CLINICAL AUDIT

Raised cardiac troponin T levels in patients without acute coronary syndrome

P Wong, S Murray, A Ramsewak, A Robinson, C van Heyningen, E Rodrigues

Postgrad Med J 2007;83:200–205. doi: 10.1136/pgmj.2006.049080

See end of article for authors' affiliations

Correspondence to: P Wong, Aintree Cardiac Centre, University Hospital Aintree, Liverpool L9 7AL, UK; peter.wong@aintree.nhs.uk

Received 28 April 2006
Accepted 15 May 2006

Objective: To investigate the frequency, diagnosis and outcome of patients admitted to hospital with acute coronary syndrome (ACS) or other conditions associated with raised levels of cardiac troponin T.

Design: Observational study.

Setting: A large university hospital.

Patients: Consecutive patients admitted over an 8-week period who had a serum troponin T test as part of their clinical assessment were included. Patients were separated into those with raised (≥ 0.01 µg/l) or normal (< 0.01 µg/l) troponin T levels, and further categorised into those with or without a diagnosis of ACS. **Main outcome measures:** In-hospital mortality in all patients; and 6-month hospital re-admissions and all-cause mortality in patients without or with ACS and raised levels of troponin T.

Results: Of 1021 patients, 118 patients had no ACS but raised troponin T levels, 195 had ACS with raised troponin T, 80 had ACS with normal troponin T and 628 had no ACS with normal troponin T. Their in-hospital all-cause mortalities were 36%, 18%, 0% and 3%, respectively ($p < 0.001$, highest mortality v other groups). 6-month all-cause mortality remained higher in patients without ACS and with raised levels of troponin T than in those with ACS and raised troponin T (42% v 29%; $p = 0.020$).

Conclusions: Patients without ACS but with raised levels of troponin T comprised 38% of all hospitalised patients found to have raised troponin T. These patients had worse in-hospital and 6-month outcome than those having ACS with raised levels of troponin T.

Cardiac troponins are highly specific markers for detecting myocardial injury. The Joint European Society of Cardiology and American College of Cardiology have redefined acute, evolving or recent myocardial infarction as the presence of an abnormally raised level of cardiac troponin (or creatine kinase-MB) in the blood associated with ischaemic symptoms, or changes indicative of ischaemia or new Q waves on an electrocardiogram, or in patients with recent coronary artery intervention.¹ The cardiac troponin-tropomyosin complex forms part of the contractile apparatus and consists of three subunits: troponin T, troponin I and troponin C.² In acute myocardial infarction, cardiac troponins are released into the blood as ternary (troponin T-I-C) and binary (troponin I-C) complexes, and as free troponin T.³ Since the original work by Cummins *et al*⁴ in developing the troponin radioimmunoassay, highly sensitive and specific monoclonal antibodies to cardiac troponins T and I have evolved to facilitate the diagnosis of

acute coronary syndrome (ACS).⁵ Besides ACS, raised levels of cardiac troponins in the blood can also be found in patients with a wide variety of conditions other than ACS.^{6–9} We examined a cohort of hospitalised patients in whom troponin T assay was carried out as part of their clinical assessment.

METHODS

Consecutive patients who were admitted to University Hospital Aintree, Liverpool, UK, over an 8-week period, between 5 January and 29 February 2004, and had one or more troponin T blood tests were included in the study. Troponin T blood test was requested by the admitting physicians when the patients were suspected of having ACS, and their decision for measuring troponin T was not influenced by this study. The study protocol was prospectively written and approved by the Sefton Local Research Ethics Committee. Patients were identified by reviewing the daily hospital admissions list and the list of troponin T blood test results. Serum troponin T level was routinely measured at 12 h from the onset of symptoms in patients who were suspected of having ACS in accordance with a hospital-wide policy. Troponin T level was measured by the Elecsys troponin T electrochemiluminescence immunoassay ECLIA (4th generation) with the Roche Elecsys 2010 analyser (Hofman-La Roche Ltd, Basel, Switzerland). The Elecsys troponin T assay consists of two monoclonal antibodies specifically directed against human cardiac troponin T, and detects free cardiac troponin T, as well as its binary and ternary complexes.¹⁰ The lowest detection limit of troponin T concentration that can be distinguished from zero is 0.01 µg/l, and the lowest troponin T concentration that meets a 10% coefficient of variation requirement is 0.03 µg/l. Patients were separated into two groups according to their troponin T level: those with

Key points

- Raised cardiac troponin T levels can be seen in both acute coronary syndrome (ACS) and many other conditions
- Patients without ACS but with raised cardiac troponin T have a poor prognosis irrespective of their diagnosis
- Any detectable cardiac troponin T level was associated with adverse clinical outcome in patients without ACS
- Cardiac troponin T level and other clinical variables can help in determining whether patients have ACS or other conditions
- Clinicians should be cautious about diagnosing ACS in patients with raised cardiac troponin T levels

Abbreviations: ACS, acute coronary syndrome

normal ($<0.01 \mu\text{g/l}$) and those with raised ($\geq 0.01 \mu\text{g/l}$) troponin T levels.

Medical records were reviewed to ascertain the primary diagnosis, and patients were categorised into four diagnostic groups: (1) without ACS but with raised levels of troponin T; (2) ACS with raised troponin T; (3) ACS with normal troponin T; and (4) without ACS and with normal troponin T. ACS comprises ST segment elevation myocardial infarction and non-ST segment elevation ACS. Non-ST segment elevation ACS can be further subdivided into unstable angina or non-ST segment elevation myocardial infarction. Myocardial infarction is accompanied by an abnormally raised cardiac troponin T level as a result of myocyte necrosis. The diagnosis of ACS (with or without raised troponin T) required the presence of ischaemic cardiac symptoms, or electrocardiographic changes indicative of ischaemia. The absence of these features, alongside the clinical picture of an alternative diagnosis, confirmed conditions other than ACS. Furthermore, the primary diagnosis of absence of ACS but presence of raised troponin T level required two clinicians (S Murray, A Ramsewak, A Dhanasekaran) to confirm the same diagnosis after their independent reviews. Any disagreement in the diagnosis required a further diagnostic review (PW).

In-hospital all-cause mortality data were available for all patients. Six-month all-cause mortality and hospital re-admission details were complete in all patients without ACS and with raised troponin T level, and in those with ACS with raised troponin T.

Data were statistically analysed using the χ^2 and Fisher's exact tests for comparing categorical variables, Student's *t* test for comparing group means and Mann-Whitney *U* test for comparing group medians, where appropriate. Logistic regression analysis using logarithmic transformation of troponin T and other clinical variables was carried out to investigate for significant prognostic factors affecting mortality in patients without or with ACS. Furthermore, on the basis of presenting characteristics of patients, multiple logistic regression was used to develop a model for helping in the diagnosis of conditions other than ACS. This diagnostic model may help clinicians to make their diagnosis more accurately as a raised level of cardiac troponin was often regarded as synonymous with having an ACS. Data were statistically analysed using SPSS V.13.0 for Windows.

RESULTS

During the study period, 1021 patients were hospitalised and one or more serum troponin T tests were carried out as part of their clinical assessment (fig 1). Of these, 313 patients had raised troponin T level ($\geq 0.01 \mu\text{g/l}$), of which 118 did not have ACS and 195 had ACS. In-hospital all-cause mortality was 36%

among patients without ACS but with raised troponin T level. This was significantly higher than in patients having ACS with raised or normal troponin T, and in those without ACS and with normal troponin T ($p<0.001$; table 1). Death due directly to cardiac causes accounted for 9% (4/43) of all deaths in patients who did not have ACS but had raised troponin T, and this compared with 92% (33/36) of all deaths in patients presenting with ACS and raised troponin T. Sensitivity and negative predictive value of a raised troponin T level in predicting in-hospital cardiac mortality in the entire cohort were both 100%, and the corresponding values in predicting in-hospital all-cause mortality were 79% and 97%, respectively (table 2).

Further analyses were focused on the two groups of patients without and with ACS who had raised troponin T levels.

Baseline characteristics and medical history of patients with raised troponin T levels

Both patients without and with ACS had broadly similar characteristics. These patients presented at an older age (mean age 75 *v* 73 years; $p = \text{NS}$; table 3). The proportion of patients who had a history of angina, myocardial infarction or coronary revascularisation was not different in the two groups. Likewise, we found no significant difference in the prevalence of hypertension, diabetes mellitus, current smoking, asthma or chronic obstructive pulmonary disease, peripheral vascular disease, chronic kidney disease and cerebrovascular disease. However, patients without ACS were more likely to be female (59% *v* 42%; $p = 0.005$), to have a history of congestive cardiac failure (25% *v* 10%; $p<0.001$) and multiple comorbidities as measured by the Charlson's Comorbidity Score (median 2 *v* 1; $p = 0.006$).¹¹

Presenting symptoms, electrocardiographic changes and cardiac markers in patients with raised troponin T levels

Patients without ACS were less likely than those with ACS to present with chest pain as a major symptom (12% *v* 57%; $p<0.001$; table 4), and were more likely to complain of breathlessness (32% *v* 17%; $p = 0.003$), collapse (19% *v* 11%; $p = 0.050$) and other symptoms not associated with chest pain (37% *v* 14%; $p<0.001$). Electrocardiographic ST elevation (2% *v* 23%; $p<0.001$) or ST depression (5% *v* 27%; $p<0.001$) was less frequent among patients without ACS than in those with ACS, whereas atrial fibrillation or flutter (41% *v* 11%; $p<0.001$) was more common among patients without ACS. Median values of troponin T (0.05 *v* 0.34 $\mu\text{g/l}$; $p<0.001$) and creatine kinase (115 *v* 284 IU/l; $p<0.001$) were lower in patients without ACS than in those with ACS.

Primary diagnosis, in-hospital and 6-month all-cause mortality in patients with raised troponin T levels

Cardiovascular disease was the most common diagnosis (36%) in patients without ACS but with raised troponin T levels

Figure 1 Flow diagram for hospitalised patients who underwent troponin T (TnT) test. Raised troponin T level $\geq 0.01 \mu\text{g/l}$. ACS, acute coronary syndrome.

Table 1 In-hospital mortality of patients with and without acute coronary syndrome with raised or normal troponin T level

	Raised TnT		Normal TnT	
	No ACS, n=118	ACS, n=195	No ACS, n=628	ACS, n=80
In-hospital cardiac mortality (%)	3	17	0	0
All-cause mortality (%)	36	18	3	0

ACS, acute coronary syndrome; TnT, troponin T.

Table 2 Usefulness of raised troponin T level in predicting in-hospital cardiac and all-cause mortality

In-hospital	Cardiac mortality (%)	All-cause mortality (%)
Sensitivity	100	79
Specificity	72	75
Positive predictive value	12	25
Negative predictive value	100	97

(table 5). Within this group, congestive cardiac failure was the most frequent primary diagnosis, with in-hospital and 6-month all-cause mortality of 32% and 42%, respectively. Patients with pulmonary embolism and cardiac arrest that was secondary to intracranial sepsis were more at risk of death than those with a supraventricular tachycardia (mostly atrial fibrillation or flutter), hypotension, myopericarditis or malignant hypertension. Respiratory disease (infection or exacerbation of chronic obstructive pulmonary disease) was the second most common diagnosis in patients without ACS, with 46% and 57% in-hospital and 6-month all-cause mortality, respectively. Among these 28 patients, 19 had one or more secondary diagnosis, including five with respiratory failure and four with congestive cardiac failure. The remaining patients without ACS had sepsis or septicaemia, gastrointestinal perforation, bleed or hepatorenal syndrome, stroke, malignancy, collapse or fall and renal failure; two patients had no apparent cause for a raised troponin T (paracetamol overdose, and no diagnosis made).

In-hospital all-cause mortality was high among patients who had raised troponin T levels and gastrointestinal perforation, bleed or hepatorenal syndrome (75%), stroke (63%), sepsis or septicaemia (50%), malignancy (43%) and renal failure (25%). However, the mortality in these subgroups of patients without ACS seemed to have reached a plateau during the index admission, and remained unchanged at 6 months. Furthermore, we found that in-hospital (19% *v* 46%; *p* = 0.004) and 6-month (26% *v* 50%; *p* = 0.012) all-cause mortality values among 42 patients with a cardiovascular diagnosis were lower than those among the remaining 76 patients with a non-cardiovascular diagnosis. Compared with patients who had ACS with raised troponin T levels, those without ACS but with raised troponin T levels were at a greater risk of dying in hospital (36% *v* 18%; *p* < 0.001) and at 6 months (42% *v* 29%; *p* = 0.020). Of the 195 patients with ACS and raised troponin T levels, 45 underwent coronary angiography, 34 of whom received coronary revascularisation.

Six-month hospital re-admissions in patients with raised troponin T levels

Rates of hospital re-admissions at 6 months were similar in patients with and without ACS (25% *v* 22%; *p* = NS; table 6). Of 19 patients without ACS who required hospital re-admission, 11 were due to cardiac causes and six of these had decompensated cardiac failure. Of the 35 patients with ACS, 30 were re-admitted with recurrent cardiac problems and 19 of these had a further ACS. All-cause mortality was lower among patients without ACS who required hospital re-admission than among those with ACS (5% *v* 34%; *p* = 0.021).

Logistic regression analysis in identifying significant prognostic factors and constructing a model to improve the diagnosis in patients without ACS

The effect of troponin T level on clinical outcome was investigated by logarithmic transformation of troponin T and separating it into quintiles among patients without (*n* = 118) or

Table 3 Baseline characteristics and medical history of patients with or without acute coronary syndrome and with raised troponin T levels

	No ACS, n = 118	ACS, n = 195	p Value
Age in years, mean (SD)	75 (12)	73 (13)	NS
Female	69 (59)	82 (42)	0.005
Angina	27 (23)	49 (25)	NS
Myocardial infarction	29 (25)	66 (34)	NS
PCI or CABG	5 (4)	11 (6)	NS
Congestive cardiac failure	29 (25)	19 (10)	<0.001
Hypertension	54 (46)	102 (52)	NS
Diabetes mellitus	28 (24)	36 (19)	NS
Current smoker	26 (22)	50 (26)	NS
Asthma or COPD	25 (21)	43 (22)	NS
Peripheral vascular disease	5 (4)	14 (7)	NS
Chronic renal impairment	10 (8)	8 (4)	NS
Stroke or TIA	25 (21)	37 (19)	NS
Charlson's Comorbidity Score			
50th centile (25th, 75th centiles)	2 (1, 3)	1 (1, 3)	0.006

Numbers in parentheses are percentages unless otherwise mentioned. ACS, acute coronary syndrome; CABG, coronary artery bypass graft; COPD, chronic obstructive pulmonary disease; PCI, pulmonary cutaneous intervention; TIA, transient ischaemic attack.

with (*n* = 195) ACS. Increasing troponin T level was associated with an increase in in-hospital mortality (*p* = 0.016), 6-month mortality (*p* = 0.019), and 6-month mortality or hospital re-admissions (*p* = 0.026) among patients without ACS, but not in those with ACS. Using the entire cohort (*n* = 313), having a diagnosis of conditions other than ACS and increasing troponin T levels among patients without ACS were found to be independent predictors for in-hospital mortality (*p* < 0.001; *p* = 0.016), 6-month mortality (*p* = 0.002; *p* = 0.019), and 6-month mortality or hospital re-admissions (*p* = 0.003; *p* = 0.026), respectively. The significance of these factors were independent of age and sex.

Multiple logistic regression analysis identified an absence of chest pain (*p* < 0.001), lower value of troponin T (*p* < 0.001), absence of ST segment depression (*p* < 0.001), and presence of atrial fibrillation or flutter (*p* = 0.001) to be independent predictors for diagnosis of patients without ACS. By using the above diagnostic model, a score can be developed to aid the diagnosis of conditions other than ACS:

$$\text{Score} = -0.7 \times \ln(\text{troponin T}) - \text{presence of chest pain} \\ - \text{presence of ST depression} + \text{presence of} \\ \text{atrial fibrillation or flutter}$$

A patient with chest pain, ST depression, or atrial fibrillation or flutter was given a score of 1 for each variable if present. The sensitivity and specificity for correctly diagnosing a patient without ACS by having a score ≥ 1.5 were 0.81 and 0.84, respectively. Using a single variable of troponin T, the best clinical cut-off for diagnosing ACS was $\geq 0.09 \mu\text{g/L}$, with a sensitivity of 77% and a specificity of 75%.

DISCUSSION

Among our unrandomised cohort of hospitalised patients with raised serum level of cardiac troponin T ($\geq 0.01 \mu\text{g/L}$), 38% of patients did not present with ACS. A wide variety of conditions other than ACS were found to be responsible for a rise in their cardiac troponin T levels. Collectively, these patients without ACS but with raised cardiac troponin T had significantly higher in-hospital and 6-month mortality than those having ACS with raised cardiac troponin T. Logistic regression analysis showed

Table 4 Presenting symptoms, changes on the electrocardiogram and cardiac markers in patients with and without acute coronary syndrome and with raised troponin T levels

	No ACS, n=118	ACS, n=195	p Value
Symptoms			
Chest pain	15 (12)	112 (57)	<0.001
Breathlessness	38 (32)	34 (17)	0.003
Collapse	22 (19)	21 (11)	0.050
Others	44 (37)	28 (14)	<0.001
ECG*			
ST elevation	2 (2)	45 (23)	<0.001
ST depression	6 (5)	52 (27)	<0.001
T-wave inversion	11 (9)	33 (17)	NS
LBBB or RBBB	18 (15)	19 (10)	NS
Atrial fibrillation or flutter	48 (41)	21 (11)	<0.001
Cardiac markers			
Creatine kinase (U/l)	115 (62, 216)	284 (110, 787)	<0.001
Troponin T (µg/l)	0.05 (0.03, 0.08)	0.34 (0.09, 1.52)	<0.001
Number of troponin T measurement	1 (1, 1)	1 (1, 1)	NS

ACS, acute coronary syndrome; LBBB, left bundle branch block; RBBB, right bundle branch block.

Values in parentheses are percentages or 25th and 75th centiles.

*Presenting electrocardiogram (ECG) was unavailable in four patients without ACS.

that increasing values of troponin T were associated with an increase in in-hospital mortality, 6-month mortality, and 6-month mortality or hospital re-admissions among patients without ACS. Furthermore, having a clinical diagnosis of conditions other than ACS was associated with a worse clinical outcome, and was independent of age or sex.

Three main areas have to be considered in the clinical application of the troponin T test:

1. *Troponin T assay performance and reliability*: Unlike the many available troponin I assays, there is only one patented troponin T assay. We used the 4th generation Elecsys Cardiac Troponin T assay, which has a lower detection limit of 0.01 µg/l. In contrast

Table 5 Primary diagnosis, in-hospital and 6-month all-cause mortality in patients with and without acute coronary syndrome with raised troponin T levels

	n	TnT, median (range)	In-hospital mortality, n (%)	6-month mortality, n (%)
No ACS				
Cardiovascular				
Congestive cardiac failure	19	0.05 (0.01–0.12)	6 (32)	8 (42)
Supraventricular tachycardia	10	0.04 (0.01–0.13)	0 (0)	1 (10)
Hypotension	6	0.03 (0.01–0.11)	0 (0)	0 (0)
Myopericarditis	3	0.02 (0.02–0.03)	0 (0)	0 (0)
Pulmonary embolism	2	0.11 (0.06–0.16)	1 (50)	1 (50)
Malignant hypertension	1	0.02	0 (0)	0 (0)
Cardiac arrest	1	0.60	1 (100)	1 (100)
Subtotal	42	0.05 (0.01–0.60)	8 (19)	11 (26)
Respiratory				
Chest infection or exacerbation of COPD	28	0.04 (0.02–0.15)	13 (46)	16 (57)
Gastrointestinal				
Bowel perforation	4	0.06 (0.02–0.13)	2 (50)	2 (50)
Bleed	3	0.03 (0.03–1.02)	3 (100)	3 (100)
Hepatorenal syndrome	1	0.05	1 (100)	1 (100)
Subtotal	8	0.05 (0.02–1.02)	6 (75)	6 (75)
Renal failure	4	0.06 (0.02–0.40)	1 (25)	1 (25)
Stroke	8	0.09 (0.02–0.17)	5 (63)	5 (63)
Sepsis or septicaemia	12	0.05 (0.02–1.72)	6 (50)	6 (50)
Malignancy	7	0.05 (0.02–0.46)	3 (43)	3 (43)
Collapse or fall	7	0.03 (0.02–0.29)	1 (14)	1 (14)
Others	2	0.05 (0.01–0.09)	0 (0)	0 (0)
Total	118	0.05 (0.01–1.72)	43 (36)*	49 (42)†
ACS				
Total	195	0.34 (0.01–33.61)	36 (18)*	56 (29)†

ACS, acute coronary syndrome; COPD, chronic obstructive pulmonary disease; TnT, troponin T.

*In-hospital mortality, non-ACS v ACS; p<0.001.

†6-month mortality, non-ACS v ACS; p=0.020.

Table 6 Six-month hospital re-admissions in patients with and without acute coronary syndrome with raised troponin T levels

	No ACS, n = 19	ACS, n = 35
Cardiac re-admissions		
ACS neg TnT	1	4
ACS pos TnT	2	15
Congestive cardiac failure	6	8
Supraventricular tachycardia	1	1
Bradycardia or hypotension	1	2
All-cause mortality	1 (9%)	10 (29%)
Non-cardiac re-admissions	8	5
All-cause mortality	0 (0%)	2 (40%)
Total all-cause mortality (cardiac and non-cardiac)	1 (5%)	12 (34%)*

*p=0.021.

ACS, acute coronary syndrome; neg TnT, without raised troponin T; pos TnT, with raised troponin T; TnT, troponin T.

with earlier troponin T assays, cross-reactivity with skeletal muscle troponin T was negligible.¹⁰ The troponin T concentration at which a 10% coefficient of variation is met as recommended by the Joint European Society of Cardiology and American College of Cardiology was 0.03 µg/l. Twenty seven of our patients without ACS had raised troponin T levels of 0.01–0.02 µg/l (equivocal but not normal level), which were within the assay imprecision range. We found their in-hospital mortality to be high and comparable with the remaining 91 patients without ACS, who also had raised troponin T levels of ≥0.03 µg/l (26% v 40%; p = NS), and also significantly higher than the 628 patients without ACS who had normal troponin T levels (26% v 3%; p<0.001). In a case-control study by Gudmundsson *et al*,¹² a minor rise in troponin I (including troponin I level below 10% coefficient of variation) among hospitalised patients was associated with a high 12-month all-cause mortality. Similarly, a random case selection study by Cook *et al*¹³ also found a graded increase in mortality among hospitalised patients with increasing troponin T level in the range of 0.01–0.099 µg/l, although there was no statistical difference found between patients who had a raised troponin T level between 0.01 and 0.03 µg/l and those with a normal troponin T level of <0.01 µg/l.

2. Troponin T in the diagnosis of acute myocardial infarction: Since the introduction of the revised definition of myocardial infarction,¹ highly sensitive cardiac troponin assays have been developed for detecting myocardial damage. It has been estimated that the incidence of acute myocardial infarction could increase by 26%, by using the level at which a 10% coefficient of variation was met as cut-off.¹⁴ Sensitivity of the Elecsys Troponin T 2nd generation assay in diagnosing acute myocardial infarction has been reported to be 100%,¹⁵ and there is a high degree of consistency between this earlier and present generation of troponin T assays.¹⁰ From our results, the best clinical troponin T cut-off value was ≥0.09 µg/l for diagnosing ACS, with sensitivity 77% and specificity 75%. Specificity of cardiac troponin assays in confirming ACS depends on the likelihood of finding a false-positive raised cardiac troponin level in conditions other than ACS. Specificity was 84% in our cohort, which included patients without ACS but who had raised cardiac troponin T levels. A rise in troponin T level occurs in a large number of conditions other than ACS.^{6–9} These included the primary diagnoses in our patients having congestive cardiac failure, supraventricular tachycardia, hypotension, myopericarditis, pulmonary embolism, malignant

hypertension, cardiac arrest caused by conditions other than ACS, acute exacerbation of chronic obstructive pulmonary disease, gastrointestinal perforation, bleed or hepatorenal syndrome, renal failure, stroke, septicemia or sepsis, and malignancy. The relatively benign outcome in our patients with hypotension contrasted with that in patients with hypotension who were managed by critical care.¹⁶ Coronary angiographic studies showed that patients who had raised cardiac troponin I levels not related to ACS could have angiographically normal coronary arteries, and these patients shared our list of diagnoses other than ACS.^{17–18} Conversely, it is also possible to miss the diagnosis of ACS in patients who seemed to have conditions other than ACS with raised cardiac troponin (false negative).¹⁹ We had no postmortem data to show the frequency of occurrence of acute myocardial infarction among our patients who were diagnosed of having conditions other than ACS with raised cardiac troponin T levels. Some of our patients may have their primary condition complicated by ACS. These patients limit our ability to diagnose coexisting ACS with other conditions associated with raised cardiac troponin T levels.

3. Correlation between cardiac troponins and outcome: Earlier studies have established the independent prognostic value of raised cardiac troponins in patients with ACS.²⁰ Moreover, the risk for death was proportional to the rise in cardiac troponin level.²¹ As a result, cardiac troponins have become important markers in risk stratification of ACS, and guide further prognostically important therapeutic and invasive management decisions in these patients.^{22–23} Among patients with conditions other than ACS, raised levels of cardiac troponins were found to be associated with an increase in mortality in patients with congestive cardiac failure,^{24–27} pulmonary embolism,^{28–29} chronic obstructive pulmonary disease,³⁰ sepsis³¹ and renal failure.³² In addition to prognostic outcome, raised levels of cardiac troponins were found to be markers for left ventricular dysfunction in patients with septic shock.^{33–34}

Despite the important prognostic value of cardiac troponin T level in conditions other than ACS, the practical value of measuring cardiac troponin T in these patients remains unclear as their management is not currently affected by the result. Finding a raised cardiac troponin T level in conditions other than ACS can present a diagnostic challenge, as misdiagnosing for ACS can lead to inappropriate treatment that may cause harm, and also a failure to recognise and treat the primary diagnosis appropriately. Cardiac troponin T level rises as a result of myocyte necrosis, but does not automatically mean an ACS. In patients without ACS, raised cardiac troponin T indicates high risk for mortality. Clinicians should be cautious about diagnosing ACS in patients with raised cardiac troponin T levels.

ACKNOWLEDGEMENTS

We thank Drs Arun Dhanasekaran and Azhar Khan for their contribution in data collection. We also thank Dr Derek Robinson, Senior Lecturer, Department of Mathematics, School of Science and Technology, University of Sussex, Brighton, UK, and Mr Steve Taylor, Research Associate in Medical Statistics, Centre for Medical Statistics and Health Evaluation, University of Liverpool, Liverpool, UK, for their statistical assistance.

Authors' affiliations

P Wong, S Murray, A Ramsewak, A Robinson, E Rodrigues, Aintree Cardiac Centre, University Hospital Aintree, Liverpool, UK

C van Heyningen, Clinical Laboratories, University Hospital Aintree, Liverpool, UK

Competing interests: PW received an unconditional research grant for the study from Bristol-Myers Squibb and Sanofi-Aventis Pharmaceuticals.

The Sefton Local Research Ethics Committee approved the study.

REFERENCES

- 1 **Alpert JS**, Thygesen K, Antman E, *et al*. Myocardial infarction redefined—a consensus document of the Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. *J Am Coll Cardiol* 2000;**36**:959–69.
- 2 **Collinson PO**, Boa FG, Gaze DC. Measurement of cardiac troponins. *Ann Clin Biochem* 2001;**38**:423–49.
- 3 **Wu AHB**, Feng Y-J, Moore R, *et al*. Characterisation of cardiac troponin subunit release into serum after acute myocardial infarction and comparison of assays for troponin T and I. *Clin Chem* 1998;**44**:1198–208.
- 4 **Cummins B**, Auckland ML, Cummins P. Cardiac specific troponin-I radioimmunoassay in the diagnosis of acute myocardial infarction. *Am Heart J* 1987;**113**:1333–44.
- 5 **Apple FS**. Analytical issues for cardiac troponin. *Prog Cardiovasc Dis* 2004;**47**:189–95.
- 6 **Khan IA**, Tun A, Wattanasauwan N, *et al*. Elevation of serum cardiac troponin I in noncardiac and cardiac diseases other than acute coronary syndromes. *Am J Emerg Med* 1999;**17**:225–9.
- 7 **Higgins JP**, Higgins JA. Elevation of cardiac troponin I indicates more than myocardial infarction. *Clin Invest Med* 2003;**26**:133–47.
- 8 **Roongsritong C**, Warraich I, Bradley C. Common causes of troponin elevations in the absence of acute myocardial infarction. Incidence and clinical significance. *Chest* 2004;**125**:1877–84.
- 9 **Jeremias A**, Gibson M. Narrative review: alternative causes for elevated cardiac troponin levels when acute coronary syndromes are excluded. *Ann Intern Med* 2005;**142**:786–91.
- 10 **Roche Diagnostics**. Basel, Switzerland. *Troponin T STAT (Short Turn Around Time)*, Cardiac T, Cobas, 2005–07, V.1 [English version].
- 11 **Charlson ME**, Pompei P, Ales KL, *et al*. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chron Dis* 1987;**40**:373–83.
- 12 **Gudmundsson GS**, Kahn SE, Moran JF. Association of mild transient elevation of troponin I levels with increased mortality and major cardiovascular events in the general patient population. *Arch Pathol Lab Med* 2005;**129**:474–80.
- 13 **Cook G**, Taylor D, France M, *et al*. Survival among hospital in-patients with troponin T elevation below levels defining myocardial infarction. *Q J Med* 2005;**98**:275–82.
- 14 **Lin JC**, Apple FS, Murakami MM, *et al*. Rates of positive cardiac troponin I and creatine kinase MB mass among patients hospitalized for suspected acute coronary syndromes. *Clin Chem* 2004;**50**:333–8.
- 15 **Kobayashi S**, Tanaka M, Tamura N, *et al*. Serum cardiac troponin T in polymyositis/dermatomyositis. *Lancet* 1992;**340**:726.
- 16 **Arlati S**, Brenna S, Prencipe L, *et al*. Myocardial necrosis in ICU patients with acute non-cardiac disease: a prospective study. *Intensive Care Med* 2000;**26**:31–7.
- 17 **Mahajan N**, Mehta Y, Rose M, *et al*. Elevated troponin level is not synonymous with myocardial infarction. *Int J Cardiol* 2006;**111**:442–9.
- 18 **Nageh T**, Sherwood RA, Roy J, *et al*. The clinical relevance of raised cardiac troponin I in the absence of significant angiographic coronary artery disease. *Int J Cardiol* 2005;**100**:325–30.
- 19 **Ooi DS**, Isotalo PA, Veinot JP. Correlation of antemortem serum creatinine kinase, creatine kinase-MB, troponin I, and troponin T with cardiac pathology. *Clin Chem* 2000;**46**:338–44.
- 20 **Heidenreich PA**, Alloggiamento T, Meslop K, *et al*. The prognostic value of troponin in patients with non-ST elevation acute coronary syndromes: a meta-analysis. *J Am Coll Cardiol* 2001;**38**:478–85.
- 21 **Antman EM**, Tanasijevic MJ, Thompson 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**:1342–9.
- 22 **Bertrand ME**, Simoons ML, Fox KAA, *et al*. Management of acute coronary syndromes in patients without persistent ST-segment elevation. The Task Force on the Management of Acute Coronary Syndromes of the European Society of Cardiology. *Eur Heart J* 2002;**23**:1809–40.
- 23 **Braunwald E**, Antman EM, Beasley JW, *et al*. ACC/AHA 2002 guideline update for the management of patients with unstable angina and non-ST-segment elevation myocardial infarction: summary article. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients with Unstable Angina). *Circulation* 2002;**106**:1893–900.
- 24 **Horwich TB**, Patel J, MacLellan WR, *et al*. Cardiac troponin I is associated with impaired haemodynamics, progressive left ventricular dysfunction, and increased mortality rates in advanced heart failure. *Circulation* 2003;**108**:833–8.
- 25 **Setsuba K**, Seino Y, Takahashi N, *et al*. Clinical significance of elevated levels of cardiac troponin T in patients with chronic heart failure. *Am J Cardiol* 1999;**84**:608–11.
- 26 **Perna ER**, Macin SM, Parras JL, *et al*. Cardiac troponin T levels are associated with poor short- and long-term prognosis in patients with acute cardiogenic pulmonary oedema. *Am Heart J* 2002;**143**:814–20.
- 27 **Healey JS**, Davies RF, Smith SJ, *et al*. Prognostic use of cardiac troponin T and troponin I in patients with heart failure. *Can J Cardiol* 2003;**19**:383–6.
- 28 **Yalamanchili K**, Sukhija R, Aronow WS, *et al*. Prevalence of increased cardiac troponin I levels in patients with and without acute pulmonary embolism and relation of increased cardiac troponin I levels with in-hospital mortality in patients with acute pulmonary embolism. *Am J Cardiol* 2004;**93**:263–4.
- 29 **Giannitsis E**, Muller-Bardorff M, Kurowski V, *et al*. Independent prognostic value of cardiac troponin T in patients with confirmed pulmonary embolism. *Circulation* 2000;**102**:211–17.
- 30 **Baillard C**, Boussarsar M, Girou E. Cardiac troponin I in patients with severe exacerbation of chronic obstructive pulmonary disease. *Intensive Care Med* 2003;**29**:584–9.
- 31 **Spies C**, Haude V, Fitzner R, *et al*. Serum cardiac troponin T as a prognostic marker in early sepsis. *Chest* 1998;**113**:1055–63.
- 32 **Needham DM**, Shufelt KA, Tomlinson G, *et al*. Troponin I and T level in renal failure patients without acute coronary syndrome: a systematic review of the literature. *Can J Cardiol* 2004;**20**:1212–18.
- 33 **Ammann P**, Maggiorini M, Bertel O, *et al*. Troponin as a risk factor for mortality in critically ill patients without acute coronary syndromes. *J Am Coll Cardiol* 2003;**41**:2004–9.
- 34 **ver Elst KM**, Spapen HD, Nguyen DN, *et al*. Cardiac troponins I and T are biological markers of left ventricular dysfunction in septic shock. *Clin Chem* 2000;**46**:650–7.