

SCIENTIFIC LETTER

Prospective evaluation of the role of routine cardiac troponin T measurement to identify left ventricular ejection fraction < 40% after first myocardial infarction

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Serial measurements of creatine kinase (CK) and its MB isoenzyme (CK-MB) and calculation of area under the curve (AUC) or peak value can be used to estimate infarct size. Peak values usually occur 20–24 hours postinfarction but release kinetics are affected by reperfusion (spontaneous or therapeutic). Regular, frequent samples must be obtained following admission, not a convenient approach for busy clinical or nursing staff. In a previous retrospective study¹ we demonstrated that an angiographically determined left ventricular ejection fraction (LVEF) < 40% could be identified by a single cardiac troponin T (cTnT) measurement at the diagnostically efficient time point of 12–24 hours from admission. We performed a larger prospective study and compared the measurement of cTnT and peak CK with early estimation of LVEF by echocardiography.

METHODS

Consecutive admissions to a typical UK district general hospital (DGH) with suspected acute coronary syndromes (ACS) and a final diagnosis of acute myocardial infarction (AMI) had measurement of cTnT and LVEF performed. Myocardial infarction was diagnosed according to World Health Organization criteria² if two of the following were present: cardiac chest pain; S-T segment elevation of at least 2 mm in chest leads or 1 mm in limb leads or new Q waves in at least two contiguous leads; elevation of CK to at least twice the upper limit of the reference range. Patients were excluded from the study if they had one or more of the following: age \geq 80 years; significant renal impairment (creatinine > 220 $\mu\text{mol/l}$); history of previous heart failure; previous myocardial infarction on the basis of history or ECG changes.

Samples for cTnT were obtained 12–24 hours from admission. Samples for CK were taken on admission and 4, 12, 24, and 48 hours from admission. Samples were either analysed immediately or were frozen without delay, stored at -70°C and thawed immediately before analysis. Analysis was completed within five days for all samples. CK was measured on an Axon analyser (Bayer Diagnostics, Basingstoke, UK; CV 2.9% at 179.5 u/l, 2.2% at 671.3 u/l, range 0–760 u/l). Measurement of cTnT was undertaken with an Elecsys 1010 using the second generation assay (Roche Diagnostics, Lewes, UK, CV 5.5% at 0.32 $\mu\text{g/l}$, 5.4% at 6.0 $\mu\text{g/l}$; range 0.04–25 $\mu\text{g/l}$).

LVEF was estimated echocardiographically using the Simpson's method of discs³ 3–14 days from admission. Experienced operators who were blinded to the cTnT results performed on all echocardiograms on a Hewlett-Packard Sonos 1000 machine.

Data analysis was performed by non-parametric methods and by receiver operator characteristic curve (ROC) analysis using the Analyse-It add in for Excel (Analyse-It, Leeds, UK). Patients were dichotomised into those with LVEF \geq 40% and those with LVEF < 40%. ROC curve analysis was performed using cTnT and peak CK value in each patient as the continuous variable.

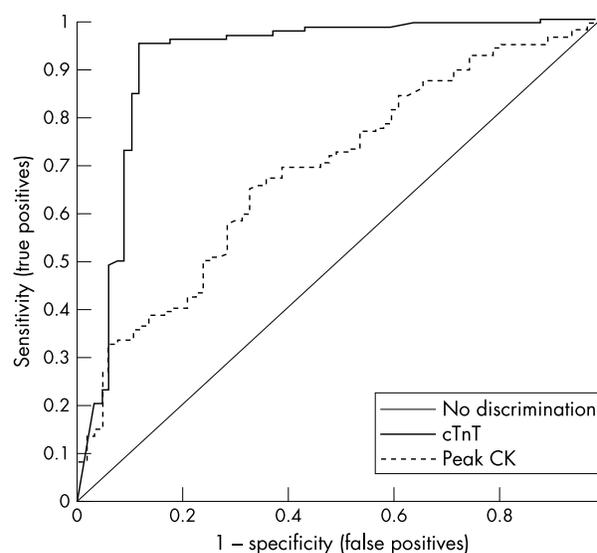


Figure 1 Receiver operator characteristic curves for peak creatine kinase (CK) and cardiac troponin T (cTnT) using a left ventricular ejection fraction of < 40% as the discriminant.

RESULTS

A total of 239 patients met the inclusion criteria for the study. In 38 patients, an inadequate echocardiogram was obtained and LVEF could not be accurately estimated. Good quality echocardiograms were obtained in 201/239 (84.1%) patients, 146 males, 55 females, median age 63.2 years (range 36.1–80.8, upper quartile 70.3, lower quartile 53.8). One hundred and twenty eight patients received thrombolytic treatment and 10 received DC cardioversion for ventricular fibrillation. Twenty six patients had diabetes mellitus (four insulin dependent), 11 had previous hypertension (a relatively small number), and three were shown to have left ventricular hypertrophy on echocardiography.

There was a significant negative correlation between CK and LVEF, $r_s -0.35$ (-0.46 to -0.22). By ROC analysis area, AUC and 95% confidence intervals (CI) were 0.913 (95% CI 0.860 to 0.967) for cTnT and 0.689 (95% CI 0.614 to 0.764) for peak CK (fig 1). A troponin concentration of \geq 2.8 $\mu\text{g/l}$ predicted a left ventricular ejection fraction of < 40% with a sensitivity of 95.5% (95% CI 90.5% to 98.3%) and specificity of 88.1% (95%

Abbreviations: ACS, acute coronary syndrome; AMI, acute myocardial infarction; AUC, area under the curve; CK, creatine kinase; cTnT, cardiac troponin T; CV, coefficient of variation; DGH, district general hospital; LVEF, left ventricular ejection fraction; ROC, receiver operator characteristic curve

CI 77.8% to 94.7%). Positive predictive accuracy was 94.1% and negative predictive accuracy 90.8%. Excluding unthrombolysed patients yielded almost identical results with the AUC for cTnT of 0.908 (95% CI 0.827 to 0.988) and for peak CK of 0.618 (95% CI 0.488 to 0.748).

DISCUSSION

Though myocardial infarct size can be estimated by using CK or CK-MB, repeated estimations during a small time window are required. These are non-structural cytosol proteins, also found in somatic muscle. Reperfusion significantly alters the kinetics of conventional cardiac markers. Consequently their use in the estimation of infarct size (and hence LVEF) in patients receiving thrombolysis is limited. The plateau phase of the plasma concentration of cTnT has been shown to correlate with size of myocardial scar after acute infarction.⁴ After acute myocardial infarction, cardiac troponins have an early peak due to the combined release of the cytosol and the structural components from infarcted myocytes. The cytosol component is small so little is released from damaged myocytes.⁵ The plateau phase is caused by the release of cTnT from the structural protein of infarcted myocytes and allows quantification of myocardial infarction. Current data indicate that cardiac troponin concentrations are affected only for the first 12 hours after thrombolysis and reperfusion. Sampling at more than 12 hours from admission will miss the peak value but sample the plateau phase which lasts for 48 hours, permitting a large time window. This means repeated sampling is unnecessary, hence it is practical and cost effective. Estimation of LVEF by cTnT measurement showed good diagnostic performance with the ROC AUC exceeding 0.9 with 95% sensitivity at a troponin concentration of > 2.8 µg/l. The results were significantly better than if AUC for peak CK was used. The results were being compared with echocardiography rather than an independent "gold standard". This may account for the lower sensitivity than our previous study, since there are technical limitations in echocardiographic estimation of LVEF.

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