

Impact of guidelines-directed very-high-risk criteria in the identification and management of occlusion myocardial infarction in patients with NSTEMI-ACS

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Aims

Guidelines recommend immediate invasive management for non-ST-segment elevation acute coronary syndrome (NSTEMI-ACS) patients meeting very high-risk (VHR) criteria. Whether these criteria identify occlusion myocardial infarction (OMI) and expedite reperfusion is uncertain.

Methods and results

This *post-hoc* analysis included 2979 NSTEMI-ACS patients undergoing percutaneous coronary intervention (PCI) in the MATRIX programme with available culprit-lesion flow. OMI was defined as culprit-vessel TIMI flow 0–1. We evaluated European Society of Cardiology (ESC) and American College of Cardiology/American Heart Association (ACC/AHA) VHR criteria for OMI detection and time from first medical contact (FMC) to PCI. OMI occurred in 592 patients (19.9%). At least one VHR criterion was present in 52.9% according to ESC and 14.1% according to ACC/AHA definitions. Among patients with OMI, only 58.1% fulfilled ESC and 24.1% ACC/AHA criteria. Median FMC-to-PCI time was shorter in patients fulfilling ESC criteria (27.0 vs. 40.5 h) or ACC/AHA VHR criteria (12.2 vs. 69.9 h; both $P < 0.001$). Nevertheless, PCI within 2 h occurred in only 2.6% and 7.7% of patients meeting ESC and ACC/AHA criteria, respectively, and in 3.6% of patients with OMI. Even among OMI patients fulfilling VHR criteria, timely reperfusion within 2 h occurred only 4.7% and 9.9%.

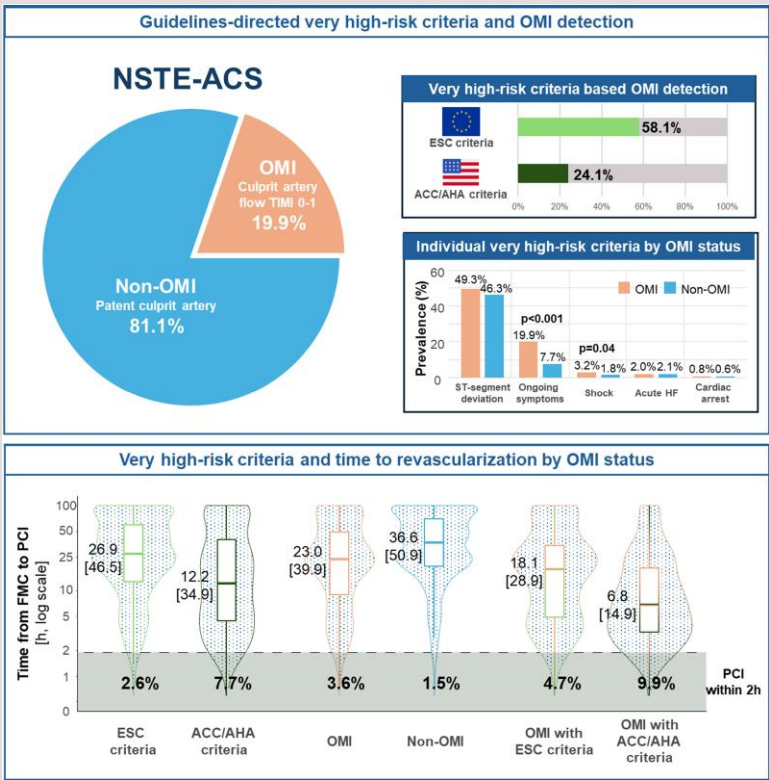
Conclusion

Guideline-directed VHR criteria had limited sensitivity for OMI and rarely translated into guideline-recommended immediate PCI. Current NSTEMI-ACS classification and triage strategies require reconsideration to improve recognition and timely reperfusion of acute coronary occlusion.

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Graphical Abstract



Impact of guidelines-directed very high-risk criteria in the detection and management of occlusion myocardial infarctions (OMIs). The green-coloured area in the lower panel marks the proportion of patients undergoing percutaneous coronary intervention within 2 h from first medical contact, according to the guidelines-suggested STEMI-like pathway for patients with very high-risk criteria. Abbreviations: FMC = first medical contact; HF = heart failure; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction; VHR = very-high-risk criteria.

Keywords Occlusion myocardial infarction • Non-ST-segment elevation acute coronary syndrome • Very-high-risk criteria • Immediate invasive strategy • Time to revascularization • Acute coronary occlusion

While coronary reperfusion should be performed within 2 h from first medical contact (FMC) in patients with ST-segment elevation myocardial infarction (STEMI), the recommended time window for invasive management is broader for non-ST-segment elevation acute coronary syndrome (NSTEMI).¹ In fact, NSTEMI presentations include both ACS with myocardial necrosis (termed non-ST-segment elevation myocardial infarction, or NSTEMI) and without evidence of myocardial necrosis (i.e. unstable angina). Up to 25% of NSTEMI patients present an acutely occluded culprit coronary artery, a condition called occlusion myocardial infarction (OMI), and experience higher mortality than those without OMI.²

The 2023 European Society of Cardiology (ESC) and the 2025 American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommended the use of very-high-risk criteria for a ‘STEMI-like’ immediate invasive management in NSTEMI-ACS.^{1,3} Both guidelines endorse the use of ongoing or recurrent symptoms/refractory angina, electrical or haemodynamic instability, and acute heart failure. The 2023 ESC—but not the 2025 ACC/AHA guidelines—also endorses the use

of recurrent dynamic ECG changes suggestive of ischaemia.^{1,3} The impact of these criteria on the identification of OMIs and on time to invasive management among NSTEMI-ACS is unknown. We investigated the accuracy of guidelines-directed very-high-risk criteria to identify OMI and their impact on time to invasive management in a large cohort of ACS patients within the MATRIX programme.

The MATRIX programme comprised three independent randomized trials (NCT 01433627) in ACS patients undergoing invasive management.^{4,5} Among 4394 NSTEMI-ACS, 3163 underwent percutaneous coronary intervention (PCI), and 2979 had complete information on culprit-lesion flow and were included in this post hoc analysis. OMI was defined as investigator-reported TIMI flow 0–1 in the culprit lesion. Mechanical complications, as exclusively proposed by the ESC guidelines, were not collected as a stand-alone item and were therefore not analysed. ST-segment deviation was used as a proxy for dynamic ST changes.

A total of 592 patients had OMI (19.9%), whereas 1557 (52.9%) and 420 (14.1%) fulfilled ≥ 1 very-high-risk criterion according to

the ESC and ACC/AHA guidelines, respectively. Patients with OMI fulfilled at least one ESC very-high-risk criterion in 58.1% of cases compared with 51.7% in non-OMI ($P = 0.006$), whereas the corresponding figures for ACC/AHA criteria were 24.1% and 11.6% ($P < 0.001$), respectively. Specificity was 48.3% for ESC and 88.4% for ACC/AHA criteria, with positive predictive values of 21.8% and 34.0% and negative predictive values of 82.3% and 82.4%, respectively. The most frequent very-high-risk criterion in the OMI cohort was ST-segment deviation (49.3%). However, only ongoing symptoms (19.9% vs. 7.7%, $P < 0.001$) and cardiogenic shock (3.2% vs. 1.8%, $P = 0.04$) differed between OMI and non-OMI ([Graphical Abstract](#), Upper Panel).

Time from FMC to PCI time was shorter in patients with vs. without ≥ 1 very-high-risk criterion (27.0 h [interquartile range (IQR): 46.5] vs. 40.5 h [IQR: 50.8] for ESC, 12.2 h [IQR: 34.9 h] vs. 69.9 h [IQR: 49.7] for ACC/AHA criteria; both $P < 0.001$) and in OMI vs. non-OMI patient (23.0 h [IQR: 39.9] vs. 36.6 h [IQR: 50.9], $P < 0.001$). Nonetheless, PCI within 2 h was exceedingly rare (2.6% for ESC, 7.7% for ACC/AHA criteria) in patients with ≥ 1 very-high-risk criterion as well as among OMI patients (3.6%), and increased only marginally for the combination of the two (respectively, 4.7% for ESC and 9.9% for ACC/AHA criteria) ([Graphical Abstract](#), Lower Panel).

This is the first analysis, to the best of our knowledge, investigating the prevalence of OMI and time to revascularization in patients fulfilling ESC and ACC/AHA guidelines directed very-high-risk criteria in a large NSTEMI-ACS cohort. The main results of this analysis are three-fold. First, patients fulfilling guidelines-directed very high-risk criteria had shorter delay to PCI, and yet only one in every 13–30 patients (according to the considered criteria) adhered to the guidelines-directed STEMI-like approach.

Second, the fulfilment of the guidelines-directed very high-risk criteria had low accuracy, with negligible sensitivity and limited specificity for OMI. Third, one out of five patients had OMI, and although OMI patients had shorter time to PCI, time to PCI within 2 h was exceedingly low at less than 1 in every 20 patients—with limited improvement even when very-high-risk criteria were present.

These results challenge the assumption that very-high-risk criteria meaningfully mitigate the STEMI/NSTEMI-ACS dichotomous ECG-based classification dominating triage and timing of invasive management, despite its well-known limitations. Within the current binary paradigm, ST-segment elevation triggers immediate reperfusion, whereas its absence permits a deferral up to 24 h in the presence of positive biomarkers (i.e. in NSTEMI), dynamic ECG changes or an elevated GRACE score. Very-high-risk criteria are intended to expedite invasive management in selected NSTEMI-ACS patients, potentially capturing those with acute coronary occlusion who may benefit from earlier reperfusion. The specificity of these criteria—especially the ACC/AHA—is good, highlighting the need to consider immediate angiography in these patients. However, in our cohort, ESC and ACC/AHA very-high-risk criteria missed $>40\%$ and $>75\%$ of OMIs, respectively. These findings suggest that additional strategies are needed to improve OMI identification beyond current guidelines. In particular, growing interest has been directed towards OMI-specific ECG patterns able to identify patients with an acute coronary occlusion despite the absence of ST-segment elevation. Because recognition of these patterns requires substantial expertise, dedicated artificial intelligence-based ECG interpretation tools have been developed for OMI detection. Their potential role in improving early detection and treatment of OMI is currently being evaluated in two randomized trials (NCT07077057 and NCT06570759).

Furthermore, although very high-risk features were associated with shorter FMC-to-PCI time, their presence almost never translated into a STEMI-like reperfusion, suggesting that current pathways for timely reperfusion in patients without STEMI need reconsideration.

Some limitations of our analysis must be acknowledged. First, as dynamic ST changes were not collected in the MATRIX trial, we used any ST-segment deviation as a proxy. Although this may reduce the specificity of the ESC guideline-directed very high-risk criteria, it should have no negative impact on their sensitivity, not affecting the main message of our analysis. Second, the MATRIX trial was performed before the publication of the assessed guidelines—our analysis should not be intended as a real-world implementation assessment, but rather as a critical appraisal of the ability of these very high-risk criteria to identify OMIs.

In conclusion, guidelines-directed very-high-risk criteria appear largely uninformative regarding OMI vs. non-OMI detection and do not meaningfully increase the proportion of the former undergoing treatment within 2 h in NSTEMI-ACS. Reconsiderations of current ACS classification and triage strategies are warranted.

Author contributions

Andrea Milzi (Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing—original draft [lead]), Antonio Landi (Investigation, Methodology, Writing—review & editing [supporting]), Sergio Leonardi (Data curation, Methodology, Writing—review & editing [supporting]), Marco Frazzetto (Investigation, Writing—review & editing [supporting]), Marco Covani (Investigation, Writing—review & editing [supporting]), Enrico Frigoli (Data curation, Writing—review & editing [supporting]), Project administration [equal]), Arnoud W J Vant'hof (Investigation, Writing—review & editing [supporting]), Pascal Vranckx (Investigation, Writing—review & editing [supporting]), and Marco Valgimigli (Conceptualization, Project administration, Supervision, Writing—review & editing [lead], Investigation, Methodology [equal])

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Data availability

Data available on request.

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