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USE OF HIGH SENSITIVITY CARDIAC TROPONIN AS AN EARLY DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION (IMA): SYSTEMATIC REVIEW

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ABSTRACT
Acute myocardial infarction (IMA) is a leading cause of morbidity and mortality worldwide, so early diagnosis is needed to detect the disease. High sensitivity troponin assessment is a biomarker examination that can diagnose Acute Myocardial Infarction. The purpose of this study is to determine the effectiveness of the use of High Sensitivity Cardiac Troponin and as an early diagnosis of Acute Myocardial Infarction (IMA). This study is a systematic review study of 4 databases, namely Scopus, PubMed, EBSCO Host, and Sage Journals, with the keywords "high sensitivity cardiac troponin" AND "acute myocardial infarction". The results of the study followed the protocol and rules of Preferred Reporting Items for Systematic Reviews (PRISMA) and used the JBI tool to assess the quality of the articles to be analyzed. The inclusion criteria in this study are articles taken in the last 5 years using the Randomized Control Trials (RCT) method and observational studies. A literature search yielded 452 research articles, of which 10 were included after several selections in a systematic review and were eligible for analysis. The ten articles used random comparison and observation research methods. All articles show that high sensitivity cardiac troponin has high sensitivity and specificity in supporting the diagnosis of acute myocardial infarction. This shows that high sensitivity cardiac troponin is one of the biomarker examinations that has high sensitivity in identifying patients with a high risk of acute myocardial infarction. This finding is expected to be a reference for health workers to determine the initial diagnosis of Acute Myocardial Infarction (IMA).

Keywords: acute myocardial infarction; diagnosis; high sensitivity cardiac troponin

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INTRODUCTION

Acute Myocardial Infarction (IMA) is one of the cardiovascular emergency diseases that is the leading cause of morbidity and mortality globally (Artawan *et al.*, 2022; PERKI, 2024). Acute myocardial infarction, often referred to as a heart attack, is a serious, life-threatening condition in which an area of local dead tissue within the heart muscle occurs. This condition requires immediate treatment to prevent more serious or fatal complications (Sofiah & Roswah, 2022). In 2020, it is estimated that around 19 million deaths (37%) worldwide are caused by cardiovascular diseases including Acute Myocardial Infarction (PERKI, 2024). In Indonesia, although there is no specific epidemiological data on Acute Myocardial Infarction, the overall prevalence of heart disease is recorded at 1.5%, or around 1,017,290 cases, which also includes Acute Myocardial Infarction (Riskesdas, 2018).

As ischemic heart disease remains the leading cause of death globally, a prompt and precise diagnosis is essential for patients suspected of suffering from Acute Myocardial Infarction to achieve this, requiring not only a clear definition of myocardial infarction (IM), but also a simple and easy-to-understand diagnosis algorithm (Lazar et al., 2022). Based on the World Health Organization (WHO), the diagnosis of IMA is based on the acquisition of 2 or more than 3 criteria, namely: based on anamnesis or history of chest pain, electrocardiography changes, and increased biochemical markers of heart muscle necrosis (Rochfika, 2019).

Several biomarkers play an important role in diagnosis, risk stratification, management guidance, and clinical decision-making in patients with symptomatic signs of myocardial infarction (Christenson & Christenson, 2013). Specific cardiac markers, such as cardiac troponin formed by myocardial cell damage, have a very important role in the diagnosis of Acute Myocardial Infarction (AMI) (Harahap & Margata, 2018). The use of high-sensitivity cardiac troponin (hs-cTn) tests has now become an integral part of routine practice in many laboratories around the world in the early assessment of typical chest pain. High-sensitivity cardiac troponins are also a significant prognostic marker for long-term incidence and mortality, both in cardiovascular disease (CVD) and some non-CVD conditions. The assessment of hs-cTn plays a very important role as a prognostic factor in Acute Myocardial Intuition. The use of hs-cTn can speed up the diagnosis process of myocardial infarction (IM), which is crucial for patients who come with complaints of chest pain (Lazar et al., 2022). The aim of this study was to determine the use of High Sensitivity Cardiac Troponin as an early diagnosis of Acute Myocardial Infarction (AMI).

METHOD

A systematic review is a comprehensive summary of various studies conducted with a focus on a specific theme. A literature search was conducted in November 2024. In this study, the data used is secondary data obtained not through direct observation but from the results of research that has been carried out by previous researchers. This secondary data source is in the form of reputable journal articles published at the national and international levels and have themes that are in accordance with the predetermined research focus. The literature search process was carried out in the last 5 years (2019-2024) in English, selected from several indexed electronic databases such as Scopus, PubMed, EBSCO Host, and Sage Journals, and the writing of article search results followed the appropriate protocols and rules using Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA). Article or journal searches use keywords and boolean operators (AND, OR NOT or AND NOT) that are used to expand or define the search, making it easier to determine which article or journal to use. The keywords in the systematic review adjusted to the Medical Subject Heading (MeSH) of the article were identified with keywords ("High Sensitivity Cardiac Troponin" AND "Diagnosis" AND Acute Myocardial Infarction") The article search strategy was carried out using the PICOT framework. Article searches were focused on studies that met certain inclusion criteria, including studies that reviewed patients who underwent a High Sensitivity Cardiac Troponin biomarker examination. Studies must show positive results and follow randomized controlled trials (RCTs) or observations.

Search Methods

Table 1.
PICOT Framework

PICOT	Inclusion Criteria	Exclusion Criteria
Population	Acute Myocardial Infarction (IMA)	Studies that did not review patients with Acute Myocardial Infarction (IMA)
Intervention	*High Sensitivity Cardiac Troponin Examination*	Research on biomarker examinations other than *High Sensitivity Cardiac Troponin*
Comparison	*No inclusion criteria*	No exclusion criteria
Outcomes	*A study explaining that High Sensitivity Cardiac Troponin has* high sensitivity in detecting Acute Myocardial Infarction (IMA)	Studies that did not discuss *High Sensitivity Cardiac Troponin as a biomarker test that can detect* Acute Myocardial Infarction (IMA)
Time	2019-2024	Before 2019
Design	Randomised control trials (RCTs) , Observational design	Review and analysis: literature review, systematic review, meta analysis,
Language	English	In addition to English

The inclusion criteria in this study include articles published in the last five years using the Randomized Control Trial (RCTs) and observation methods. The purpose of this study is to analyze in depth the sensitivity of High Sensitivity Cardiac Troponin in detecting acute myocardial infarction. Based on the search using keywords and the selection carried out, 10 articles were found out of a total of 452. Selection is carried out using PRISMA (Figure 1) in accordance with PRISMA guidelines. The first step after conducting a search of 4 databases, the researcher found 452 articles. Then duplicate deletion was carried out through the delay application and 449 articles were left for feasibility review. Screening articles based on title identification were obtained 97 articles. The feasibility test of full text articles left 28 research articles and articles for review there are 10 articles. After identifying, there were all articles using randomized control trials (RCTs) and observational.

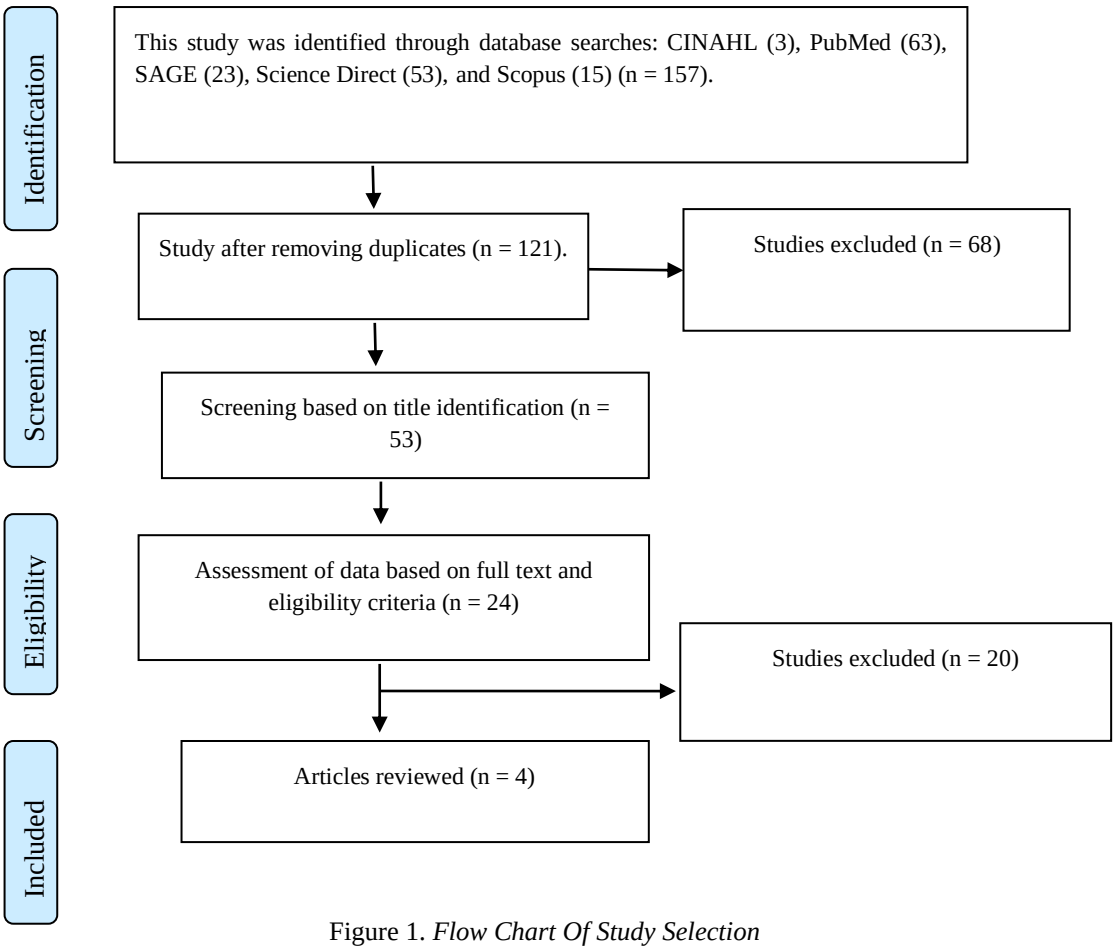

Figure 1. *Flow Chart Of Study Selection*

The inclusion criteria in this study include articles published in the last five years using the Randomized Control Trial (RCTs) and observation methods. The purpose of this study is to analyze in depth the sensitivity of High Sensitivity Cardiac Troponin in detecting acute myocardial infarction. Based on the search using keywords and the selection carried out, 10 articles were found out of a total of 452. To determine the bias of a study, The Joanna Briggs Institute (JBI) for Randomised Controlled Trials (RCTs) and the Observational methodology with a cross sectional approach were used to analyse the quality of each methodology from each study (n=10) to assess the criteria using 'yes', 'no', or 'unclear' 'Not applicable' scores. The results of this assessment are then calculated and summed up. In order for a study to meet the critical assessment criteria, a minimum of 50% of the existing criteria must be met. These boundary values have been approved by the study researchers who were included in the inclusion criteria. Systematic Literature Review (SLR) is the approach used in this study. The systematic observation method aims to obtain maximum results through a structured and organized literature review process. After analyzing the relevant literature, all the data collected will be

evaluated, and from the analysis conclusions will be drawn to provide an accurate, clear, and relevant picture of the situation being studied. The Systematic Literature Review (SLR) method consists of three main components: first, we conduct research to gather information; second, we apply the information that has been obtained; and third, we review what we have learned from the information. In carrying out literature research, there are three stages that must be passed, namely conducting an investigation and identifying research questions; The research stage includes the collection of research questions and sources, the implementation of research, the collection of quality data, as well as data testing and the preparation of the final report.

RESULT

Researchers use narrative tables to compile and summarize relevant studies. This table serves to identify findings that are in accordance with the questions and objectives of the research. The data entered in the table includes information such as author's name, year of publication, research design, sample size, findings and conclusions. Of the 10 articles analyzed, 1 article discusses hs-cTn in general for the identification of Acute Myocardial Infarction, 5 articles discuss hs-cTnI for the identification of Acute Myocardial Infarction, and 4 articles discuss hs-cTnT for the identification of Acute Myocardial Infarction. The results of the analysis of 10 journals prove that both hs-cTnI and hs-cTnT have high sensitivity in diagnosing patients with a high risk of acute myocardial infarction.

Table 2.
JBI Critical appraisal checklist for randomized controlled trials

Citation	Criteria													Results
	1	2	3	4	5	6	7	8	9	10	11	12	13	
(Chapman et al., 2020)	√	√	√	√	√	√	√	√	√	√	√	√	√	13/13 (100%)
(Lee et al., 2023)	√	√	√	√	√	√	√	√	√	√	√	√	√	13/13 (100%)

Table 3.
JBI Critical Appraisal Checklist for Analytical Cross Sectional Studies

Citation	Criteria								Results
	1	2	3	4	5	6	7	8	
(Andersen et al., 2021)	√	√	√	√			√	√	6/8 (75%)
(McCord et al., 2021)	√	√	√	√	√	√	√	√	8/8 (100%)
(Kim et al., 2020)	√	√	√	√	√	√	√	√	8/8 (100%)
(Cullen et al., 2023)	√	√	√	√	√		√	√	7/8 (88%)
(Gilje et al., 2024)	√	√	√	√	√	√	√	√	8/8 (100%)
(Silva et al., 2023)	√	√	√	√	√		√	√	7/8 (88%)
(Chen et al., 2024)	√	√	√	√	√	√	√	√	8/8 (100%)
(Johannessen et al., 2021)	√	√	√	√	√	√	√	√	8/8 (100%)

Table 4.
Study Characteristics

Writer	Method	Sample	Early Diagnosis	Research Results	Conclusion
(Chapman et al., 2020)	Randomised Clinical Trial	48,282 patients	hs-cTn	The application of high-sensitivity cardiac troponin tests increased the diagnosis of type 1 myocardial infarction by 11% (510 out of 4,471), type 2 myocardial infarction by 22% (205 out of 916), and acute and chronic myocardial injury by 36% (443 out of 1,233) and 43% (389 out of 898), respectively.	Based on the results of the research and discussion, it can be concluded that the implementation of the cardiac troponin test with high sensitivity and identifying patients with a high risk of myocardial infarction events.
(Lee et al., 2023)	Randomised Clinical Trial	10,360 patients	*hs-cTnI*	A total of 10,360 patients showed cardiac troponin concentrations higher than the 99th percentile, with 1,771 (17.1%) of them experiencing a change in	The application of the high-sensitivity cardiac troponin I test in the evaluation of patients

Writer	Method	Sample	Early Diagnosis	Research Results	Conclusion
				classification after the application of the high sensitivity test. The incidence of myocardial infarction or death in the five years before and after the application of the high-sensitivity test was recorded at 29.4% (5,588/18,978) and 25.9% (7,591/29,304), respectively, in overall patients (adjusted hazard ratio 0.97, 95% confidence interval 0.93 to 1.01), as well as 63.0% (456/720) and 53.9% (567/1,051), in patients reclassified by high-sensitivity test (0.82, 0.72 to 0.94). After the application of the high-sensitivity test, a decrease in myocardial infarction or subsequent death was seen in patients with non-ischemic myocardial injury (0.83, 0.75 to 0.91), but not in patients with type 1 or type 2 myocardial infarction (0.92, 0.83 to 1.01 and 0.98, 0.84 to 1.14).	with suspected acute coronary syndrome was associated with a reduced risk of myocardial infarction or death within five years in patients reclassified by the test. The most significant improvement in clinical outcomes was found in patients with non-ischemic myocardial injury, suggesting that the benefits of this test extend beyond just the identification of myocardial infarction.
(Andersen et al., 2021)	*Observational study*	1370 patients	*hs-cTnI*	1370 patients who had hs-cTnI results at admission: with a median age (Q1-Q3) of 65 (52–74) years, 43% of whom were female, and 22% had a history of myocardial infarction (IM). Successfully confirmed IM in 118 patients (8.6%). Overall, 470 patients (34%) were classified as early presenters, 770 patients (56%) as late presenters, and 130 patients (9%) had unknown onset. By applying diagnostic thresholds, IM was successfully ruled out in 370 patients (27%) at the time of admission: consisting of 134 patients (29%) early presenters, 206 patients (27%) late presenters, and 30 patients (23%) with unknown onset. These results showed an overall negative predictive value of 100% (CI 95%: 99.0–100%), with a value of 100% (97.3–100%) for early presenters and 100% (98.2–100%) for late presenters. The sensitivity was also very high in both groups.	Myocardial infarction (IM) can be safely detected in all patients presenting with chest pain ≤3 hours, when using a single hs-cTnI value of <3 ng/L as the diagnostic threshold.
(McCord et al., 2021)	*Observational study*	575 patients	*hs-cTnI*	A total of 567 subjects had all the necessary data for data analysis. AMI is diagnosed in 46 (8.1%) patients. Two hundred and thirty-two (40.9%) individuals had an hs-cTnI presentation outcome of <4.0 ng/L. None of the patients with an initial hs-cTnI <4.0 ng/L experienced AMI, resulting in a negative predictive value of 100.0% and a sensitivity of 100%, and a good prognosis (no AMI or heart-related death at 30 days). In this single-center ED study, a new initial hs-cTnI value of <4.0 ng/L effectively detected AMI in 40.9% of all patients who came to the ED and had suspicious symptoms for AMI.	Based on the results of the study, it can be concluded that the implementation of the hs-cTnI test can identify patients with a high risk of myocardial infarction.
(Kim et al., 2020)	*Observational study*	581 patients	*hs-cTnI*	The threshold value for predicting acute myocardial infarction (AMI) is 16.2 ng/L for the absolute change of hs-cTnI and 42.1% for the relative change of hs-cTnI. The area under the hs-cTnI curve (AUC) for the diagnosis of AMI was greater for	The absolute change in hs-cTnI levels within 3 hours of the patient coming to the ER proved to be more effective compared to the relative

Writer	Method	Sample	Early Diagnosis	Research Results	Conclusion
				absolute change compared to relative change, which was 0.96 (95% confidence interval [CI], 0.92–0.98) compared to 0.89 (95% CI, 0.85–0.93) (P = 0.014).	change in diagnosing acute myocardial infarction (AMI). An increase or decrease in hs-cTnI of more than 16.2 ng/L in this 3-hour period can be a useful indicator for identifying AMI in patients presenting with suspicious symptoms in the emergency room.
(Cullen et al., 2023)	*Observational study*	1994 patients	*hs-cTnI*	A total of 1,994 patients were involved in this study, with an average age of 56.2 years (SD = 15.6), and 44.9% of them were women. Of these, 118 patients (5.9%) were diagnosed with acute myocardial infarction (AMI). The 2-hour algorithm classified 61.3% of patients as low-risk, with a sensitivity of 99.1% (94.0%–99.9% confidence interval) and a negative predictive value (NPV) of 99.9% (99.3%–100% confidence interval). As many as 24.4% of patients are considered to be at medium risk. When using criteria to identify high risk, a total of 252 patients (14.3%) were detected, with a specificity of 91.5% (confidence interval 88.7%–93.6%) and a positive predictive value (PPV) of 42.0% (confidence interval 35.6%–48.7%).	hs-cTnI is a safe and efficient risk assessment in emergency patients with suspected AMI.
(Gilje et al., 2024)	*Observational study*	24,973 patients	*hs-cTnT*	The threshold of hs-cTnT at 0 hours indicating an NPV of ≥99.5% for the primary endpoint was <9 ng/L (NPV: 99.6% with 95% CI: 99.5–99.7). With this threshold, the sensitivity obtained reached 96.2% (95% CI: 95.2–97.1), and 59.7% of patients were classified as low risk, higher compared to 35.8% and 43.9% at the 0-hour hs-cTnT thresholds <5 ng/L and <6 ng/L. Similar results were also found in the validation group and showed better performance in patients whose 0-hour hs-cTnT measurements were taken more than 3 hours after symptom onset, as well as in patients with non-ischemic ECG and a history of low risk.	The hs-cTnT limit of 0 hours <9 ng/L can safely identify AMI or death within 30 days in the majority of patients with chest pain, and is shown to be more effective than the currently recommended <5 ng/L and <6 ng/L limits.
(Silva et al., 2023)	*Observational study*	5,497 patients	*hs-cTnT*	In the retrospective analysis, 1,091 patients had troponin values of <5 ng/L and no cardiovascular deaths at day 30 in this group. Among all 4,914 patients, the risk of AMI or death from cardiovascular disease within 30 days increased according to troponin levels: 0% in the < group 5 ng/L, 0.6% between 5 and 14 ng/L, 2.2% between 14 and 42 ng/L, 6.3% between 42 and 90 ng/L, and 7.7% at ≥ 90 ng/L level.	The hs-cTnT level category has also been shown to have good accuracy in differentiating the risk level of patients, with an excellent prognosis of cardiovascular mortality
(Chen et al., 2024)	*Observational study*	12.900 patient	*hs-cTnT*	In 12,900 patients, 3,247 patients had an estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73 m2. Even in the absence of AMIs, 50.2% of participants with an eGFR of <60 mL/min/1.73 m2 had an hs-cTnT	The specific limit value of kidney function of hs-cTnT can help doctors to accurately diagnose AMI and avoid the potential for overtreatment in practice.

Writer	Method	Sample	Early Diagnosis	Research Results	Conclusion
				concentration of ≥14 ng/L. Using 14 ng/L as the threshold for hs-cTnT to diagnose AMI led to significantly reduced specificity and positive predictive values in patients with renal dysfunction, compared to patients with normal renal function. Specific limits of renal function were set at 14, 18 and 48 ng/L for patients with eGFR >60, 60–30 and <30 mL/min/1.73 m2, respectively. Using the new cut-off values, the specificity for diagnosing AMI in participants with varying degrees of renal dysfunction increased significantly (from 9.1%–52.7% to 52.8–63.0%) without sacrificing sensitivity (96.6%–97.9%). A similar improvement in diagnostic accuracy was observed in the validation group (n = 8012).	
(Johannessen et al., 2021)	*Observational study*	1711 patients	*hs-cTnT*	Among the 1711 patients, 61 (3.6%) were diagnosed with AMI, and 569 (33.3%) patients were prescribed for a single examination (<5 ng/L). Without AMI in this group, the negative predictive value (NPV) and sensitivity were both 100.0% (95% CI 99.4% to 100.0% and 94.1% to 100.0%, respectively), and specificity 34.5% (32.2% to 36.8%). The original HEART score sorted out more patients as low risk (n=871), but missed five AMIs (NPV 99.4% (98.7% to 99.8%); sensitivity 91.8% (81.9% to 97.3%) and specificity 52.5% (50.0% to 54.9%)). The modified HEART score increased low risk sensitivity to 98.4% (91.2% to 100.0%), with a specificity of 38.7% (36.3% to 41.1%). The incidence of AMI or 90-day mortality in the single rule-out group and the original and modified low-risk HEART group were 0.0%, 0.7%, and 0.2%, respectively.	In primary care emergency situations, the approach with a single hs-cTnT strategy is more effective than the HEART score in ruling out AMIs. This rapid and safe approach can improve the assessment of patients with chest pain outside of hospital with adequate medical support.

DISCUSSION

Heart disease is a major public health problem recently. Delays in treatment are still the main problem in treating acute myocardial infarction (Rosjidi, 2019). A Delay in diagnosis of Acute Myocardial Infarction (AMI) can increase the risk of death in patients. Although there are some cases where patients survive despite late diagnosis, patients who survive the early stages of treatment tend to die within the first year after an AMI diagnosis is made (Pickering et al., 2018). This delay is often due to lack of suspicion of acute myocardial infarction, the presence of unusual symptoms, and the peak time of onset of non-cardiac causes of chest pain (Safdar, 2019). Fast and appropriate treatment by a doctor is very important to increase the chances of recovery and reduce the death rate due to AMI. Therefore, it is important to speed up the diagnosis and treatment process, as well as increase medical alertness in dealing with symptoms that lead to AMI (Amrullah *et al*., 2022)

After evaluating and ruling out clinical signs as well as ECGs indicating Acute Myocardial Infarction with ST Elevation (IMA-EST) or Acute Coronary Syndrome Non-Elevation ST (SKA-NEST) with very high risk, biomarkers have an important role as an aid in the diagnosis, risk assessment, and management of patients suspected of having Acute

Myocardial Infarction. Measurement of biomarkers for injury to heart cells, especially using high-sensitivity cardiac troponin (hs-cTn), is highly recommended for all patients suspected of having Acute Myocardial Infarction. In patients with myocardial infarction, cTn levels will increase rapidly (usually within an hour using the hs-cTn test) after the onset of symptoms and remain high for several days. The best cardiac biomarker to use is high-sensitivity cardiac troponin T or I (hs-cTnT/I), with a minimum value higher than the 99th percentile of the upper reference limit The hs-cTn test has various advantages, including a very high negative predictive value and a shorter "troponin blind" interval, which allows for faster detection of Acute Myocardial Infarction (AMI) (Chapman et al., 2017). This systematic review found 10 research articles that revealed that the examination of the biomarker hs-cTn either hs-cTnT or hs-cTnI has high sensitivity in diagnosing patients at high risk of developing Acute Myocardial Infarction.

Several large multicenter studies have consistently shown that hs-cTn improves the diagnostic accuracy of myocardial infarction (IM) compared to conventional troponin I/T tests, especially in patients who arrive immediately after starting to feel chest pain. This makes it possible to immediately carry out the 'rule-in' and 'rule-out' process of myocardial infarction (PERKI, 2024a). It can be concluded that high-sensitivity cardiac troponin (hs-cTn) is currently the gold standard in the diagnosis of Acute Myocardial Infarction (IMA), as it is a specific indicator for heart tissue damage (Wu et al., 2021).

This is supported by research conducted by Chapman *et al* (2020) which shows that the cardiac troponin test has high sensitivity and identifies patients at high risk of experiencing myocardial infarction.Application of high-sensitivity cardiac troponin testing increased the diagnosis of type 1 myocardial infarction by 11% (510 of 4,471), type 2 myocardial infarction by 22% (205 of 916), and acute and chronic myocardial injury by 36% (443 of 1,233) and 43% (389 of 898), respectively. Other research that supports this is research conducted by McCord *et al* (2021) that the hs-cTnI test can identify patients who are at high risk of experiencing myocardial infarction. A total of 567 subjects had all the data required for data analysis. AMI was diagnosed in 46 (8.1%) patients. Two hundred thirty-two (40.9%) people had a presenting result of hs-cTnI <4.0 ng/L. No patients with initial hs-cTnI <4.0 ng/L experienced AMI, resulting in a negative predictive value of 100.0% and sensitivity of 100%, as well as a good prognosis (no AMI or cardiac-related death within 30 days). In this single-center ED study, a new baseline hs-cTnI value of <4.0 ng/L effectively detected AMI in 40.9% of all patients who presented to the ED and had symptoms suspicious for AMI. This is also supported by research conducted by Cullen *et al* (2023) which shows that hs-cTnI is a safe and efficient risk assessment in emergency patients with suspected AMI. A total of 1,994 patients were involved in this study, with an average age of 56.2 years (SD = 15.6), and 44.9% of them were women. Of these, 118 patients (5.9%) were diagnosed with acute myocardial infarction (AMI). The 2-hour algorithm classified 61.3% of patients as low-risk, with a sensitivity of 99.1% (94.0%–99.9% confidence interval) and a negative predictive value (NPV) of 99.9% (99.3%–100% confidence interval). As many as 24.4% of patients are considered to be at medium risk. When using criteria to identify high risk, a total of 252 patients (14.3%) were detected, with a specificity of 91.5% (confidence interval 88.7%–93.6%) and a positive predictive value (PPV) of 42.0% (confidence interval 35.6%–48.7%).

CONCLUSION

The review showed that the measurement of biomarkers hs-cTn, either hs-cTnT or hs-cTnI, has high sensitivity in diagnosing patients at high risk of acute myocardial infarction because it is a specific

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