Cardiac Risk Stratification Scoring Systems for Suspected Acute Coronary Syndromes in the Emergency Department

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Abstract Considerable time and resources are consumed investigating the many patients who present to emergency departments but who do not have an acute coronary syndrome. Consequently, researchers are increasingly modifying or developing cardiovascular risk-scoring systems for rule-out of acute coronary syndrome in patients who present to emergency departments with chest pain. Scoring systems range from those developed from statistical weighting of variables collected in observational studies to those developed from clinical judgment, logic, and common sense. The trend is towards systems using clinical logic and simple criteria. Although sensitivity and negative predictive value are the key parameters of interest when deciding to use a risk-assessment score to assist with chest-pain rule-out decision-making, it is important to consider the proportion of patients that will be classified as low risk. If the numbers are significantly low, then adopting a risk-scoring system in an early rule-out strategy is unlikely to impact upon patient flow and emergency-department overcrowding.

Keywords Emergency department · Acute coronary syndrome · Cardiovascular risk score system · Cardiovascular risk assessment · Chest pain · Early rule-out strategy · Hospital overcrowding · Low risk · Acute myocardial infarction

Introduction

Clinicians involved in acute care often worry that patients may come to harm, soon after discharge, from the medical complaint that they presented to the hospital with. Therefore, discharge decisions in emergency medicine are difficult to make and are frequently more challenging than treatment of an immediately life-threatening disease. Patients with symptoms suggestive of acute coronary syndromes (ACS) contribute approximately 5–10 % of annual presentations to emergency departments and up to 25 % of hospital admissions [1]. Accordingly, assessment and safe disposition of these patients is a major challenge. Their safe workup generally requires considerable time and often includes in-patient observation, which adds to emergency-department and hospital overcrowding. Despite prolonged workup, the actual number of patients finally diagnosed with ACS is often 25 % or less [2–4]. Considerable time and resources are consumed investigating the many patients who do not have an ACS. Consequently, some researchers are investigating risk score systems that identify patient-groups that can be discharged early with a low risk of harm from adverse cardiac events.

For an emergency physician, the short-term prognosis of a patient is paramount and therefore effectively defines the required accuracy of an investigative pathway. A recent survey of approximately 1,000 emergency-medicine physicians found that most doctors preferred a 1 in 100 (1 %) or 1

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in 1,000 (0.1 %) acceptable error rate in discharging patients from ED with an unrecognized ACS [5]. These findings suggest that a sensitivity of 99 % or higher is the minimum standard that most physicians will accept for a risk scoring system that classifies chest-pain patients for early discharge.

Cardiac-troponin analysis and the electrocardiogram (ECG) are the principal tests used to assess patients with chest pain. However, some estimation of the pre-test probability of patients having an ACS is necessary to interpret these tests. This is a fundamental principle of Bayes theorem. Historically, pre-test probability has been determined using clinical acumen primarily involving historical variables and risk factors learnt at medical school and reinforced during clinical practice. Unfortunately, evidence suggests that neither symptomatic history nor presence of chronic risk factors for coronary artery disease are as predictive as initially thought, when used in the emergency-department context [6–10]. In addition, the experience of the initial-assessing doctors in emergency departments may vary considerably depending on the hospital setting (i.e., an academic department or a rural hospital). Since assessments contain an element of subjectivity, there is often poor inter-rater agreement between clinicians when comparing gestalt pre-test probability determinations. Risk-scoring systems can improve inter-rater agreement by providing some structure around the pre-test probability assessment process. There are many approaches to risk scoring ranging from those developed on statistical weighting of variables collected in observational studies to those developed using clinical judgment, logic, and common sense. Few systems have been widely adopted for disposition decisions in the emergency department because they were not designed for emergency-department use. They generally focus on the identification of high-risk patients and/or are too complicated to gain wide user acceptance. The thrombolysis in myocardial infarction (TIMI), Goldman Rule, ACITIPI, PURSUIT, and GRACE have recently been reviewed by Hess et al. (2008) and Steurer et al. (2010) [11–17]. The reviews concluded that published validation studies of these risk scores have substantial methodological limitations, and have not been successfully implemented safely in the clinical setting. Newer scoring systems such as the HEART score [18], the North American chest pain rule [19] and a new pathway developed in Vancouver [20] have been purpose designed for emergency-department use. Also of interest is a recently published article by Aldous et al. [21]. This attempts to directly compare the diagnostic performance of the majority of existing risk-scores for the detection of ACS in a 1,000 patient cohort in New Zealand. The article highlights the differences in outcomes reported and variations in accuracy in different study cohorts. In the direct comparison the TIMI risk score and the North American

chest pain rule produced the highest sensitivities (99.2 and 99.7 % respectively). In this review, we will present a broader range of published risk-scoring systems with summary statistics, discuss how they were developed, comment on their strengths and weaknesses, and discuss the future direction of this area of medicine.

Pre-Existing Risk Scores

Differences in reporting styles and populations make it difficult to compare many of the common risk scoring systems. The manner of reporting diagnostic statistics varies considerably—in many cases, the area under the receiver-operating curve (AUC or C statistic) is all that is available. Tables 1 and 2, respectively, summarize the common risk scoring systems and their diagnostic statistics.

GoldMan

Goldman et al. [11] originally derived The Goldman rule in 1982 from a cohort of 482 patients from a single center using recursive partitioning techniques, and validated the rule in 468 patients from a second center. In 1988, they modified the rule using recursive partitioning on a derivation sample of 1,379 patients, and validated it on a cohort of 4,770 patients [22]. The rule included ECG findings, age, time since symptom onset, prior history of angina or myocardial infarction, and pain characteristics (Table 1). Of note, the rule did not include biomarker results. The rule achieved 88 % sensitivity, and 74 % specificity in the validation cohort (Table 2). Grijseels et al. [23] subsequently externally validated the modified Goldman rule in 1995 achieving 74 % sensitivity and a 40 % specificity (Table 2).

The Acute Cardiac Ischaemia Time-Insensitive Prediction Instrument (ACI-TIPI)

Selker et al. in 1991, published the acute cardiac ischaemia time-insensitive prediction instrument (ACI-TIPI) score [13], which was trialed on a population of 3,453 patients presenting to six hospitals with symptoms suggesting acute cardiac ischaemia. The score was derived by means of logistic regression, and included age, sex, chest/arm pain, Q-waves, ST deviation, and T wave elevation/inversion. The ACI-TIPI uses special software in order to categorize risk. The score was subsequently validated on a new cohort of 2,320 patients, showing a C-statistic of 0.88 [13]. The score has since been validated in five other studies, with sensitivity ranging from 84 to 100 %, and specificity ranging from 4 to 84 % [24–28].

Table 1 Summary of earlier risk score systems and rules

Goldman rule [11, 22]	TIMI (scores 0–7) [12]	NHF AUS [43] ^b
Typical new onset chest pain at rest	Age ≥ 65 years	<i>High-risk NSTEMACS</i>
Constricting discomfort in the front of the chest, with radiation to the neck, jaw, shoulders or arms	≥ 3 Risk factors ^a for coronary artery disease	Presentation with clinical features consistent with ACS and any of:
Pain the same as previous MI	Use of aspirin in the last 7 days	Repetitive or prolonged (>10 min) ongoing chest pain/discomfort
Pain not relieved by own GTN within 15 min	Significant coronary stenosis (e.g. prior coronary stenosis ≥ 50 %)	Elevation of at least one cardiac biomarker (troponin or CK-MB)
Pain lasting more than 60 min	Severe angina (e.g. ≥ 2 angina events in last 24 h or persisting discomfort)	Persistent or dynamic ST depression >0.5 mm or new T wave inversion >2 mm
Pain occurring with increasing frequency	ST-segment deviation of 0.05 mV on first ECG	Transient ST segment elevation (>0.5 mm) in more than two contiguous leads
Hypotension (SBP <100 mmHg)	Elevated troponin and/or CK-MB on initial blood tests	Haemodynamic compromise: systolic blood pressure <90 mmHg, cool peripheries, diaphoresis, Killip class >1 and/or new onset mitral regurgitation
Acute shortness of breath	^a FHx of coronary artery disease, HTN, hypercholesterolemia, DM, or Smoker	Sustained ventricular tachycardia
Pain within 6 weeks of AMI or revascularisation	Low risk: No to all	Syncope
Very low risk: No to all	Not low risk: Yes to 1 or more	LV systolic dysfunction (LVEF <40 %)
Low risk: Yes to 1	Prognosis—14 days	Prior PCI within 6 months or prior CABG surgery
Intermediate risk: Yes to 2 or more		Presence of known diabetes (with typical symptoms of ACS)
		Chronic kidney disease-estimated GFR <60 mL/min (with typical symptoms of ACS)
PURSUIT (scores 0–18) [14, 36]	GRACE (scores 0–258) [37]	<i>Intermediate-risk NSTEMACS</i>
Age, separate points for enrolment diagnosis	Age (>40 years in 10 year bands)	Presentation with clinical features consistent with ACS and any of:
Decade bands [for UA (MI); starting at 50 years]	Heart rate (>70 bpm; in bands of 10 up to >200 bpm)	Chest pain or discomfort within past 48 h that occurred at rest, or was repetitive or prolonged but currently resolved
Sex (male or female)	Systolic BP (>80 mmHg in bands of 10 up to >200 mmHg)	Age >65 years
Worst CCS-class in previous 6 weeks	Creatinine (0 to >4 mg/dL in bands of 0.39)	Known CHD: prior MI with LVEF >40 % or known coronary lesion >50 % stenosed
No angina or CCS I/II	Killip class (I, II, III, or IV)	No high-risk ECG changes (see above)
CCS III/IV	Cardiac arrest at admission	Two or more of: known hypertension, family history, active smoking or hyperlipidaemia
Signs of heart failure	Elevated cardiac markers	Presence of known diabetes (with atypical symptoms of ACS)
ST-depression on presenting ECG	ST-segment deviation	Chronic kidney disease-estimated GFR <60 mL/min (with atypical symptoms of ACS)
Prognosis—30 days	Prognosis—events in hospital	Prior aspirin use AND NOT meeting the criteria for high-risk NSTEMACS
Vancouver [41]	MARSAN et al. [39, 40]	<i>Low-risk NSTEMACS</i>
In the final model, a patient was considered low-risk if either of the following criteria were met:	Adults, 40 years	Presentation with clinical features consistent with ACS without intermediate- or high-risk features, for example
<40 years old, with a normal initial ECG, and no prior history of ischaemic chest pain	No cardiac risk factors and/or normal ECG	Onset of anginal symptoms within the last month; or
≥ 40 years old with normal ECG results, no previous ischemic chest pain, low risk chest pain characteristics, and either an initial creatine kinase-MB (CK-MB) <3.0 μ g/L or an initial CK-MB ≥ 3.0 μ g/L, but without an increase or ECG changes within 2 h	At low risk (<1 %) for ACS and 30-day adverse cardiovascular events	Worsening in severity or frequency of angina; or
		Lowering in anginal threshold

ACS acute coronary syndrome, CABG coronary artery bypass grafting, CHD coronary heart disease, GFR glomerular filtration rate, LVEF left ventricle ejection fraction, MI myocardial infarction, NSTEMACS non-ST elevation acute coronary syndrome, PCI percutaneous coronary intervention, TIMI thrombolysis in myocardial infarction score, PURSUIT Platelet glycoprotein IIb/IIIa in Unstable angina, GRACE Global Registry of Acute Coronary Events, NHF Aus National Heart Foundation of Australia

^a FHx of coronary artery disease, HTN, hypercholesterolemia, DM, or smoker

^b The National Heart Foundation of Australia/Cardiac Society of Australia and New Zealand guidelines for ED management of suspected acute coronary syndrome 2006

Table 2 Summary of risk score diagnostic accuracy parameters

Rule	Derivation publication	Validation publication	<i>n</i>	Sensitivity	Specificity	PPV	NPV	LR+	LR–	C-Stat
Goldman rule	Goldman et al. [11]	Goldman et al. [22]	482	98	66				0.03	
		Grijseels et al. [23]	4,770	88	74				0.2	
				74	40				0.7	
AC TIPI	Selker et al. 1991		3,453	98	32				0.06	
		Selker et al. [13]	2,320	99	34				0.02	0.88
		Seyal et al. [24]		98	4				0.4	
		Miller et al. [26]		95	18				0.3	
		Miller et al. [26]		98	8				0.3	
		Mitchell et al. [27]		100	6				<.01	
		Kellett [28]		84	84				0.2	
TIMI	Antman et al. [12]		1,957							
		Macdonald et al. [29]	1,758							0.76
		Than et al. [30]	3,582	99.3	11	12.9	99.1			
		Hess et al. [31]	17,265 (Systematic review)	97.2	25			1.3	0.11	
		Conway et. al. [32]		100	28					
		Tong et al. [33]		98	19					
		Chase et al. [34]		94	35					
PURSUIT		Boersma et al. [14]	9,461							0.669
		Araujo Goncalves et al. [36]	460							0.62
Grace	Granger et al. [37]		11,389							0.83
		Granger et.al [37]	3,972							0.84
		Granger et. al. [37]	12,142							0.79
		Yusufali et al. 2011 ^a	7,709							0.86
		Lyon et al. 2007 ^a	734	100	13	19	100			0.8
		Eggers et al. 2010 ^a	453							0.81
Marsan's rule	Marsan et al. [39]		1,023	98	31					
Vancouver	Christenson et al. [41]		769	99	32	28	99			
		Jalili et al. [42]	593	95	56	26	99			
NHF Aus	ACS Guidelines Working Group [43]	Macdonald et al. [29]	1,758							0.82
		Kelly [44]	768							0.74
Heart	Six et al. [47]		120	97	43					
		Backus et al. [48]	880	98	42					0.897
		Mahler et al. [49]	1,070	58	85					
NACPR	Hess et al. [19]		2,718	100						
Vancouver CPA	Scheuermeyer et al. [20]		1,116							

AC TIPI acute cardiac ischaemia time-insensitive prediction instrument, TIMI thrombolysis in myocardial infarction score, PURSUIT Platelet glycoprotein IIb/IIIa in Unstable agina, GRACE Global Registry of Acute Coronary Events, NHF Aus National Heart Foundation of Australia, NACPR North American Chest Pain Rule, Vancouver CPA Vancouver diagnostic chest pain algorithm, *n* number of patients in cohort, PPV positive predictive value, NPV negative predictive value, LR+ Positive likelihood ratio, LR– negative likelihood ratio, C-stat area under receiver operating curve

^a Yusufali et al. Angiology 2011, Lyon et al. Resuscitation 2007;74:90–3., Eggers et al. Am Heart J 2010 (Not in main reference list)

The Thrombolysis in Myocardial Infarction (TIMI) Score

The TIMI risk score for unstable angina/non-ST elevation myocardial infarction was published by Elliott Antman et al. in 2000 [12]. It was validated on 1,957 patients recruited in the multi-national, randomized clinical TIMI 11B trial, which compared treatment with unfractionated heparin or enoxaparin. Of note, participants were required to have unstable angina or a non-ST elevation myocardial infarction in order to be included in the study. 12 baseline characteristics were screened as candidate predictor variables for developing a risk score and univariate and multivariate analyses were performed to identify seven independent predictive parameters (Table 1).

The initial results demonstrated that the prevalence of cardiac disease increased as the score increased, from 4.7 % for a score of 0–1, to 40.9 % with a score of 6–7. The initial score derivation did not involve its use as a rule-out tool, but it has subsequently been validated for this purpose in six other separate studies [29–34]. The sensitivity for these rule-out strategies incorporating the TIMI score ranged from 99.3 to 100 %. It has been common for validators and users of the TIMI score to modify it to accommodate a broader definition of ischemia on the ECG and currently available cardiac biomarkers. For example, ASPECT and ADAPT studies modified the score to include ‘any new’ ischemia on the ECG, and troponin or multi-marker panel testing at 0 and 2 h after presentation to hospital [30, 35].

Pursuit

The (PURSUIT) risk score published by Boersma et al. [14] was derived from a population of 9,461 patients enrolled in the PURSUIT randomised controlled trial (comparing glycoprotein IIB/IIIa inhibitor therapy vs placebo in unstable angina or non-ST elevation myocardial infarction). The score was derived using multiple regression, which included the parameters: age, heart rate, systolic blood pressure, ST-segment depression, signs of heart failure, and cardiac enzymes. It yielded a C-statistic of 0.814 for predicting mortality, but only produced a C-statistic of 0.669 for predicting disease. Araujo Gonçalves et al. [36] validated the Pursuit score in 2005 in a cohort of 460 patients admitted to a single centre with ACS. They found the score to have a C-statistic of 0.62. The PURSUIT risk score is little used for emergency department rule-out decision making because it is not designed for rule-out.

Grace

The Global Registry of Acute Coronary Events (GRACE) score was published by Granger et al. in 2003 [37] and was the product of a multinational collaboration involving 94 hospitals in 14 countries. The score was derived from a cohort of 11,389 patients using multiple regression, and subsequently validated in two separate cohorts of 3,972 and 12,142 patients, respectively. Patients needed to have either ECG changes suggesting ACS, serial increase in cardiac enzymes, or documented coronary artery disease to be included. It was found that inclusion of age, Killip class (severity of heart failure) [38], systolic blood pressure, ST-segment deviation, cardiac arrest during presentation, serum creatine, cardiac enzymes, and heart rate accounted for 89.9 % of the prognostic information. The final model yielded a C-statistic of 0.83 in the derivation cohort, 0.84 in the smaller validation cohort, and 0.79 in the larger validation cohort. Since its initial publication, the GRACE score has been externally validated in two separate studies, yielding c statistics of 0.86 and 0.81 respectively. It is regarded as a useful tool for predicting those patients that will be at higher risk and as a guide to therapy but not as a rule-out tool.

Marsan (A Clinical Decision Rule for Young Adult Patients with Chest Pain)

In 2005, Marsan et al. modified a rule produced by Walker et al. in 2001 [39, 40]. Marsan et al. trialed a population of 1,023 patients and found that chest- patients who were <40 years old, with no known cardiac disease, with neither classic cardiac risk factors or an abnormal ECG, and normal biomarkers at presentation were unlikely to suffer an adverse cardiac event within 30 days.

Vancouver Chest Pain Rule

The Vancouver Chest Pain Rule was derived in 2006 by Christenson et al. [41] from a cohort of 769 patients (aged at least 25 years old) presenting to a single center in Vancouver. It is important to note that this decision aid was specifically designed for rule-out purposes. The rule was derived using recursive partitioning, with the result that it is slightly more complex than some of the other risk scoring systems.

In the final model, a patient was considered low-risk if s/he was <40 years old, with a normal initial ECG, and no prior history of ischaemic chest pain; or ≥ 40 years old with normal ECG results, no previous ischemic chest pain, low risk chest pain characteristics, and either an initial creatine kinase-MB (CK-MB) <3.0 $\mu\text{g/L}$ or an initial CK-MB $\geq 3.0 \mu\text{g/L}$, but without an increase or ECG changes within 2 h.

This rule proved to be 98.8 % sensitive and 32.5 % specific in the derivation cohort, with a 28.5 % predictive value and 99.0 % negative predictive value. This rule was validated by Jalili et al. [42] who achieved 95.1 % sensitivity, 56.3 % specificity, 98.6 % negative predictive value, and 25.9 % positive predictive value in a cohort of 593 consecutive patients aged 25 or older presenting to a single center in Iran.

National Heart Foundation of Australia

In 2006, the Cardiac Society of Australia and New Zealand in collaboration with the National Heart Foundation of Australia published national guidelines for the management of ACS [43]. The guidelines were formulated by committee consensus using expert opinion and published evidence available at that time. The document included a method for stratifying chest-pain patients at risk of non ST-elevation acute coronary syndromes (NSTEMI). The risk score divided patients into low, intermediate and high risk of NSTEMI using ECG findings, biomarker results, haemodynamic status, syncope, left ventricular ejection fraction, history of PCI, diabetes, heart disease, age, hypertension, family history, smoking, hyperlipidaemia, aspirin use, and prior myocardial infarction. The score was later validated by Macdonald et al. in 2011 [29] on a population of 1,758 patients, yielding a C-statistic of 0.82, and Kelly in 2012 [44] in a population of 768 patients yielding a C-statistic of 0.74 (CI 0.71–0.77) for ACS, and acute myocardial infarction.

Summary

Of the pre-existing risk scores, the TIMI score is probably most widely used for rule-out of ACS purposes. In contrast, the Grace score is more commonly used to assist with rule-in management decisions. It is worth noting that of the early scoring systems, only the Vancouver chest pain rule was intentionally developed to facilitate early discharge of patients with possible cardiac chest pain from emergency departments. This means that there is plenty of work left to do in the development of purpose designed risk assessment tools for the emergency department.

Newly Developed Risk Scores

The Heart Score

The heart score was developed by Jacob Six and Barbra Backus and colleagues, in 2007 [45]. The manner in which

the score was developed is interesting. It differs from the other scoring systems in that it is based on a clinical approach rather than purely mathematical approach. A respected local cardiologist (Jacob Six) in Utrecht (The Netherlands), was undertaking a teaching ward round with some medical students at a local hospital. In the process of this ward round he taught students that the key factors to consider when assessing chest-pain patients were their history, ECG results, age, risk factors, and their troponin test result. He then realized that these factors actually formed quite a good mnemonic, and work began to see if a score would be useful in clinical practice. It is noticeable that the starting point for the score was clinical knowledge and understanding of the medical scenario and knowledge of the medical literature. This information was used to develop a score that is logical and simple to use. The authors had noted that the Apgar score (a score to assess neonatal well-being immediately after birth) [46] is regarded as very easy to use because of its simplicity. Backus et al. wished simplicity to be a founding principle of the score to help clinicians accept and adopt the risk score system.

The score consists of points given for history, ECG results, age, risk factors and troponin concentrations. For history, two points are given if the history is highly suspicious, one point if it is moderately suspicious, and zero if slightly suspicious. For ECG results, two points are given for significant ST depression, one point for non-specific repolarization disturbance, and no points for a normal ECG. For age, two points are given for age ≥ 65 years, one point for age 45–65 years and no points for age ≤ 45 years. For risk factors, two points are given for ≥ 3 risk factors or a history of atherosclerotic disease, one point is given for one or two risk factors, and no points are given for no risk factors. For troponin concentrations, two points are given if the troponin level is greater than or equal to three times the normal limit, one point if the level is one, two, or three times the normal limit, and no points if the troponin is less than or equal to the normal limit. The score is summarized in Table 3.

In 2008, Six et al. [47] tested the heart score on 120 patients. It achieved a 96.5 % sensitivity, and a 42.7 % specificity. Backus et al. also tested the score on 880 patients in 2010, yielding a 98.1 % sensitivity, and a 41.6 % specificity [48]. Finally, Mahler et al. [49] validated the heart score on a cohort of 1,070 patients. In this population, the score achieved a 58.3 % sensitivity, and an 85.0 % specificity; however it must be noted that this population had a very low prevalence of disease (1 %).

The North American Chest Pain Rule

The North American Chest Pain Rule was developed by Erik Hess and colleagues and published in 2012 [19]. The

Table 3 Summary of new risk score systems and rules

HEART [45]	North American chest pain rule [19]	Vancouver chest pain diagnostic algorithm [20]
Composition of the HEART score for chest pain patients	A patient with chest pain and possible acute coronary syndrome can be safely discharged from the ED without additional diagnostic testing if NONE of the following criteria are met:	Patients are discharged with no further investigations if deemed very low risk by an ending emergency physician
History		
Highly suspicious 2		0-h assessment. If yes to any of: High risk clinical features ^c , EKG suspicious for ischemia ^f , Initial troponin positive, ^g then refer to cardiology. If No then low risk. If unclear then assess at 2 h.
Moderately suspicious 1	(1) New ischemia on initial ECG ^a	
Slightly suspicious 0	(2) History of coronary artery disease	
ECG	(3) Pain is typical for acute coronary syndrome ^b	2 h assessment. If yes to any of: New high risk clinical features, EKG suspicious for ischemia, 2 h troponin positive, then refer to cardiology. If No then low risk. If unclear then assess at 6 h.
Significant ST-depression 2	(4) Initial cardiac troponin is positive AND	
Non-specific repolarisation disturbance 1	(5) Age ≤ 40 years OR	
Normal 0	Age 41–50 years and repeat troponin at least 6 h from symptom onset is negative ^{c, d}	6 h assessment. If yes to any of: New high risk clinical features, EKG suspicious for ischemia, 6 h troponin positive, then refer to cardiology. If no then low risk. If unclear then outpatient provocative testing arranged within 48 h ^h .
Age		All low-risk patients followed up at 30 days.
≥ 65 year 2		
45–65 year 1		
≤ 45 year 0		
Risk factors		
≥ 3 Risk factors or history of atherosclerotic disease 2		
1 or 2 Risk factors 1		
No risk factors known 0		
Troponin		
$\geq 3 \times$ Normal limit 2		
1–3 $\times$ Normal limit 1		
$\leq$ Normal limit 0		

^a Defined as ST-segment deviation greater than or equal to 1 mm or T-wave inversion greater than or equal to 0.2 mm in at least 2 contiguous leads

^b As determined by the attending emergency physician. Samples for contemporary cardiac troponin assay analysis were obtained at presentation and at least 6 h from symptom onset in this cohort. Positive was defined as greater than 99th percentile reference limit

^c In addition, an age cutoff of 60 years or younger can be used with a less than 2 % miss rate and lower proportion of patients who require urgent stress testing in practice settings in which this miss rate is acceptable

^d Does not apply to patients with acute ST-segment elevation, hemodynamic instability, a clear traumatic cause of chest pain, a history of cocaine use or tested positive for cocaine, a terminal non-cardiac illness, or who were considered to have an unreliable history by the treating physician

^e High-risk clinical features: hemodynamically unstable, typical crescendo angina, rest pain > 20 min identical to past ACS, or on-going pain in ED

^f EKG suspicious for ischemia: ST elevation > 2 mm in 2 precordial leads, ST elevation > 1 mm in 2 inferior or lateral leads, ST elevation in right ventricular or posterior leads, ST depression > 0.5 mm in 2 contiguous leads, pathologic Q waves in 2 contiguous leads, or T wave inversion in 2 contiguous leads

^g Troponin T elevation: (Roche Elecsys, Hoffman LaRoche, Laval, PQ) elevation > 0.04 ng/mL

^h Although patients were typically referred at 0-, 2-, or 6-h decision points, they could be referred any time if clinical status changed; therefore some referral and discharge times are approximate

initial derivation paper included an internal validation using statistical bootstrapping techniques, and included 2,718 patients from three academic emergency departments in Ottawa Ontario, Kingston Ontario, and Rochester Minnesota. The robust methodology for the study was published in advance in [50]. In this chest-pain rule, patients were classified as low-risk if they met the following criteria: <50 years old, atypical chest pain, no history of

known coronary disease, non-ischaemic ECG results, and negative troponin test results during 6 h (Table 3). The derived rule was 100 % sensitive for a cardiac event within 30 days (Table 2). The model was internally validated using statistical bootstrapping techniques. The authors comment that the rule will differentially affect resource use depending on local practice patterns. They noted that a decrease in resource would be likely in centers where a

high proportion of patients undergo prolonged observation. External validation data is awaited.

The Vancouver Chest Pain Diagnostic Algorithm (2012)

Scheuermeyer et al. in Vancouver built on previous work in this area by conducting a single cohort implementation study on 1,116 patients with careful monitoring of patient outcomes [20] (Tables 2 and 3). Patients were categorized as low-risk if they did not have any high risk features. Patients with perceived high-risk features were referred to inpatient cardiology for further assessment and management.

High-risk features included:

- (a) *History* Pain similar to prior ACS, rest pain for greater than 20 min, ongoing pain in the ED, or typical crescendo angina, or a change in angina pattern such as new rest angina.
- (b) *Physical findings* such as a new murmur or clinical heart failure or haemodynamic instability;
- (c) *ECG results* suggestive of ischaemia; and
- (d) *Cardiac troponin* elevated

Patients that were classified as low-risk were eligible for early discharge after 2–6 h. The decision on whether to observe and test for follow-up troponin at 2 or 6 h was left to the clinician's judgment as to whether the patient was very low risk or not. At the time of discharge, follow-up provocative testing was arranged to take place within 48 h. After 30-day follow-up, no patients (0 %) had had a missed ACS. A "missed" case of ACS was defined as patient that was discharged from the ED with no cardiology referral or outpatient stress testing who proved to have ACS or died at 30 days. At the index visit, 271 patients (24.2 %) were referred to cardiology, 579 (51.8 %) were discharged home with no follow-up testing, and 254 (22.7 %) were discharged with follow-up testing. At 30 days, of the 120 patients with ACS, none (0 %, 95 % CI 0–2.5 %) were missed. However, 21 patients had evidence of reversible ischaemia on provocative testing and were readmitted for further investigation without incident. Of the 50 patients who had evidence of reversible ischemia on provocative testing, all were immediately re-referred to the ED for mandatory cardiology consultation; 21 of those patients ultimately proved to have unstable angina. Of the 254 patients referred for stress testing, none re-presented to the ED prior to their testing, and none had a myocardial infarction. This diagnostic algorithm shows great promise, especially as it was actually implemented in practice. External validation is clearly required for wider adoption.

The Future of Cardiac Risk Scoring Systems

There is no consensus on what is the best approach to develop risk stratification tools, although there is an international guidelines group working on this at present. A large variation of approaches to developing risk scores has been used, ranging from statistical weighting of variables collected in observational studies to clinical judgment, logic, and common sense. In mathematical models, all relevant clinical variables are collected in their prospective cohort of patients and objective outcomes are determined. Statistical techniques are subsequently employed, most commonly logistic regression analysis or recursive partitioning to identify those variables which are independent; these are then weighted. There are many variations in techniques on how to develop mathematical models, which are summarized in an excellent textbook by Ewout Steyerberg [51]. Statistically created models tend to be more mathematically sound, but run the risk of being overcomplicated and hard to use. Alternatively, risk scores developed using clinical judgment (such as the heart score) are more simplistic, but can work very well.

This analysis of risk scores suggests that the ideal characteristics of a risk stratification system would be:

- It achieves the required diagnostic accuracy when tested externally and put into clinical practice outside its derivation locations.
- It is simple to use.
- Not too long (i.e., not too many variables).
- It is easy to reproduce in different settings.
- It is easy to reproduce by different doctors with different experience.
- It is easy to calculate the score, if this needs to be done.
- It can be calculated without the aid of a calculator or computer.
- It can be easily remembered without needing to refer to a secondary source.
- It is logical to the user.

While debate about the best method for the development of risk scores may continue, it would seem that if the score works well in clinical practice with appropriate diagnostic accuracy then how it was created may not matter. It is also likely that whichever scores are adopted by clinicians, there will be an ongoing process of modification and improvement. This is nicely demonstrated by the history of the development and further improvement of scoring systems for the assessment of suspected pulmonary embolism in the emergency department. The

Geneva score [52] has gone through several modifications and simplifications since it was originally published. We are aware of a number of research groups in Australasia, Canada, the USA, the United Kingdom, Germany, and Switzerland that are in the process of developing new, purpose designed risk scores.

Other Considerations

Although sensitivity and negative predictive value are the key parameters of interest when deciding to use a risk assessment score to assist with chest-pain rule-out decision-making, it is important to consider the proportion of patients that will be classified as low risk. If the numbers are significantly low, then adopting a risk scoring system in an early rule-out strategy is unlikely to impact upon patient flow and ED overcrowding.

One other consideration is the rapidly changing field of cardiac biomarkers. The risk scoring systems we discuss were designed to be used in conjunction with cardiac biomarkers (and ECG). A new generation of high sensitivity troponin I assays is almost upon us and high sensitivity troponin T has been in use in many countries for several years. The inclusion of other supplementary biomarkers such as heart fatty acid binding protein and copeptin may also need to be investigated in future early rule-out strategies. As such, scoring systems should be flexible to include new technologies.

Conclusion

The judicious use of diagnostic tests should involve some assessment of pre-test probability, and this is relevant to assessing patients with possible ACS in the emergency department. In addition, reliable identification of patients who are at low risk will allow fast tracking of some tests and enable early discharge or progression to further investigations. Risk stratification scores represent a proven method of identification of such low-risk patients. Importantly, such scores are generally more reproducible amongst users than using clinician gestalt.

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