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THE ANALYSIS STUDY OF DIAGNOSTIC ACCURACY OF SINGLE SAMPLE RULE-OUT OF HIGH-SENSITIVITY CARDIAC TROPONIN IN DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION IN EMERGENCY DEPARTEMENT: A COMPREHENSIVE SYSTEMATIC REVIEW FROM LABORATORY DEPARTMENT

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ABSTRACT

Background: High-sensitivity cardiac troponin (hs-cTn) assays has significantly enhanced the diagnostic of acute myocard infark (AMI). Recent studies have shown that hs-cTn assays can effectively rule out AMI with a single sample. This systematic review aim to evaluate the diagnostic accuracy of single sample rule-out of high-sensitivity cardiac troponin in diagnosis of acute myocardial infarction in emergency departement based on literatures of the last 10 years.

Methods: The study adhered to PRISMA 2020 standards, examining English literature from 2014 to 2024. It excluded editorials, reviews from the same journal, and submissions without a DOI. PubMed, SagePub, SpringerLink, and Google Scholar were utilized as literature sources.

Result: Initially retrieving 360 articles from online databases (PubMed, SagePub, SpringerLink and Google Scholar) eight relevant papers were selected after three rounds of screening for full-text analysis.

Conclusion: High-sensitivity cardiac troponin I assays enable rapid AMI rule-out in emergency departments, offering high sensitivity and negative predictive value. However, caution is needed when ruling in AMI, and further research is required to optimize their use.

Keyword: High-sensitivity cardiac troponin, acute myocardial infarction, single-sample rule-out

INTRODUCTION

Acute myocardial infarction (AMI) is a critical condition frequently encountered in emergency departments (EDs), where timely and accurate diagnosis is essential to prevent adverse outcomes. Patients presenting with chest pain or symptoms suggestive of acute coronary syndrome account for 5% to 10% of all ED visits, making effective triage and diagnosis crucial.[1] Historically, the diagnostic process for AMI has relied on a combination of clinical assessment, electrocardiograms (ECGs), and standard cardiac troponin assays. However, these traditional methods often required extended periods of observation, leading to increased hospital admissions and delayed diagnosis, despite the fact that only a fraction of these patients actually had AMI.[2,3]

The advent of high-sensitivity cardiac troponin (hs-cTn) assays has significantly enhanced the diagnostic landscape. For an assay to be classified as high sensitivity, it must have a total imprecision of 10% or less at the 99th percentile of the reference population and be able to measure concentrations above the limit of detection in at least 50% of the reference population.[4] These criteria ensure that hs-cTn assays provide more accurate and reliable results compared to their standard counterparts. As a result, hs-cTn assays have the potential to rule out AMI more efficiently, allowing for faster decision-making and potentially reducing unnecessary hospital admissions.[5]

Recent studies have shown that hs-cTn assays can effectively rule out AMI with a single sample. For instance, the Elecsys Troponin T high-sensitive assay and the ARCHITECTSTAT high-sensitivity troponin I assay have been evaluated for their effectiveness in early rule-out protocols.[6,7] These assays, when used at presentation and with a follow-up sample, offer high negative predictive values (NPV) and sensitivity. Additionally, the potential for using lower cut-off values, such as the limit of detection or limit of blank, has been explored as a strategy to identify very low-risk patients and exclude AMI without the need for a second measurement.[8,9]

In the UK, the National Institute for Health and Care Excellence (NICE) has provided guidelines for the clinical application of hs-cTn assays, recommending their use in early rule-out protocols.[10,11] Despite this, anecdotal evidence suggests that the transition from standard troponin assays to high-sensitivity assays has been uneven, with many institutions still relying on traditional methods. This highlights the need for further research and standardization to fully capitalize on the benefits of hs-cTn assays.[12–14]

The hs-cTnT assay, a fourth-generation modification of the standard troponin T assay, serves as a central focus of this review. Its limit of blank, limit of detection, and limit of quantification are key parameters that influence its diagnostic performance.[15,16] Understanding these technical specifications and their implications for clinical practice is essential for optimizing the use of hs-cTn assays in the ED.[17] This systematic review aim to evaluate the diagnostic accuracy of single sample rule-out of high-sensitivity cardiac troponin in diagnosis of acute myocardial infarction in emergency departement based on literatures of the last 10 years.

METHODS

PROTOCOL

The author carefully followed the rules laid out in the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020. This was done to make sure the study met all its standards. The selection of this methodological approach was specifically aimed at ensuring the precision and reliability of the conclusions drawn from the investigation.

CRITERIA FOR ELIGIBILITY

This systematic to evaluate diagnostic accuracy of single sample rule-out of high-sensitivity cardiac troponin in diagnosis of acute myocardial infarction in emergency departement based on literatures of the last 10 years. This study meticulously analyzed data on literatures to provide insights and enhance patient treatment strategies. The primary objective of this paper is to highlight the collective significance of the identified key points.

Inclusion criteria for this study entail: 1) Papers must be in English, and 2) Papers must have been published between 2014 and 2024. Exclusion criteria comprise: 1) Editorials; 2) Submissions without a DOI; 3) Previously published review articles; and 4) Duplicate entries in journals.

SEARCH STRATEGY

The keywords used for this research are diagnostic high-sensitivity cardiac troponin, acute myocardial infarction, single-sample rule-out. The Boolean MeSH keywords inputted on databases for this research are: *"High-Sensitivity"[All Fields] AND ("cardiacs"[All Fields] OR "heart"[MeSH Terms] OR "heart"[All Fields] OR "cardiac"[All Fields]) AND ("troponin"[MeSH Terms] OR "troponin"[All Fields] OR "troponins"[All Fields] OR "troponine"[All Fields]) AND (("acute"[All Fields] OR "acutely"[All Fields] OR "acutes"[All Fields]) AND ("myocardial infarction"[MeSH Terms] OR ("myocardial"[All Fields] AND "infarction"[All Fields]) OR "myocardial infarction"[All Fields])) AND ("Single-Sample"[All Fields] AND "Rule-Out"[All Fields])*

DATA RETRIEVAL

The authors assessed the studies by reviewing their abstracts and titles to determine their eligibility, selecting relevant ones based on their adherence to the inclusion criteria, which aligned with the article's objectives. A consistent trend observed across multiple studies led to a conclusive result. The chosen submissions had to meet the eligibility criteria of being in English and a full-text.

This systematic review exclusively incorporated literature that met all predefined inclusion criteria and directly pertained to the investigated topic. Studies failing to meet these criteria were systematically excluded, and their findings were not considered. Subsequent analysis examined various details uncovered during the research process, including titles, authors, publication dates, locations, study methodologies, and parameters.

QUALITY ASSESSMENT AND DATA SYNTHESIS

Each author independently evaluated the research presented in the title and abstract of the publication to determine which ones merited further exploration. The subsequent stage involved assessing all articles that met the predefined criteria for inclusion in the review. Decisions on including articles in the review were based on the findings uncovered during this evaluation process.

Table 1. Article Search Strategy

Database	**Strategi Pencarian**	***Hits***
Pubmed	*"High-Sensitivity"[All Fields] AND ("cardiacs"[All Fields] OR "heart"[MeSH Terms] OR "heart"[All Fields] OR "cardiac"[All Fields]) AND ("troponin"[MeSH Terms] OR "troponin"[All Fields] OR "troponins"[All Fields] OR "troponine"[All Fields]) AND (("acute"[All Fields] OR "acutely"[All Fields] OR "acutes"[All Fields]) AND ("myocardial infarction"[MeSH Terms] OR ("myocardial"[All Fields] AND "infarction"[All Fields]) OR "myocardial infarction"[All Fields])) AND ("Single-Sample"[All Fields] AND "Rule-Out"[All Fields])*	100
Science Direct	*((High-Sensitivity Cardiac Troponin) AND (Acute Myocardial Infarction)) AND (Single-Sample Rule-Out)*	150
Sagepub	*((High-Sensitivity Cardiac Troponin) AND (Acute Myocardial Infarction)) AND (Single-Sample Rule-Out)*	50
Google Scholar	*((High-Sensitivity Cardiac Troponin) AND (Acute Myocardial Infarction)) AND (Single-Sample Rule-Out)*	160

Table 2. JBI *Critical appraisal of Study*

Parameters	Gimenez (2015)	Boeddinghaus (2020)	Van der Linden (2018)	Pickering (2016)	Jaeger (2016)	Fabre-Estremera (2023)	Body (2020)	Nowak (2020)
1. Bias related to temporal precedence Is it clear in the study what is the "cause" and what is the "effect" (ie, there is no confusion about which variable comes first)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Bias related to selection and allocation Was there a control group?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Bias related to confounding factors Were participants included in any comparisons similar?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Bias related to administration of intervention/exposure Were the participants included in any comparisons receiving similar treatment/care, other than the exposure or intervention of interest?	No.	No.	No.	No.	No.	No.	No.	No.
5. Bias related to assessment, detection, and measurement of the outcome Were there multiple measurements of the outcome, both pre and post the intervention/exposure?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the outcomes of participants included in any comparisons measured in the same way?	No.	No.	No.	No.	No.	No.	No.	No.
Were outcomes measured in a reliable way?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
6. Bias related to participant retention Was follow-up complete and, if not, were differences between groups in terms of their follow-up adequately described and analyzed?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
7. Statistical conclusion validity Was appropriate statistical analysis used?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

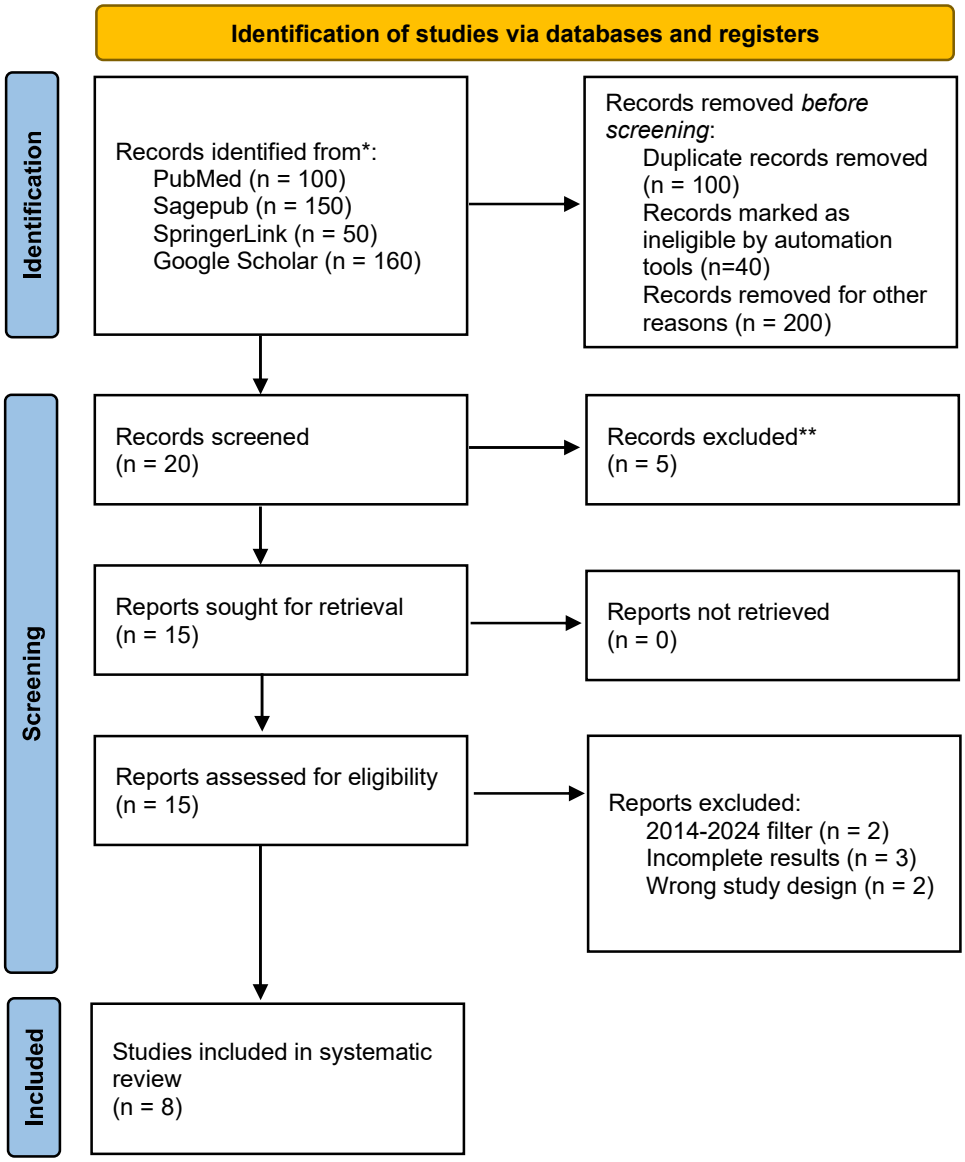

Figure 1. Article search flowchar

RESULT

The initial number of articles retrieved from online databases (PubMed, SagePub, SpringerLink, and Google Scholar) is 360 articles. After conducting three levels of screening, eight articles that directly relate to the current systematic review have been chosen for further assessment through full-text reading and analysis. Table 1 presents the selected literature included in this analysis.

Table 1. The literature included in this study

No.	Author	Origin	Method	Sample	Result
1.	Gimenez, et al.[18] (2015)	Switzerland	Prospective cohort study	1811 patients	The study evaluated the effectiveness of a 1-hour algorithm using high-sensitivity cardiac troponin I (hs-cTnI) for diagnosing acute myocardial infarction (AMI). In the validation cohort, 18% of patients were ultimately diagnosed with AMI. The algorithm classified 50.5% of patients as "rule-out," 19% as "rule-in," and 30.5% as

					"observe." The negative predictive value (NPV) for AMI in the "rule-out" group was exceptionally high at 99.6%, while the positive predictive value (PPV) in the "rule-in" group was 73.9%. Both NPV and PPV were significantly higher when compared to the classical hs-cTnI interpretation and the standard of care, which includes electrocardiograms.
2.	Boeddinghaus, et al.[19] (2020)	Switzerland	Prospective cohort study	1261 patients	In this study, myocardial infarction (MI) was the final diagnosis in 14% of the 1,261 patients. The point-of-care high-sensitivity cardiac troponin I (POC-hs-cTnI) TriageTrue assay demonstrated a high diagnostic accuracy with an area under the curve (AUC) of 0.95, which was comparable to the hs-cTnT-Elecsys (AUC: 0.94) and hs-cTnI-Architect (AUC: 0.92) assays. A single cutoff of <3 ng/l at presentation identified 45% of patients as low risk, with a negative predictive value (NPV) of 100%. Conversely, a cutoff >60 ng/l identified high-risk patients with a positive predictive value (PPV) of 76.8%. The 0/1-hour algorithm successfully ruled out 55% of patients (NPV: 100%) and ruled in 18% (PPV: 76.8%). Patients ruled out had a 0% cumulative event rate at 30 days and 1.6% at 2 years.
3.	Van der Linden, et al.[20] (2018)	Netherlands	Prospective cohort study	2225 patients	The study found that combining hs-cTnI and hs-cTnT did not significantly improve overall diagnostic accuracy for acute myocardial infarction (AMI) compared to using each marker alone. However, the combination increased the number of patients eligible for very early rule-out. Applying optimized cut-off values for the sum and product of hs-cTnI and hs-cTnT concentrations allowed 34% to 41% of patients to be ruled out with high negative predictive values. Despite these improvements in early rule-out, the combination did not enhance the ability to rule in AMI.
4.	Pickering, et al.[21] (2016)	New Zealand	Prospective cohort study	1061 patients	The study included 1,061 patients with hs-cTnI and 985 with hs-cTnT. The European Society of Cardiology (ESC) rule-in algorithm showed a positive predictive value (PPV) of 83.5% for hs-cTnI and 72.0% for hs-cTnT. However, 34.9% of AMIs were not identified using hs-cTnI, and 46.2% were missed using hs-cTnT. The sensitivity of the 99th percentile to rule out AMI was 93.2% for hs-cTnI and 94.8% for hs-cTnT, which is considered too low for clinical use.

5.	Jaeger, et al.[22] (2016)	Switzerland	Prospective cohort study	1500 patients	In this study, acute myocardial infarction (AMI) was diagnosed in 16% of patients. Using the hs-cTnI 0-/1-hour algorithm, 57% of patients were classified as "rule-out," 10% as "rule-in," and 33% as "observe." In the validation cohort, the algorithm showed a sensitivity and negative predictive value (NPV) of 100% for ruling out AMI. For ruling in AMI, the specificity was 96%, and the positive predictive value (PPV) was 70%. The NPV and PPV of this algorithm were significantly higher than the standard of care, which combines hs-cTnI with an electrocardiogram
6.	Fabre-Estremera, et al.[23] (2023)	Spain	Prospective cohort study	1171 patients	In a study of 1,171 patients, myocardial infarction (MI) occurred in 8.3%, with 78.3% being type 2 MI. The optimal rule-out threshold for hs-cTnI was <10 ng/L, identifying 44.3% of patients as low risk at presentation. This threshold had a sensitivity of 99.0% and a negative predictive value (NPV) of 99.8%. For type 1 MI, both sensitivity and NPV were 100%. The strategy also effectively identified myocardial injury with a sensitivity of 99.5% and an NPV of 99.8%. Sensitivity for predicting 30-day adverse events was 96.8%, with an NPV of 97.9%.
7.	Body, et al.[24] (2020)	UK	Prospective cohort study	999 patients	In this study involving 999 patients, 13.1% were diagnosed with acute myocardial infarction (AMI). The Siemens ADVIA Centaur hs-cTnI assay showed high sensitivity and negative predictive value (NPV) for ruling out AMI with a single blood test in the emergency department. Using the limit of quantitation (LoQ) cut-off, the assay achieved 100% sensitivity and a 99.7% NPV, ruling out 28.6% of patients. A lower cut-off of 5 ng/L had slightly lower sensitivity (99.2%) but similar NPV (99.8%), allowing for the rule-out of 50.4% of patients. Major adverse cardiac events (MACE) were rare, occurring in 0.7% of patients below the LoQ and 1.4% below the 5 ng/L cut-off.
8.	Nowak, et al.[25] (2020)	USA	Prospective cohort study	2113 patients	In a study across 29 U.S. medical centers involving 2,113 patients, the Siemens Atellica Immunoassay hs-cTnI 0/1-hour algorithm effectively ruled out acute myocardial infarction (AMI) in 50.4% of patients, with a high negative predictive value (99.7%) and sensitivity (98.7%). It ruled in 12.6% of patients, showing a positive

					predictive value of 69.4% and specificity of 95.7%. The remaining 37.1% required further evaluation, with a 5.6% incidence of AMI. The 30-day risk of death or post-discharge AMI was very low in ruled-out patients (0.2%), but higher in the other groups (2.1% for continued evaluations and 4.8% for rule-in). Similar results were observed using a 0/2- to 3-hour algorithm.

Gimenez, et al.[18] (2015) concluded that this algorithm could safely and accurately classify 70% of patients with suspected AMI, enabling rapid decision-making.

Boeddinghaus, et al.[19] (2020) showed that POC-hs-cTnI-TriageTrue assay was found to be highly accurate and comparable to well-established central laboratory assays in diagnosing suspected MI.

Van der Linden, et al.[20] (2018) showed that concluded that while new strategies combining hs-cTnI and hs-cTnT may increase the number of patients eligible for early and safe rule-out, they are less effective for ruling in AMI.

Pickering, et al.[21] (2016) concluded that while the ESC rule-in algorithm has good PPV, especially with hs-cTnI, the sensitivity for ruling out AMI is insufficient for reliable clinical application.

Jaeger, et al.[22] (2016) concluded that the hs-cTnI 0-/1-hour algorithm is a safe and effective method for early diagnosis of AMI, potentially reducing the time to diagnosis when combined with other clinical information.

Fabre-Estremera, et al.[23] (2023) showed that a single hs-cTnI measurement can quickly identify patients at low risk for MI and 30-day adverse events, potentially allowing early discharge from the emergency department.

Body, et al.[24] (2020) showed that the hs-cTnI assay is highly effective for quickly ruling out AMI, with the potential to rule out over 50% of patients using the 5 ng/L cut-off.

Nowak, et al.[25] (2020) showed that the European rapid rule-out/rule-in algorithm can be effectively applied to a diverse U.S. emergency department population.

DISCUSSION

The diagnostic accuracy of single-sample rule-out strategies using high-sensitivity cardiac troponin (hs-cTnI) for acute myocardial infarction (AMI) has shown substantial promise across various clinical studies. From a laboratory perspective, these studies highlight the significant potential of hs-cTnI assays in providing rapid and reliable results, which are crucial for effective patient management in emergency departments.[26]

The high negative predictive value (NPV) and sensitivity of hs-cTnI assays, as demonstrated in multiple studies, underscore their value in ruling out AMI with a single blood test. This capability is particularly beneficial in emergency settings, where timely decision-making is critical. The ability to accurately exclude AMI early in the diagnostic process can reduce unnecessary admissions and allow for more efficient allocation of medical resources.[18]

One of the key strengths of hs-cTnI assays is their robustness across different patient populations and clinical settings. Studies have shown that these assays maintain high diagnostic accuracy, whether used in central laboratories or as point-of-care tests. This versatility enhances their utility in various healthcare environments, making them a reliable tool for clinicians when rapid diagnosis is essential.[19]

However, while hs-cTnI assays are effective for ruling out AMI, their role in ruling in the condition is more complex. Some studies indicate that although hs-cTnI has a good positive predictive value (PPV), the sensitivity for ruling in AMI may not be sufficient for confident clinical decisions. This highlights the need for careful interpretation of hs-cTnI results, particularly when considering treatment options for patients suspected of having AMI.[20,21]

The integration of hs-cTnI assays into clinical workflows also presents opportunities for optimizing patient care. By providing rapid results with high accuracy, these assays can support more efficient patient triage, reducing the time to

diagnosis and enabling quicker treatment decisions. This is particularly important in emergency departments, where the timely identification and management of AMI can significantly impact patient outcomes.[22]

Moreover, the ability of hs-cTnI assays to perform well in diverse populations suggests their broad applicability in various healthcare settings. This makes them a valuable asset in laboratories that serve a wide range of patients, ensuring consistent diagnostic performance regardless of demographic or risk factor differences.[23]

From a laboratory management perspective, the use of hs-cTnI assays can contribute to improved workflow efficiency. The ability to rule out a significant proportion of patients with a single test reduces the need for additional testing and resource utilization, allowing laboratories to focus on more complex cases that require further evaluation.[24,25]

CONCLUSION

High-sensitivity cardiac troponin I assays enable rapid AMI rule-out in emergency departments, offering high sensitivity and negative predictive value. However, caution is needed when ruling in AMI, and further research is required to optimize their use.

REFERENCES

[1] Zhelev Z, Hyde C, Youngman E, et al. Diagnostic accuracy of single baseline measurement of Elecsys Troponin T high-sensitive assay for diagnosis of acute myocardial infarction in emergency department: systematic review and meta-analysis. *BMJ*. 2015;350:h15. doi:10.1136/bmj.h15

[2] Twerenbold R, Boeddinghaus J, Nestelberger T, et al. Clinical Use of High-Sensitivity Cardiac Troponin in Patients With Suspected Myocardial Infarction. *J Am Coll Cardiol*. 2017;70(8):996-1012. doi:10.1016/j.jacc.2017.07.718

[3] Clerico A, Zaninotto M, Aimo A, et al. Use of high-sensitivity cardiac troponins in the emergency department for the early rule-in and rule-out of acute myocardial infarction without persistent ST-segment elevation (NSTEMI) in Italy: Expert opinion document from the Study Group of Cardiac Biomarkers associated to the Italian Societies ELAS (European Ligand Assay Society, Italy Section), SIBIoC (Società Italiana di Biochimica Clinica), and SIPMeL (Società Italiana di Patologia Clinica e Medicina di Laboratorio). *Clin Chem Lab Med CCLM*. 2022;60(2):169-182. doi:10.1515/cclm-2021-1085

[4] Wu AHB. A practical guide to the implementation of high-sensitivity cardiac troponin assays into the clinical lab. *J Lab Precis Med*. 2023;8(0). doi:10.21037/jlpm-22-61

[5] Sandoval Y, Smith SW, Love SA, Sexter A, Schulz K, Apple FS. Single High-Sensitivity Cardiac Troponin I to Rule Out Acute Myocardial Infarction. *Am J Med*. 2017;130(9):1076-1083.e1. doi:10.1016/j.amjmed.2017.02.032

[6] Boeddinghaus J, Nestelberger T, Twerenbold R, et al. High-Sensitivity Cardiac Troponin I Assay for Early Diagnosis of Acute Myocardial Infarction. *Clin Chem*. 2019;65(7):893-904. doi:10.1373/clinchem.2018.300061

[7] Greenslade J, Cho E, Van Hise C, et al. Evaluating Rapid Rule-out of Acute Myocardial Infarction Using a High-Sensitivity Cardiac Troponin I Assay at Presentation. *Clin Chem*. 2018;64(5):820-829. doi:10.1373/clinchem.2017.283887

[8] Body R, Burrows G, Carley S, et al. High-Sensitivity Cardiac Troponin T Concentrations below the Limit of Detection to Exclude Acute Myocardial Infarction: A Prospective Evaluation. *Clin Chem*. 2015;61(7):983-989. doi:10.1373/clinchem.2014.231530

[9] Mueller-Hennessen M, Lindahl B, Giannitsis E, et al. Combined testing of copeptin and high-sensitivity cardiac troponin T at presentation in comparison to other algorithms for rapid rule-out of acute myocardial infarction. *Int J Cardiol*. 2019;276:261-267. doi:10.1016/j.ijcard.2018.10.084

[10] Giannitsis E, Slagman A, Hamm CW, Gehrig S, Vollert JO, Huber K. Copeptin combined with either non-high sensitivity or high sensitivity cardiac troponin for instant rule-out of suspected non-ST segment elevation myocardial infarction. *Biomarkers*. 2020;25(8):649-658. doi:10.1080/1354750X.2020.1833084

[11] Chapman AR, Mills NL. High-sensitivity cardiac troponin and the early rule out of myocardial infarction: time for action. *Heart*. 2020;106(13):955-957. doi:10.1136/heartjnl-2020-316811

[12] Lopez-Ayala P, Boeddinghaus J, Koechlin L, Nestelberger T, Mueller C. Early Rule-Out Strategies in the Emergency Department Utilizing High-Sensitivity Cardiac Troponin Assays. *Clin Chem*. 2021;67(1):114-123. doi:10.1093/clinchem/hvaa226

[13] Westwood M, van Asselt T, Ramaekers B, et al. High-sensitivity troponin assays for the early rule-out or diagnosis of acute myocardial infarction in people with acute chest pain: a systematic review and cost-effectiveness analysis. *Health Technol Assess*. 2015;19(44):1-234. doi:10.3310/hta19440

[14] Joyce LR, Pickering JW, Than M. Ruling out acute myocardial infarction based on a single high-sensitivity troponin measurement in the emergency department: a clinical practice review. *J Lab Precis Med*. 2023;8(0). doi:10.21037/jlpm-23-20

[15] Giuliani S, Dieplinger B, Mueller T. Head-to-head comparison of three different high-sensitivity cardiac troponin assays for early rule-in and rule-out of acute myocardial infarction. *J Lab Precis Med*. 2019;4(0). doi:10.21037/jlpm.2018.12.07

[16] Twerenbold R, Boeddinghaus J, Nestelberger T, et al. How to best use high-sensitivity cardiac troponin in patients with suspected myocardial infarction. *Clin Biochem*. 2018;53:143-155. doi:10.1016/j.clinbiochem.2017.12.006
[17] Ricci F, Neumann JT, Rübsamen N, et al. High-sensitivity troponin I with or without ultra-sensitive copeptin for the instant rule-out of acute myocardial infarction. *Front Cardiovasc Med*. 2022;9. doi:10.3389/fcvm.2022.895421
[18] Rubini Gimenez M, Twerenbold R, Jaeger C, et al. One-hour Rule-in and Rule-out of Acute Myocardial Infarction Using High-sensitivity Cardiac Troponin I. *Am J Med*. 2015;128(8):861-870.e4. doi:10.1016/j.amjmed.2015.01.046
[19] Boeddinghaus J, Nestelberger T, Koechlin L, et al. Early Diagnosis of Myocardial Infarction With Point-of-Care High-Sensitivity Cardiac Troponin I. *J Am Coll Cardiol*. 2020;75(10):1111-1124. doi:10.1016/j.jacc.2019.12.065
[20] van der Linden N, Wildi K, Twerenbold R, et al. Combining High-Sensitivity Cardiac Troponin I and Cardiac Troponin T in the Early Diagnosis of Acute Myocardial Infarction. *Circulation*. 2018;138(10):989-999. doi:10.1161/CIRCULATIONAHA.117.032003
[21] Pickering JW, Greenslade JH, Cullen L, et al. Validation of presentation and 3 h high-sensitivity troponin to rule-in and rule-out acute myocardial infarction. *Heart*. 2016;102(16):1270-1278. doi:10.1136/heartjnl-2015-308505
[22] Jaeger C, Wildi K, Twerenbold R, et al. One-hour rule-in and rule-out of acute myocardial infarction using high-sensitivity cardiac troponin I. *Am Heart J*. 2016;171(1):92-102.e5. doi:10.1016/j.ahj.2015.07.022
[23] Fabre-Estremera B, Smith SW, Sandoval Y, et al. Rapid Rule-Out of Myocardial Infarction Using a Single High-Sensitivity Cardiac Troponin I Measurement Strategy at Presentation to the Emergency Department: The SAFETY Study. *Clin Chem*. 2023;69(6):627-636. doi:10.1093/clinchem/hvad033
[24] Body R, Morris N, Collinson P. Single test rule-out of acute myocardial infarction using the limit of detection of a new high-sensitivity troponin I assay. *Clin Biochem*. 2020;78:4-9. doi:10.1016/j.clinbiochem.2020.02.014
[25] Nowak RM, Christenson RH, Jacobsen G, et al. Performance of Novel High-Sensitivity Cardiac Troponin I Assays for 0/1-Hour and 0/2- to 3-Hour Evaluations for Acute Myocardial Infarction: Results From the HIGH-US Study. *Ann Emerg Med*. 2020;76(1):1-13. doi:10.1016/j.annemergmed.2019.12.008
[26] Reichlin T, Twerenbold R, Wildi K, et al. Prospective validation of a 1-hour algorithm to rule-out and rule-in acute myocardial infarction using a high-sensitivity cardiac troponin T assay. *Can Med Assoc J*. 2015;187(8):E243-E252. doi:10.1503/cmaj.141349