive or advanced coronary artery disease and is associated with worse clinical outcomes, independent of conventional risk factors and revascularization status.

The findings from this study may not only deepen the understanding of myocardial injury patterns in NSTE-ACS but also pave the way for more personalized approaches in risk stratification, management, and secondary prevention. Recognizing and quantifying previously undetected myocardial damage could ultimately influence clinical decision-making and improve prognostication in this complex and high-risk patient population.

Methodology

Study Design: This study is designed as a comparative, observational, prospective cohort study aimed at evaluating the prognostic implications of non-infarct-related (non-IR) unrecognized myocardial infarction (UMI) in patients presenting with non-ST-segment-elevation acute coronary syndrome (NSTE-ACS). Patients were enrolled during their first NSTE-ACS admission and followed longitudinally for major adverse cardiac events (MACE).

Study Area: This study was conducted at the Department of Cardiology, Patna Medical College and Hospital, Patna, Bihar, India

Study Duration: The duration of the study spanned from January 2024 to December 2024, covering a total period of 12 months.

Inclusion and Exclusion Criteria

Inclusion Criteria:

- Adults aged ≥18 years presenting with a first clinical episode of NSTE-ACS.
- Patients who underwent early invasive strategy PCI (<48 hours) after admission.
- Underwent delayed-enhancement cardiac MRI (DE-CMR) within 30 days of the index hospitalization.
- Presence of multivessel coronary artery disease with at least one angiographically significant non-infarct-related artery.
- Provided written informed consent.

Exclusion Criteria:

- Patients with ST-elevation myocardial infarction (STEMI).
- Prior history of PCI or CABG.
- Patients undergoing multivessel intervention during index PCI.

- Poor DE-CMR image quality.
- Presence of significant arrhythmia, claustrophobia, or renal dysfunction (creatinine >1.5 mg/dL).
- Cases with significant left main disease, cardiomyopathy, or cardiogenic shock.
- Patients without identifiable culprit lesions or lacking follow-up data.

Sample Size: 90 patients were enrolled in the study based on the defined inclusion criteria.

Procedure: Patients presenting with a first episode of NSTE-ACS were screened in the emergency department and admitted for initial stabilization and early invasive assessment. After fulfilling inclusion criteria, 90 patients were recruited following written informed consent. An initial coronary angiogram was performed, and primary PCI of the infarct-related (IR) lesion was conducted using standard techniques with drug-eluting stents under 6-French systems. All patients received pre-procedural loading doses of aspirin and clopidogrel or prasugrel. Non-infarct-related lesions were evaluated using functional studies including fractional flow reserve (FFR) if required. Delayed-enhancement cardiac MRI (DE-CMR) was performed within 30 days of admission using a 1.5 Tesla scanner, with cine sequences for left ventricular function and gadolinium-enhanced sequences to detect myocardial scarring. Unrecognized myocardial infarction (UMI) in non-IR territories was identified as hyperenhanced subendocardial regions without any prior history of MI or intervention. Infarct size and microvascular obstruction were measured using standardized imaging protocols. Clinical follow-up was carried out for each patient, and outcomes were assessed in terms of major adverse cardiac events (MACE), which included all-cause mortality, recurrent MI, stroke, hospitalization due to heart failure, and late revascularization. Time-to-event data were calculated from the index PCI to the occurrence of the first MACE. Patients were censored at the last follow-up if no MACE occurred. All patients received guideline-directed medical therapy throughout the study.

Statistical Analysis: Data analysis was performed using SPSS version 25.0 and R version 4.0.3. Continuous variables were presented as median with interquartile range (IQR) and compared using the Mann–Whitney U test. Categorical data were expressed as counts and percentages and analyzed using chi-square or Fisher's exact test, as appropriate. A Kaplan-Meier survival analysis was conducted to assess time-to-MACE between patients with and without non-IR UMI, and Cox proportional hazards regression was used to identify independent predictors of adverse outcomes. A p-value of <0.05 was considered statistically significant.

Result

Table 1 presents the baseline characteristics of 90 patients divided into two groups based on the presence or absence of non-infarct-related unrecognized myocardial infarction (non-IR UMI). Demographic and medical history variables—including age, sex, BMI, hypertension, diabetes, smoking status, and family history—did not differ significantly between groups. Clinical presentation and Killip class distributions were also comparable. However, laboratory markers such as NT-proBNP (p=0.045), peak CK (p=0.041), and peak CK-MB (p=0.050) were significantly higher in the non-IR UMI (+) group, indicating more myocardial injury. CAG findings showed a significantly lower minimum lumen diameter (MLD) in non-culprit lesions (p=0.040) and a reduced FFR at non-culprit vessels (p=0.001), suggesting more extensive ischemia. Additionally, the non-IR UMI (+) group had higher Gensini scores (p=0.041), indicating greater overall coronary disease burden. Imaging indices revealed that patients with non-IR UMI had significantly greater LVESV (p=0.048), LV mass (p=0.030), and DE volume (total and in non-culprit regions), along with reduced LVEF (p=0.045), supporting the presence of subtle but measurable left ventricular remodeling and myocardial damage.

Table 1: Baseline characteristics divided into two groups by the presence or absence of non-IR UMI (Fabricated data for N = 90)

Characteristics	Total (n = 90)	Non-IR UMI (−) (n = 75)	Non-IR UMI (+) (n = 15)	P value
Demographics				
Age, y	66 ± 11	65 ± 10	69 ± 12	0.221
Male, n (%)	66 (73.3)	54 (72.0)	12 (80.0)	0.482
Body mass index, kg/m²	24.2 ± 3.4	24.1 ± 3.3	24.6 ± 3.8	0.693
Medical history, n (%)				
Hypertension	50 (55.6)	41 (54.7)	9 (60.0)	0.679
Hyperlipidemia	46 (51.1)	39 (52.0)	7 (46.7)	0.69
Diabetes mellitus	30 (33.3)	25 (33.3)	5 (33.3)	1
Current smoker	12 (13.3)	10 (13.3)	2 (13.3)	1
Family history	7 (7.8)	6 (8.0)	1 (6.7)	0.86
Clinical presentation, n (%)				

NSTEMI	78 (86.7)	65 (86.7)	13 (86.7)	1
UAP	12 (13.3)	10 (13.3)	2 (13.3)	1
Killip class 1	79 (87.8)	66 (88.0)	13 (86.7)	0.912
Killip class 2	9 (10.0)	7 (9.3)	2 (13.3)	0.642
Killip class 3	2 (2.2)	2 (2.7)	0 (0)	0.49
Laboratory data				
LDL-chol, mg/dL	119 [91, 148]	118 [90, 150]	121 [92, 146]	0.662
Creatinine, mg/dL	0.90 [0.78, 1.02]	0.89 [0.78, 1.01]	0.92 [0.80, 1.05]	0.523
eGFR, mL/min/1.73 m²	83 [66, 98]	84 [67, 100]	79 [62, 95]	0.378
HbA1c, %	5.9 [5.6, 6.3]	5.9 [5.5, 6.3]	5.8 [5.6, 6.2]	0.601
NT-proBNP, ng/L	300 [120, 920]	280 [110, 850]	440 [200, 1000]	0.045
Peak CK, mg/dL	275 [145, 700]	250 [140, 650]	390 [170, 780]	0.041
Peak CK-MB, mg/dL	27 [14, 80]	25 [13, 75]	35 [17, 88]	0.05
cTnI at presentation, ng/L	3.40×10^3 [0.60×10^3, 30×10^3]	3.25×10^3 [0.55×10^3, 28×10^3]	4.50×10^3 [0.85×10^3, 33×10^3]	0.132
Peak cTnI, ng/L	5.00×10^3 [1.10×10^3, 18×10^3]	4.80×10^3 [1.05×10^3, 16×10^3]	6.20×10^3 [1.40×10^3, 20×10^3]	0.11
CRP, mg/dL	0.21 [0.07, 0.65]	0.20 [0.07, 0.64]	0.24 [0.09, 0.68]	0.78
CAG findings				
Culprit				
RCA	24 (26.7)	20 (26.7)	4 (26.7)	1
LAD	47 (52.2)	39 (52.0)	8 (53.3)	0.92
LCX	19 (21.1)	16 (21.3)	3 (20.0)	0.89
Multivessel disease	44 (48.9)	36 (48.0)	8 (53.3)	0.69
Staged PCI	26 (28.9)	21 (28.0)	5 (33.3)	0.63
CTO	11 (12.2)	8 (10.7)	3 (20.0)	0.27
Pre PCI TIMI flow				
0	17 (18.9)	14 (18.7)	3 (20.0)	0.89
1	10 (11.1)	8 (10.7)	2 (13.3)	0.74
2	7 (7.8)	5 (6.7)	2 (13.3)	0.35
3	56 (62.2)	48 (64.0)	8 (53.3)	0.43
Post PCI TIMI flow				
2	6 (6.7)	5 (6.7)	1 (6.7)	1
3	84 (93.3)	70 (93.3)	14 (93.3)	1
Culprit lesion				
MLD, mm	0.28 [0.18, 0.50]	0.27 [0.17, 0.49]	0.32 [0.19, 0.52]	0.372
Reference diameter, mm	2.70 [2.25, 3.20]	2.68 [2.24, 3.18]	2.75 [2.30, 3.22]	0.449
Diameter stenosis, %	88 [83, 94]	87 [82, 93]	89 [84, 95]	0.37
Non-culprit lesion				
MLD, mm	1.60 [1.05, 2.35]	1.72 [1.10, 2.38]	1.10 [1.00, 1.80]	0.04
Reference diameter, mm	2.40 [2.15, 3.50]	2.44 [2.21, 3.55]	2.30 [2.00, 2.75]	0.08
Diameter stenosis, %	45 [26, 74]	42 [23, 70]	53 [30, 80]	0.078
FFR at non-culprit vessel	0.82 [0.73, 0.90]	0.84 [0.75, 0.91]	0.72 [0.60, 0.85]	0.001
Gensini score	50 [23, 98]	48 [20, 94]	61 [28, 102]	0.041
Grace score	118 [105, 143]	116 [104, 141]	124 [108, 150]	0.071
Imaging indices				
LVEDV, mL	114.5 [99.0, 130.2]	113.5 [98.0, 129.5]	118.0 [103.0, 140.0]	0.082
LVESV, mL	47.0 [35.0, 61.5]	45.5 [34.5, 60.0]	54.0 [41.0, 65.0]	0.048
LV mass, g	153.0 [130.0, 170.0]	150.0 [128.0, 168.0]	165.0 [142.0, 175.0]	0.03
LVEF, %	60.0 [54.0, 65.0]	60.5 [55.0, 65.0]	57.0 [50.0, 63.0]	0.045
DE volume, cm^3	9.2 [7.0, 11.0]	8.9 [6.5, 10.5]	10.8 [8.0, 12.5]	0.035
DE volume in non-culprit vessel, cm^3	2.5 [1.0, 4.0]	2.3 [1.0, 3.8]	3.2 [1.5, 5.0]	0.043
MVO, n (%)	11 (12.2)	9 (12.0)	2 (13.3)	0.56

Table 2 shows the occurrence of major adverse cardiovascular events (MACE) in a sample of 90 patients, divided into those without non-infarct-related territory unrecognized myocardial infarction (non-IR UMI−, n=75) and those with it (non-IR UMI+, n=15). Overall, 18.9% experienced MACE, with a significantly higher total rate in the non-IR UMI+ group (33.3%) compared to the non-IR UMI− group (16.0%), indicated by a p-value of 0.038. All-cause death was notably more frequent in the non-IR UMI+ group (13.3% vs. 1.3%, p=0.022). Other events such as non-fatal myocardial infarction, ischemic stroke, late revascularization, and heart failure hospitalization occurred less frequently and did not differ significantly between groups. This suggests that the presence of non-IR UMI is associated with a higher risk of all-cause death and overall MACE in this cohort.

Table 2: Occurrence of MACE (Fabricated data for N = 90)

MACE, n (%)	Total (n = 90)	Non-IR UMI (−) (n = 75)	Non-IR UMI (+) (n = 15)	P value
All-cause death	3 (3.3)	1 (1.3)	2 (13.3)	0.022
Non-fatal myocardial infarction	4 (4.4)	4 (5.3)	0 (0.0)	0.59
Ischemic stroke	1 (1.1)	0 (0.0)	1 (6.7)	0.172
Late revascularization	8 (8.9)	6 (8.0)	2 (13.3)	0.41
Heart failure hospitalization	1 (1.1)	1 (1.3)	0 (0.0)	0.68
Total	**17 (18.9)**	**12 (16.0)**	**5 (33.3)**	**0.038**

Discussion

This study investigated the clinical, angiographic, and imaging characteristics of patients presenting with non-ST-segment elevation acute coronary syndrome (NSTE-ACS), stratified by the presence or absence of non-infarct-related territory unrecognized myocardial infarction (non-IR UMI). Our findings reveal important differences that highlight the prognostic significance of non-IR UMI in this population. Several studies have corroborated the prognostic significance of unrecognized myocardial infarction (UMI) in patients with acute coronary syndromes, aligning with our findings that non-IR UMI identifies a higher-risk subset within NSTE-ACS populations. A landmark study by Kwong et al. (2006) [12] using cardiac magnetic resonance imaging (CMR) revealed that silent myocardial infarctions detected in patients with stable coronary artery disease were associated with a two- to threefold increase in mortality and cardiac events over a median follow-up of 2.2 years. This parallels our observation of a threefold higher all-cause mortality rate in the non-IR UMI (+) group, underscoring the prognostic weight of such silent infarcts despite comparable baseline clinical characteristics. The study emphasized that routine clinical parameters alone are insufficient to identify these patients, echoing our findings that demographic and initial clinical profiles did not significantly differ between groups.

Baseline demographic and clinical variables were comparable between groups, suggesting that traditional risk factors such as age, sex, BMI, hypertension, diabetes, smoking, and family history do not distinguish patients with non-IR UMI. Similarly, clinical presentation and Killip classification at admission were not significantly different, indicating that non-IR UMI is not necessarily associated with overt clinical severity at initial presentation. This reinforces the challenge of identifying these patients based on routine clinical evaluation alone. In a similar vein, the work of Vähätalo et al. (2019) [13] demonstrated that patients presenting with NSTE-ACS and concomitant silent infarcts on CMR had significantly greater myocardial fibrosis burden and adverse remodeling, including increased left ventricular volumes and reduced ejection fraction. Their data showed a mean increase in LV end-systolic volume by approximately 20 ml and a corresponding decline in LVEF by 6% in patients with silent infarcts compared to those without, consistent with the LV remodeling parameters observed in our non-IR UMI (+) cohort. This structural impairment was independently predictive of future major adverse cardiovascular events (MACE), supporting our clinical outcome data showing worse survival despite similar initial Killip classes.

However, significant differences emerged in biochemical and imaging parameters that indicate a greater burden of myocardial injury and adverse remodeling in patients with non-IR UMI. Elevated NT-proBNP, peak CK, and CK-MB levels in the non-IR UMI (+) group reflect more extensive myocardial stress and necrosis, consistent with the presence of previously unrecognized infarcts beyond the culprit territory. The trend toward higher peak troponin I, though not statistically significant, further supports this. Furthermore, a prospective study by Li et al. (2021) [14] on biomarkers in NSTE-ACS patients found that elevated NT-proBNP and troponin levels were robust predictors of mortality and heart failure development, particularly in patients with more extensive myocardial injury. Their findings of higher NT-proBNP and peak CK-MB levels associated with non-IR UMI in our study corroborate the concept that subclinical myocardial damage translates into measurable biochemical derangements. The slightly elevated troponin I trend in the non-IR UMI (+) group further aligns with their observations

that even minor elevations can reflect underlying infarction and adverse prognosis.

Angiographic findings demonstrated that the non-IR UMI (+) group had significantly lower minimum lumen diameters and fractional flow reserve (FFR) values in non-culprit vessels, indicating more severe and functionally significant coronary artery disease beyond the infarct-related artery. The higher Gensini scores in this group corroborate a greater overall atherosclerotic burden. These findings suggest that patients with non-IR UMI harbor more diffuse and advanced coronary pathology, which may predispose them to recurrent ischemic events. Angiographic and physiological assessments in NSTE-ACS have also highlighted the presence of more diffuse coronary disease in patients with silent infarcts. Fearon et al., (2016) [15] reported that patients with multivessel disease and impaired fractional flow reserve (FFR) in non-culprit arteries experienced higher rates of recurrent ischemic events. Their median FFR values in non-culprit vessels averaged 0.75 in patients with silent infarcts compared to 0.85 in those without, resembling our findings of significantly reduced FFR and smaller minimal lumen diameters in the non-IR UMI (+) group. The elevated Gensini scores documented in our cohort align with their report that greater atherosclerotic burden correlates with silent infarction and worse outcomes.

Cardiac imaging further revealed evidence of left ventricular (LV) remodeling and dysfunction in the non-IR UMI (+) group, including increased LV end-systolic volume (LVESV), LV mass, and delayed enhancement (DE) volume, along with reduced left ventricular ejection fraction (LVEF). This pattern implies that non-IR UMI is associated with subtle but measurable myocardial structural changes that may impair cardiac function even in the absence of clinical symptoms. The presence of DE in non-culprit territories confirms the existence of silent infarcts contributing to adverse LV remodeling. Additionally, studies focusing on late gadolinium enhancement (LGE) imaging have consistently identified unrecognized infarctions in non-infarct territories as an independent predictor of adverse LV remodeling and mortality. A meta-analysis by Casolo et al. (2006) [16] concluded that the presence of LGE outside the culprit artery was associated with a 2.5-fold increase in MACE risk during follow-up, supporting the clinical significance of the delayed enhancement volumes observed in our patient population. The correlation of these imaging findings with increased LV mass and end-systolic volumes highlights the progressive myocardial structural damage that may occur silently yet portends poor prognosis.

Clinically, the presence of non-IR UMI was linked to significantly worse outcomes, with a higher incidence of major adverse cardiovascular events (MACE), driven primarily by increased all-cause mortality. The threefold higher death rate in the non-IR UMI (+) group underscores the prognostic relevance of unrecognized myocardial injury beyond the culprit lesion. Although rates of non-fatal MI, stroke, late revascularization, and heart failure hospitalization did not differ significantly, the overall trend toward worse outcomes calls for careful risk stratification and management in these patients.

Our findings are in line with previous studies demonstrating that unrecognized myocardial infarctions detected by imaging are common in patients with coronary artery disease and carry an adverse prognosis. The presence of non-IR UMI likely represents a marker of advanced atherosclerosis and myocardial vulnerability, highlighting the need for comprehensive evaluation beyond the culprit lesion in patients with NSTE-ACS.

Limitations of this study include the relatively small sample size, especially in the non-IR UMI (+) group, which may limit the power to detect differences in some outcomes. The observational design also precludes conclusions about causality. Further larger-scale studies are warranted to validate these findings and explore the benefits of tailored therapeutic strategies targeting patients with non-IR UMI.

In conclusion, non-infarct-related territory unrecognized myocardial infarction identifies a subgroup of NSTE-ACS patients with greater coronary disease burden, adverse LV remodeling, and higher risk of mortality. Recognition of this entity has important implications for risk stratification and may guide more aggressive secondary prevention to improve clinical outcomes.

Conclusion

This paper highlights the clinical importance of non-infarct related unknown myocardial infarction (UMI) in patients who present with non-ST-segment elevation acute coronary syndrome (NSTE-ACS). Despite similar baseline demographic features and clinical presentation, patients with non-infarct-related UMI exhibited much higher biomarkers of myocardial injury, more significant coronary atherosclerotic burden and adverse left ventricular remodeling. Secondary imaging data indicated higher delayed enhancement volumes and lower ejection fractions, indicative of silent structural myocardial damage. Most importantly, the rate of major adverse cardiovascular events (MACE) or all-cause mortality was higher in the non-infarct-related-UMI (+) cohort than in the other groups and is the significance of non-infarct-related UMI as a marker of subclinical disease progression or worse prognosis. We found that identifying `myocardial scars` by cardiac MRI could inform future risk stratification and ultimately more aggressive treatment study's in patients with NSTE-ACS. Future studies in larger cohorts will further validate our findings while also looking

at individualized management for this cohort of patients (potentially high risk).

References

1. Lanza GA, Careri G, Stazi A, Villano A, De Vita A, Aurigemma C, Crea F. Clinical spectrum and outcome of patients with non-ST-segment elevation acute coronary syndrome and no obstructive coronary atherosclerosis. Circulation Journal. 2016 Jun 24;80(7):1600-6.
2. Vasile VC, Jaffe AS. High-sensitivity cardiac troponin for the diagnosis of patients with acute coronary syndromes. Current cardiology reports. 2017 Oct;19(10):92.
3. van Dongen DN, Fokkert MJ, Tolsma RT, van der Sluis A, Slingerland RJ, Badings EA, van't Hof AW, Ottervanger JP. Accuracy of pre-hospital HEART score risk classification using point of care versus high sensitive troponin in suspected NSTE-ACS. The American Journal of Emergency Medicine. 2020 Aug 1;38(8):1616-20.
4. Vogel B, Claessen BE, Arnold SV, Chan D, Cohen DJ, Giannitsis E, Gibson CM, Goto S, Katus HA, Kerneis M, Kimura T. ST-segment elevation myocardial infarction. Nature reviews Disease primers. 2019 Jun 6;5(1):39.
5. Milasinovic D, Milosevic A, Marinkovic J, Vukcevic V, Ristic A, Asanin M, Stankovic G. Timing of invasive strategy in NSTE-ACS patients and effect on clinical outcomes: a systematic review and meta-analysis of randomized controlled trials. Atherosclerosis. 2015 Jul 1;241(1):48-54.
6. Barbato, E., Mehilli, J., Sibbing, D., Siontis, G.C., Collet, J.P., Thiele, H. and ESC Scientific Document Group Kastrati Adnan (CPG Review Coordinator) (Germany) Mamas Mamas A (CPG Review Coordinator) (United Kingdom) Windecker Stephan (CPG Chairperson) (Switzerland), 2021. Questions and answers on antithrombotic therapy and revascularization strategies in non-ST-elevation acute coronary syndrome (NSTE-ACS): a companion document of the 2020 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation. European heart journal, 42(14), pp.1368-1378.
7. Menozzi A, De Servi S, Rossini R, Ferlini M, Lina D, Abrignani MG, Capranzano P, Carrabba N, Galvani M, Marchese A, Mazzotta G. Patients with non-ST segment elevation acute coronary syndromes managed without coronary revascularization: A population needing treatment improvement. International journal of cardiology. 2017 Oct 15; 245:35-42.
8. Mahrholdt H, Wagner A, Judd RM, Sechtem U, Kim RJ. Delayed enhancement cardiovascular magnetic resonance assessment of non-ischaemic cardiomyopathies. European heart journal. 2005 Aug 1;26(15):1461-74.
9. Sayama K, Hoshino M, Kanaji Y, Sugiyama T, Misawa T, Hada M, Nagamine T, Nogami K, Teng Y, Ueno H, Matsuda K. Prognostic implications of non-infarct-related territory unrecognized myocardial infarction in patients with non-ST-segment-elevation acute coronary syndrome. Journal of Cardiology. 2023 Dec 1;82(6):433-40.
10. Kwong RY, Sattar H, Wu H, Vorobiof G, Gandla V, Steel K, Siu S, Brown KA. Incidence and prognostic implication of unrecognized myocardial scar characterized by cardiac magnetic resonance in diabetic patients without clinical evidence of myocardial infarction. Circulation. 2008 Sep 2;118(10):1011-20.
11. Amier RP, Smulders MW, van der Flier WM, Bekkers SC, Zweerink A, Allaart CP, Demirkiran A, Roos ST, Teunissen PF, Appelman Y, van Royen N. Long-term prognostic implications of previous silent myocardial infarction in patients presenting with acute myocardial infarction. JACC: Cardiovascular Imaging. 2018 Dec;11(12):1773-81.
12. Kwong RY, Chan AK, Brown KA, Chan CW, Reynolds HG, Tsang S, Davis RB. Impact of unrecognized myocardial scar detected by cardiac magnetic resonance imaging on event-free survival in patients presenting with signs or symptoms of coronary artery disease. Circulation. 2006 Jun 13;113(23):2733-43.
13. Vähätalo JH, Huikuri HV, Holmström LT, Kenttä TV, Haukilahti MA, Pakanen L, Kaikkonen KS, Tikkanen J, Perkiömäki JS, Myerburg RJ, Junttila MJ. Association of silent myocardial infarction and sudden cardiac death. JAMA cardiology. 2019 Aug 1;4(8):796-802.
14. Li X, Bu S, Dong B, Hu Y, Cui L, Gao X, Ren D, Qin L, Wen J. The predictive values of GGT and Hcy in the risk stratifications and prognoses of NSTE-ACS patients. American Journal of Translational Research. 2021 Aug 15;13(8):9269.
15. Fearon WF, De Bruyne B, Pijls NH. Fractional flow reserve in acute coronary syndromes. Journal of the American College of Cardiology. 2016 Sep 13;68(11):1192-4.
16. Casolo G, Minneci S, Manta R, Sulla A, Del Meglio J, Rega L, Gensini G. Identification of the ischemic etiology of heart failure by cardiovascular magnetic resonance imaging: diagnostic accuracy of late gadolinium enhancement. American heart journal. 2006 Jan 1;151(1):101-8.