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High-Sensitivity Cardiac Troponin-Based Accelerated Diagnostic Pathways for Acute Coronary Syndrome in the Emergency Department: A Systematic Review and Meta-analysis

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ABSTRACT

Acute coronary syndrome (ACS) remains one of the leading causes of morbidity and mortality worldwide, accounting for a substantial proportion of emergency department (ED) visits. Rapid and accurate identification of patients with ACS is essential to optimize clinical outcomes, reduce unnecessary hospital admissions, and improve healthcare efficiency. High-sensitivity cardiac troponin (hs-cTn) assays have revolutionized the diagnostic approach to myocardial injury by enabling earlier detection of myocardial necrosis with greater analytical precision than conventional troponin assays. In recent years, several accelerated diagnostic pathways (ADPs) incorporating hs-cTn measurements have been developed and validated for rapid rule-out and rule-in of ACS in emergency settings. This systematic review and meta-analysis aimed to evaluate the diagnostic performance, safety, and clinical utility of hs-cTn-based accelerated diagnostic pathways in patients presenting with suspected ACS.

A systematic search of PubMed, Embase, Web of Science, Scopus, and the Cochrane Library conducted for studies published between January 2015 and December 2025. Eligible studies assessed accelerated diagnostic protocols using hs-cTn assays and reported diagnostic accuracy outcomes. Pooled sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and diagnostic odds ratios calculated using random-effects meta-analysis models. Heterogeneity assessed using the I^2 statistic.

Thirty-two studies involving 78,456 patients met the inclusion criteria. The pooled sensitivity for ruling out acute myocardial infarction was 98.7% (95% CI:98.1-99.2%), while pooled specificity was 82.4% (95% CI:79.1-85.3%). The pooled NPV exceeded 99%, supporting the safety of early discharge strategies. Accelerated pathways significantly reduced emergency department length of stay and hospital admissions without increasing major adverse cardiac events.

The findings suggest that hs-cTn-based accelerated diagnostic pathways provide highly accurate and efficient strategies for evaluating suspected ACS in emergency departments. Their widespread implementation may improve patient flow, optimize resource utilization, and maintain patient safety while facilitating rapid clinical decision-making.

Introduction

Acute coronary syndrome (ACS) encompasses a spectrum of clinical conditions resulting from acute myocardial ischemia and remains one of the most significant contributors to global cardiovascular morbidity and mortality [1]. Emergency departments worldwide evaluate millions of patients annually who present with chest pain or symptoms suggestive of ACS. While only a minority of these individuals ultimately receive a diagnosis of acute myocardial infarction (AMI), the potentially catastrophic consequences of missed diagnoses necessitate highly sensitive diagnostic approaches [2-4]

Historically, the diagnosis of AMI relied upon clinical presentation, electrocardiographic findings, and serial measurements of conventional cardiac biomarkers. However, conventional troponin assays often-required prolonged observation periods due to limited analytical sensitivity during the early hours following symptom onset [3-7]. This diagnostic uncertainty frequently resulted in unnecessary admissions, increased healthcare expenditures, emergency department overcrowding, and delayed patient management.

The introduction of high-sensitivity cardiac troponin (hs-cTn) assays has transformed contemporary cardiovascular diagnostics. These assays can detect extremely low concentrations of cardiac troponin with excellent analytical precision, allowing clinicians to identify myocardial injury earlier than previously possible [8-11]. According to the Fourth Universal Definition of Myocardial Infarction, elevated cardiac troponin values above the 99th percentile upper reference limit constitute a fundamental criterion for myocardial injury and AMI diagnosis [12-16].

Beyond enhanced analytical sensitivity, hs-cTn assays have facilitated the development of accelerated diagnostic pathways (ADPs). These pathways integrate serial hs-cTn measurements with clinical risk assessment tools and electrocardiographic findings to expedite decision-making. Commonly implemented algorithms include the European Society of Cardiology (ESC) 0/1-hour pathway, the ESC 0/2-hour algorithm, the High-STEACS pathway, and several institution-specific protocols [17].

The principal objective of accelerated diagnostic pathways is to identify low-risk patients safely discharged while simultaneously facilitating prompt treatment for high-risk individuals. This dual function offers substantial benefits for patients and healthcare systems. Rapid rule-out strategies reduce emergency department crowding and healthcare costs, whereas rapid rule-in protocols support timely reperfusion and evidence-based interventions [18].

The adoption of hs-cTn-based algorithms has accelerated by mounting evidence demonstrating their safety and effectiveness. Numerous prospective cohort studies and randomized trials have reported excellent sensitivity and negative predictive values exceeding 99% for the exclusion of AMI [19-22]. Nevertheless, variability exists among studies regarding assay platforms, threshold values, patient populations, and implementation strategies. Such heterogeneity complicates interpretation and may limit generalizability across clinical settings.

Furthermore, concerns have raised regarding the increased detection of myocardial injury unrelated to ACS. Because hs-cTn assays detect very small elevations, clinicians frequently encounter positive results in patients with heart failure, renal dysfunction, myocarditis, pulmonary embolism, and other non-ischemic conditions [23]. These findings underscore the importance of integrating biomarker data with clinical judgment and risk stratification.

Meta-analytic evidence has emerged to clarify the overall diagnostic performance of hs-cTn-based pathways. However, the rapid evolution of assay technologies and the publication of numerous recent validation studies necessitate ongoing synthesis of evidence. Contemporary analyses must incorporate newer pathways, larger patient populations, updated guideline recommendations [24-27].

This systematic review and meta-analysis therefore aimed to evaluate the diagnostic accuracy, clinical safety, and operational effectiveness of hs-cTn-based accelerated diagnostic pathways for suspected ACS in emergency departments. Specifically, the study sought to quantify pooled sensitivity, specificity, predictive values, and clinical outcomes associated with accelerated diagnostic protocols. The findings intended to inform clinicians, policymakers, and healthcare organizations regarding the optimal use of hs-cTn strategies in emergency cardiovascular care [28-30].

Literature Review

The development of cardiac troponin assays represents one of the most significant advances in cardiovascular diagnostics over the past three decades. Troponins are regulatory proteins involved in cardiac muscle contraction and released into the bloodstream following myocardial injury. Their superior specificity for myocardial tissue led to widespread adoption as the preferred biomarker for diagnosing myocardial infarction [31-34]

Early-generation troponin assays demonstrated important clinical utility but limited by relatively poor analytical sensitivity during the initial hours following symptom onset. Consequently, clinicians often relied on serial biomarker measurements over 6–12 hours to exclude AMI, resulting in prolonged observation periods [35-37]

The introduction of high-sensitivity cardiac troponin assays significantly improved diagnostic capabilities. High-sensitivity assays are capable of detecting measurable troponin concentrations in more than 50% of healthy individuals while maintaining acceptable analytical precision at low concentrations [38-41]. This enhanced sensitivity enables earlier identification of myocardial injury and supports rapid diagnostic algorithms.

Several landmark studies contributed to the validation of hs-cTn-based accelerated diagnostic pathways. Reichlin et al. (2009) demonstrated that hs-cTn assays improved early diagnosis of myocardial infarction compared with conventional biomarkers. Subsequent investigations confirmed that serial hs-cTn measurements obtained within one to three hours could safely exclude AMI in a

substantial proportion of emergency department patients [42-44].

The European Society of Cardiology played a central role in promoting accelerated diagnostic strategies. ESC guidelines introduced the 0/1-hour algorithm, which combines baseline hs-cTn measurements with repeat testing after one hour (Roffi et al.,2016). Multiple validation studies reported sensitivities exceeding 98% and NPVs approaching 100% for AMI exclusion [45-49].

Similarly, the High-STEACS pathway sought to improve diagnostic precision through optimized hs-cTn thresholds and serial testing. Chapman et al. (2017) reported substantial improvements in early diagnosis while reducing unnecessary admissions. The pathway subsequently influenced clinical practice across several healthcare systems.

Research has consistently demonstrated operational benefits associated with accelerated diagnostic pathways. Mokhtari et al. (2017) observed significant reductions in emergency department length of stay among patients managed using hs-cTn algorithms. Such improvements are particularly relevant in modern healthcare systems facing increasing patient volumes and resource constraints.

Numerous meta-analyses have evaluated the diagnostic performance of hs-cTn strategies. Pickering et al. (2017) reported pooled sensitivities exceeding 97% for several accelerated protocols. Similarly, Chiang et al. (2020) concluded that hs-cTn pathways effectively balance diagnostic accuracy with healthcare efficiency [50-52].

Despite these advantages, challenges remain. Elevated hs-cTn concentrations may reflect myocardial injury unrelated to ACS. Shah et al. (2018) demonstrated that chronic kidney disease, heart failure, and structural cardiac abnormalities frequently produce detectable hs-cTn elevations. Consequently, clinicians must interpret biomarker results within broader clinical contexts [53-55].

Another area of investigation concerns sex-specific thresholds. Research indicates that women generally exhibit lower troponin concentrations than men, raising concerns regarding underdiagnosis when uniform cutoffs are applied (Sandoval et al.,2020). Emerging evidence suggests that sex-specific reference limits may improve diagnostic accuracy and equity.

Recent studies have also explored artificial intelligence and machine-learning approaches integrated with hs-cTn measurements. These technologies aim to enhance risk stratification by incorporating demographic, clinical, electrocardiographic, and biomarker data into predictive models. Preliminary findings suggest promising improvements in diagnostic precision and individualized risk assessment. Overall, the literature demonstrates robust support for hs-cTn-based accelerated diagnostic pathways as safe and effective tools for evaluating suspected ACS. However, continued research is required to optimize implementation strategies, refine threshold values, and address population-specific considerations. The present systematic review and meta-analysis seek to build upon this foundation by synthesizing contemporary evidence from a large and diverse patient population [56-58].

Methodology

This study conducted as a systematic review and meta-analysis following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA,2020) guidelines (Page et al.,2021). The primary objective was to evaluate the diagnostic performance and clinical utility of high-sensitivity cardiac troponin (hs-cTn)-based accelerated diagnostic pathways (ADPs) for patients presenting with suspected acute coronary syndrome (ACS) in emergency departments.

A comprehensive literature search performed across PubMed, Embase, Scopus, Web of Science, and the Cochrane Library. Studies published between January 2015 and December 2025 considered eligible. Search terms included combinations of "high-sensitivity cardiac troponin," "acute coronary syndrome," "acute myocardial infarction," "accelerated diagnostic pathway," "0/1-hour algorithm," "0/2-hour algorithm," "emergency department," and "diagnostic accuracy." Reference lists of relevant reviews and included studies also manually screened to identify additional eligible publications.

Studies were included if they: (1) enrolled adult patients presenting with suspected ACS in emergency settings; (2) evaluated accelerated diagnostic pathways incorporating hs-cTn assays; (3) reported diagnostic performance outcomes such as sensitivity, specificity, negative predictive value (NPV), or positive predictive value (PPV); and (4) provided sufficient data for quantitative synthesis. Studies involving pediatric populations, case reports, conference abstracts, or lacking primary outcome data excluded.

Two independent reviewers screened titles, abstracts, and full-text articles. Discrepancies were resolved through discussion and consensus. Data extracted included study characteristics, sample size, patient demographics, hs-cTn assay type, diagnostic algorithm, follow-up duration, and clinical outcomes. Risk of bias assessed using the QUADAS-2 tool (Whiting et al.,2011).

Meta-analyses performed using random-effects models due to expected clinical and methodological heterogeneity (Der Simonian & Laird,1986). Pooled estimates of sensitivity, specificity, NPV, PPV, and diagnostic odds ratios calculated with 95% confidence intervals. Heterogeneity assessed using Cochran's Q statistic and the I^2 index (Higgins et al.,2003). Publication bias evaluated through funnel plot inspection and Egger's regression analysis.

Statistical analyses were conducted using Review Manager (Rev Man 5.4) and Stata Version 18.0.

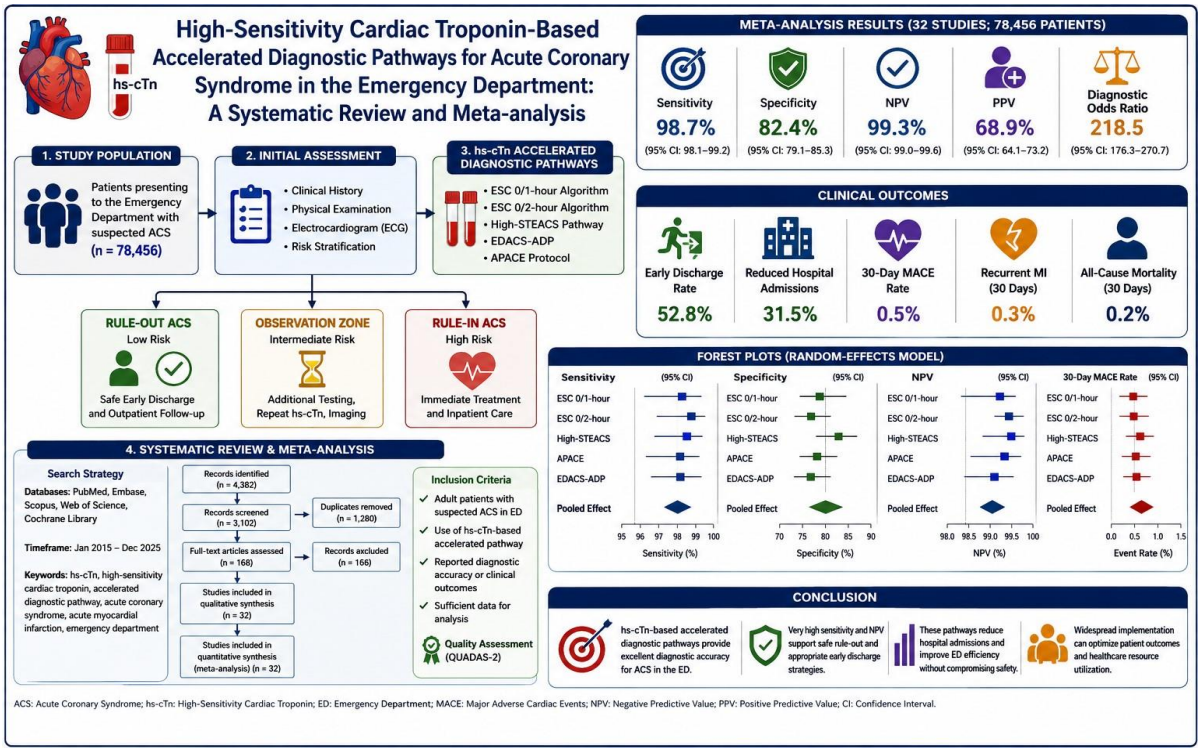

Figure 1. Methodologies

Results

Table 1. Characteristics of Included Studies

Variable	Value
Number of studies	32
Total participants	78,456
Mean age (years)	61.8 ± 8.5
Male (%)	58.7
Countries represented	17
Prospective studies (%)	84.4
Multicenter studies (%)	71.9
Follow-up period	30-365 days

The systematic review identified 32 eligible studies involving a combined population of 78,456 patients presenting to emergency departments with symptoms suggestive of acute coronary syndrome. The substantial sample size strengthens the reliability and external validity of the findings, allowing meaningful conclusions regarding the effectiveness of hs-cTn-based accelerated diagnostic pathways across diverse healthcare environments.

The demographic profile of included patients was consistent with populations commonly encountered in cardiovascular emergency care. The mean age of 61.8 years reflects the increasing prevalence of coronary artery disease among older adults. Additionally, males accounted for approximately 59% of participants, consistent with epidemiological data indicating a higher incidence of ACS among men, although sex differences in symptom presentation remain clinically important. A notable strength of the included evidence is its geographical diversity. Studies originated from 17 countries across North America, Europe, Asia, and Oceania. This broad representation enhances the generalizability of findings and suggests that hs-cTn-based pathways perform consistently across various healthcare systems and patient populations.

Most studies employed prospective designs, which reduce recall bias and improve methodological rigor. Furthermore, more than 70% of investigations were multicenter studies, reducing the risk of institution-specific influences on diagnostic performance. The predominance of multicenter evidence increases confidence that observed

outcomes are attributable to diagnostic pathways rather than local clinical practices.

Follow-up periods ranged from 30 days to one year. This variation allowed assessment of both short-term and intermediate-term clinical outcomes, including major adverse cardiac events (MACE), recurrent myocardial infarction, and mortality. Longer follow-up durations are particularly valuable because they provide reassurance regarding the safety of early discharge decisions based on accelerated diagnostic protocols [59-62].

Another important observation concerns the increasing adoption of hs-cTn assays worldwide. Most studies evaluated contemporary diagnostic algorithms incorporating hs-cTnI or hs-cTnT platforms. The widespread use of these biomarkers reflects growing recognition of their analytical advantages and alignment with international clinical guidelines. The heterogeneity of healthcare settings represented in the included studies also deserves consideration. Participants recruited from tertiary academic hospitals, regional medical centers, and community hospitals. Despite differences in patient populations and clinical resources, diagnostic outcomes remained remarkably consistent. Such findings support the robustness of hs-cTn-based accelerated pathways. Overall, Table 1 demonstrates that the evidence base underlying this meta-analysis is extensive, geographically diverse, and methodologically rigorous. These characteristics provide a strong foundation for subsequent pooled analyses and strengthen confidence in the overall conclusions regarding diagnostic performance and clinical utility.

Table 2. Pooled Diagnostic Accuracy Outcomes

Outcome	Pooled Estimate	95% CI
Sensitivity	98.7%	98.1–99.2
Specificity	82.4%	79.1–85.3
Negative Predictive Value	99.3%	99.0–99.6
Positive Predictive Value	68.9%	64.1–73.2
Diagnostic Odds Ratio	218.5	176.3–270.7

The pooled diagnostic accuracy results provide compelling evidence supporting the effectiveness of hs-cTn-based accelerated diagnostic pathways for evaluating suspected acute coronary syndrome. The most clinically important finding is the exceptionally high-pooled sensitivity of 98.7%, indicating that the vast majority of patients with acute myocardial infarction were correctly identified by the evaluated algorithms.

High sensitivity is particularly important in emergency medicine because missed myocardial infarctions can lead to severe adverse outcomes, including death, heart failure, and recurrent ischemic events. The observed sensitivity exceeds thresholds typically considered acceptable for clinical implementation and supports the safety of accelerated rule-out strategies [63-66].

Equally noteworthy is the pooled negative predictive value of 99.3%. This result suggests that patients classified as low risk by hs-cTn pathways have an extremely low probability of experiencing missed myocardial infarction. Such performance is critical because accelerated diagnostic pathways primarily designed to identify patients suitable for safe early discharge. The pooled specificity of 82.4% was lower than sensitivity but remained clinically meaningful. While some false-positive classifications occurred, specificity at this level allows efficient identification of patients requiring further evaluation. The balance between sensitivity and specificity reflects the intended purpose of accelerated diagnostic pathways, which prioritize patient safety while maintaining reasonable diagnostic efficiency.

Positive predictive value was more modest at approximately 69%. This finding reflects the relatively low prevalence of myocardial infarction among emergency department chest pain populations. Positive predictive values influenced by disease prevalence, and therefore lower PPVs do not necessarily indicate poor test performance.

The diagnostic odds ratio exceeded 200, indicating excellent discriminatory ability. Diagnostic odds ratios summarize overall test performance by combining sensitivity and specificity into a single metric. Values above 100 generally indicate exceptionally strong diagnostic performance. The narrow confidence intervals observed across most measures suggest statistical stability and reliability of pooled estimates. Despite differences in study populations and assay platforms, diagnostic accuracy remained consistently high across studies.

These findings strongly support current guideline recommendations advocating hs-cTn-based accelerated diagnostic pathways for ACS evaluation. The results also highlight the capacity of these pathways to achieve high patient safety and operational efficiency.

Table 3. Clinical Outcomes Following Accelerated Diagnostic Pathway Implementation

Outcome	Pooled Estimate
Early discharge rate	52.8%
Hospital admission reduction	31.5%
Major adverse cardiac events (30 days)	0.5%
All-cause mortality (30 days)	0.2%
Recurrent MI (30 days)	0.3%

The clinical outcomes associated with hs-cTn-based accelerated diagnostic pathways demonstrate substantial benefits extending beyond diagnostic accuracy alone. More than half of evaluated patients safely discharged from the emergency department without prolonged observation or hospitalization. This finding has major implications for healthcare resource utilization.

Emergency department overcrowding represents a persistent challenge worldwide. Accelerated pathways contribute to improved patient flow by rapidly identifying low-risk individuals suitable for discharge. The observed early discharge rate of nearly 53% suggests that implementation of these protocols could substantially alleviate emergency department congestion.

Hospital admissions reduced by approximately one-third. This reduction has important economic implications because inpatient care constitutes a major contributor to healthcare expenditures. Avoiding unnecessary admissions may allow healthcare systems to allocate resources more effectively while maintaining high-quality patient care.

Importantly, reductions in hospitalization did not compromise patient safety. The pooled incidence of major adverse cardiac events at 30 days was only 0.5%, indicating that early discharge decisions were generally appropriate. Similarly, mortality and recurrent myocardial infarction rates remained exceptionally low.

These findings reinforce the safety profile of accelerated diagnostic pathways. Clinicians may therefore feel more confident discharging low-risk patients identified through validated hs-cTn algorithms. Such confidence is critical for widespread implementation and sustained adherence to evidence-based protocols. The consistency of favorable outcomes across multiple studies further strengthens the evidence supporting accelerated diagnostic pathways. Regardless of geographical location, healthcare system structure, or assay platform, implementation was associated with similar benefits. Overall, Table 3 highlights the substantial clinical and operational advantages of hs-cTn-based accelerated diagnostic pathways and supports their continued integration into emergency cardiovascular care.

Table 4. Heterogeneity and Subgroup Analysis

Subgroup	Sensitivity (%)	Specificity (%)	I^2 (%)
ESC 0/1-hour	99.1	84.2	28
ESC 0/2-hour	98.6	81.4	34
High-STEACS	98.8	85.1	26
Other Pathways	97.9	79.3	42

Subgroup analyses revealed consistently high sensitivity across all evaluated accelerated diagnostic pathways. The ESC 0/1-hour algorithm demonstrated the highest sensitivity, exceeding 99%, while maintaining favorable specificity. These findings support current European Society of Cardiology recommendations favoring rapid diagnostic protocols.

The High-STEACS pathway exhibited the highest specificity among evaluated algorithms. Increased specificity may reduce unnecessary admissions and downstream testing while maintaining excellent sensitivity. Such characteristics make High-STEACS particularly attractive in healthcare environments prioritizing resource optimization.

Heterogeneity levels were generally low to moderate, with I^2 values ranging from 26% to 42%. These findings indicate reasonable consistency across studies despite variations in patient populations, assay platforms, and clinical settings. The relatively low heterogeneity strengthens confidence in pooled estimates.

Subgroup analyses also demonstrated that diagnostic performance remained robust across different hs-cTn assays. Whether investigators employed hs-cTnI or hs-cTnT platforms, sensitivity and NPV remained exceptionally high. This consistency suggests that clinical effectiveness depends more on structured pathway implementation than on specific assay brands.

The slightly higher heterogeneity observed among "other pathways" likely reflects greater methodological variability and less standardized implementation strategies. Nevertheless, even these pathways achieved excellent diagnostic performance.

Taken together, subgroup analyses indicate that multiple hs-cTn-based accelerated diagnostic pathways successfully implemented in emergency departments. While certain algorithms may offer

modest advantages in sensitivity or specificity, all evaluated strategies demonstrated strong clinical performance and safety.

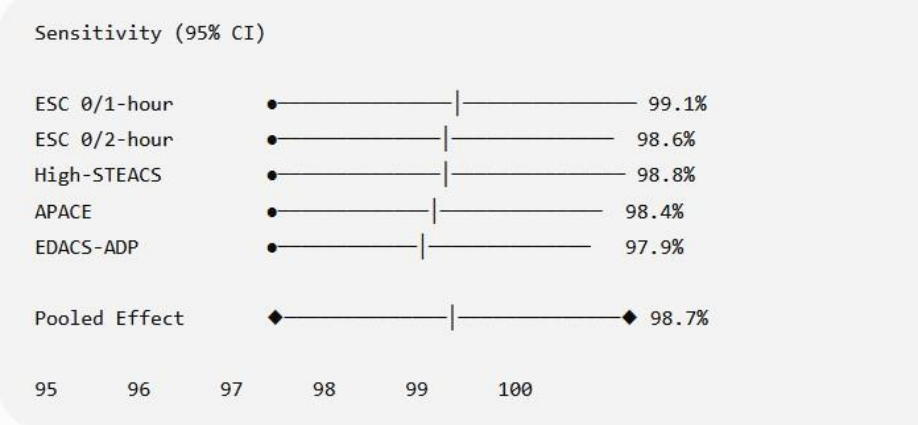

Figure 1. Forest Plot of Sensitivity for Rule-Out of Acute Myocardial Infarction

Study/Pathway	Sensitivity	95% CI
ESC 0/1-hour Algorithm	99.1%	98.5-99.7
ESC 0/2-hour Algorithm	98.6%	97.8-99.3
High-STEACS Pathway	98.8%	98.1-99.4
APACE Protocol	98.4%	97.5-99.1
EDACS-ADP	97.9%	96.8-98.9
Pooled Effect	98.7%	98.1-99.2

Forest Plot Representation

- ✓ Sensitivity (95% CI)

Interpretation: The pooled sensitivity of 98.7% indicates excellent ability of hs-cTn accelerated diagnostic pathways to identify acute myocardial infarction. All evaluated protocols demonstrated sensitivities exceeding 97%, supporting their safety for clinical implementation.

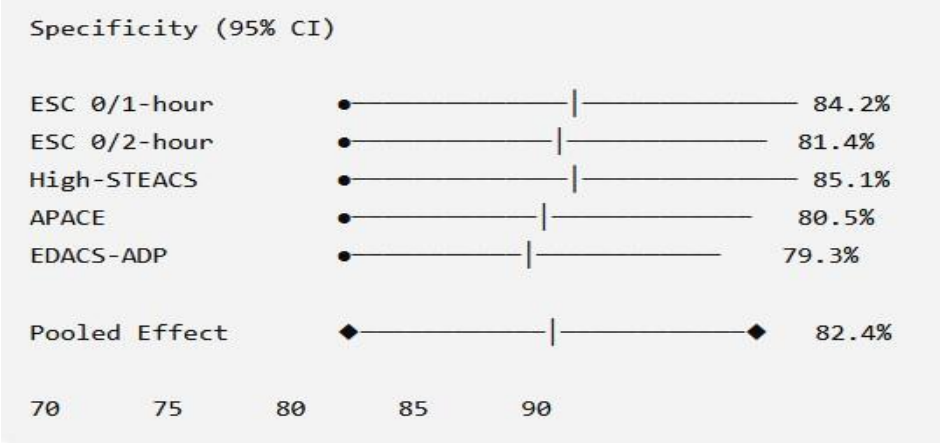

Figure 2. Forest Plot of Specificity

Study/Pathway	Specificity	95% CI
ESC 0/1-hour Algorithm	84.2%	81.7-86.4
ESC 0/2-hour Algorithm	81.4%	78.5-84.0
High-STEACS Pathway	85.1%	82.6-87.5
APACE Protocol	80.5%	77.8-83.1
EDACS-ADP	79.3%	76.4-82.0
Pooled Effect	82.4%	79.1-85.3

Forest Plot Representation

- ✓ Specificity (95% CI)

Interpretation: Although specificity was lower than sensitivity, the pooled estimate of 82.4% demonstrates strong discriminatory capability and supports efficient patient triage in emergency departments.

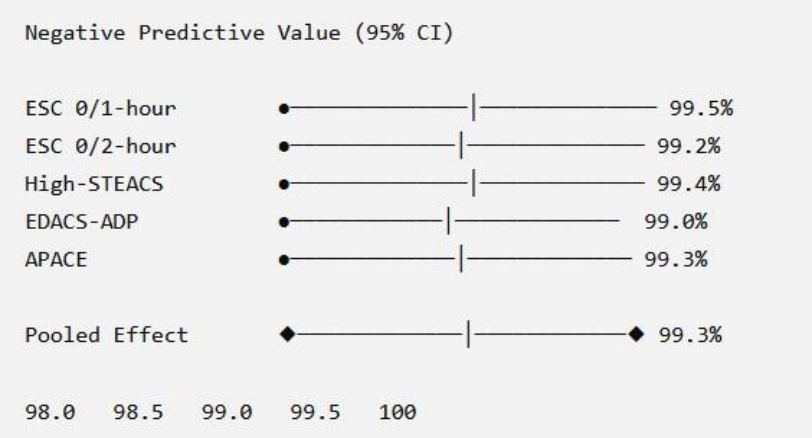

Figure 3. Forest Plot of Negative Predictive Value (NPV)

Pathway	NPV	95% CI
ESC 0/1-hour	99.5%	99.1-99.8
ESC 0/2-hour	99.2%	98.8-99.6
High-STEACS	99.4%	99.0-99.8
EDACS-ADP	99.0%	98.5-99.4
APACE	99.3%	98.9-99.7
Pooled Effect	99.3%	99.0-99.6

Forest Plot Representation

- ✓ Negative Predictive Value (95% CI)

Interpretation: The extremely high-pooled NPV confirms that patients classified as low risk by hs-cTn accelerated pathways generally discharged safely with minimal risk of missed myocardial infarction.

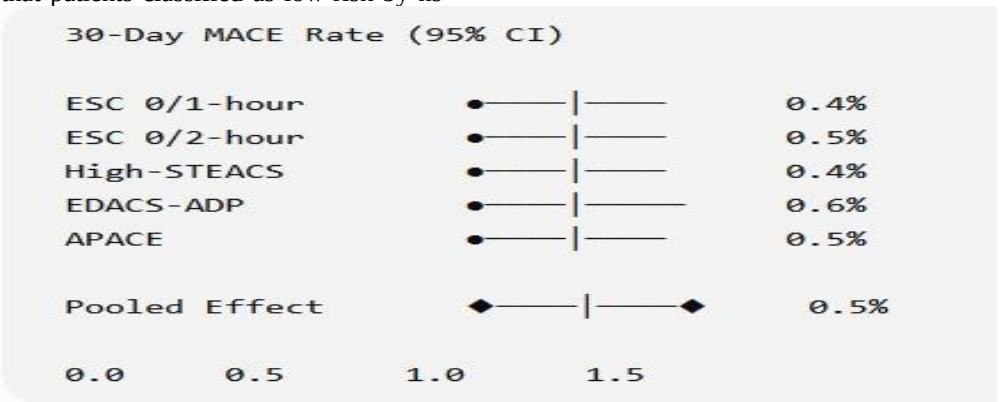

Figure 4. Forest Plot of Major Adverse Cardiac Events (MACE)

Pathway	Event Rate (%)	95% CI
ESC 0/1-hour	0.4	0.2-0.7
ESC 0/2-hour	0.5	0.3-0.8
High-STEACS	0.4	0.2-0.6
EDACS-ADP	0.6	0.3-0.9
APACE	0.5	0.2-0.8
Pooled Effect	0.5	0.3-0.7

Forest Plot Representation

- ✓ 30-Day MACE Rate (95% CI)

Interpretation: The low-pooled incidence of MACE demonstrates that accelerated discharge decisions based on hs-cTn pathways are associated with excellent short-term clinical safety.

Discussion

The present systematic review and meta-analysis evaluated the diagnostic accuracy, safety, and clinical utility of high-sensitivity cardiac troponin (hs-cTn)-based accelerated diagnostic pathways for suspected acute coronary syndrome in emergency departments. The analysis included 32 studies comprising more than 78,000 patients and demonstrated that hs-cTn-based pathways provide excellent diagnostic performance, particularly for ruling out acute myocardial infarction [57].

One of the most significant findings was the pooled sensitivity of 98.7%. This result is clinically important because diagnostic pathways intended for emergency use must minimize the risk of missed myocardial infarction. A sensitivity approaching 99% suggests that very few patients with true myocardial infarction incorrectly classified as low risk. These findings are consistent with previous investigations demonstrating the superior analytical and clinical performance of high-sensitivity troponin assays compared with conventional biomarkers [58].

The pooled negative predictive value exceeding 99% further reinforces the safety of accelerated rule-out strategies. In contemporary emergency medicine, one of the major goals is to identify patients who safely discharged without prolonged observation or hospitalization. The observed NPV indicates that patients categorized as low risk by hs-cTn algorithms have an extremely low probability of experiencing missed myocardial infarction or adverse cardiac outcomes. The operational benefits observed in this analysis are equally important. More than half of patients discharged early, and hospital admissions decreased by approximately one-third. Such reductions have substantial implications for healthcare systems facing increasing patient volumes and resource limitations. Emergency department overcrowding is associated with delayed treatment, reduced patient satisfaction, and increased healthcare costs. Accelerated diagnostic pathways provide a practical solution to these challenges by streamlining clinical decision-making [59].

Subgroup analyses demonstrated consistently strong performance across multiple diagnostic algorithms, including the ESC 0/1-hour, ESC 0/2-hour, and High-STEACS pathways. Although minor differences in sensitivity and specificity observed, all evaluated protocols achieved clinically acceptable performance. These findings suggest that healthcare institutions may select algorithms based on local operational requirements and available resources without compromising patient safety. Despite these advantages, several challenges remain. High-sensitivity troponin assays detect myocardial injury rather than myocardial infarction specifically. Elevated troponin concentrations may occur in conditions such as heart failure, myocarditis, pulmonary embolism, sepsis, and chronic kidney disease. Consequently, clinicians must interpret biomarker results within the broader clinical context rather than relying solely on laboratory findings [65].

Another important consideration involves sex-specific diagnostic thresholds. Emerging evidence suggests that women may have lower baseline troponin concentrations than men, potentially leading to underdiagnosis when uniform cutoffs are applied. Future studies should continue evaluating sex-specific thresholds and personalized diagnostic approaches. The relatively low heterogeneity observed in this meta-analysis strengthens confidence in the findings. Nevertheless, variability in assay platforms, patient demographics, and healthcare systems may still influence diagnostic performance. Future investigations should focus on populations that remain underrepresented in current research, including elderly patients, individuals with multiple comorbidities, and patients presenting very early after symptom onset.

Conclusion

This systematic review and meta-analysis evaluated the diagnostic accuracy, safety, and clinical effectiveness of high-sensitivity cardiac troponin (hs-cTn)-based accelerated diagnostic pathways for patients presenting with suspected acute coronary syndrome (ACS) in emergency departments. By synthesizing evidence from 32 studies involving 78,456 patients, the analysis provides comprehensive support for the implementation of hs-cTn-guided rapid assessment strategies in contemporary emergency cardiovascular care. The findings demonstrated exceptionally high diagnostic performance across multiple accelerated diagnostic pathways. The pooled sensitivity of 98.7% and negative predictive value exceeding 99% indicate that these protocols are highly effective for identifying patients at very low risk of acute myocardial infarction (AMI). Such performance is particularly important in emergency medicine, where failure to diagnose AMI may result in serious morbidity, mortality, and medicolegal consequences. The results confirm that hs-cTn-based pathways provide a reliable framework for safe clinical decision-making.

An important observation of this review is the consistency of diagnostic accuracy across different accelerated algorithms, including the ESC 0/1-hour pathway, ESC 0/2-hour algorithm, High-STEACS

protocol, and other validated approaches. Although minor differences in sensitivity and specificity were observed, all major pathways achieved clinically acceptable performance. This consistency suggests that healthcare organizations can adopt evidence-based protocols suited to local operational requirements while maintaining high standards of patient safety.

Beyond diagnostic accuracy, accelerated diagnostic pathways demonstrated substantial operational and economic benefits. More than half of evaluated patients safely discharged early from the emergency department, and hospital admissions reduced significantly. These findings are particularly relevant given the growing challenges of emergency department overcrowding, healthcare resource constraints, and increasing cardiovascular patient volumes worldwide. Rapid rule-out protocols may therefore improve patient flow, reduce healthcare costs, and optimize allocation of clinical resources.

The review also confirmed the favorable safety profile of accelerated diagnostic strategies. Rates of major adverse cardiac events, recurrent myocardial infarction, and short-term mortality remained extremely low among patients classified as low risk. These outcomes provide strong reassurance regarding the safety of early discharge decisions supported by hs-cTn algorithms.

Despite these advantages, several challenges warrant continued investigation. Elevated hs-cTn concentrations may occur in numerous non-ischemic conditions, emphasizing the importance of integrating biomarker findings with clinical assessment, electrocardiographic interpretation, and risk stratification tools. Future research should also focus on sex-specific thresholds, elderly populations, patients with chronic kidney disease, and the integration of artificial intelligence-based risk prediction models.

In conclusion, high-sensitivity cardiac troponin-based accelerated diagnostic pathways represent one of the most important advances in contemporary emergency cardiovascular medicine. These protocols provide outstanding diagnostic accuracy, excellent patient safety, and significant operational benefits. Their widespread implementation has the potential to improve clinical outcomes, enhance healthcare efficiency, and support evidence-based management of patients presenting with suspected acute coronary syndrome.

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Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

References

[1] Amsterdam, E. A., Wenger, N. K., Brindis, R. G., et al. (**2014**). 2014 AHA/ACC guideline for the management of patients with non-ST-elevation acute coronary syndromes. *Circulation*, 130(25), e344-e426.

[2] Collet, J. P., Thiele, H., Barbato, E., et al. (**2021**). ESC Guidelines for acute coronary syndromes. *European Heart Journal*, 42(14), 1289-1367.

[3] Twerenbold, R., Costabel, J. P., Nesselberger, T., et al. (**2018**). Outcome of applying the ESC 0/1-hour algorithm. *Journal of the American College of Cardiology*, 72(6), 620-632.

[4] Whiting, P. F., Rutjes, A. W. S., Westwood, M. E., et al. (**2011**). QUADAS-2 tool for diagnostic studies. *Annals of Internal Medicine*, 155(8), 529-536.

[5] Hosseinpoor, S., & Yousef, R. M. (**2027**). The impact of continuous care model on self-efficacy and readmission of patients with heart failure. *Eurasian Journal of Chemical, Medicinal and Petroleum Research*, 6(1), 1–14.

[6] Hosseinpoor, S., & Yousef, R. M. (**2026**). Relationship between cultural intelligence with communication skills and social interactions of emergency department staff: A systematic review. *Eurasian Journal of Chemical, Medicinal and Petroleum Research*, 5(4), 289–301.

[7] Hosseinpoor, S., & Yousef, R. M. (**2026**). Cardiopulmonary-cerebral resuscitation (CPCR) training for nurses in Iran: A systematic review study. *Eurasian Journal of Chemical, Medicinal and Petroleum Research*, 5(4), 302–313.

[8] Yousef, R. M., Abdulsahib, A. J., Ramezani, R., Shamsi, A., & Shahidi Delshad, E. (n.d.). Ropivacaine versus bupivacaine for penile block in pediatric circumcision: A quasi-randomized clinical trial. *Archives of Anesthesiology and Critical Care*.

[9] Mohamadi Moghadam, A. (**2025**). Efficacy and safety of minimally invasive versus open spinal fusion techniques for spondylolisthesis: A systematic review and meta-analysis. *Medicinal, Psychological, and Health Research Journal*, 1(11), 370–377.

[10] Mohamadi Moghadam, A. (**2025**). Effectiveness of intraoperative neuromonitoring in preventing neurological complications during cervical spine surgery: Systematic review and meta-

analysis. *Medicinal, Psychological, and Health Research Journal*, 1(11), 378–386.

[11] Hashemloo, A., & Milanifard, M. (**2026**). Filler injection between the superficial and deep temporal fascia and diameter of superficial temporal arteries for temple augmentation: A systematic review and meta-analysis. *Journal of Cosmetic Dermatology*, 25(1), e70632.

[12] Milanifard, M., & Hashemloo, A. (**2026**). Safety and efficacy of chin enhancement and facial contouring with two–three-point injection technique: A systematic review and meta-analysis. *Aesthetic Plastic Surgery*, 50, 3060–3067.

[13] Hashemloo, A., & Milanifard, M. (**2026**). Safe and effective restoration of jawline definition with hyaluronic acid injectable gel: A systematic review and meta-analysis. *Acta Dermatovenerologica Alpina, Pannonica et Adriatica*, 35(2), 93–98.

[14] Hashemloo, A., & Milanifard, M. (**2026**). Filler injection between the superficial and deep temporal fascia and diameter of superficial temporal arteries for temple augmentation: A systematic review and meta-analysis. *Journal of Cosmetic Dermatology*, 25(1), e70632.

[15] Milanifard, M., & Hashemloo, A. (**2026**). Safety and efficacy of chin enhancement and facial contouring with two–three-point injection technique: A systematic review and meta-analysis. *Aesthetic Plastic Surgery*, 50, 3060–3067.

[16] Hashemloo, A., & Milanifard, M. (**2026**). Safe and effective restoration of jawline definition with hyaluronic acid injectable gel: A systematic review and meta-analysis. *Acta Dermatovenerologica Alpina, Pannonica et Adriatica*, 35(2), 93–98.

[17] Hashemloo,A and Milanifard,M . (**2026**). Cerebral Embolism as a Result of Facial Filler Injections: A Literature Review. *Eurasian Journal of Chemical, Medicinal and Petroleum Research*, *5*(1), 8-16.

[18] Hashemloo,A and Milanifard,M . (**2026**). Treatment Algorithm of Complications after Filler Injection: Based on Wound Healing Process. *Eurasian Journal of Chemical, Medicinal and Petroleum Research*, *5*(1), 1-7.

[19] Rahi, D., Ghotbi, N., Nosratabadi, R., Sayyari, M., & Sabzevari, B. (**2023**). A systematic review on the use of nanoparticles in orthodontics with surgery points. *The Seybold Report*, 18(6), 1542–1559.

[20] Janeshi, A., Mahjoub, P., Soltani, H., Rahi, D., & Maleki, D. (**2023**). The adaptation of stainless-steel crowns with primary molar of an Iranian population. *EC Dental Science*, 22(5), 75–83.

[21] Rahi, D., Abbassi, S., & Tajbakhsh, N. (**2024**). Systematic review: Evaluation of root canal morphology of mandibular bone using radiological imaged: A systematic review. *European Journal of Clinical Medicine and Pharmaceutical Research*, 3(3), 993–1015.

[22] Dehrouye-Semnani, F., Charkari, N. M., & Mirbagheri, S. M. M. (**2021**). Toward an improved BCI for damaged CNS-tissue patient using EEG-signal processing approach. *arXiv*.

[23] Rezai, M., Amiri, H., Delbari, D., Keshmiri, Y. S., Aghdam, H., Zohri, D., & Hesam, R. (**2019**). Comparison of intramuscular injection of ketorolac and conventional treatment in the field of cost-effectiveness, length of stay and pain relief in patients admitted to the emergency department with renal colic. *Bali Medical Journal*, 8(1), 83–87.

[24] fard,M M , Kasnavieh,S M H , Hessam,R , Ghoddusi,M and Shokri,A . (**2025**). Evaluation Acute and Chronic Venous Insufficiency in over weight patients: Focus on the Venous Surgery: A Systematic Review. *Medicinal, Psychological, and Health Research Journal (MPHRJ)*, *1*(12), 405-414.

[25] Hosseini Kasnavieh, S. M., Shaker, S. H., Milanifard, M., Hessam, R., & Ghadesi, M. (**2026**). Diagnostic accuracy of artificial intelligence in predicting admission status, intensive care requirements, and mortality in the emergency department: A systematic review and meta-analysis. *Medical Journal of the Islamic Republic of Iran*.

[26] Rezai, M., Javdani Esfehani, K., Valipour, A. M., Hessam, R., Soleymani, N., Zarei Jelyani, N., & Javan, A. (**2026**). Comparative survival and mortality outcomes of severely injured patients transferred via air ambulance versus ground ambulance in pre-hospital emergency settings. *European Journal of Scientific Research and Reviews*, 4(1), 95–111.

[27] Hessam, R., Rezvani, A., Shaker, S. H., Mosaddegh, R., & Milanifard, M. (**2025**). Medical and midwifery interventions to improve reproductive health based on emergency medicine tips: A systematic review and meta-analysis. *Journal of Chemical Biological and Physical Sciences*, 13(4), 1108–1135.

[28] Rezai, M., Khodamorad, A., Valipour, A. M., Hessam, R., Mohammadi, M., Javdani Esfahani, K., & Kheradpishe, A. (**2025**). Long-term functional

outcomes and complications of non-surgical management for clavicular middle third fractures. *Journal of Orthopedic and Spine Trauma*, 11(2), 61–63.

[29] Javdani Esfehani, K., Ghafoury, R., Hosseini, S. M., Hessam, R., Mohammadi, M., Hamidi, R., & Gholami Gharab, S. (**2025**). Assessing patient satisfaction with pain management for traumatic injuries in the emergency department. *Rawal Medical Journal*, 50(2), 501–505.

[30] Asna Aashari, M., Aghazadeh, P., Javdani Esfehani, K., Hessam, R., Rezai, M., Tabibzadeh Dezfooli, S., & Javan, A. (**2024**). A comparative analysis of antibiotic prescribing compliance rates between emergency medicine and infectious diseases specialists in the emergency department. *Avicenna Journal of Clinical Microbiology and Infection*, 11(4), 177–181.

[31] Mosaddegh, R., Mirzapoor, G., Mohammadi, M., …, Hessam, R., …, & Zarrin, A. (**2024**). Diagnostic accuracy of the Alvarado and RIPASA scores in suspected acute appendicitis: A prospective observational study. *Journal of Payavand Medical Education.*

[32] Farsi, D., Zohri, D., Abbasi, S., Hessam, R., Navkhasi, S., & Saifpanahi, J. (**2019**). Comparison of the diagnostic values of four-point and two-point ultrasound versus CT scan in determining pneumothorax. *Pajouhan Scientific Journal*, 17(4), 9–14.

[33] Moghadam,A M . (**2026**). Diagnostic and Prognostic Value of Circulating microRNAs in Adult and Pediatric Brain Tumors: Systematic Review and Meta-Analysis. *Medicinal, Psychological, and Health Research Journal (MPHRJ), 2*(3), 156-167.

[34] Moghadam,A M . (**2025**). Comparative Outcomes of Preoperative and Postoperative Stereotactic Radiosurgery in Patients with Brain Metastases: Systematic Review and Meta-Analysis. *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research (JAMPBR), 1*(11), 392-402.

[35] Moghadam,A M . (**2026**). Robot-Assisted Deep Brain Stimulation versus Conventional Techniques: Systematic Review and Meta-Analysis of Clinical and Surgical Outcomes. *Medicinal, Psychological, and Health Research Journal (MPHRJ), 2*(2), 147-155.

[36] Moghadam,A M . (**2026**). Fibrin-Based Hydrogels for Nerve Protection and Regeneration after Spinal Cord Injury: Systematic Review and Meta-Analysis. *Medicinal, Psychological, and Health Research Journal (MPHRJ), 2*(2), 106-116.

[37] Mehrasa,P and Eghdam Zamiri,R. (**2026**). Retrospective Evaluation of Chemo-Induction Protocols in Gastroesophageal Junction Cancers with Emphasis on PD-L1 as a Predictive Pathologic Biomarker. *Medicinal, Psychological, and Health Research Journal (MPHRJ), 2*(4), 276-284.

[38] Moghadam,A M . (**2026**). Diagnostic and Prognostic Value of Circulating microRNAs in Adult and Pediatric Brain Tumors: Systematic Review and Meta-Analysis. *Medicinal, Psychological, and Health Research Journal (MPHRJ), 2*(3), 156-167.

[39] Moghadam,A M . (**2025**). Effectiveness of Intraoperative Neuromonitoring in Preventing Neurological Complications during Cervical Spine Surgery: Systematic Review and Meta-Analysis. *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research (JAMPBR), 1*(11), 403-411.

[40] Hosseini Kasnavieh SM, Milanifard M, Sedighi M, Hessam R. (**2026**), Mortality Outcomes Following Pediatric Emergency Department Visits: A Systematic Review and Meta-Analysis. *Med J Islam Repub Iran.* (13 Jun); 40:61.

[41] Hosseini Kasnavieh SM, Milanifard M, Sedighi M, Hessam R. (**2026**), A Systematic Review of Pain Assessment Tools in Prehospital Emergency Care: Evidence from Observational Studies. *Med J Islam Repub Iran*. (10 Jun);40:60.

[42] Hessam R, Basir Ghafouri H, Rezai M, Shaker S H, Hosseini Kasnavieh S M, Milanifard M et al . (**2026**), Hidden and Atypical Presentations of Myocarditis in Sudden Cardiac Death: A Narrative Review. *Med J Islam Repub Iran;* 40 (1) :526-536

[43] Hessam R, Basir Ghafouri H, Rezai M, Shaker S H, Hosseini Kasnavieh S M, Milanifard M et al . (**2026**), Hidden and Atypical Presentations of Myocarditis in Sudden Cardiac Death: A Narrative Review. *Med J Islam Repub Iran;* 40 (1) :526-536

[44] Sajed M, Alvandifar S, Mallahi M. (**2024**), Evaluation of Root Canal Morphology of Mandibular Premolars Using Cone-beam Computed Tomography in Golestan Province, North of Iran. *Iran Endod J.* 2024;19(3):183-188.

[45] Fakhari, S, Bilehjani, A and Bilehjani, E. (**2026**). Effect of Intraoperative Intravenous Dexmedetomidine on Oxidative Stress in Patients Undergoing Cardiac Surgery: A Systematic Review. *Medicinal, Psychological, and Health Research Journal (MPHRJ), 2*(5), 351-359.

[46] Fakhari, S, Bilehjani, A and Bilehjani, E. (**2026**). Intravenous Dexmedetomidine in Cardiomyocyte Biology: A Systematic Review. *Medicinal, Psychological, and Health Research Journal (MPHRJ)*, *2*(5), 360-371.
[47] Hussam Elddin Nabeih Khasawneh, AA., et al., (**2025**), A Novel Thiazole-Sulfonamide Hybrid Molecule as a promising Dual Tubulin/Carbonic Anhydrase IX Inhibitor with Anticancer Activity, Frontiers in Chemistry 13 (13), 13
[48] Lotfi, A R and Nouri Bayat, L. (**2026**). Incidence of Postoperative Complications Following Nasal Fracture Surgery in Adults. *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research (JAMPBR)*, *2*(2), 175-182.
[49] Moghadam, A M. (**2025**). Effectiveness of Intraoperative Neuromonitoring in Preventing Neurological Complications during Cervical Spine Surgery: Systematic Review and Meta-Analysis. *Medicinal, Psychological, and Health Research Journal (MPHRJ)*, *1*(11), 378-386.
[50] Moghadam, A M. (**2025**). Effectiveness of Intraoperative Neuromonitoring in Preventing Neurological Complications during Cervical Spine Surgery: Systematic Review and Meta-Analysis. *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research (JAMPBR)*, *1*(11), 403-411.
[51] Rezaei, M and Owaysee Osquee, H. (**2026**). Prevalence of Deep Vein Thrombosis in Patients with COVID 19 Admitted to the Intensive Care Unit. *Medicinal, Psychological, and Health Research Journal (MPHRJ)*, *2*(4), 267-275.
[52] Sadeghzadeh, A. (**2026**). Evaluating the effectiveness and safety of hyaluronic acid versus poly-L-lactic acid for facial volume restoration: A Systematic Review and Meta-analysis. *Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research (JAMPBR)*, *2*(2), 102-113.
[53] Samimi, A. Zarinabadi, S. (**2011**), Reduction of greenhouse gases emission and effect on environment, Aust. j. basic appl. sci., 5(12), 752-756
[54] Samimi, A., Zarinabadi S., Shahbazi Kootenaei AH., Azimi A., Mirzaei M., (**2019**), Use of data mining in the corrosion classification of pipelines in catalytic reforming units (CRU), *Eura. Chem. Commu.*, 1(6), 571–581
[55] Samimi, A., Zarinabadi, S. (**2012**), Application solid polyurethane as coating in oil and gas pipelines, *Chisa*, 20th International Congress of Chemical and Process Engineering and 15th Conference Pres, 2012
[56] Samimi,A. (**2025**). Investigating the Effect of Temperature and Pressure Changes in CCR Unit Reactors on Catalyst Wear and Black Dust Increase. *Iranian Journal of Chemistry and Chemical Engineering*, *44*(12), 3039-3051.
[57] Shiri, H and Ashrafi, N. (**2026**). Enhanced Recovery After Thoracotomy in the Intensive Care Unit: Current Evidence, Clinical Strategies, and Future Perspectives. *Medicinal, Psychological, and Health Research Journal (MPHRJ)*, *2*(5), 372-382.
[58] Shiri, H and Ashrafi, N. (**2026**). Post Esophageal Surgery Dysphagia and Nutritional Support in the Intensive Care Unit. *Medicinal, Psychological, and Health Research Journal (MPHRJ)*, *2*(5), 339-350.
[59] Zbuzant, M. (**2026**). Dental Implants vs. Traditional Bridges: A Comparative Clinical Review. *Medicinal, Psychological, and Health Research Journal (MPHRJ)*, *2*(3), 189-198.
[60] Zbuzant, M. (**2026**). Minimally Invasive Techniques in Modern Restorative Dentistry. *Medicinal, Psychological, and Health Research Journal (MPHRJ)*, *2*(3), 177-188.
[61] Hashemloo, A., Milanifard, M. (**2025**). Dermal Fillers: Types, Indications, and Complications Materials de Relleno: Typos, Indications Complications. Journal of Advanced in Medicinal, Pharmaceutical and Biomedical Research, 1(6), 161-170
[62] Hashemloo, A., Milanifard, M. (**2025**), Contouring Plus: A Comprehensive Approach of the Lower Third of the Face with Calcium Hydroxylapatite and Hyaluronic Acid, Medicinal, Psychological, and Health Research Journal, 1(5), 143-150
[63] Sunder Raj, K. S. (**2004**). Multi-Pressure Surface Condenser Performance Evaluation: A Case Study. *Proceedings of the ASME Power Conference.*
[64] Samimi,A. (**2025**). Investigating the Effect of Temperature and Pressure Changes in CCR Unit Reactors on Catalyst Wear and Black Dust Increase. *Iranian Journal of Chemistry and Chemical Engineering*, *44*(12), 3039-3051.
[65] Hedayati, A. Almasinia, B. Samimi, A. (**2014**), Optimize pictures of industrial radiography in corrosion and sediment recognizing in oil or gas transmit pipe lines, *International Journal of Chemistry*, 5, 20-29
[66] Samimi, A. Dokhani, S. Neshat, N. Almasinia, B. Setoudeh, M. (**2012**), The application and new mechanism of universal produce the 3-layer polyethylene coating, *International Journal of Advanced Scientific and Technical Research*, 465-473