An investigation into the prognostic value of the cardiac marker troponin T in patients with suspected acute coronary syndrome without ST segment elevation

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Abstract

This study was set up to investigate the prognostic significance of different bands of troponin T in the diagnosis and management of patients presenting with suspected acute coronary syndrome without ST segment elevation. The study was a cohort study, set in a District General Hospital in the north west of England. The participants were 421 patients admitted with suspected acute coronary syndrome without ST segment elevation over a three-month period. Analysis was carried out depending on whether the level of troponin elevation was in a negative (< 0.03 µg/L), intermediate (0.03–0.1 µg/L) or positive (> 0.1 µg/L) band. The outcome was a composite of all-cause mortality or hospital admission due to non-fatal myocardial infarction at 30 days and 12 months.

Both intermediate and positive levels of elevated troponin increased the risk of all-cause mortality and non-fatal myocardial infarction at least two-fold, both at 30 days and 12 months (p<0.01). People over 50 were found to have a worse prognosis than younger patients at 12 months (p<0.05) but gender had no significant effect.

Patients with suspected acute coronary syndromes without ST segment elevation who have either intermediate or positive levels of troponin T show a substantial increase in adverse outcomes during short- and long-term follow-up. Further research is required on these bandings as new generations of troponin assays are developed with improved levels of precision.

Key words: troponin T, chest pain, acute coronary syndrome, risk, prognosis

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Introduction

The management of patients presenting to hospital emergency departments with chest pain suspected to be of cardiac origin poses a diagnostic challenge. These patients represent a considerable burden for the NHS, comprising 20–30% of all emergency medical admissions.[1,2] Cardiac troponins, highly specific biochemical markers of myocardial damage, can help improve quality of care. However, troponins have not been universally adopted by all UK hospitals[3] and further work is still required on the different bands of troponin that have a significant adverse prognosis.[4]

This prognostic study therefore seeks to add to the available evidence base in the following ways:

- Whilst the majority of prognostic studies have dichotomised troponin levels as normal or elevated, this study considers three bands of troponin values.
- It specifically considers a lower decision limit in line with the recommendations of the International Federation of Clinical Chemistry (IFCC),[5] which in the case of troponin T is currently assessed at 0.03 µg/L, as well as the conventional decision limit of 0.1 µg/L used by many existing studies in this field.
- It uses a standardised troponin sampling time of 12 hours after onset of symptoms.

The study considers these issues in the context of the Joint European Society of Cardiology/American College of Cardiology Committee (JESC/ACC) consensus statement on the redefinition of myocardial infarction.[6]

Methodology

To examine the potential prognostic value of this test in a typical population, a cohort study with 12-month follow-up was conducted of patients presenting with acute chest pain to a district general hospital (DGH) in the north west of England (Stockport NHS Trust). This hospital primarily serves Stockport Primary Care Trust (PCT), which has a population all-age standardised mortality ratio (SMR) due to cardiovascular diseases of 101.[7]

Stockport PCT residents with chest pain suspected to be of cardiac origin, without evidence of ST segment elevation, and who were admitted during a three-month period during the year 2000 were included in the study. The methodologies used for case identification and diagnostic classification have been described previously.[8] Briefly, prospective case identification based on intensive surveillance of daily admissions took place and baseline data collection included ECG and troponin values (12 hours post onset of symptoms). National and international consensus statements[5,9-11] were used to determine troponin status as follows: negative (troponin T < 0.03 µg/L); intermediate (troponin T 0.03–0.1 µg/L); positive (troponin T > 0.1 µg/L).

Cardiac interventions (such as early angiogram and revascularisation were not provided on site; emergency and routine access to such interventions was available at two local tertiary centres.

Follow-up composite events (all-cause mortality or hospital admission due to non-fatal myocardial infarction [MI]) were ascertained through data linkage to the Public Health Mortality File and the Commissioning Data Set (both provided by the Office for National Statistics). Information on coronary angiography and revascularisation procedures, as defined by relevant OPCS codes, that occurred during the follow-up period was also collected.

A univariate analysis was conducted to examine the effect of troponin status on survival, followed by a multivariate Cox regression analysis adjusting for sex, age and revascularisation status.

Results

A total of 421 patients were included, 223 men (53.0%) and 198 women (47.0%). There were 73 patients (17.3%) under age fifty, 127 patients (30.2%) between 50 and 75 years and 221 patients (52.5%) over the age of 75. An additional 34 patients were excluded as no troponin level had been recorded.

Age greater than 50 years was associated with an adverse prognosis for the 12-month composite outcome of mortality or non-fatal MI, though not for a similar 30-day outcome. Gender did not have any prognostic significance.

Kaplan-Meier 'time-to-event' curves for the composite outcome of mortality or non-fatal MI show that patients who had intermediate and positive troponin levels both had significantly higher event rates (figure 1).

The associated relative risks for composite adverse outcomes (and their lower and upper 95% confidence intervals) are shown in table 1 for different bands of troponin elevation and for different follow-up times, using a multivariate Cox regression analysis adjusted for sex, age and revascularisation status.

Figure 1. Cumulative event rate for composite outcome by differing troponin T bands over a 12-month period (n=421)

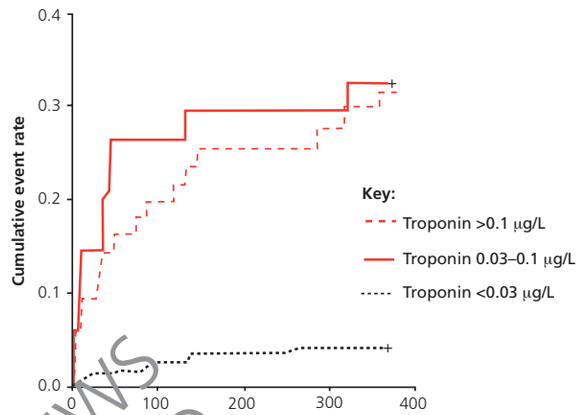

Table 1. Prognostic value of troponin T in patients with suspected acute coronary syndrome without ST elevation

	Troponin-negative < 0.03 µg/L	Troponin-intermediate 0.03–0.1 µg/L	Troponin-positive > 0.1 µg/L
Patients with chest pain without STEMI cases (n=421 patients)			
Crude event rates	n=333	n=34	n=54
30-day mortality or non-fatal MI	5/333 (1.5%)	5/34 (14.7%)	6/54 (11.1%)
12-month mortality or non-fatal MI	14/333 (4.2%)	11/34 (32.4%)	17/54 (31.5%)
Relative risk (with 95% CI) adjusted for age, sex and revascularisation			
30-day mortality or non-fatal MI	1	10.1 (2.8–36.8)***	6.9 (2.0–24.2)**
12-month mortality or non-fatal MI	1	6.9 (3.0–15.5)***	7.4 (3.6–15.2)***

Numbers in parenthesis indicate percentages or 95% confidence intervals (CI) as appropriate.
** p<0.01; *** p<0.001; d = day; m = month

Table 2. Number of angiograms and revascularisation procedures during follow-up

Troponin band	Angiogram performed		Revascularisation performed	
	Absolute numbers	Percentage	Absolute numbers	Percentage
Troponin-negative	17/333	5.11%	7/333	2.10%
Troponin-intermediate	2/34	5.88%	2/34	5.88%
Troponin-positive	7/54	12.96%	7/54	12.96%

Key messages

- The patients in this study were admitted to hospital with suspected acute coronary syndrome
- Those with troponin T levels in the upper two bands had higher all-cause mortality and hospitalisation for non-fatal MI at 30 days and 12 months
- Those patients in the 'intermediate' band had a similar risk to those in the highest one

Angiogram and revascularisation status during follow-up, are shown in table 2.

Discussion

Patients with suspected acute coronary syndrome without ST segment elevation with either an intermediate or positive level of elevated troponin T (as defined in this study) have a two- to three-fold increase in both short- and long-term adverse outcomes.

The angiogram and revascularisation rates, although low by current practices, are in keeping with nationally measured figures for Scotland[12] during an equivalent time period when glycoprotein IIb/IIIa inhibitors were not in common use and when revascularisation rates were correspondingly lower. A further significant contributing factor, as explored by Miller *et al.*[13] may be the recognised inequity of access around early invasive assessment and revascularisation services in those patients admitted to district general hospitals (DGHs) compared to those admitted to tertiary cardiac centres.

These findings nevertheless are consistent with four meta-analyses[14-17] of acute coronary syndrome patients without ST segment elevation, showing a two- to three-fold increase in the risk of composite outcome (death or non-fatal MI) associated with an elevated troponin level both at 30 days and 12 months. Such meta-analyses, however, are primarily composed of studies which use a dichotomised view of troponin levels with a detection limit typically of 0.1 µg/L or 0.2 µg/L. Individual studies such as that of Lindahl *et al*.[18] have, in contrast, considered a range of troponin bands and his recent studies have published a lower decision limit level as low as 0.06 µg/L.[18] This is still above the lower decision limit for myocardial damage at which the current IFCC recommendations[4] regarding the precision of troponin assays would still be met, however. Indeed, in the case of third generation troponin T assays, it has been demonstrated that a decision limit as low as 0.03 µg/L[5] would still be in line with these recommendations.

This study re-examines the definition of an elevated troponin by demonstrating that 'intermediate' troponin levels indicate a similar high risk to that seen in those patients with troponin values in the 'positive' range. This 'intermediate' range has been demonstrated to extend as far as 0.03 µg/L, a figure which is in line with the recommendations of the IFCC and which is also substantially lower than the conventional decision limit of 0.1 µg/L used by many existing studies in this field. Indeed, as future generations of troponins are developed with improved levels of precision, even lower decision limits for troponin T may be used to identify at-risk patients in line with the Joint European Society of Cardiology/American College of Cardiology (JESC/ACC) consensus statement on the redefinition of myocardial infarction.[6] Such a redefinition incorporates a troponin T elevation above the 99th centile of a normal reference population as evidence for myocardial damage, currently calculated for third generation troponins as 0.01 µg/L.[4]

Study strengths and limitations

Our study has a relatively small sample size, as indicated by the often wide confidence intervals around statistically significant values. Other potential limitations include case selection bias, variation in cardiovascular risk factors and different medication regimes whilst in hospital.

It is possible that different follow-up arrangements (such as cardiac rehabilitation) could partly account for the results, but intuitively patients with higher troponin values would be more likely to have access to such treatments and to benefit from them. Therefore the findings most likely under-estimate the prognostic significance of troponin status.

In contrast to clinical trials which include a well defined but highly selected population, this cohort study used patients presenting as emergencies in a typical UK general hospital, and hence provides 'real world' evidence about the prognostic ability of cardiac troponins.

Further research issues

Further work is required to explore the extent to which troponin elevation might influence subsequent outcomes, particularly at lower decision limits. As new generations of troponin T assays are developed, the ability to detect even lower levels of troponin that could indicate a prognostically significant adverse outcome will be enhanced.

Conclusions

Patients with suspected acute coronary syndromes without ST

segment elevation who have either positive or intermediate levels of troponin T elevation, as defined here, show a substantial increase in adverse outcomes during both short- and long-term follow-up. With the development of new generation of troponin T assays, there is scope to improve the precision of troponin measurements at lower decision limits that would be in accordance with the JESC/ACC consensus statement[6] on the redefinition of MI.

Conflict of interest

The study received a grant of £12,000 from MSD, manufacturer of a glycoprotein IIb-IIIa receptor inhibitor. The authors have no other conflict of interest to declare.

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