High-sensitivity cardiac troponin concentrations at presentation in patients with ST-segment elevation myocardial infarction

ORIGINAL RESEARCH LETTER

High-sensitivity cardiac troponin concentrations at presentation in patients with ST-segment elevation myocardial infarction

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Running title: *Troponin concentrations at presentation in STEMI*

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Word Count: 598

Table and Figures: 1

References: 6

Introduction

The introduction of high-sensitivity cardiac troponin testing into clinical practice has transformed the assessment of patients with suspected acute coronary syndrome in the Emergency Department.[1] The majority of patients can be discharged using accelerated diagnostic pathways that do not require hospital admission for peak cardiac troponin testing.[2] These pathways are not recommended for patients with ST-segment elevation on the electrocardiogram,[3,4] but given interpretation is dependent on experience, there is a risk patients could be inappropriately assessed.

Methods

Between June 2013, and March 2016, consecutive patients with suspected acute coronary syndrome were recruited across ten hospitals in the High-STEACS cluster randomized controlled trial.[5] High-sensitivity cardiac troponin I was measured using the Abbott ARCHITECT$_{STAT}$ assay (Abbott Laboratories, Abbott Park, IL), which has a limit of detection of 1.2 ng/L, and a 99th-centile upper reference limit of 34 ng/L in men and 16 ng/L in women. The index diagnosis was independently adjudicated by two physicians, on review of all clinical information, according to the Universal Definition of Myocardial Infarction.[6] Patients with type 1 ST-segment elevation myocardial infarction (STEMI) were stratified according to cardiac troponin concentration at presentation using a validated risk-stratification threshold (5 ng/L),[1] the sex-specific 99th-centile, and the European Society of Cardiology (ESC) 0/1 hour pathway rule-in threshold (52 ng/L).[4] Posterior STEMI was defined as those with STEMI and an acute occlusion of the circumflex, obtuse marginal, or posterior left ventricular artery on angiography. Time from symptom onset was recorded prospectively by attending clinicians. Comparisons between groups were performed using the *Chi*-squared test for categorical variables, and an unpaired *t*-test or the Kruskal-Wallis test for continuous variables. Statistical analysis was performed using R (v.3.6.1, R Foundation). The trial was approved by our

research ethics committee, and as randomisation was at the hospital-level, individual patient consent was not sought.[5]

Results

The trial enrolled 48,282 consecutive patients of whom 925 had an adjudicated diagnosis of STEMI (67.8% male, mean age 65 [SD 14] years). At presentation the median troponin concentration was 196 ng/L (interquartile range [IQR] 46-21,611 ng/L), with 2.2% (20/925) and 14.4% (133/925) of patients having concentrations <5 ng/L and the 99th-centile, respectively (***Figure***). Just 73.2% (677/925) of patients had troponin concentrations above the rule-in threshold of 52 ng/L. Patients presenting within 2 hours of symptom onset (23.4%, 216/809) had lower troponin concentrations (96 [26- 494] *versus* 294 [59-3042] ng/L; P<0.001), and were more likely to have concentrations below the 99th-centile (26.4%, (57/216) *versus* 14.1%, (95/674); P<0.001), compared to those presenting later. Posterior STEMI was more common in patients presenting with troponin below the 99th-centile (18.1%, (26/144) *versus* 9.8%, (61/618); P=0.008).

Discussion

Despite significant advances in the sensitivity of cardiac troponin testing, more than 1 in 4 patients with STEMI have troponin concentration below the ESC-recommended rule-in threshold at presentation. Patients presenting within 2 hours were more likely to have a troponin concentration below the 99th-centile, however even in those who presented later, 1 in 6 had troponin concentrations below the diagnostic threshold. During myocardial infarction, abrupt coronary occlusion may prevent the release of troponin into the circulation until reperfusion has occurred. Our observations are an important reminder of the limited role of troponin testing in the early assessment of patients with ST-segment elevation. Where clinical suspicion is high, troponin concentrations within the reference range should not delay the initiation of therapeutic agents, or urgent coronary angiography. This is particularly relevant in patients with electrocardiographic changes suspicious of posterior myocardial

infarction, but our findings are relevant to a wider group of patients with conduction abnormalities, such as bundle branch block or ventricular pacing, where interpretation of the electrocardiogram is challenging.

Acknowledgements

The trial was funded by the British Heart Foundation (SP/12/10/29922 and PG/15/51/31596). The funder had no role in design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication. NLM is supported by the Butler Senior Clinical Research Fellowship (FS/16/14/32023), and KL and RW are supported by a Clinical Research Training Fellowship (FS/18/25/33454), and a Research Excellence Award (RE/18/5/34216), respectively from the British Heart Foundation. ARC receives support from a Starter Grant for Clinical Lecturers by the Academy of Medical Sciences (SGL021/1075). RW and ARC had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. The High-STEACS investigators were responsible for the conception and design of the High-STEACS trial, and the acquisition of data used in this analysis.

High-STEACS investigators

Chief Investigator: Prof Nicholas L Mills (University of Edinburgh) **Trial managers:** Dr Fiona E Strachan (University of Edinburgh); and Mr Christopher Tuck (Edinburgh Clinical Trials Unit). **Trial research team:** Dr Anoop S V Shah, Dr Fiona E Strachan, Dr Atul Anand, Dr Anda Bularga, Dr Ryan Wereski, Dr Amy V Ferry, Dr Kuan Ken Lee, Dr Andrew R Chapman, Mr Dennis Sandeman, Dr Philip D Adamson, Dr Catherine L Stables, Dr Catalina A Vallejo, Dr Athanasios Tsanasis, Ms Lucy Marshall, Ms Stacey D Stewart, Dr Takeshi Fujisawa, Ms Mischa Hautvast, Ms Jean McPherson, and Ms Lynn McKinlay (University of Edinburgh). **Grant applicants:** Prof Nicholas L Mills, Prof David E Newby, Prof Keith AA Fox, Dr Simon Walker, and Dr Christopher J Weir

(University of Edinburgh); Prof Colin Berry (University of Glasgow). **Adjudication panel:** Dr Anoop S V Shah, Dr Atul Anand, Dr Andrew R Chapman, Dr Kuan Ken Lee, Dr Jack Andrews, Dr Phil Adamson, Dr Alastair Moss, Dr Mohamed Anwar, Dr John Hung, an Prof Nicholas L Mills (University of Edinburgh). **Trial steering committee**: Prof Nicholas L Mills, Prof David Newby, Prof Alasdair Gray, Prof Keith AA Fox, Dr Simon Walker, Prof John Norrie, Prof Christopher Weir (University of Edinburgh); Prof Colin Berry, Prof Ian Ford, Dr David A McAllister, (University of Glasgow); Prof Paul O Collinson (St George's University Hospitals); Prof Fred S Apple (University of Minnesota), Mr Alan Reid (UKNEQAS); Dr Anne Cruikshank, Dr Iain Findlay, Dr Donogh Maguire (NHS Greater Glasgow and Clyde); Dr Shannon Amoils (British Heart Foundation), Ms Jennifer Stevens. **Biochemistry sub-group committee:** Dr Simon Walker (University of Edinburgh); Dr Jonathan Malo (NHS Lothian); Mr Alan Reid (UKNEQAS); Dr Anne Cruikshank (NHS Greater Glasgow and Clyde); and Prof Paul O Collinson (St George's University Hospitals). **Data monitoring committee:** Prof Colin Fischbacher (Public Health Scotland), Dr Bernard Croal (NHS Grampian), and Prof Stephen J Leslie (NHS Highland). **Edinburgh Clinical Trials Unit**: Ms Catriona Keerie, Prof Christopher Weir, Mr Richard Parker, Mr Allan Walker, Mr Ronnie Harkess, Mr Chris Tuck, and Mr Tony Wackett. **NHS Greater Glasgow & Clyde Safe Haven:** Dr Roma Armstrong, Ms Marion Flood, Ms Laura Stirling, Ms Claire MacDonald, Mr Imran Sadat, and Mr Frank Finlay. **NHS Lothian eHealth and Safe Haven:** Dr Heather Charles, Ms Pamela Linksted, Mr Stephen Young, Mr Bill Alexander, and Mr Chris Duncan.

Declaration of Interests

NLM has received honoraria or consultancy from Abbott Diagnostics, Roche Diagnostics, Siemens Healthineers, and LumiraDx. All other authors have no conflicts of interest.

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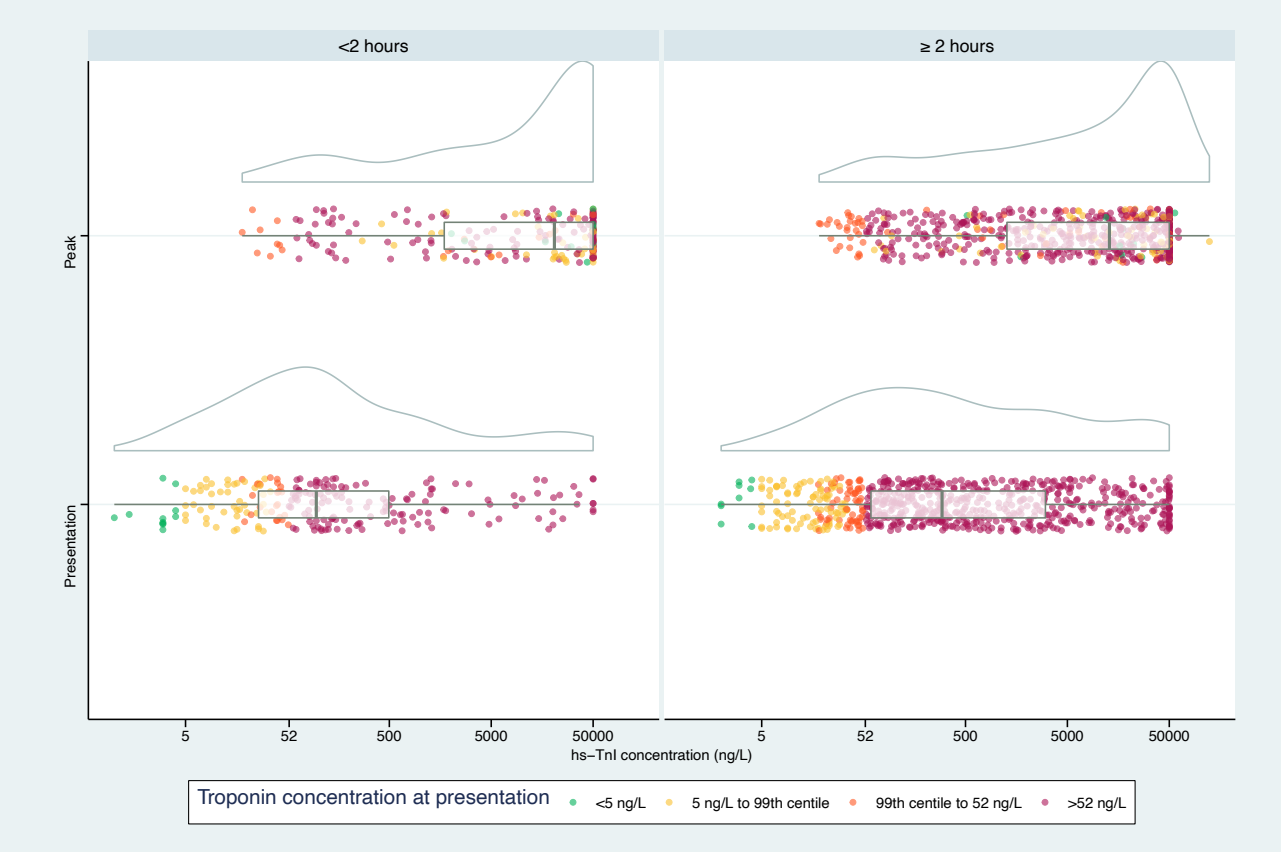
Figure.



High-sensitivity cardiac troponin I concentrations in consecutive patients with ST-segment elevation myocardial infarction stratified by troponin concentration at presentation

Patients were stratified by time of onset of symptoms (<2 hours, ≥2 hours) and according to cardiac troponin concentration at presentation. Individual patient concentrations (below the rule-out threshold of <5 ng/L (green), 5 ng/L to the 99th-centile diagnostic threshold (yellow), 99th-centile to 52 ng/L rule-in threshold for the ESC 0/1 hours pathway (orange), and >52 ng/L (red)) are shown with box and whisker distribution and probability density plots. Peak concentration is the highest troponin concentration obtained on serial sampling.

Abbreviations: hs-TnI, high-sensitivity cardiac troponin; ng/L, nanograms per liter