Can troponin I measurement predict short-term serious cardiac outcomes in patients presenting to the emergency department with possible acute coronary syndrome?

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ABSTRACT

Objective: To determine the ability of troponin I (TnI) measurement to predict the likelihood of a serious cardiac outcome over the subsequent 72 hours in patients presenting to the emergency department (ED) with symptoms suggestive of an acute coronary syndrome.

Methods: This prospective observational study enrolled consecutive patients presenting to 2 urban tertiary care hospital EDs over a 5-week period. Eligible patients included those for whom a TnI test was ordered within 24 hours of arrival and in whom no serious cardiac outcome occurred before the test result was available. Patients were followed for 72 hours and serious cardiac outcomes documented; these included cardiovascular death, myocardial infarction, congestive heart failure, serious arrhythmia and refractory pain. We calculated likelihood ratios (LRs) to describe the association of the TnI result with serious cardiac outcomes.

Results: Of the 352 enrolled patients, 20 had a serious cardiac outcome within 72 hours of ED presentation. The derived LRs (and 95% confidence interval [CI]) were 0.5 (0.3–0.9) for TnI values <0.5 μg/L, 1.6 (0.4–6.5) for TnI values from 0.5 to 2.0 μg/L, 5.8 (1.7–19.5) for TnI values from >2.0 to 10.0 μg/L and 14.4 (4.8–42.9) for TnI values >10.0 μg/L.

Conclusions: TnI values >2.0 μg/L are associated with an increased probability of serious cardiac outcomes within 72 hours. TnI values between 0.5 and 2.0 μg/L are weakly positive predictors. TnI values <0.5 μg/L have LRs in the range of 0.5 and thus are weakly negative predictors, not substantially decreasing the likelihood of serious cardiac outcomes, particularly in patients with a moderate or high pretest probability.

Key words: cardiac troponin; acute coronary syndrome; prognosis; likelihood ratios

Objectif : Déterminer dans quelle mesure la troponine I (TnI) peut prévoir la probabilité d'un incident cardiaque sérieux au cours des 72 heures suivantes chez les patients qui se présentent à l'urgence avec des symptômes indiquant un syndrome coronarien aigu.

Méthodes : Dans le contexte de cette étude prospective par observation, on a inscrit les patients

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consécutifs qui se sont présentés à l'urgence de deux hôpitaux urbains de soins tertiaires pendant cinq semaines. Les patients admissibles comprenaient ceux pour lesquels on a prescrit un test TnI dans les 24 heures suivant leur arrivée et qui n'ont pas eu d'incident cardiaque grave avant que le résultat du test soit disponible. On a suivi les patients pendant 72 heures et documenté les incidents cardiaques graves qui comprenaient la mort cardiovasculaire, l'infarctus du myocarde, l'insuffisance cardiaque globale, l'arythmie grave et la douleur réfractaire. Nous avons calculé des rapports de vraisemblances (RV) pour décrire le lien entre le résultat du test TnI et les incidents cardiaques graves.

Résultats : Sur les 352 patients inscrits, 20 ont eu un incident cardiaque grave dans les 72 heures après leur arrivée à l'urgence. Les RV dérivés (et intervalle de confiance [IC] à 95 %) s'établissaient à 0,5 (0,3–0,9) pour les valeurs TnI de < 0,5 µg/L, à 1,6 (0,4–6,5) pour les valeurs TnI de 0,5 à 2,0 µg/L, à 5,8 (1,7–19,5) pour les valeurs TnI de > 2,0 à 10,0 µg/L et à 14,4 (4,8–42,9) dans le cas des valeurs TnI > 10,0 µg/L.

Conclusions : On établit un lien entre les valeurs TnI de > 2,0 µg/L et une probabilité accrue d'incidents cardiaques graves dans les 72 heures. Les valeurs TnI qui se situent entre 0,5 et 2,0 µg/L sont de faibles prédicteurs positifs. Les valeurs TnI de < 0,5 µg/L ont des RV de l ordre de 0,5 et sont donc des prédicteurs faiblement négatifs qui ne réduisent pas de façon substantielle la probabilité d'incidents cardiaques graves, en particulier chez les patients qui présentent une probabilité moyenne ou élevée au prétest.

Introduction

Patients who present with potential acute coronary syndrome (ACS) represent an important diagnostic and dispositional challenge. Cost and system constraints increasingly pressure clinicians to optimize the use of resources by admitting only the highest-risk patients to coronary care units (CCUs) and either streaming others into short-stay diagnostic units or referring them for outpatient investigation. In order to make safe, cost-effective decisions, emergency physicians must determine, on a patient-by-patient basis, the likelihood of a serious outcome (death, myocardial infarction [MI], congestive heart failure [CHF] or refractory pain) in the near future. When evaluating risk, clinicians intuitively use Bayesian logic: they gather information from the history and physical examination to generate a pretest probability of disease or an estimate of the likelihood of an outcome, then they modify this probability on the basis of new clinical information and diagnostic test results.[1]

Cardiac markers, particularly the troponins, have been advocated as a tool for objective risk stratification in patients with possible ACS. Many studies have evaluated the troponins (I and T) as predictors of death, MI and other serious cardiac outcomes, such as CHF.[2–23] Others have addressed the usefulness of troponin measurement to rule out MI or unstable angina.[17–20] Likelihood ratios (LRs) are the most useful single indicator of a test's diagnostic strength and therefore the degree to which the test result can modify the pretest probability and facilitate clinical decision-making.[24] Many test results are considered positive or negative according to a single threshold or cut-off value, but this approach ignores much important information. For example, a troponin result above a threshold of 2.0 µg/L may have different diagnostic and prognostic implications than a value above a threshold of 0.5 µg/L. Multilevel likelihood ratios can help us to use tests more effectively by quantifying the predictive strength of a test result across a full range of possible values.

Our primary objective in this prospective cohort study was to assess the ability of troponin I (TnI) assays to predict serious 72-hour cardiac outcomes in patients presenting to the emergency department (ED) with possible ACS. Our secondary objective was to establish multilevel LRs that would help clinicians use troponin assays optimally in deciding the need for hospitalization and CCU admission.

Methods

Setting and patients

The study was conducted in the EDs of the Hamilton Health Sciences Centre (Hamilton General Hospital and McMaster sites) during 5 consecutive weeks in July and August 2000. Eligible patients included all those who presented with possible ACS between 0800 Sunday and 0800 Friday and for whom a TnI test was ordered within 24 hours of presentation. We identified consecutive eligible patients in the laboratory-order database and subsequently excluded those who had a serious outcome before the first TnI result was available, those who were referred directly to the trauma or surgery service, those who had their first TnI assay ordered after an admission decision was documented, and those who had troponin assays performed in error, the

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result of an inadvertent order. In all cases of suspected error, trained research assistants reviewed the chart to ensure that ACS was not a diagnostic possibility. Prespecified serious outcomes included cardiovascular death, MI, CHF, serious arrhythmia and significant refractory ischemic pain.

Laboratory measurements

For all patients, total creatine kinase (CK) and TnI assays were performed according to hospital protocols, and the results were available to clinical staff. Excess plasma was recovered from the samples and frozen at –70ºC for later measurement of the MB fraction of CK; these results were not made available to clinical staff. The total CK level was measured by means of a Roche Integra 700 (Roche Diagnostics, Laval, Que.). CKMB and TnI assays were performed with an Abbott Axsym (Abbott Laboratories, Mississauga, Ont.), using upper reference limits of 225 U/L for total CK and 10 µg/L for CKMB. TnI threshold values recommended by the manufacturer, and the corresponding narrative interpretations developed by the Hamilton Regional Laboratory Medicine Program, are as follows: <0.5 µg/L, no evidence of myocardial injury; 0.6–2.3 µg/L, consistent with myocardial injury or ischemia; >2.3 µg/L, consistent with myocardial ischemia or infarct.

Data collection

After the initial clinical assessment and before the first TnI result was available, physicians recorded key data, including the most likely diagnosis and the US Agency for Health Care Policy and Research (AHCPR) risk category (low, intermediate or high),[25] on standardized data forms. At 72 hours, research assistants reviewed the charts of all patients who were still in the hospital. Between 72 and 110 hours, the assistants conducted a telephone follow-up interview on all patients who had been discharged home before 72 hours. Primary outcomes were based on the patient's status (alive or dead) and location (inpatient, home or hospital again) at 72 hours and whether the patient had undergone a therapeutic intervention or had a serious cardiac outcome during this time. Also recorded were new medication orders and modifications to existing prescriptions for acetylsalicylic acid, sublingual or transdermal nitrate therapy, ß-blockers, ACE inhibitors, heparin or calcium channel blockers.

Outcome definitions

Two investigators (P.J.D. and J.O.), blinded to the TnI test results, independently evaluated all instances of suspected serious cardiac outcomes. Disagreements were resolved by consensus discussion. Serious cardiac outcomes were defined a priori as follows. Cardiovascular death was defined as death during a revascularization procedure, cardiac arrest, MI, stroke, or death from unknown cause (noncardiovascular death included such causes as infection, trauma and malignant disease). The definition of MI was based on World Health Organization (WHO) criteria[26] and required 2 of the following 3 criteria: ischemic symptoms consistent with MI, characteristic electrocardiographic (ECG) changes, and characteristic rise and subsequent fall in total CK and CKMB values. A diagnosis of CHF required all 3 of the following: documented signs and symptoms consistent with heart failure, chest radiograph consistent with CHF and administration of a diuretic. Serious arrhythmias included ventricular fibrillation, sustained ventricular tachycardia (>30 seconds), asystole, electromechanical dissociation, supraventricular tachycardia, atrial fibrillation, sinus bradycardia, or second- or third-degree heart block; to qualify as a serious cardiac outcome, the arrhythmia had to have required 1 of the following treatments: cardioversion, administration of an antiarrhythmic, rate-slowing or sympathomimetic drug or of atropine, or temporary implantation of a pacemaker. Significant refractory ischemic pain was defined as recurrent chest pain lasting longer than 5 minutes, with ECG changes consistent with ischemia and requiring the administration of nitroglycerin or morphine.

Data analysis

We calculated sensitivity, specificity and LRs to describe the association of TnI results (first value, maximum within 12 hours, and maximum within 24 hours) with the occurrence of a serious cardiac outcome. These parameters were described using 3 TnI thresholds: 0.5, 2.0 and 10.0 µg/L. We attempted to maximize the number of cut-off points while including sufficient data points in each category to ensure a smooth gradient of LRs. We also calculated the LRs associated with AHCPR risk stratification.

Ethics approval

The study was approved by the Research Ethics Board of the Hamilton Health Sciences Centre as a quality-assurance audit and protocol. The patients provided informed consent for study participation at the follow-up telephone interview.

Results

During the study period, 440 patients had TnI testing and 88 were excluded, including 62 who had serious cardiac outcomes before their first TnI result became available, 11 who were referred directly to the trauma or surgery ser-

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vice, and 15 for whom the first TnI test was ordered after the decision to admit or was performed in error. Table 1 summarizes baseline characteristics of the 352 patients who fulfilled the entry criteria. For 347, the first TnI test

Table 1. Baseline characteristics of eligible patients with and without serious cardiac outcomes after presenting to EDs with possible acute coronary syndrome

	Patients; no. (and %) or mean ± SD		
	All (*N* = 352)	With serious outcome (*N* = 20)	Without serious outcome (*N* = 332)
Male	181 (51.4)	10 (50.0)	171 (51.5)
Age, yr	65.4 ± 15.8	72.3 ± 10.0	65.0 ± 16.0‡
Presenting symptoms*			
Chest pain	183 (52.0)	13 (65.0)	170 (51.2)
Syncope or pre-syncope	50 (14.2)	0 (0.0)	50 (15.1)
Palpitations	18 (5.1)	0 (0.0)	18 (5.4)
Anginal equivalent	32 (9.1)	5 (25.0)	27 (8.1)‡
Other	234 (66.5)	12 (60.0)	222 (66.9)
Previous MI			
Yes	90 (25.6)	5 (25.0)	85 (25.6)
No	237 (67.3)	15 (75.0)	222 (66.9)
Unknown	25 (7.1)	0 (0.0)	25 (7.5)
Tobacco smoking			
Never	100 (40.2)	6 (37.5)	94 (40.5)
Currently	85 (34.1)	3 (18.8)	82 (35.3)
Formerly	63 (25.3)	7 (43.8)	56 (24.1)
Diabetes	87 (25.7)	8 (42.1)	79 (24.8)
Provisional diagnosis†			
Non-cardiac	161 (46.0)	6 (31.6)	155 (46.8)
Stable angina	11 (3.1)	0 (0.0)	11 (3.3)
Unstable angina	76 (21.7)	9 (47.4)	67 (20.2)‡
Myocardial infarction	1 (0.3)	1 (5.3)	0 (0.0)
Undiagnosed chest pain	40 (11.4)	1 (5.3)	39 (11.8)
Congestive heart failure	10 (2.9)	0 (0.0)	10 (3.0)
Other cardiac diagnosis	84 (24.0)	6 (31.6)	78 (23.6)
AHCPR risk category†			
High	36 (10.3)	3 (15.0)	33 (10.1)‡
Intermediate	77 (22.1)	10 (50.0)	67 (20.4)‡
Low	109 (31.3)	1 (5.0)	108 (32.9)‡
N/A (no chest pain)	126 (36.2)	6 (30.0)	124 (36.6)‡
Probable disposition†			
Continued observation	246 (69.9)	9 (45.0)	237 (71.4)
Referral to internist or cardiologist	57 (16.2)	5 (25.0)	52 (15.7)
Other medical referral	9 (2.5)	0 (0.0)	9 (2.7)
Surgical referral	9 (2.5)	2 (10.0)	7 (2.1)
Discharge home	3 (0.9)	0 (0.0)	3 (0.9)
Self-discharge	4 (1.1)	0 (0.0)	4 (1.2)
No ED assessment	27 (7.6)	4 (20.0)	23 (6.9)

SD = standard deviation; ED = emergency department; AHCPR = Agency for Health Care Policy and Research
*Total is >352 because some patients had >1 symptom. "Other" included nausea, dyspnea and arm, back, neck or other pain.
†After initial physician assessment and before availability of first troponin I (TnI) test result.
‡$p > 0.05$

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was ordered within 12 hours of ED arrival; for the other 5 it was delayed. Seventeen of 20 patients with serious cardiac outcomes had serial TnI assays, but 145 (43.7%) of the 332 patients without serious cardiac outcomes had only a single TnI determination.

Disposition

Figure 1 shows that 325 patients (92.3%) were evaluated first by emergency physicians; the other 27 were referred directly to an internist or cardiologist. Of the patients seen first by emergency physicians, 116 (35.7%) were discharged, 189 (58.2%) were referred to an internist or cardiologist, and 20 (6.2%) were referred to other specialty services. Of the 209 patients referred to a specialty service, 94 (45.0%) were ultimately discharged and 115 (55.0%) admitted to hospital. Of the 27 patients seen initially by a cardiologist or internist, 13 were discharged and 14 admitted.

Follow-up

Of the 219 patients sent home from the ED or discharged from the hospital within 72 hours, 17 were lost to follow-up (12 had no phone and 5 did not answer repeated calls) and 4 refused to take part in the 72-hour interview. None of these 21 patients had a documented serious cardiac outcome or returned to the study EDs within 72 hours.

Serious cardiac outcomes

Of the 20 patients with serious outcomes after the first TnI result became available and within 72 hours, 7 had an uncomplicated acute MI, 4 significant refractory ischemic pain, 3 cardiovascular death, 2 CHF, 2 serious arrhythmias, and 2 acute MI with CHF. No revascularization procedures were performed during the 72 hours after presentation. The overall kappa value for evaluator agreement (serious outcome v. no serious outcome) was 0.59 (95% confidence interval [CI], 0.34–0.84). Kappa values for agreement on individual outcomes were 1.0 for refractory pain, 0.36 for acute MI, 0.67 for CHF and 0.20 for cardiac death

Table 2 shows the management and 72-hour disposition of the study patients. Of the 20 patients with a serious cardiac outcome, 17 remained alive at 72 hours and were still in hospital. Of the 332 patients who did not have a serious cardiac outcome, 219 (66.0%) had been discharged home by 72 hours; the other 34% remained in hospital. A new cardiac medication was started during the study period in 75% of the patients with a serious cardiac outcome and in 31.6% of those without.

TnI diagnostic parameters

Table 3 summarizes TnI diagnostic parameters, using the highest value obtained within 12 hours after presentation. This table shows that TnI identified only half of the patients who had a serious cardiac outcome and that only one fifth of the patients with elevated TnI values went on to have a serious outcome. Table 4 presents the TnI diagnostic parameters for the initial and the highest TnI values in

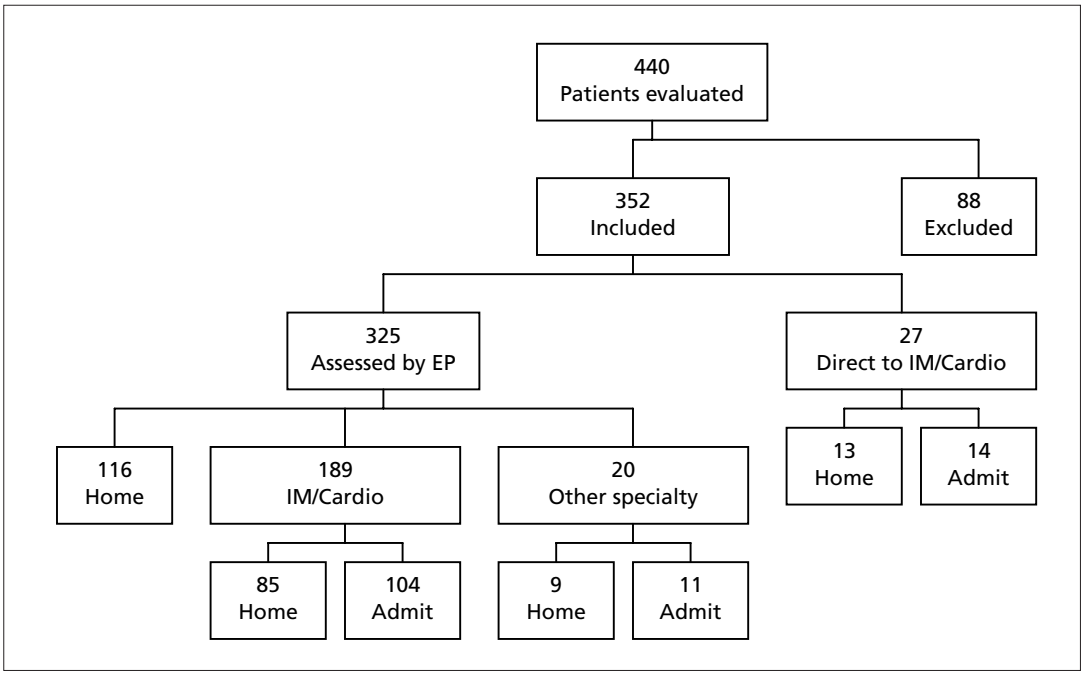

Fig. 1. Patient disposition. EP = emergency physician; IM/Cardio = internal medicine or cardiology

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the same period. Table 5 presents the LRs for predicting serious cardiac outcomes, stratified by the first TnI result, the highest value within 12 hours and the highest value within 24 hours. Of the 20 patients who had a serious cardiac outcome, 12 (including 2 who died and 3 who had an acute MI) had an initial TnI value <0.5 μg/L, and 7 of these (including 1 who died and 1 who had an acute MI) still had such a value at 24 hours.

The emergency physicians categorized the patients by AHCPR risk as follows: high, 36 patients (10.3%); intermediate, 77 (22.1%); and low, 109 (31.3%). The LRs associated with these 3 categories were 1.4, 2.2 and 0.14, respectively. Because of the absence of chest pain, 130 patients could not be placed in an AHCPR risk category.

Discussion

When patients present to the ED with potential cardiac symptoms, physicians often use cardiac biomarkers to assess risk and help determine the need for hospitalization.

Table 2. Patient management in the first 72 hours

	Patients; no. (and %) or mean/median		
Management feature	All (*N* = 352)	With serious outcome (*N* = 20)	Without serious outcome (*N* = 332)
Location at 72 hours			
Ward, telemetry monitored	48 (13.6)	6 (30.0)	42 (12.7)
Ward, unmonitored	65 (18.5)	3 (15.0)	62 (18.7)
Coronary/intensive care unit	16 (4.6)	8 (40.0)	8 (2.4)
Home	219 (62.2)	0 (0.0)	219 (66.0)
Deceased	4 (1.1)	3 (15.0)	1 (0.3)
Cardiac monitoring	241 (68.5)	18 (90.0)	223 (67.2)
Duration, hours			
Mean ± SD	29.5 ± 28.3	63.2 ± 18.1	26.7 ± 27.2
Median (and range)	12 (1–72)	72 (13–72)	11 (1–72)
New medications*			
None	232 (65.9)	5 (25.0)	227 (68.4)
Heparin	49 (13.9)	10 (50.0)	39 (11.8)
ASA	41 (11.7)	4 (20.0)	37 (11.1)
Nitroglycerine spray	38 (10.8)	7 (35.0)	31 (9.3)
Nitroglycerine patch	35 (9.9)	9 (45.0)	26 (7.8)
Beta-blocker	28 (8.0)	7 (35.0)	21 (6.3)
ACE inhibitor	19 (5.4)	5 (25.0)	14 (4.2)
Calcium-channel blocker	7 (2.0)	2 (10.0)	5 (1.5)

SD = standard deviation; ASA = acetylsalicylic acid; ACE = angiotensin-converting enzyme
*Total is >352 because some patients received >1 new medication.

Table 3. Occurrence of serious cardiac outcomes according to maximum TnI test result in the first 12 hours

	No. of patients		
TnI value, μg/L	With serious outcome	Without serious outcome	All*
≥0.5†	10	36	46
<0.5	9	292	301
	19	328	347

*Data were missing for 5 patients.
†This cut-off was used to maximize test sensitivity.
Sensitivity = 52.6% (10/19); specificity = 89.0% (292/328); positive predictive value = 21.7% (10/46); negative predictive value = 97.0% (292/301).

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Our study shows that TnI values >2.0 μg/L are associated with a substantial increase in the likelihood of a serious cardiac outcome. It may be reasonable to treat such patients in a CCU; however, the interpretation of lower TnI levels is more difficult. We found that most patients with TnI values = 0.5 μg/L did not suffer serious cardiac outcomes within 72 hours and that the TnI test identified only half the patients who had serious outcomes. Physicians should therefore be cautious in using normal TnI values as markers for safe discharge. AHCPR scoring identified low-risk patients better than a TnI value of <0.5 μg/L; thus the decision to discharge patients from the ED should be based more on a low pretest probability as determined by clinical features such as history, physical and ECG findings, and perhaps the response to exercise testing.

Predictive strength of the TnI test

We reported our findings as LRs because LRs are the most useful indicator of a test's diagnostic strength.[24] LRs between 0.3 and 3.0 result in only small changes in the probability of disease or, in this case, a serious cardiac outcome. LRs less than 0.1 and greater than 10 generate large changes in the post-test probability. Our data showed that TnI values <0.5 μg/L were associated with LRs of 0.7 (first value), 0.5 (maximum value in the first 12 hours) and 0.4 (maximum value in the first 24 hours), signifying only a modest reduction in the probability of serious cardiac outcomes in the first 72 hours. More than half the patients with such outcomes (12/20) had an initially normal TnI value, which confirms the inability of the initial result to identify patients at risk. Furthermore, 7 of the 20 patients had negative results of serial TnI tests in the first 24 hours.

TnI values between 2.0 and 10.0 μg/L produced LRs of 6.6, 5.8 and 5.5, respectively, whereas values > 10 μg/L produced LRs greater than 10. Increasing TnI levels appear to identify a subset of patients at greater risk for a serious cardiac outcome within the first 72 hours.

Previous studies

Previous studies have generally been more optimistic about the predictive strength of troponin assays. These studies tended to focus on outcomes such as death, MI and revascularization, and many failed to follow patients initially discharged from the ED. Overall, 11 studies[2,5,7,8,11–14,17–19] took an approach similar to the one we chose, which was to assess the value of troponin measure-

Table 4. Sensitivity and specificity of TnI test results in the first 12 hours in predicting serious cardiac outcomes

TnI cut-off value, μg/L	TnI result category*	Sensitivity (and 95% CI)	Specificity (and 95% CI)
0.5	First	40.0 (19.1–63.9)	91.3 (87.7–94.1)
	Maximum	52.6 (28.9–75.6)	89.0 (85.1–92.2)
2.0	First	25.0 (8.7–49.1)	97.3 (94.9–98.8)
	Maximum	42.1 (20.3–66.5)	95.4 (92.6–97.4)
10.0	First	15.0 (3.2–37.9)	98.8 (96.9–99.7)
	Maximum	26.3 (9.1–51.2)	98.2 (96.1–99.3)

*"First" is the TnI result for the first sample drawn after presentation; "Maximum" is the maximum TnI value documented in the first 12 hours after arrival at the ED.
CI = confidence interval.

Table 5. Likelihood ratios for predicting serious cardiac outcomes from TnI test results

	First result			Maximum in first 12 hours*			Maximum in first 24 hours		
TnI value, μg/L	Serious outcome; no. of patients		Ratio (and 95% CI)	Serious outcome; no. of patients		Ratio (and 95% CI)	Serious outcome; no. of patients		Ratio (and 95% CI)
	Yes	No		Yes	No		Yes	No	
<0.5	12	303	0.7 (0.5–0.9)	9	292	0.5 (0.3–0.9)	7	293	0.4 (0.2–0.7)
0.5–2.0	3	20	2.5 (0.8–7.7)	2	21	1.6 (0.4–6.5)	4	19	3.5 (1.3–9.3)
>2.0–10	2	5	6.6 (1.4–32.1)	3	9	5.8 (1.7–19.5)	4	12	5.5 (2.0–15.6)
>10	3	4	12.5 (3.0–51.9)	5	6	14.4 (4.8–42.9)	5	8	10.4 (3.7–28.8)

*One patient with a serious cardiac outcome and 4 patients without did not have a TnI test within the first 12 hours.

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ments in predicting adverse outcomes. Seven of these[2,5,7,8,12,14,17] suggested that troponin measurement was of little value, whereas 3[11,18,19] suggested that it was of substantial value. It is not clear from these papers, however, whether the troponin result modified the physicians' diagnostic judgment or merely concurred with already correct clinical impressions.

Many studies involved longer follow-up time frames — from 1 week to 57 months.[3–6,9–13,19] Several[2,8,14–18,20] used short time points (6 to 72 hours and "in hospital"), and two[8,14] used outcomes similar to ours.[8,14] We selected a 72-hour time frame because events during this interval dictate the need for immediate CCU admission. A strong design feature of this study is that we conducted follow-up interviews, between 72 and 110 hours, for all patients, including those discharged from the ED. Our results are therefore directly applicable to the decision facing physicians seeing patients with potential cardiac symptoms in the ED.

Study strengths and limitations

Strengths of this study include our explicit predefined outcomes, which are highly relevant to ED practice, and our 95% follow-up success rate. Weaknesses include the relatively small number of outcome events and poor interobserver agreement on some of the outcomes identified. More specific concerns include the following.

We used the Abbott Laboratories TnI assay, which is widely used in North America.[27] This assay classifies values up to 0.5 μg/L as negative, values from 0.5 to 2.0 μg/L as worrisome and values >2.0 μg/L as positive. The imprecision of this assay in the low end of the analytic range (10% coefficient of variation [CV] at 1.2 μg/L[28]) may have contributed to the LR near 1.0 for results in this range. Because TnI assays produced by other equipment manufacturers use different antibodies to the troponin molecule and have different thresholds and normal values, the TnI values and ranges cited in this study do not necessarily correlate with quantitative TnI values generated by different assays in other settings. However, our results are applicable in general terms to the use of troponin assays for adverse event prediction.

Physicians in our study ordered the TnI test for many patients who had a low pretest probability of a serious cardiac outcome in the next 72 hours. Because sensitivity and specificity are intrinsic test characteristics and relatively constant across populations, the LRs associated with this test can be generalized to other patient populations. Physicians in our study also ordered a TnI test for patients in whom the risk of a serious cardiac outcome was high enough to justify admission regardless of the test result. In order to examine the usefulness of this test in the situations in which it is most needed — that is, when the clinical and ECG findings are not diagnostic — we excluded all those in whom a serious cardiac outcome was predicted without the aid of a test (e.g., those admitted before TnI testing, those with diagnostic ECGs and those who suffered serious cardiac outcomes before the TnI result was available). The consequence of this decision, however, was that, with these patients eliminated, the number of serious cardiac outcome events was low, leading to wide CIs around our point estimates.

The European Society of Cardiology and the American College of Cardiology[29] recently defined MI as a rise in troponin concentration in addition to ischemic symptoms, ECG findings (new pathologic Q-waves or ischemic changes) or coronary artery intervention. To qualify, troponin values must be greater than the 99th percentile of a reference population or above the 10% CV for the assay (1.2 μg/L for the Abbott assay that we used[28]), whichever is greater. We were aware of this new standard for acute MI diagnosis but chose the WHO definition of MI, which uses CK and CKMB as the biochemical markers of interest. We did so because it is inappropriate to use a diagnostic test as its own gold standard. Using the TnI test as both the diagnostic test being studied for acute MI and as the gold standard for acute MI diagnosis is a self-fulfilling process that, in this study, would have falsely increased the LR of a positive test result to approximately 200, although it would have had little or no effect on the LR of a negative test result (0.6).

Conclusions

Substantial troponin-I elevations > 2.0 ng/mL increase the likelihood of a serious cardiac event in the next 72 hours and suggest the need for intensive care admission. Negative troponin values, on the other hand, have little impact on the post-test likelihood of such an event. Physicians should exercise caution in the interpretation of Tn assays and base disposition decisions on all available information-particularly clinical and ECG findings.

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