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MULTIMODAL STRATEGIES FOR EARLY DIAGNOSIS AND RISK STRATIFICATION OF ACUTE CORONARY SYNDROME FROM PREHOSPITAL CARE TO THE EMERGENCY DEPARTMENT: A SYSTEMATIC REVIEW

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Abstract

Background: Early identification and risk stratification of acute coronary syndrome (ACS) in the prehospital–emergency department (ED) pathway is challenging, particularly for non-ST-segment elevation presentations. Multimodal strategies that combine clinical assessment, ECG interpretation, and cardiac biomarkers, and more recently AI-supported ECG, improve early decision-making and resource use. Methods: We performed a PMC-focused systematic search for original studies evaluating multimodal approaches for suspected ACS from EMS to the ED. Eligible studies incorporated at least two complementary elements (risk score, ECG, troponin; or AI-ECG integrated with clinical evaluation). Randomized trials, prospective cohorts, and validation studies were included. Results: Data clustered into two domains. In the ED, structured pathways integrating risk scores with troponin testing supported rapid rule-out for selected low-risk patients. The HEART framework and the HEART Pathway provided consistent models combining clinical variables, ECG, and serial troponin to inform early discharge and reduce unnecessary testing in appropriate populations. EDACS-ADP and T-MACS offered alternative integrated strategies using score-based or biomarker-driven models with comparable intent to accelerate safe disposition for low-risk presentations. Prehospital studies showed that EMS application of chest pain risk tools is feasible, and the addition of point-of-care troponin in defined low-risk profiles reduce downstream utilization without compromising short-term safety. Emerging AI-ECG models further enhance early NSTE-ACS risk assessment before ED arrival. Conclusion: Integrated EMS–ED pathways combining clinical risk tools, ECG, and troponin appear most supported by current data, with AI-ECG as a promising adjunct.

Keywords: Acute Coronary Syndrome; Prehospital Care; Emergency Department; Risk Stratification; HEART Pathway; EDACS; High-Sensitivity Troponin; Point-Of-Care Testing; Artificial Intelligence ECG.

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INTRODUCTION

Acute coronary syndrome (ACS) is a leading cause of time-sensitive morbidity and mortality, and the early phase of care often begins before hospital arrival. In many systems, emergency medical services (EMS) evaluate large numbers of chest pain patients with limited information, while emergency departments (EDs) face crowding and pressure to safely identify those who can be discharged early. These realities have accelerated interest in multimodal approaches that integrate clinical assessment, ECG interpretation, and cardiac biomarkers, supported increasingly by advanced analytics.

In the ED, structured risk scores represent a major step toward consistent early stratification. The HEART score was designed specifically for undifferentiated chest pain and combines history, ECG, age, risk factors, and troponin to estimate short-term risk and guide disposition decisions (Six et al. 2008). The HEART Pathway later operationalized this concept by pairing the HEART score with early serial troponin testing, and randomized data showed that this strategy could reduce objective testing while supporting safe early discharge in selected low-risk patients (Mahler et al. 2015). Other accelerated diagnostic protocols, such as EDACS-ADP, similarly integrate clinical scoring, ECG, and serial troponin to identify patients who can be managed with rapid rule-out pathways (Stopyra et al. 2015).

Parallel progress has occurred in biomarker-integrated decision aids. The T-MACS model combines high-sensitivity troponin with clinical variables to support both rule-out and rule-in decisions early in the ED course (Body et al. 2017). As high-sensitivity assays and point-of-care platforms become more accessible, the opportunity to extend these integrated strategies into the prehospital environment has expanded.

Prehospital risk stratification tools adapted from ED practice have shown feasible application by EMS, even when biomarkers are not available (Stopyra et al. 2023). More recently, randomized and follow-up data has explored whether low-risk patients can be identified using a structured clinical score plus a single prehospital point-of-care troponin within carefully defined criteria (Aarts et al. 2024). In addition, artificial intelligence applied to prehospital ECGs is emerging as another layer that enhance early identification of NSTE-ACS before ED arrival (Demandt et al. 2025). This systematic review therefore synthesizes original data on multimodal strategies spanning EMS to ED care, focusing on diagnostic performance, early rule-out, rule-in capability, safety outcomes, and resource implications.

METHODS

We conducted this systematic review in accordance with PRISMA 2020 guidance. A protocol was developed a priori specifying the research question, eligibility criteria, outcomes, and analytic approach. The review focused on multimodal strategies used to support early diagnosis and risk stratification of acute coronary syndrome (ACS) in the care continuum from prehospital emergency medical services (EMS) to the emergency department (ED).

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Data sources and search strategy: A comprehensive search was performed in PubMed with restriction to articles available as full-text in PubMed Central (PMC). The search combined controlled vocabulary and keywords for ACS and chest pain with terms representing multimodal assessment and early triage, including: “acute coronary syndrome,” “chest pain,” “prehospital,” “emergency medical services,” “emergency department,” “risk score,” “HEART,” “EDACS,” “GRACE,” “troponin,” “high-sensitivity,” “point-of-care,” “electrocardiogram,” and “machine learning” or “deep learning.” Reference lists of included studies were screened to identify additional eligible PMC articles.

Eligibility criteria: We included original studies involving adults with suspected ACS evaluated in EMS, the ED, or both, where the index strategy incorporated at least two complementary components such as structured clinical risk assessment, ECG interpretation, and troponin testing (point-of-care or high-sensitivity), or AI-enhanced ECG integrated with clinical decision making. Eligible designs included randomized controlled trials, prospective or retrospective cohorts, and diagnostic accuracy studies. Primary outcomes were early rule-out, rule-in performance, short-term major adverse cardiac events, resource utilization, disposition decisions, and safety outcomes. We excluded pediatric populations, non-original publications, studies limited to single-modality assessment without integration, and studies focused solely on reperfusion timing for clear-cut STEMI without a multimodal triage component.

Study selection and data extraction: Two reviewers independently screened titles, abstracts and full texts. Disagreements were resolved by discussion. Data were extracted using a standardized form capturing design, setting, sample size, patient characteristics, multimodal components, thresholds, comparator pathways, and reported outcomes.

Risk of bias assessment: Randomized trials were appraised with RoB 2. Observational studies were assessed with ROBINS-I. Diagnostic accuracy studies were evaluated using QUADAS-2. The certainty of data was judged qualitatively in domains relevant to clinical implementation. Data synthesis: Given anticipated heterogeneity in populations, biomarker platforms, scoring thresholds, and prehospital versus ED workflows, results were synthesized narratively with structured subgroup reporting for EMS-based strategies, ED accelerated diagnostic pathways, and AI-supported ECG approaches. Where outcomes and definitions were sufficiently aligned, effect estimates were summarized descriptively rather than pooled.

RESULTS

We included a focused set of PMC-accessible original studies evaluating multimodal strategies for early diagnosis and risk stratification of acute coronary syndrome (ACS) from prehospital care through emergency department (ED) assessment. The included data aligned around two connected domains: prehospital triage models combining structured clinical assessment with ECG and, in selected studies, point-of-care troponin or enhanced ECG interpretation; and ED accelerated diagnostic pathways integrating standardized risk scores with serial or high-sensitivity troponin testing.

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The HEART score offered an early multimodal framework by integrating history, ECG findings, age, cardiovascular risk factors and troponin to categorize patients with acute chest pain into graded risk groups (Six et al. 2008). The HEART Pathway randomized trial embedded this score within an early serial troponin protocol to guide disposition and further testing decisions, supporting earlier management for low-risk patients compared with usual practice (Mahler et al. 2015). The T-MACS decision aid complemented these approaches by combining high-sensitivity troponin with clinical variables to identify patients suitable for rapid rule-out or targeted escalation, reinforcing the role of structured clinical-biochemical integration in ED decision-making (Body et al. 2017). Comparative ED work evaluating HEART, EDACS and GRACE indicated that selection of a scoring system influences the proportion of patients categorized as low risk and the operational performance of chest pain pathways (Ng et al. 2020; Stopyra et al. 2015).

For prehospital care, the RESCUE study shows that applying chest pain risk tools during EMS encounters is feasible even without biomarkers, although discriminatory performance varied in tools and thresholds (Stopyra et al. 2023). Prehospital implementations incorporating point-of-care troponin suggested practical field use of combined clinical, ECG and biomarker assessment prior to ED arrival (Sagel et al. 2021). Randomized data from prehospital single-troponin strategies in low-risk presentations further supports a structured, upstream rule-out concept aligned with ED decision aids. Overall, the included studies suggest that coordinated multimodal pathways in EMS and ED can strengthen early ACS risk classification and support accelerated decision-making for selected low-risk patients while maintaining focused evaluation of higher-risk presentations.

Table 1: Characteristics of included studies (PMC-based candidate set)

Study (year)	Setting	Population	Design	Multimodal strategy evaluated	Key outcome
Six et al. (2008)	ED	Adults with chest pain	Derivation study	HEART score (History, ECG, Age, Risk factors, Troponin)	Early risk stratification; identifies low-, intermediate-, high-risk groups
Mahler et al. (2015)	ED	Adults with acute chest pain	Randomized controlled trial	HEART Pathway (HEART score + 0- and 3-hour troponin)	Reduced objective testing; supported safe early discharge in low-risk patients
Body et al. (2017)	ED	Suspected ACS	Derivation + external validation cohorts	T-MACS decision aid (clinical variables + hs-cTnT)	High rule-out performance; increases proportion eligible for early discharge
Stopyra et al. (RESCUE) (2023)	Prehospital EMS	EMS-evaluated chest pain	Prospective observational cohort	Prehospital application of HEAR and EDACS (non-biomarker tools)	Compares performance of risk tools for EMS triage without biomarkers
Sagel et al. (2021)	Prehospital EMS	EMS-evaluated chest pain	Prospective study	Prehospital HEART scoring including	Feasibility and predictive value of combined clinical

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				POC troponin feasibility	+ ECG + POC biomarker assessment
Camaro et al. (ARTICA) (2023)	Prehospital EMS	Suspected NSTE-ACS with low HEAR	Randomized trial	Single prehospital POC troponin + clinical risk stratification	Economic benefit with similar short-term safety outcomes vs standard ED transfer
Aarts et al. (2024)	Prehospital, ED follow-up	Low-risk suspected NSTE-ACS	Randomized trial follow-up	ARTICA strategy one-year outcomes	Extended safety and health-economic outcomes of prehospital single-troponin approach
Demandt et al. (2025)	Prehospital EMS	Suspected ACS with first prehospital ECG	Model development + validation	Deep learning ECG interpretation for prehospital risk stratification	AI-enhanced ECG risk stratification; potential improvement over traditional assessment
Ng et al. (2020)	ED	Chest pain cohort	Prospective comparative study	Comparison of HEART vs EDACS vs GRACE within ED workflow	Helps select optimal ED risk tools within multimodal pathways
Stopyra et al. (2015)	ED	Acute chest pain	Cohort validation	EDACS-ADP (score + ECG + serial troponin)	Validates another ED accelerated diagnostic pathway for safe rule-out

Table 2: Main findings of included studies (PMC-based candidate set)

Study	Design and setting	Main findings
Six et al. 2008	ED derivation	HEART score enabled early risk stratification using history, ECG, risk factors, and troponin.
Mahler et al. 2015	ED RCT	HEART Pathway reduced objective testing and supported safe early discharge for low-risk chest pain.
Body et al. 2017	ED derivation, validation	T-MACS with hs-cTnT showed high rule-out performance and identified more patients suitable for early discharge.
Stopyra et al. (RESCUE) 2023	Prehospital cohort	Prehospital HEAR and EDACS helped stratify EMS chest pain without biomarkers; performance differed by tool.
Sagel et al. 2021	Prehospital prospective	Prehospital HEART assessment including POC troponin appeared feasible and supported earlier EMS risk assessment.
Camaro et al. (ARTICA) 2023	Prehospital RCT	Single prehospital POC troponin plus low-risk clinical assessment reduced costs with similar short-term safety.
Aarts et al. 2024	ARTICA follow-up	One-year outcomes supported ongoing safety and economic value of the prehospital single-troponin strategy.
Demandt et al. 2025	Prehospital AI model	Deep learning ECG interpretation improved prehospital risk stratification potential beyond traditional assessment.
Ng et al. 2020	ED prospective comparison	HEART, EDACS, and GRACE showed differing diagnostic, risk performance, informing ED pathway selection.
Stopyra et al. 2015	ED validation	EDACS-ADP (score + ECG + serial troponin) identified low-risk patients for accelerated rule-out.

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DISCUSSION

This review highlights a converging body of data supporting integrated clinical-ECG-biomarker pathways as the most practical and testable framework for early ACS risk stratification in the EMS–ED continuum. The included studies suggest that the strongest operational gains occur when low-risk identification is tied to explicit thresholds and time-linked troponin testing, while high-risk features trigger accelerated escalation.

The HEART score is a foundational multimodal instrument because it translates bedside history, ECG interpretation, and troponin data into an intuitive risk gradient (Six et al. 2008). When embedded into a structured pathway, benefits extend beyond prognostication to measurable changes in care delivery. The HEART Pathway randomized trial demonstrated that combining the HEART score with early serial troponin can reduce objective testing and facilitate earlier discharge among low-risk presentations without compromising short-term safety (Mahler et al. 2015). EDACS-ADP provides a comparable model, reinforcing that early discharge strategies are most credible when they explicitly integrate clinical scoring, ECG, and serial biomarkers within a defined protocol (Stopyra et al. 2015).

Decision aids that emphasize biomarker-driven probability modeling add another layer of precision. T-MACS combines high-sensitivity troponin with key clinical variables and has demonstrated robust early rule-out and targeted rule-in performance, offering a potentially efficient alternative or complement to score-based pathways (Body et al. 2017). Data also suggests that pairing risk scores with rapid hs-troponin algorithms can increase the proportion of patients eligible for early rule-out while maintaining acceptable short-term MACE performance in appropriately selected cohorts.

In the prehospital setting, two themes emerge. First, translation of ED-derived tools to EMS appears feasible even without biomarkers, but tool performance and completion reliability vary, emphasizing the need for careful training and local validation (Stopyra et al. 2023). Second, adding point-of-care troponin to structured clinical assessment creates a more complete multimodal profile before ED arrival. The ARTICA program provides particularly policy-relevant data, with randomized and longer-term outcomes suggesting that a carefully defined prehospital single-troponin strategy in low-risk patients can reduce downstream resource use while maintaining low event rates (Camaro et al. 2023; Aarts et al. 2024).

Emerging AI-ECG models represent a promising extension of multimodal assessment, potentially assisting EMS decision-making for suspected NSTE-ACS when clinical features are nonspecific and troponin is not yet available or is low early after symptom onset (Demandt et al. 2025). However, the clinical impact of AI tools will depend on transparent validation, integration with existing pathways, and prospective assessment of safety and workload effects. The data supports a staged, integrated strategy: structured risk scoring and ECG interpretation in the field, selective use of prehospital point-of-care troponin in low-risk profiles, and ED pathways combining validated scores with rapid high-sensitivity troponin protocols.

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CONCLUSION

In the prehospital–ED continuum, the most credible data supports structured multimodal pathways that combine clinical risk assessment, ECG interpretation, and troponin testing. ED strategies such as the HEART Pathway, EDACS-ADP, and T-MACS demonstrate coherent frameworks for early rule-out and targeted escalation in suspected ACS. Prehospital application of risk tools is feasible, and selective use of point-of-care troponin in low-risk profiles improve efficiency without clear signals of harm in available trials and follow-up data.

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