Original article

A clinical scoring system in undifferentiated chest pain predicting undetectable troponin concentration

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ABSTRACT

Background: Chest pain is the most common reason for emergency admission to hospital, but the majority of these are due to non-cardiac pain. We sought to determine which combination of clinical features is more likely to predict an undetectable troponin level in patients presenting with chest pain.

Methods: We collected data over a two-month period on consecutive patients presenting acutely to hospital with chest pain and who had a troponin I measured. We recorded basic demographics, risk factors, pain distribution, associated symptoms, physical findings and ECG changes. The parameters significantly associated with troponin positivity were entered into a stepwise logistic regression analysis and the resulting model's coefficients were used to construct a simple clinical score to categorise patients into low, medium or high probability of having a positive troponin.

Results: 26 of 157 (16.6%) patients had a positive troponin. The variables retained in the regression model were: age >65, heart rate >80, previous myocardial infarction, diabetes and pain radiating to either arm. The model showed good discrimination (area under ROC curve 0.869, 95% CI 0.806 – 0.917). Using the regression model's coefficients, patients were grouped into low, intermediate or high probability groups. Being in the low probability group had a negative predictive value of 97.8% and being in the high probability group had a positive predictive value of 65.2%. The majority (73.9%) of patients could be categorised as either low or high probability.

Discussion: This simple scoring system, if prospectively validated, may be useful in identifying low risk patients with chest pain who are unlikely to have elevation of serum troponin concentration.

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1. Introduction

Chest pain is the most common reason for attendance at emergency departments and accounts for 20–30% of all medical admissions,^{1,2} contributing to overcrowded hospitals and rising hospital costs. Acute chest pain is a diagnostic challenge due to the variety of causes for the symptom, however the majority of patients turn out to have a benign, non-cardiac cause of pain.^{1,2} Despite this two-thirds of patients with acute chest pain are admitted for further investigation, and only a small minority of these admissions are subsequently diagnosed with acute coronary syndromes.¹ Recent years have seen an increase in chest pain related admissions to Scottish hospitals; between 2001 and 2008 there was a 30% increase.³

Wealth of evidence and guidelines exist^{4–6} on the management of patients with confirmed or suspected acute coronary syndromes. Often these patients have diagnostic or abnormal ECGs to aid

diagnosis. In contrast there is relatively little evidence on how to manage “low-risk” patients with chest pain where physician suspicion of acute coronary syndrome is low, the ECG is normal or non-diagnostic, or where the diagnosis is in doubt. Increased physician anxiety regarding potentially missed acute coronary syndrome diagnoses and subsequent medico-legal claims in recent years has led to increased admission rates⁷ in patients considered to be low-risk for ACS in order to “rule out” ACS through troponin measurement.

Troponin measurement has become an integral part of assessing patients presenting with suspected cardiac chest pain, and elevated troponin concentrations consistently predict adverse outcome in patients with acute coronary syndromes.⁸ Troponin testing and assessment generally requires admission to a secondary or tertiary centre. For patients that live in rural communities with only primary care medical services nearby this may not be straightforward. Patients often have to travel long distances that may heighten patient anxiety and add to the burden already on the ambulance service.

Previous studies have identified clinical features that predict the likelihood of acute coronary syndromes, such as chest pain being

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“indigestion-like” or “burning” in character; radiation to either arms, neck or shoulder; precipitation by exertion, presence of a third heart sound and hypotension,^{9–11} but most of these studies involved patients with diagnostic ECGs or confirmed acute coronary syndromes where the diagnosis is clearer. In contrast, a recent study involving patients with normal or non-diagnostic ECGs reveal that isolated clinical features have very limited diagnostic value,¹² and measurement of troponin is therefore of paramount importance.

Evidence is lacking as to which groups of clinical features predict patients with chest pain who are likely to have undetectable troponin concentrations in the context of a normal or non-diagnostic ECG, where the aetiology is in doubt. We sought to investigate whether a combination of simple clinical parameters could identify patients presenting with chest pain and a normal or non-diagnostic ECG who are unlikely to have an elevation in troponin concentration. If this could be done, it could help identify a low-risk group of patients with chest pain, who in the setting of a normal ECG and low clinical suspicion of acute coronary syndrome would not necessarily require urgent referral to secondary care for troponin measurement.

2. Methods

We collected anonymised data prospectively between October and December 2009 from all adult patients (age >18) who had troponin I measured in Stobhill hospital, Glasgow, as part of their investigation for an acute episode of chest pain. The only exclusion criterion was age less than 18.

As well as basic demographics, we collected data from examination of patient case notes on major cardiovascular risk factors, past history, clinical observations at presentation, the distribution and character of pain, autonomic symptoms and ECG abnormalities. Troponin I was deemed elevated if the 12 h (or admission measurement if over 12 h from onset of pain) exceeded the threshold level of 0.04 ug/L using Abbott Laboratories Troponin I Immunoassay. The cut-off of 0.04 ug/L was chosen as this was the point below which our laboratory did not report specific measurements, and was regarded by the local cardiology service as an undetectable level.

For each of the variables, we tested their independence from troponin positivity using a Chi-square test with Yate's continuity correction or Fisher's exact test where appropriate. The continuous variables were first dichotomised by finding their point of maximum discrimination through analysis of their receiving-operator characteristic (ROC) curves, and selecting the nearest clinically relevant number as a cut-off point. Those variables with non-significant correlations were omitted from further analysis.

All of the remaining variables were entered into a stepwise multivariate logistic regression analysis (Medcalc v11.1.1, MedCalc Software, Mariakerke, Belgium) and those whose regression coefficients had a significance level of $p < 0.05$ were retained. These coefficients were used to create the weightings for each parameter in a simple clinical scoring system.

We assessed the discriminating power of our derived scoring system by measuring the area under its ROC curve, and measured the predictive values at each score level. The scoring system was used in turn to categorise patients into low, medium and high-risk groups based on the predictive values of each score point.

3. Results

We collected data on 157 consecutive adult patients who had a troponin measured and a history of chest pain, comprising 73 men and 84 women with a median age of 63 (range 18–94). Of these, 26

Table 1

Univariate associations between clinical features and troponin positivity.

Univariate associations			
Variable	Relative risk (95% CI)	Variable	Relative risk (95% CI)
<i>Demographics</i>		<i>ECG findings</i>	
Age >65	4.3 (1.8–10.0)	Heart rate >80	4.1 (1.9–8.7)
Male sex	1.0 (0.5–2.0)	Abnormal ECG	3.1 (1.5–6.4)
		AF	3.6 (1.8–7.3)
<i>Site of pain</i>		<i>Risk factors</i>	
Retrosternal	1.0 (0.5–2.2)	Diabetes	3.5 (1.8–6.9)
Epigastric	1.0 (0.2–6.2)	Smoking	2.0 (1.0–3.9)
Upper chest	1.6 (0.6–4.1)	Hypertension	1.6 (0.8–3.3)
Left chest	0.9 (0.3–2.3)	Hypercholesterolaemia	1.0 (0.4–2.6)
Right chest	2.1 (0.6–6.9)	Family history	1.0 (0.4–2.6)
Across chest	3.2 (1.1–9.1)		
Jaw/teeth	1.4 (0.6–3.1)	Previous MI	3.2 (1.7–6.3)
Posterior	1.2 (0.4–2.9)	Known CAD	2.8 (1.4–5.6)
Either arm	2.3 (1.2–4.7)	Previous CVA	1.1 (0.4–3.2)
<i>Associated features</i>		<i>Character</i>	
Dyspnoea	1.8 (0.9–3.8)	Pleuritic	0.6 (0.1–3.9)
Sweating	1.8 (0.9–3.8)	Sharp	0.8 (0.3–2.0)
N&V	2.0 (1.0–3.9)	Ache	1.8 (0.6–5.1)
Palpitations	1.2 (0.4–2.9)	Burning	0.9 (0.1–5.5)
Anxiety	1.5 (0.3–8.7)	Tight/crushing	1.2 (0.6–2.5)

(16.6%) had an elevated troponin. No patients had ST segment elevation or new bundle branch block on the ECG. The relative risk of having an elevated troponin for each of the clinical parameters considered is shown in Table 1, with the significant associations shown in bold.

When these variables were entered in a stepwise logistic regression analysis with troponin elevation as a binary dependant variable, the independent variables retained in the model were: age >65, heart rate >80, previous myocardial infarction, diabetes and pain radiating to either arm.

The logistic regression coefficients from this model are shown in Table 2. To obtain simple weightings for each parameter for the clinical score, the regression coefficients were rounded to the nearest whole multiple of the smallest coefficient. This resulted in each parameter receiving equal weighting, meaning the total clinical score is therefore simply the number of these parameters present (Table 3).

The clinical score showed good discrimination for troponin positivity, with an area under the ROC curve of 0.869 (95% confidence interval 0.806–0.917). The ROC curve is shown in Fig. 1, and the distribution of scores with the frequency of troponin elevation for each score are shown in Table 4.

Further splitting the scores into low (0–1), intermediate (2) and high-probability (3–5) groups gave a negative predictive value of 97.8% (95% confidence interval 92.4–99.7%) for a low-probability score and a positive predictive value of 65.2% (95% confidence

Table 2

Logistic regression model.

Variable	Coefficient	p value
Age >65	1.76	0.003
Pain in either arm	1.68	0.005
Heart rate >80	2.32	<0.001
Diabetes	1.84	0.021
Previous MI	1.55	0.008
Constant	–5.13	

Overall model fit $p < 0.0001$.

Table 3
Clinical score to predict troponin positivity.

Clinical feature	Score
Age >65	+1 point
Heart rate >80	+1 point
Previous MI	+1 point
Pain in either arm	+1 point
Diabetes	+1 point

Low-risk = 0–1; Intermediate-risk = 2; High-risk = 3–5.

Table 4
Distribution of scores and troponin positivity.

Score group	Frequency (percent of total)	Troponin positive (percent of group)
0	30 (19.1%)	1 (3.3%)
1	63 (40.1%)	1 (1.6%)
2	41 (26.1%)	9 (22.0%)
3	19 (12.1%)	11 (57.9%)
4	2 (1.3%)	2 (100%)
5	2 (1.3%)	2 (100%)

interval 42.7–83.6%) for a high-probability score (see Table 5). Almost three quarters (73.9%) of patients could be identified as either low-probability or high-probability.

4. Discussion

Our study introduces a novel simple score to predict the likelihood of an elevated troponin measurement based upon clinical features alone in patients presenting with chest pain and non-diagnostic ECGs. In particular, a low-risk score (0 or 1 points) had a negative predictive value of 97.8% and a high-risk score (3–5 points) had a positive predictive value of 65.2%. The strong negative predictive value of those with a low-risk score, 60% in this study, is where we focus our attention.

Patients presenting with chest pain to primary care physicians can broadly be split into three categories after initial assessment: those who have a clearly non-cardiac diagnosis; those who have a likely cardiac diagnosis; and those where a cardiac diagnosis is possible.

We propose that this scoring system may be of use to stratify patients who have a possible cardiac cause for their pain. Those who have a clearly non-cardiac cause for chest pain could be managed appropriate to the likely diagnosis, and those who fall into the remaining two categories could be further evaluated by means of an ECG. Those felt to be at high-risk based upon an abnormal ECG or by clinical history should be referred to the nearest secondary or tertiary centre for further investigation and assessment, including troponin measurement.

If prospectively validated we would argue a role for our scoring system for those patients in the final group; those with a possible or less likely cardiac cause of pain based upon history and examination findings in combination with a normal ECG. The strong negative predictive value of 97.8% in those with a score of zero or one would place these patients at being extremely low likelihood of having an elevated troponin.

This result would be in keeping with findings by Christenson et al.¹³ who derived the Vancouver Chest Pain Rule that was 98.8% sensitive for excluding myocardial infarction if the patient had a normal ECG, was under 40 years of age and had no previous ischaemic chest pain. Like our scoring system, this risk prediction tool has not yet been prospectively validated.

Risks are relative to the outcome of concern, and if the potential outcome is myocardial infarction, then the stakes are high. Understandably those who have a missed diagnosis of myocardial infarction have a higher mortality rate¹⁴ compared to those who are correctly identified, diagnosed and admitted to hospital for investigation and treatment. Around half of patients who have a “missed” diagnosis in retrospect have an abnormal ECG that was not detected by an often inexperienced physician.¹⁴ ECG evaluation by an experienced doctor is therefore important and would have to be an integral part of this system.

Although this scoring system predicts those at ‘low-risk’ of having an undetectable troponin it does not predict those at ‘zero risk’. This level of risk may be acceptable to some physicians however it may not be felt to be an acceptable level risk to patients, family members and relatives.

This study has limitations that should be taken into account when interpreting the findings. Firstly, this was a secondary analysis of data collected for another purpose to audit prescribing in acute coronary syndromes. Patient numbers were small as a result, there was no sample size calculation, and the study was not powered to detect associations between clinical features and troponin level. The data was obtained from case sheets rather than through direct assessment of each patient by the investigator. We therefore relied on accurate history taking and documentation by the attending doctor(s). However, the two strongest parameters that ended up in our model are age and heart rate (as recorded on initial ECG), which were both objectively verifiable. We would also argue that radiation to the arms, past history of myocardial infarction and diabetes are rarely omitted from the documented history of patients presenting with chest pain, and that this data is therefore robust.

Table 5
Distribution of probability groups and troponin positivity.

Probability group	Number of patients (percentage of total)	Troponin positive (percentage of group)
Low (0–1)	93 (59.2%)	2 (2.2%)
Intermediate (2)	41 (26.1%)	9 (22.0%)
High (3–5)	23 (14.6%)	14 (65.2%)

Fig. 1. ROC curve of clinical score.

The population our hospital in this single centre study serves has a relatively high prevalence of coronary artery disease. Therefore, this scoring system will require further evaluation in multiple centres that serve patient populations with different ethnicities and disease prevalence.

It should also be noted that patients attending with clearly non-cardiac chest pain and little diagnostic uncertainty, such as obvious musculoskeletal pain, were not included in our study if the attending doctor did not measure serum troponin levels. Our findings may therefore not apply to patients with a clearly non-cardiac diagnosis. Conversely, our results should not be generalised to higher risk patients with chest pain, such as those with new ST elevation or left bundle branch ECG changes. Patients with these ECG changes did not enter our study as they met criteria for Primary PCI and therefore did not attend our centre, however in this case the diagnosis is clearer. Our scoring system should therefore not apply to those at high clinical suspicion for ACS, a high-risk ECG, or those who had a clear non-cardiac diagnosis.

A recent multicentre emergency department¹⁵ study has shown the usefulness of point-of-care troponin assays. Their use is associated with increased discharge rates from emergency departments in patients attending hospital with chest pain. Troponin samples were taken at admission and at 90 min rather than admission and 6–12 h measurements that current national and international guidelines recommend.^{4–6} Point-of-care testing if expanded for use in primary care may be a useful adjunct to our scoring system and could be incorporated into a prospective validation study. Our study did not follow patients up to ascertain whether or not any had adverse outcomes over the coming weeks or months. It is also possible that we missed some patients with mildly elevated troponin measurements but not high enough to reach our laboratory cut-off of 0.04 ug/L.

Elevated troponin levels are found in other conditions besides acute coronary syndromes, such as heart failure, pulmonary thromboembolism and renal impairment, and therefore care must be taken in interpreting positive troponin results.¹⁶ Our data included some patients whose chest pain was associated with a tachyarrhythmia, and troponin can be elevated in such cases because of rate-related ischaemia rather than true acute coronary syndrome with plaque rupture. Nevertheless, such patients are still likely to require intensive monitoring and cardiology input, as raised troponin levels are known to carry increased mortality risk in critically ill patients.¹⁷

Finally, the study was relatively small and used multiple parameters to build its model. This increases the possibility of a type 1 error allowing clinical features that have no genuine relationship with troponin being included in the model by chance. However, each independent variable retained in our model has been previously associated with acute coronary syndromes or its mortality risk: previous MI, age and tachycardia are used to calculate risk in GRACE mortality risk scoring systems¹⁸; pain radiating to the arms has been previously shown to be a feature useful in the diagnosis of acute coronary syndromes^{11,19}; and diabetes has for a long time been known to be a risk factor for myocardial infarction.²⁰ In addition, four of the five parameters in the final model had *p* values of less than 0.0016, the cut-off for significance after Sidak's correction for multiple hypothesis testing. Only pain radiating to the arms did not meet this strict criterion, but as this has been

shown in other studies^{11,19} to be relevant, we believe the association is genuine and therefore retained it in our model.

We believe this clinical score shows promise as a tool to predict the likelihood of an elevated troponin level based upon clinical features in acute admissions with chest pain. If prospectively validated it may be useful in identifying those at low clinical suspicion of having an acute coronary syndrome in combination with a normal ECG who may not require troponin measurement. This scoring system could potentially be of most benefit to primary care doctors and to doctors in rural areas who do not have easy access to secondary care services. Ultimately this may save patients' an anxious, time consuming trip to a distant hospital, and save health boards money.

Conflicts of interest

All authors have none to declare.

References

- Blatchford O, Capewell S. Emergency medical admissions in Glasgow: general practices vary despite adjustments for age, sex and deprivation. *Br J Gen Pract.* 1999;49:551–554.
- Goodacre S, Cross E, Arnold J, et al. The health care burden of acute chest pain. *Heart.* 2005;91:229–230.
- www.isdscotland.org.
- www.sign.ac.uk/pdf/sign93.pdf.
- http://publications.nice.org.uk/chest-pain-of-recent-onset-cg95.
- http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/Guidelines-NSTE-ACS-FT.pdf.
- Katz DA, Williams GC, Brown RL, et al. Emergency physicians fear of malpractice in evaluating patients with possible acute cardiac ischaemia. *Ann Emerg Med.* 2005;46:525–533.
- Antman E, Tanasijevic MJ, Thomson B, et al. Cardiac-specific troponin I levels to predict the risk of mortality in patients with acute coronary syndromes. *N Engl J Med.* 1996;335:1342–1349.
- Goodacre SW, Angelini K, Arnold J, et al. Clinical predictors of acute coronary syndrome in patients with undifferentiated chest pain. *Q J Med.* 2003;96:893–898.
- Swap CT, Nagurney JT. Value and limitations of chest pain history in the evaluation of patients with suspected acute coronary syndromes. *JAMA.* 2005;294:2623–2629.
- Panju AA, Hemmelgarn BR, Guyatt GH, et al. The rational clinical examination. Is this patient having a myocardial infarction? *JAMA.* 1998;280:1256–1263.
- Goodacre S, Pett P, Arnold J, et al. Clinical diagnosis of acute coronary syndrome in patients with chest pain and a normal or non-diagnostic electrocardiogram. *Emerg Med J.* 2009;26:866–870.
- Christenson J, Innes G, McKnight D, et al. A clinical prediction rule for early discharge of patients with chest pain. *Ann Emerg Med.* 2006;47:1–10.
- Lee TH, Rouan GW, Weisberg MC, et al. Clinical characteristics and natural history of patients with acute myocardial infarction sent home from the emergency room. *Am J Cardiol.* 1987;60:219–224.
- The Randomised Assessment of Treatment using Panel Assay of Cardiac Markers (RATPAC) trial: a randomised controlled trial of point-of-care cardiac markers in the emergency department. *Heart.* 2011;97:190–196.
- De Gennaro L, Brunetti ND, Cucola A, et al. Increased troponin levels in non-ischemic cardiac conditions and non-cardiac diseases. *J Interv Cardiol.* 2008;21:129–139.
- Lim W, Qushmaq I, Devereaux PJ, et al. Elevated cardiac troponin measurements in critically ill patients. *Arch Intern Med.* 2006;166:2446–2454.
- Granger CB, Goldberg RJ, Dabbous OH, et al. For the global registry of acute coronary events investigators. Predictors of hospital mortality in the global registry of acute coronary events. *Arch Intern Med.* 2003;163:2345–2353.
- Goodacre S, Locker T, Morris F, et al. How useful are clinical features in the diagnosis of acute, undifferentiated chest pain? *Acad Emerg Med.* 2002;9:203–208.
- Woods KL, Samanta A, Burden AC. Diabetes mellitus as a risk factor for acute myocardial infarction in Asians and Europeans. *Br Heart J.* 1989;62:118–122.