#### REVIEW

# Chest Pain Risk Stratification in the Emergency Department: Current Perspectives

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**Abstract:** Chest pain is the second leading cause of all emergency department (ED) visits in adults in the United States, with nearly 11 million encounters yearly. While identifying low-risk patients is crucial for early discharge, identifying high-risk patients in ED is vital in timely and appropriate acute coronary syndrome (ACS) management. Traditional methods such as physical examination, cardiac markers, or imaging tests cannot reliably confirm or rule out ACS; they cannot be singularly incorporated to risk stratify patients. Various clinical risk scores have been proposed to address this challenge for risk stratification in patients being evaluated for suspected ACS. The ideal risk score should demonstrate high sensitivity and specificity to accurately differentiate between patients with varying levels of risk, particularly in identifying those at high risk for major adverse cardiovascular events. Simultaneously, an ideal scoring system should also be able to compute information for other non-coronary etiologies of chest pain that require time-sensitive interventions and workups (eg, aortic dissection and pulmonary embolism). In this review, we have assembled major risk scores used for risk stratification in patients with acute chest pain in ED. We have abbreviated their salient features to assist readers in their clinical decision-making.

Keywords: angina, acute coronary syndrome, ED, cardiac mortality, adverse events

#### Introduction

Chest pain is the second leading cause of emergency department (ED) visits in adults in the United States. Each year, there are nearly 11 million chest pain encounters, accounting for approximately 5.5% of all visits to the ED.<sup>1</sup> Although less than 10% of patients with chest pain are diagnosed with acute coronary syndrome (ACS), testing for diagnosis burdens the healthcare system in the United States, costing \$ 10–13 billion annually.<sup>2</sup> A low risk for chest pain is a 30-day risk of death or major adverse cardiac events (MACE), which is less than 1%.<sup>3</sup> Different strategies for chest pain risk stratifications used by ED physicians to identify such low-risk patients are crucial to optimizing resource allocation, early discharge, and avoiding unnecessary hospital admissions.<sup>4,5</sup> However, identifying high-risk patients in the emergency room is vital in ensuring timely and appropriate acute coronary syndrome (ACS) care.<sup>6</sup> Additionally, discharge of patients with high risk from the emergency room is associated with increased medical liability lawsuits, as chest pain and ACS are the most common causes of malpractice lawsuits against ED physicians in the United States.<sup>7</sup>

Clinical assessment of patients with the utility of history, physical examination, or initial diagnostic tools, such as the electrocardiogram (EKG) or cardiac biomarkers, have been traditionally used methods to distinguish low-risk patients from patients with ACS; however, none of these methods can reliably rule in or exclude ACS. To meet this challenge, several clinical risk scores (eg, HEART, TIMI, etc.) have emerged for risk stratification of patients to evaluate suspected ACS.<sup>8</sup> Recently, a new biomarker, high-sensitivity cardiac troponin (hs-cTn), has further enhanced the chest pain risk stratification, allowing for a rapid rule-in and rule-out strategy.<sup>9</sup>

This review will examine and evaluate the various risk stratification methods used to assess patients with chest pain. We will explore the effectiveness and reliability of different clinical tools, cardiac markers, and pathways in identifying

© 024 Yukselen et al. This work is published and licensed by Dove Medical Press Limited. The full terms of this license are available at https://www.dovepress.com/terms. work you hereby accept the Terms. Non-commercial uses of the work are permitted without any further permission for Dove Medical Press Limited, provided the work is properly attributed. For permission for commercial use of this work, please se paragraphs 4.2 and 5 of our Terms (https://www.dovepress.com/terms.php). low-risk individuals who can be safely discharged from the emergency department. Furthermore, we will assess the role of scoring systems, such as TIMI and HEART scores, in aiding clinicians in decision-making and optimizing resource allocation. By synthesizing the current evidence and highlighting the strengths and limitations of various risk stratification approaches, this review aims to provide a comprehensive understanding of the best practices for risk assessment in chest pain patients in ED settings.

# Discussion

#### Cardiac Biomarkers

#### cTn and Hs-cTn

Cardiovascular biomarkers play a crucial role in evaluating chest pain for the diagnosis of acute myocardial infarction (AMI), risk stratification, and differentiation of cardiac and non-cardiac causes. Cardiac troponins (cTn-I and cTn-T) are cardiac-specific enzymes extensively studied and validated as diagnostic markers for AMI. A cTn concentration above the 99th percentile upper reference limit indicates myocardial injury.<sup>10</sup> It is important to note that different assays may have slightly different 99th percentile upper reference limits due to variations in sensitivity and specificity. Therefore, the manufacturer's assay should be considered when interpreting cTn results in clinical practice.<sup>11</sup> Although creatine kinase MB (CK-MB) and myoglobin are also widely used cardiac enzymes, cTn is preferred for chest pain assessment for being superior to these enzymes.<sup>3</sup>

The introduction of high-sensitivity cardiac troponin (hs-cTn) assays has brought significant advancements to the diagnostic testing landscape for ACS. The greater sensitivity and negative predictive value (NPV) of hs-cTn assays compared with cTn have led to the widespread adoption of hs-cTn as the preferred biomarker to rule out patients in ED. In addition, the higher sensitivity of hs-cTn assays provides a shorter time interval to the second measurement of troponin, significantly reducing the time to diagnosis and improving efficiency in the ED. Older-generation assays often require a longer time interval between troponin measurements to allow for a sufficient increase in troponin levels for detection. However, with hs-cTn assays, detecting even small changes in troponin levels is possible, allowing for a more rapid diagnosis of AMI.<sup>9,12</sup> 0/1-h protocol with hs-cTn suggested by the European Society of Cardiology (ESC) is a useful risk assessment tool for emergency physicians to rapidly rule out AMI.<sup>13</sup>

#### Other Biomarkers

Although various other biomarkers have been suggested, none are recommended for chest pain assessment. An elevated N-terminal fraction of brain natriuretic peptide (NT-proBNP) level is associated with transient myocardial ischemia. This indicates the worst diagnosis,<sup>14</sup> recommended by ESC guidelines to predict prognosis in patients with ACS.<sup>15</sup>

High-sensitivity C-reactive protein (hs-CRP), a biochemical marker of inflammation in ischemia, has also shown value in predicting death in patients with a clinical syndrome consistent with ACS. Although measurements of hs-CRP and NT-pro-BNP are class IIa recommendations by the National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines for early risk stratification in ACS, they do not benefit management.<sup>10</sup>

D-dimer, a widely used noncardiac biomarker, holds significance in the comprehensive evaluation of patients presenting with chest pain. D-dimer should be part of initial assessment, especially if clinical suspicion is high for aortic dissection or pulmonary embolisms.<sup>9</sup>

### Early Risk Stratification and Clinical Risk Scores

Over the years, several scoring methods have been developed for early risk stratification in patients with chest pain presenting to the ED (Figure 1). By systematically assessing factors like age, risk factors, and clinical presentation; risk scores provide a standardized method for estimating the likelihood of adverse cardiac events.

The primary objectives of early risk stratification are to optimize resource allocation, guide further diagnostic testing, reduce unnecessary hospital admissions, and enhance overall patient care. These strategies facilitate efficient decision-making in busy emergency department settings, helping physicians to tailor interventions based on individual patient risks and needs, ultimately leading to improved outcomes and timely interventions for those at greatest risk.<sup>5</sup>



Figure I Timeline of Chest Pain Scoring systems created for use in the emergency department.

Abbreviations: ASPECT, Asia-Pacific Evaluation of Chest Pain Trial; ADAPT, Accelerated Diagnostic Protocol for Chest Pain Trial; EDACS, Emergency Department Assessment of Chest Pain Score; EDACS-ADP, Emergency Department Assessment of Chest Pain Score Accelerated Diagnostic Protocol; GRACE, The Global Registry of Acute Coronary Events; HEART, History, EKG, Age, Risk Factors, and Troponin; HE-MACS, History and Electrocardiogram-only Manchester Acute Coronary Syndromes; MACS, Manchester Acute Coronary Syndromes; PURSUIT, Platelet glycoprotein IIb/IIIa in Unstable angina: Receptor Suppression Using Integrilin Therapy; SVEAT, Symptoms, history of Vascular disease, Electrocardiography, Age, and Troponin; TIMI, The Thrombolysis in Myocardial Infarction; VCPR, Vancouver Chest Pain Rule.

#### **TIMI Risk Score**

Thrombolysis in Myocardial Infarction (TIMI) risk score initially focused on predicting 14-day mortality in patients with non-ST-elevation myocardial infarction (NSTEMI) and unstable angina (UA). TIMI score typically includes factors such as age, the presence of at least three risk factors for coronary artery disease, known coronary artery disease, aspirin use in the last 7 days, recent angina, elevated cardiac markers, and ST-segment changes on electrocardiogram (EKG) (Table 1).<sup>16</sup> In low-risk patients (TIMI risk score of 0 or 1) presenting to the ED with chest pain, the utility of the TIMI score may be limited.<sup>17</sup> The original study indicated that 4.7% of patients with a score of 0 or 1 experienced adverse outcomes within 14 days. Subsequent validation studies have revealed that 1.7% to 2.1% of patients with a score of 0 still had adverse outcomes of death, MI, or revascularization within 30 days, which is unacceptably high.<sup>17,18</sup> Therefore, serial biomarker measurements have been used to enhance the accuracy of the TIMI score. The ASPECT study combined troponin I, CK-MB, and myoglobin with TIMI score (Table 1). In contrast, the ADAPT study combined troponin I only with TIMI score 2-h to create an accelerated diagnostic protocol (ADP) to assess patients with chest pain presenting to the ED. While sensitivity and negative predictive value (NPV) are 99.3% and 99.1% in the ASPECT study, they showed 99.7% and 99.7% in the ADAPT study, respectively (Table 2).<sup>19,20</sup>

TIMI validation studies showed that higher TIMI scores are associated with a higher risk of 30-day adverse outcomes, including composite of death, AMI, and coronary revascularization (percutaneous coronary intervention and coronary artery bypass surgery) with a specificity of 99.6% for MACE in high-risk TIMI scores ( $\geq 6$ ).<sup>17,33</sup> Therefore, while TIMI score of 0 or 1 cannot safely rule out adverse outcomes in patients with chest pain, higher scores are more useful for ED physicians to identify patients who need to be hospitalized for more aggressive medical or procedural interventions.<sup>16</sup>

#### Grace

The Global Registry of Acute Coronary Events (GRACE) study is a large multinational, prospective observational study involving 94 hospitals across 14 countries and enrolled 43,810 patients with ACS, including ST-elevation myocardial infarction (STEMI), NSTEMI, and UA.<sup>22</sup> Variables used to calculate the GRACE score include age, heart rate, systolic blood pressure, ST changes on EKG, prehospital resuscitation, Killip class, cardiac biomarkers, and serum creatinine.<sup>34</sup> One limitation of the GRACE scoring system is that it may need to be more readily applicable in the ED setting, as some

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Scores	Year	Target Population	Outcome	Variab	bles used	Risk Category, Limitations and Recommendations
PURSUIT <sup>21</sup>	1998	NSTE-ACS	Death or nonfatal recurrent MI	Age Sex Worst CCS class past 6 weeks points) Signs of heart failure ST depression on EKG	50 (8 points) 60 (9 points) 70 (11 points) 80 (12 points) Male (1 points) Female (0 points) No angina/CCS I/II (0 CCS III/IV (2 points) (1 point)	No additional investigations are required and patients can be discharged home if none of the criteria are met
TIMI score <sup>16</sup>	2000	UA/NSTEMI	14-days MACE	<ul> <li>Age≥65 (1 poi</li> <li>≥2 anginal eve point)</li> <li>Use of aspirin v point)</li> <li>≥3 cardiac risk (hypertension, di dyslipidemia, fam smoker) (1 point)</li> <li>Known corona</li> <li>&gt;50% (1 point)</li> <li>EKG with ST-se depression &gt;1 m</li> <li>Elevated cardia point)</li> </ul>	int) nts in last 24 h (1 within last 7 days (1 c factors iabetes, hily history or t) ury artery stenosis egment elevation or hm (1 point) ic biomarkers (1	<ul> <li>Patients with a score of 0 or 1 point are at lower risk of adverse outcome.</li> <li>Patients with a higher risk score may require more aggressive medical or procedural intervention.</li> <li>Limitations:</li> <li>A TIMI Risk Score of 0 does not equal to zero risk.</li> <li>No recommendations have been provided for the patients presenting to the ED with undifferentiated chest pain.</li> </ul>
GRACE <sup>22</sup>	2001	NSTE-ACS and STE-ACS	All-cause mortality during hospitalization	<ul> <li>Age</li> <li>Heart rate</li> <li>Systolic blood</li> <li>Creatinine</li> <li>Cardiac arrest</li> <li>ST-segment dev</li> <li>Elevated cardia</li> <li>Killip class (signed)</li> </ul>	pressure at admission viation on EKG ic biomarkers ns and symptoms)	No recommendations have been provided for the patients presenting to the ED with undifferentiated chest pain.

#### Table I Summary of Risk Models Predicting the Outcome of Patients with Chest Pain in the ED

r	1				
The	2006	Risk stratification	MI (including death	The patient is low-risk and can be	No additional investigations are required, and patients can be discharged home if none
original		of undifferentiated	without other obvious	early discharge if all the following	of the criteria are met.
VCPR <sup>23</sup>		chest pain	cause) or definite UA	questions are answered 'No':	Limitations:
				Step I	Relied on CK-MB as the sole biomarker.
				<ul> <li>Abnormal initial EKG</li> </ul>	
				(if 'no', continue to step 2. If 'yes',	
				not candidate for early discharge)	
				Step 2	
				• Prior MI, angina, or nitrate use	
				(if 'no', continue to step 3. If 'yes',	
				not candidate for early discharge)	
				Step 3	
				• Age less than 40	
				(if 'no', continue to step 4. If 'yes',	
				candidate for early discharge)	
				Step 4	
				• Pain radiates to neck, arm, or jaw	
				And	
				• Pain does not increase with deep	
				breath or palpation	
				(if 'no', continue to step 5. If 'yes',	
				not candidate for early discharge)	
				Step 5	
				• 0 HR CK-MB less than 3	
				(if 'no', continue to step 6. If 'yes',	
				candidate for early discharge)	
				Step 6	
				Ischemic indicators at 2 hours	
				• I–2-hour EKGs are abnormal OR	
				• 2 hr. CK-MB/Tn > 0	
				(if 'no', candidate for early	
				discharge. If 'yes', not candidate for	
				early discharge)	
				/ /	

(Continued)

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# Table I (Continued).

Scores	Year	Target Population	Outcome	Variables used	Risk Category, Limitations and Recommendations
Modified TIMI <sup>24</sup>	2007	ACS	30-day MACE	<ul> <li>Age≥65 (1 point)</li> <li>≥2 anginal events in last 24 h (1 point)</li> <li>Use of aspirin within last 7 days (1 point)</li> <li>≥3 cardiac risk factors (hypertension, diabetes, dyslipidemia, family history or smoker) (1 point)</li> <li>Known coronary artery stenosis &gt;50% (1 point)</li> <li>EKG with ST-segment elevation or depression &gt;1 mm (*5 points)</li> <li>Elevated cardiac biomarkers (*5 points)</li> <li>*The presence of either or both variables attracts value of five points giving a total possible mTIMI score of 10</li> </ul>	Low mTIMI score (≤2) Intermediate mTIMI score (3 or 4) High mTIMI scores (≥5) Limitations: Even a low mTIMI score alone would not allow discharge from the ED.

HEART <sup>25</sup>	2008	Risk stratification of undifferentiated chest pain	MI, PCI, CABG, and/or death	History Highly suspicious 2 points Moderately suspicious 1 point Slightly suspicious 0 point EKG Significant ST depression 2 points Nonspecific repolarization 1 point Normal 0 points Age ≥65 years 2 points Between 45–65 years 1 point ≤45 years 0 point Risk factors ≥3 risk factors or history of CAD 2 points One or two risk factors 1 point No risk factors 0 points Troponin ≥3× normal limit 2 points Between 1–3× normal limit 1 point ≤ Normal limit 0 point	Score $0-3 \rightarrow \text{Discharge home}$ Score $4-6 \rightarrow \text{Admit for clinical observation.}$ Score $7-10 \rightarrow \text{Early invasive strategy}$ Limitations: It was designed to risk stratify patients with undifferentiated chest pain, cannot be used for patients that already diagnosed with ACS.
ASPECT <sup>19</sup>	2011	Patients with chest pain	30-day MACE	TIMI score, EKG, and a point-of- care biomarker panel including troponin, CK-MB, and myoglobin at both presentation and at 2 hours	<ul> <li>No additional investigations are required, and patients can be discharged home if none of the criteria are met.</li> <li>Limitations: <ol> <li>The study's focus on the Asia-Pacific population constrains the generalizability of its findings to other geographic regions.</li> <li>The risk stratification tool identified only 9.8% of patients as being at low risk for adverse events within 30 days. However, the data does not specify how many of these low-risk patients subsequently underwent follow-up testing or received inpatient or outpatient treatment.</li> </ol> </li> </ul>
ADAPT <sup>20</sup>	2012	NSTE-ACS	30-day MACE	<ul> <li>Abnormal cTnl at 0 and 2h</li> <li>Ischemic changes on initial EKG</li> <li>TIMI &gt; 0</li> </ul>	All parameters need to be negative to be identified as low risk. Limitations: Predominantly Caucasian population studied, lacks diversity; high sensitivity troponin not used.

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# Table I (Continued).

Scores	Year	Target Population	Outcome	Variables used	Risk Category, Limitations and Recommendations
EDACS- ADP <sup>26</sup>	2014	Patients with chest pain	30-day MACE	EDACS a) Age b) Male sex c) Aged 18–50 years and either: (i) known CAD or (ii)≥3 risk factors d) Symptoms and signs Diaphoresis Radiates to arm or shoulder. Pain occurred or worsened with inspiration. Pain is reproduced by palpation. EDACS + following: • EKG results • Troponin results at 0 and 2 h	Low risk cohort: • EDACS <16 AND • EKG shows no new ischemia AND • 0-hr and 2-hour troponin both negative. Safe to discharge if low risk cohort. Limitations: Possible interrater variability.

The new	2014	Risk stratification	30-day ACS	The patient is low-risk and can be	No additional investigations are required, and patients can be discharged home if none
The new VCPR <sup>27</sup>	2014	Risk stratification of undifferentiated chest pain	30-day ACS	The patient is low-risk and can be early discharge if all the following questions are answered 'No': Step I • Abnormal initial EKG • Positive troponin at 2 hours • Prior ACS or nitrate use (if 'no' to all, continue to step 2. If 'yes' to any, not candidate for early discharge) Step 2 • Does palpation reproduce pain? (If pain is reproducible, the patient is a candidate for early discharge and does not require Step 3 questions.) Step 3 • Age 50 and above? • Does pain radiate to the neck, jaw, or left arm? (if 'no' to all, early discharge. If 'yes' to any, not candidate for early	No additional investigations are required, and patients can be discharged home if none of the criteria are met. Other etiologies of chest pain should be considered. Patients who do not meet the low-risk criteria should be managed as per usual chest pain protocols
MACS <sup>28</sup>	2014	Risk stratification of undifferentiated chest pain	30-day MACE	<ul> <li>High sensitivity troponin</li> <li>Heart-type fatty acid binding protein</li> <li>EKG ischemia</li> <li>Sweating</li> <li>Vomiting</li> </ul>	Complicated calculation which enables immediate discharge and identifies high risk patients. Limitations: Needs serial sampling at 60–70 minutes delaying early discharge, needs complex calculations and needs use of a computer.
				<ul> <li>SBP&lt;100</li> <li>Worsening angina</li> <li>Pain radiating to right arm or shoulder</li> </ul>	

(Continued)

#### Table I (Continued).

Scores	Year	Target Population	Outcome	Variables used	Risk Category, Limitations and Recommendations	
HEART Pathway <sup>29</sup>	2015	ACS	30-day MACE	History Highly suspicious 2 points Moderately suspicious 1 point Slightly suspicious 0 point EKG Significant ST depression 2 points Nonspecific repolarization 1 point Normal 0 points Age ≥65 years 2 points Between 45–65 years 1 point ≤45 years 0 point Risk factors ≥3 risk factors or history of CAD 2 points One or two risk factors 1 point No risk factors 0 points Troponin ≥3× normal limit 2 points Between 1–3× normal limit 1 point ≤ Normal limit 0 point	<ul> <li>HEART Score ≤3         <ul> <li>If initial troponin 0: Repeat troponin at 3 hours and if negative, discharge home outpatient follow-up.</li> <li>If initial troponin 1–2: Cardiology consultation and admission. Further testing required.</li> </ul> </li> <li>If initial troponin 0: Admit to hospital or observation.         <ul> <li>If initial troponin 1–2: Cardiology consultation and admission. Further testing required.</li> <li>If initial troponin 0: Admit to hospital or observation.             <ul> <li>If initial troponin 1–2: Cardiology consultation and admission. Further testing required.</li> <li>Unlike TIMI or GRACE, the HEART Pathway is used to predict the likelihood of AC the patient presenting to the ED with acute chest pain.</li> <li>Limitations: The HEART Pathway was designed for patients presenting to the ED chest pain and was not tested for patients with chest pain who are already hospital point.</li> </ul> </li> </ul></li></ul>	
HE- MACS <sup>30</sup>	2019	ACS	Risk of ACS or MACE in 30 days	n       • Age       Very low risk (Risk of ACS or MACE in 30 days is <4.0%)		
SVEAT <sup>31</sup>	2020	NSTE-ACS	30-day MACE	<ul> <li>Symptoms</li> <li>Vascular disease</li> <li>EKG</li> <li>Age</li> <li>Troponin I</li> </ul>	Low risk (<1% 30-day MACE) - Score < 4. Identified a larger proportion of low-risk patients as compared with HEART and TIMI scores. Limitations: Needs multicentric validations with diverse populations, Individual scores are assigned arbitrarily.	

Abbreviations: ACS, Acute Coronary Syndrome; ASPECT, Asia-Pacific Evaluation of Chest Pain Trial; ADAPT, Accelerated Diagnostic Protocol for Chest Pain Trial; CABG, Coronary Artery Bypass Graft; CAD, Coronary Artery Disease; CCS, Canadian Cardiovascular Society angina severity classification; CAD, Coronary artery disease; CK-MB, creatine kinase MB; ED, Emergency Department; EDACS, Emergency Department Assessment of Chest Pain Score; EDACS-ADP, Emergency Department Assessment of Chest Pain Score Accelerated Diagnostic Protocol; EKG, electrocardiogram; GRACE, The Global Registry of Acute Coronary Events; HEART, History, EKG, Age, Risk Factors, and Troponin; HE-MACS, The History and Electrocardiogram-only Manchester Acute Coronary Syndromes; MACE, Major adverse cardiovascular events; MI, myocardial infarction; NSTE-ACS, Non ST-elevation acute coronary syndrome; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; PURSUIT, Platelet glycoprotein IIb/IIIa in Unstable angina: Receptor Suppression Using Integrilin Therapy; STE-ACS, ST Elevation Acute Coronary Syndrome; SVEAT, Symptoms, history of Vascular disease, Electrocardiography, Age, and Troponin; TIMI, The Thrombolysis in Myocardial Infarction; Tn, troponin; UA, unstable angina; VCPR, Vancouver Chest Pain Rule.

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Scoring System	Sensitivity	Specificity	PPV	NPV
TIMI (score 0) <sup>32</sup>	97.4%	49.6%	22%	99.2%
Modified TIMI <sup>24</sup>	58.1%	82.6%	35.9%	92.2%
The original VCPR <sup>23</sup>	99.2%	23.4%	16.4%	99.5%
ASPECT <sup>19</sup>	99.3%	11%	12.9	99.1%
ADAPT <sup>20</sup>	99.7%	34.4%	I <b>9</b> %	99.7%
HEART (score ≤3) <sup>32</sup>	97.4%	47.7%	21.4	99.2
HEART Pathway <sup>29</sup>	100%	49.6%	10.7%	100%

**Table 2** Test Characteristic Ranges of Each Risk StratificationScoring System for 30-Day MACE or ACS

**Abbreviations:** ASPECT, Asia-Pacific Evaluation of Chest Pain Trial; ADAPT, Accelerated Diagnostic Protocol for Chest Pain Trial; HEART, History, EKG, Age, Risk Factors, and Troponin; TIMI, The Thrombolysis in Myocardial Infarction; VCPR, Vancouver Chest Pain Rule.

of the variables required for calculation may take time to be available. Additionally, the GRACE score is primarily designed for hospitalized ACS patients and may need to be more accurate for risk prediction in the ED setting.<sup>34,35</sup>

#### Vcpr

The original Vancouver Chest Pain Rule (VCPR) was derived from a research study conducted in Vancouver, Canada. A tool was derived using CK-MB as a cardiac marker (Table 1). Derivation and validation cohorts showed sensitivity of 100% and 99.2% for 30-day ACS, respectively (Table 2).<sup>23</sup> Because of having high sensitivity, VCPR helps physicians to identify low-risk patients with chest pain who could be safely discharged from the ED without further cardiac testing. The new VCPR score, an updated tool, was created using cTn instead of CK-MB and showed 99.2% sensitivity for 30-day ACS. For both the original VCPR and new VCPR scores, if none of the criteria are met, no additional investigations are required, and patients can be discharged home.<sup>23,27</sup>

#### HEART Score and the HEART Pathway

The HEART (History, EKG, Age, Risk Factors, and Troponin) score is a clinical prediction tool used to evaluate the risk of MACE in patients who present to the ED with chest pain to stratify patients into low, moderate, and high-risk groups. The HEART score was first developed and proposed in a study published in 2008 in the Archives of Internal Medicine by Six et al.<sup>25</sup> It was created from a retrospective analysis of data from two university hospitals in the Netherlands using data from 1120 patients admitted to ED with chest pain. Each of the five components receives 0, 1, or 2 points according to the criteria with a total score of 0 to 10. A score of 0 to 3 denotes low risk, with a 6-week MACE risk of less than 2%. A score of 4–6 shows intermediate risk with a 6-week MACE risk of 12–16% and score of 7–10 indicates a high risk with a 6-week MACE risk of 50–65%. According to the study, a HEART score of 0–3 supports to discharge patients home, a score of 4–6 suggests clinical observation and score  $\geq$ 7 points suggest early invasive strategy (Table 1).<sup>25</sup>

The HEART score has shown high sensitivity and negative predictive value for identifying low-risk patients who may be safely discharged from the ED.<sup>25,36</sup> The HEART score performed better in the low-risk population than other risk scores like TIMI and GRACE, with only 0.8% incidence of MACE in the low-risk group. Main limitation of the HEART score is that it is only used in patients with undifferentiated chest pain, however, it cannot be used in patients who are already diagnosed with ACS.<sup>37</sup>

The HEART Pathway was created to evaluate patients with acute chest pain based on the previously validated HEART Score (Table 1). Unlike other scores such as TIMI or GRACE, the HEART Pathway is used to evaluate the risk of ACS in patients with chest pain. However, it was designed for patients presenting to the ED with chest pain and was not studied in patients who are already hospitalized for chest pain.<sup>29</sup>

Emergency Department Assessment of Chest Pain Score (EDACS) is calculated with the variables, including age, male sex, history of CAD, risk factors, and symptoms such as diaphoresis, and characteristics of pain. EDACS was combined with EKG results and troponin results at 0 and 2 h to create an accelerated diagnostic protocol (EDACS-ADP). The original study shows that sensitivity was 99–100% to correctly identify patients as low-risk.<sup>26</sup>

If the score shows low risk (EDACS <16, no new ischemia on EKG and 0-hr and 2-hr troponin both negative), patient can be discharged early with early outpatient follow-up. For non–low-risk patients, ED physicians should continue investigating for chest pain (Table 1).<sup>26</sup>

#### Macs

Manchester Acute Coronary Syndromes (MACS) was a clinical decision rule developed and validated in 2014 and aims to identify low-risk patients in the ED who can be safely discharged without undergoing additional cardiac testing. It uses variables including high-sensitivity troponin, heart-type fatty acid-binding protein, ischemia on EKG, sweating, vomiting, systolic blood pressure <100 mmHg, worsening angina, and pain radiating to right arm or shoulder (Table 1). On external validation, MACS rule identified 27% of the patients as "very low risk" and none of these patients had AMI.<sup>28</sup>

# Aspect

The ASia-Pacific Evaluation of Chest Pain Trial (ASPECT) included 14 emergency departments in the Asia-Pacific region to validate 2-hr accelerated diagnostic pathway. ASPECT ADP integrates variables including TIMI score, EKG, and point-of-care biomarkers (troponin, creatine kinase MB, and myoglobin) with a sensitivity of 99.3% for MACE (Table 2). If the TIMI score is zero, there is no ischemic change on EKG and 0- and 2-h point-of-care biomarker results are negative, it is considered "low risk" and patients are suitable for early discharge from the ED.<sup>19</sup>

# Newer Scoring Systems

# The HE-MACS

The History and Electrocardiogram-only Manchester Acute Coronary Syndromes (HE-MACS) was created in 2019 to stratify ACS risk using data from history, EKG, age, chest pain characteristics, systolic BP, heart rate, cardiac troponin, and symptoms such as nausea, vomiting or sweating. It only includes one troponin level without requiring serial testing. It uses logistic regression models to calculate the likelihood of ACS in terms of a percentage. In the initial validation, the ACS is "ruled out" in low risk; the HE-MACS tool exhibits a pooled sensitivity of >99.5%.<sup>30</sup>

# SVEAT Score

The SVEAT (Symptoms, history of Vascular disease, Electrocardiography, Age, and Troponin) score is a clinical prediction score developed to risk stratify patients with possible acute coronary syndrome in the ED. Each factor is assigned points between -2 and +5. SVEAT score  $\leq 4$  predicted low-risk 30-d MACE, assisting in early discharge. The advantages of this score are an objective assessment of symptom stratification, negative scores for noncardiac chest pain/ normal EKG with chest pain/age less than 30/normal troponin after 4 hr of chest pain, and uses of hs-cTn. However, this score requires further validation in multicentric studies in diverse populations.<sup>31,38-40</sup>

# Hs-cTnT Strategies to Rule Out MI

# Rapid Rule-Out Strategy at Presentation

In a comprehensive meta-analysis involving 22,457 patients, nearly half (49%) had cardiac troponin I concentrations below 5 ng/L upon presentation. Within this subgroup, the negative predictive value was high at 99.5% for the primary outcome. Remarkably, no cardiac death was observed at 30 days and 0.1% of cardiac death at year 1, with a negative predictive value of 99.9%. Based on these findings, it can be inferred that a rule-out strategy utilizing a high-sensitivity cardiac troponin I concentration of less than 5 ng/L at presentation is highly effective in identifying patients at low risk of myocardial infarction or cardiac death within the first 30 days. This suggests the potential utility of this approach in the early risk stratification of patients presenting with chest pain to ED. However, further research is warranted to explore the clinical utility of this strategy.<sup>41</sup>

#### Rapid Rule-Out Strategy by 0/I-Hour Algorithm

A hs-cTnT 0/1-hr algorithm as suggested by ESC is an important tool as a fast rule-out and rule-in for patients with chest pain presenting to the ED. The ESC 0/1-h algorithm helps ED physicians triage patients based on hs-cTnT cutoff concentrations obtained at presentation and after 1 hr, in conjunction with clinical information and ECG findings. The assay-specific hs-cTnT cutoffs were established by multicenter studies as the reference standard. Simulations using the hs-cTnT 0/1-hr algorithm showed a low 30-day MACE, with a rate of 0.2% in the rule-out group and a 0.1% 30-day MACE rate among outpatients.<sup>42</sup> Because of the high NPV, many patients can be discharged home early; however, other life-threatening conditions such as aortic dissection or pulmonary embolism need to be considered as the differential of chest pain. Moreover, the hs-cTnT 0/1-hr algorithm significantly reduces the length of stay in the ED as the median ED length of stay was reported as 2.5 hr when using 0/1-hr algorithm for patients with suspected NSTEMI.<sup>43</sup>

### Rapid Rule-Out Strategy by 0/3-Hour Algorithm

According to the hs-cTnT 0/3-hr algorithm, AMI is ruled out if hs-cTn concentration remains below the 99th percentiles at presentation and 3 h, and if the patient has no chest pain with low risk of in-hospital mortality (GRACE score is <140).<sup>42</sup> When implementing 0/3-hr algorithm in HEART Pathway APD, a low-risk score (<4) is identified in 31% of ED patients with acute chest pain, if there is no history of CAD, no acute ischemia on EKG, and no troponin elevation at 0 or 3 hr. The 30-day MACE rate was 0.4%.<sup>2</sup> The 0/3-hr algorithm can be used if patients with chest pain who have intermediate hs-cTn values or NSTEMI cannot be ruled out by the 0/1-hr algorithm.

# Conclusion

Cardiac biomarkers, particularly cTn-I and cTn-T, are crucial in assessing chest pain for AMI diagnosis, risk stratification, and distinguishing cardiac from non-cardiac causes. High-sensitivity cardiac troponin assays, offering greater sensitivity and negative predictive value, have revolutionized early detection and management of patients with suspected acute coronary syndrome (ACS). The introduction of ESC hs-cTnT strategies for rapid rule-out, particularly the 0/1-hr and 0/3-hr algorithms, has shown promising results in identifying low-risk patients, allowing for early discharge. These strategies significantly reduce the length of stay in the emergency department, enhancing overall efficiency.

Early risk stratification in the emergency department relies on various clinical risk scores. While TIMI scores of 0 or 1 cannot safely rule out AMI in patients with chest pain, higher scores are used to determine the likelihood of ischemic events, therefore TIMI scores are more useful for ED physicians to identify patients who need to be hospitalized for further interventions. The HEART Score stratifies the risk of patients into low, moderate, and high-risk categories. This helps early discharge of low-risk patients and earlier interventions for moderate and high-risk patients. The original VCPR, new VCPR, ASPECT, and ADAPT scores are useful for low-risk patients considered early discharge as no additional investigations are required, and patients can be discharged home if none of the criteria are met. Newer scores such as HE-MACS and SVEAT contribute to efficient risk stratification and patient disposition. The safe and effective evaluation of chest pain can be facilitated by optimizing and validating these risk scores, avoiding needless admissions, and testing for those at low risk. Additional studies should compare and improve the diagnostic reliability and accuracy of the various available scores across a range of patient populations.

# Disclosure

All the authors declare that the research was conducted without any commercial or financial relationships that could be construed as a potential conflict of interest.

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