

Which clinical scoring system should we use for the evaluation of chest pain in the Emergency Department? A review

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Abstract

Many clinical prediction rules and scoring systems have been developed to predict Acute Coronary Syndrome in-patient with chest pain (CP) in Emergency Department. In this review we check and compare the level of validity and reliability of the TIMI (thrombolysis in myocardial infarction); HEART (history, ECG, age, risk factors, troponin); GRACE (global registry of acute coronary events). We used as eligibility criteria: all studies, reviews and meta-analysis on validity and reliability of clinical score systems for CP conducted on all ages of patients in all languages. The selection of articles included in the review was performed according to PRISMA guidelines. We collected one systematic review, one meta-analysis and eleven studies. The HEART score showed the best validity in predicting the outcomes tested with a mean AUROC value of 0.86 (range 0.83-0.88); the GRACE score showed a good validity: mean AUROC value=0.78 (range 0.70-0.82); the TIMI a moderate validity: mean AUROC=0.67 (range 0.42-0.79). The only included study on the reliability showed that the TIMI score had a poor to moderate reliability: weighted kappa range= $k=0.30-0.43$. In conclusion, in this review the HEART and GRACE scores showed the best validity in predicting acute coronary syndromes and major cardiac events. To our knowledge there is only one study on the reliability of TIMI score that showed a poor to moderate inter-rater reliability. There are no studies on the reliability of other score systems.

Introduction

Chest pain is a common complaint in Emergency Department (ED). It is often associated to serious diseases like acute coronary syndrome (ACS) with a significant morbidity and mortality.

For these reasons, many clinical prediction rules and scoring systems have been developed to manage this condition (ACS).

Ideally a clinical scoring system should help to guide clinicians during their evaluation and improve the standardization of clinical management.

For the previous reasons many Emergency and Intensive scientific societies have suggested spreading an early use of scores for the evaluation of patients in the ED with chest pain.^{1,2}

The major clinical prediction rules for chest pain are described in a recent Systematic Review:³ the TIMI (thrombolysis in myocardial infarction); HEART (history, ECG, age, risk factors, troponin); GRACE (global registry of acute coronary events).

According to the literature, a clinical score system used in ED should also be easy and rapid to use.

Stiell *et al.*⁴ suggested the methodologic standards for the development of clinical decision rules in Emergency Medicine: before using these tools they should be tested in various setting (*e.g.* primary care, hospital, emergency) for the major quality indexes (the reliability and validity in predict diagnosis and prognosis).

For these reasons we reviewed the literature to check and compare the level of validity and reliability of the major score systems developed for the evaluation of chest pain in ED.

Materials and Methods

The primary aim was to check the state of art of studies on the validity and reliability of clinical score systems for chest pain.

We used the following eligibility criteria to include reports: all studies, reviews and meta-analysis on validity and reliability of clinical score systems for CP conducted on all ages of patients in all languages. In particular, we consider the studies which used the following validity indexes: accuracy, sensitivity, specificity measures; ROC curves with areas under the ROC curves (AUCs); the following reliability indexes: kappa coefficient (weighted and un-weighted), intraclass correlation coefficient, Pearson correlation coefficient and spearman rank correlation coefficient.

The selection of articles included in the review was performed in a three-phase process (Figure 1) according to PRISMA guidelines.

In the first phase, one author conducted a literature search of PubMed database.

The systematic search of the international literature published from 1941 through June 2016 was conducted using the following key words: *chest pain and clinical prediction rule and emergency service OR chest pain and risk score and emergency service*. Ninety-seven and one hundred and sixty-eight citations have been found.

In the second phase, the author performed a

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screening by regarding eligibility criteria of the list of articles (title and abstract) selected in phase one. All duplicates were removed. In this way potentially useful articles were selected with their full text.

In the third phase, all full-text articles have been examined to select the studies that met the inclusion criteria.

The studies remaining after this phase were included in the analysis.

Results

We collected one systematic review, one meta-analysis and eleven studies:^{3,5-16} the meta-analysis, the review and ten studies tested the validity in predicting ACS and major cardiac events of TIMI, GRACE and HEART score; one study the validity and reliability. The characteristics of studies are shown in Table 1. The HEART score showed the best validity in predicting the outcomes tested with a mean AUROC value of 0.86 (range 0.83-0.88) but we found only two studies on this score.

The GRACE score has been tested in several studies and setting (emergency department, cardiology and ICU) and it showed a good validity: mean AUROC value=0.78 (range 0.70-0.82).

In this review the TIMI score showed a moderate validity: mean AUROC=0.67 (range 0.42-0.79).

The good performance of the GRACE score has also been confirmed in five comparison studies with other scores (Table 1).

The test characteristics of major clinical score systems for Chest Pain described in the

systematic review and meta-analysis are shown in Table 2. Fanaroff *et al.*³ suggested that the TIMI and HEART risk score have excellent accuracy for ACS: patients with a TIMI score of 5 or higher have a summary LR for ACS of 6,8; among high-likelihood patients (HEART score range of 7-10) the LR for diagnosis of ACS was 13.

D'Ascenzo *et al.*,¹⁶ after a revision of seven derivation studies (25,525 patients) and fifteen validation studies (257,654 patients), concluded that GRACE risk score performed better than the TIMI when predicting ACS.

The only included study on the reliability showed that the Goldman, the TIMI and Sanchis score had a poor to moderate reliability: weighted kappa range=0.18-0.30; k=0.30-0.43; K=0.18-0.43 respectively.¹⁵

A comparison of the overall validity in predicting outcome of the major clinical prediction scores for chest pain is shown in Figure 2.

Discussion

In this review the HEART and GRACE score systems for the evaluation of chest pain in Emergency Department showed the best valid-

ity in predicting acute coronary syndromes and major cardiac events. According to the systematic review³ and to the meta-analysis¹⁶ the best score systems were the TIMI and HEART; the GRACE respectively.

To our knowledge there is only one study on the reliability of TIMI score that showed a poor to moderate inter-rater reliability. There are no

studies on the reliability of other score systems. For several years, researchers tried to develop a risk score for chest pain patients. Most of these scores are difficult to use and are only validated for a selected group of patients such as STEMI or non-STEMI patients in the coronary care unit.

The major and useful scores are the TIMI,¹⁷

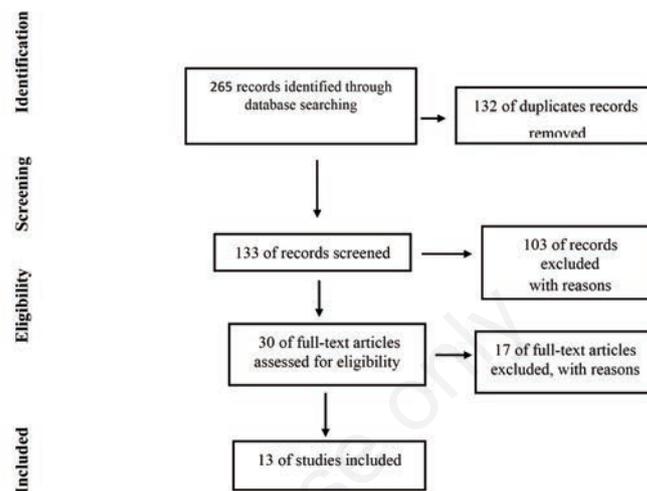


Figure 1. Review process.

Table 1. Characteristics of studies included.

Reference (author, year)	Target population setting	Score	Design	Outcome	Results
Leite <i>et al.</i> , 2015 ⁵	233 patients ED	HEART	Retrospective Observational	Mortality, AMI, Revascularization at 6 weeks	AUROC=0.88
Sanchis <i>et al.</i> , 2005 ⁶	646 patients	TIMI	Prospective	Mortality, AMI at 1 yr	AUROC=0.66
Rawlings <i>et al.</i> , 2012 ⁷	104 pat ED	TIMI	Prospective	Mortality NSTEMI at 30 days	AUROC=0.67 for death AUROC=0.42 for NSTEMI
Macdonald <i>et al.</i> , 2014 ⁸	219 pat ED	TIMI	Multicenter	Prospective obs at 30 days	Mortality AMI AUROC=0.71
Lyon <i>et al.</i> , 2007 ⁹	1000 pat ED	GRACE TIMI	Prospective	ACS, cardiac arrest, death at 30 days	GRACE: AUROC=0.80 TIMI: AUROC=0.79
De Araujo Gonçalves <i>et al.</i> , 2005 ¹⁰	460 pat	GRACE TIMI PURSUIT	Prospective	Death, AMI at 1 yrs	GRACE: AUROC=0.72 TIMI: AUROC=0.59 PURSUIT AUROC=0.63
Yan <i>et al.</i> , 2007 ¹¹	1728 pat	GRACE TIMI PURSUIT	Multicenter Prospective	In hospital and death at 1 year	GRACE: AUROC=0.79 TIMI: AUROC=0.69 PURSUIT AUROC=0.77
Ramsay <i>et al.</i> , 2007 ¹²	347 pat	GRACE TIMI	Prospective	Death, AMI, In-hospital at 3 months	GRACE: AUROC=0.82 TIMI: AUROC=0.74
Backus <i>et al.</i> , 2013 ¹³	2440 pat ED	GRACE TIMI HEART	Multicenter Prospective	Major cardiac Events at 6 weeks	GRACE: AUROC=0.70 TIMI: AUROC=0.75 HEART: AUROC=0.83
Granger <i>et al.</i> , 2003 ¹⁴	11389 pat GRACE		Retrospective	In hospital death	AUROC=0.84
Manini <i>et al.</i> , 2009 ¹⁵	148 ED pat	TIMI GOLDMAN SANCHIS	Prospective cohort	NSTEMI Reliability	Sens=35-53% Spec=72-86% Reliability=poor-moder

AMI, acute myocardial infarction; ACS, acute coronary syndromes. In this list the two meta-analyses are excluded.

the GRACE,¹⁴ and the HEART.¹³

The TIMI risk score (2000) is derived from the Thrombolysis in Myocardial Infarction (TIMI)-11B trial, a multinational, randomized clinical trial, comparing unfractionated heparin to enoxaparin, which included all patients with confirmed ACS. Seven elements compose the TIMI score for unstable angina/NSTEMI: age ≥ 65 years, ≥ 3 classical risk factors for coronary artery disease (CAD), known CAD, use of Aspirin in the past 7 days, severe angina in the past 24 hours, elevated cardiac markers and ST-deviation ≥ 0.5 mm. Each of these elements can be assigned with 0 or 1 points, resulting in a score of 0-7. The TIMI score predicts the risk of all causes mortality, MI and severe recurrent ischemia requiring urgent revascularization within 14 days after admission.

The GRACE score (2003) was developed in a multinational registry of 11,389 ACS patients (global registry of acute coronary events). The scoring system, consisting of hemodynamic, laboratory, ECG and patient specific findings: Killip class for congestive heart failure (CHF), systolic blood pressure at presentation (SBP), heart rate at presentation (HR), age, creatinine level, cardiac arrest at admission, ST-segment deviation on the index ECG and elevated cardiac enzyme levels. Each element has its own scoring, resulting in a possible score ranging from 1 to 372. Event rates increased significantly with increasing GRACE-scores, ranging from ≤ 0.2 to $\geq 52\%$ chance of in-hospital death.

Recently (2008), the HEART risk score was developed for chest pain patients presenting to the ED. The composition of the HEART score was not based on multivariate regression analysis but on the decision making clinical factors according to expert opinion. The HEART score is composed of five parameters of clinical judgement: history, ECG, age, risk factors and troponin. By appreciating each of these five elements with 0, 1 or 2 each patient will receive a score of 0-10. The HEART score divides patients into low (0-3), intermediate (4-6) or high-risk groups (7-10), with mean risks of an event of 0.9, 12 and 65%, respectively. One limit of the TIMI and GRACE scores is that they have been originally developed for patients with confirmed ACS in the setting of coronary unit. In a second time they have been tested in the ED setting.

The HEART, instead, is the only score, which was developed for chest pain patients presenting to the ED.

One other limit of all the previous scores is that they could not be used to discriminate other causes of chest pain (e.g. aortic dissection, pulmonary embolism, non cardiac chest pain).

But in our opinion the main limit of all the previous score systems is the lack of research

on their reliability. In fact, according to literature,⁴ before using a clinical score it could be very important to test its inter-rater and intra-rater reliability.

Among the studies collected in this review, the most studied score in the ED setting is the TIMI with four studies conducted on 3763 patients; the HEART and GRACE score showed the best validity in the ED setting: AUROC range 0.83-0.88 and 0.70-0.80 respectively.

But which could be the most useful and effectiveness clinical score systems to evaluate a patient with chest pain in the daily ED clinical practice?

In our opinion the best score in a suspicious of ACS in ED setting should be faster, simpler, intuitive, valid in predicting the main outcomes (short and long term mortality, AMI,

major cardiac events), reliable. But to our knowledge, until now there is not a score with all these characteristics. Moreover it is very difficult to compare the results on the performance of score models evaluated in studies with different setting, design and outcome tested.

Anyway according to the results of this and other reviews and meta-analysis, probably the useful scores in ED could be the HEART and GRACE because both showed good validity in predicting major cardiac events in short and long term. Our opinion has also been supported by European Society of Cardiology which suggests the use of GRACE¹ and recently by the experts' opinion from ACEP (American College of Emergency Physician) who proposed the HEART score.

The main advantages of HEART are that it

Table 2. Test characteristics of clinical score systems for chest pain from meta-analysis and systematic review.

SCORE	Threshold	LR	AUROC
HEART			
Low Probability	0-3	0.20	
Indeterminate	4	0.79	
Mod. Probability	5-6	2.4	
High Probability	7-10	13	
TIMI			
Low probability	0-1	0.31	$^{\circ} 0.66$ (95% CI 0.64 -0.68)
Indeterminate	2	0.94	$^{\circ} 0.73$
Mod. Probab.	3-4	2.4	(95% CI 0.69- 0.78)
High Probab.	5-7	6.8	
HFA/CSANZ			
Low probability	Low to mod high	0.24	
Mod. Probab.		2.8	
GRACE			
			$^{\circ} 0.83$ (95% CI 0.82-0.84); $^{\circ} 0.82$ (95% CI 0.80-0.89)

HEART, history, ECG, age, risk factors, troponin; TIMI, thrombolysis in myocardial infarction risk score; HFA/CSANZ, Heart Foundation of Australia and Cardiac Society of Australia and New Zealand rule; GRACE, global registry of acute coronary events. ^oThe authors considered the overall AUROC for the ability of GRACE and TIMI to predict in-hospital and first year mortality, major cardiac events, ACS diagnosis, cardiac arrest among Seven derivation studies (25,525 patients); ^o15 validation studies (257,654 patients).

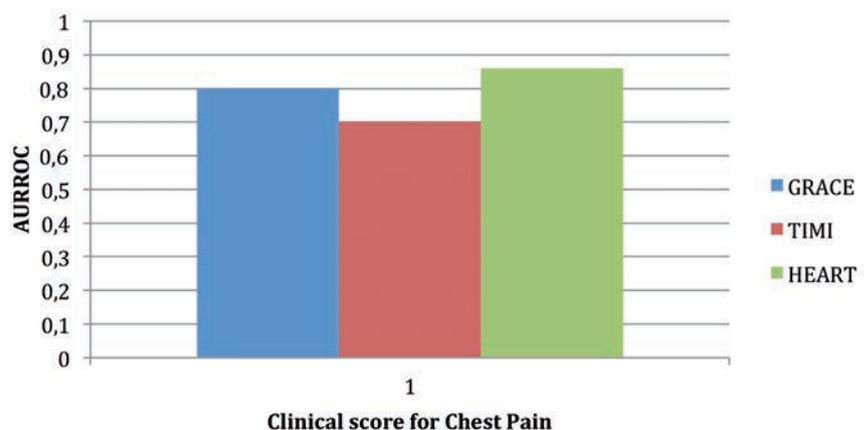


Figure 2. Comparison of validity in predicting outcome of clinical score for chest pain. All value of AUROC are means among the studies included. The outcome tested were: death at 6 weeks, at 30 days; ACS, MACE (major cardiac events).

has been developed for patients with CP in ED, it is fast, simple and intuitive, it also considers the patients history. Its limitations are: few studies published on its validity in predicting CP outcomes; no data on its reliability.

Conclusions

In our opinion the score actually in use for the management of patient with CP in the ED does not respect all the quality indexes suggested by the experts. Anyway, among the scores until now tested, probably the HEART and GRACE scores could be the most useful for their good validity in predicting outcomes and large validation in ED setting. Further research on their reliability should be conducted. More studies on their comparison are desirable.

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