Low Concentrations of High-Sensitivity Troponin T at Presentation to the Emergency Department

Link to publication record in USC Research Bank:
http://research.usc.edu.au/vital/access/manager/Repository/usc:22342

Document Version:
Author accepted manuscript (postprint)

Citation for published version:

Copyright Statement:
Copyright © 2017 The Authors. The author accepted version is reproduced here in accordance with the publisher's copyright policy. The definitive version is available here:

General Rights:
Copyright for the publications made accessible via the USC Research Bank is retained by the author(s) and / or the copyright owners and it is a condition of accessing these publications that users recognize and abide by the legal requirements associated with these rights.

Take down policy
The University of the Sunshine Coast has made every reasonable effort to ensure that USC Research Bank content complies with copyright legislation. If you believe that the public display of this file breaches copyright please contact research-repository@usc.edu.au providing details, and we will remove the work immediately and investigate your claim.
Low concentrations of high-sensitivity troponin T at presentation to the Emergency Department.

Edward Carlton¹ PhD, Jason Kendall¹ MD, Ahmed Khattab² PhD, Kim Greaves³ MD.

Authors Affiliations

1. Emergency Department, Southmead Hospital, North Bristol NHS Trust, UK.

2. School of Health and Social Care, Bournemouth University, UK.

3. Sunshine Coast Hospital and Health Services, University of the Sunshine Coast and University of Queensland, Nambour, Australia.

Key Words: Chest Pain, Myocardial infarction, High-sensitivity troponin, Emergency Department.

Word Count: 748
Dear Editor:

Several issues around rule-out strategies utilising low concentrations of high-sensitivity cardiac troponin (hs-cTn) assays taken at presentation to the Emergency Department (ED) remain unexplored. Firstly, large-scale analyses investigating cut-off concentrations for hs-cTnI (Abbott Architect) < 99th percentile, have failed to investigate outcomes which incorporate the full spectrum of clinically relevant acute coronary syndromes, namely emergency revascularization (1,2). Secondly, whether these strategies work with the hs-cTnT (Roche Elecsys) assay are under-explored. Finally, the impact of laboratory rounding (ie. rounding the reported value up or down to the next whole integer depending on the exact post-decimal point value e.g. 4.5ng/L to 5ng/L) upon diagnostic performance at low cut-off concentrations, and how this effects the proportion of patients potentially eligible for early discharge, remains unknown.

In this post-hoc analysis of a prospectively recruited cohort we aimed to establish the diagnostic performance of a single hs-cTnT result taken at ED presentation in patients with a non-ischemic ECG, using the LoD and additional cut-off concentrations <99th percentile, and also the impact of laboratory rounding. The methods and results of the primary analysis have been published previously, including reporting of diagnostic accuracy at the LoD for hs-cTnT at ED presentation (3). Patients aged ≥18 years with chest pain suggestive of cardiac ischemia and a non-ischemic ECG, for whom the treating physician determined 6-hour troponin testing was required, were prospectively recruited at a single center. Specific to this analysis hs-cTnT results from the LoD (<5ng/L) up to the 99th percentile (14ng/L) were analyzed and were available to one decimal place. Rounding occurred up or
down to the nearest integer at all cut-off concentrations between the LoD and 99th percentile. Assay results were not affected by a previously reported calibration shift (4). The outcome was the presence of MACE (death due to ischemic heart disease, cardiac arrest, emergency revascularization, cardiogenic shock, ventricular arrhythmia, high-degree atrioventricular block and incident/prevalent acute myocardial infarction) occurring within 30 days.

In total, 922 patients were included. Of these, 546 (59.2%) were male, mean age was 58.0 years (SD=13.3) and 95 (10.3%) developed MACE within 30 days. Baseline characteristics have been previously reported (3).

Troponin concentrations were <LoD (5ng/L) in 210 (22.8%) of 922 patients when laboratory rounding was applied and 262 (28.4%) with unrounded values. The rounded LoD cut-off gave a sensitivity of 97.9% (95%CI 92.0-99.6) for MACE (Figure); negative predictive value (NPV) 99.0% (96.4-99.8) and negative likelihood ratio (NLR) 0.084 (0.014-0.325) (2). The performance of the unrounded LoD cut-off value was nearly identical: sensitivity 97.9% (92.0-99.6), NPV 99.2% (97.1-99.9) and NLR 0.067 (0.012-0.259).

The sensitivity for MACE decreased with increasing cut-off concentration. Rounded and unrounded cut-off values >LoD, up to and including 14ng/L all had sensitivities <97% for MACE (Figure).

Laboratory rounding led to a decrease in the proportion of patients potentially suitable for early discharge across all cut-off concentrations. This effect only reached significance at the LoD, where 5.6% fewer patients would have been eligible for early discharge with rounding; 22.8% (20.2-25.6) rounded vs. 28.4% (CI 25.6-31.4) unrounded.
We demonstrate that hs-cTnT taken at ED presentation can, using a cut-off of <5ng/L (LoD), identify >20% of patients as potentially suitable for discharge. At this cut-off, for the outcome of MACE, diagnostic performance may fall to levels below that which is clinically acceptable (5). However, it should be noted that the composite outcome of MACE includes revascularization which, although important, is a subjective outcome. We also demonstrate that cut-off values >LoD may not have adequate diagnostic performance for clinical implementation. Laboratory rounding may significantly reduce the proportion of patients potentially suitable for early discharge using the LoD cut-off.

Importantly, we have not analyzed those patients presenting early after symptom onset. The diagnostic performance of low cut-off concentrations has been shown to fall in this subgroup (1). Furthermore, we selected patients without new onset ECG changes diagnostic of ischemia. Therefore, the population selected for this analysis were likely to be at lower risk when compared to prior studies, and diagnostic performance may be overestimated as a result.

Given the medicolegal implications for missed MACE, clinicians must carefully consider whether a LoD strategy is ready for clinical implementation. In particular, were clinicians to make a discharge decision based on an undetectable troponin, full consideration should be given to time from symptom onset, further risk-stratification, and the need for advanced cardiac testing.

Whether strategies that utilize low cut-off concentrations of hs-cTn can be successfully implemented into clinical practice remains unknown. Further studies are required to determine the clinical and cost effectiveness of such strategies.
Acknowledgements

The authors thank Dr John Beavis PhD (Bournemouth University) for statistical support. We thank staff at Poole Hospital Emergency Department and Biochemistry departments for their assistance and support. We are indebted to the patients who participated in the study.

Funding

The TRUST Study was supported by a research grant from the Royal College of Emergency Medicine of the United Kingdom and research fellowship funding from Bournemouth University, United Kingdom.

Contributors

Each author has contributed to the analysis and interpretation of the data, drafting and approval of the final manuscript. All authors have also contributed to the conception/design of the study reported in this manuscript. Drs Carlton and Greaves had full access to all study data and take responsibility for the integrity of the data and accuracy of the data analysis. The sponsors had no role in designing or conducting the study and no role in gathering or analyzing the data or writing the manuscript. The manuscript and its contents have not been published previously and are not being considered for publication elsewhere.

Ethics Approval: Frenchay Research Ethics Committee (reference 12/SW/0133).

Registry: ISRCTN No. 21109279
REFERENCES


Figure Legend

Figure. Sensitivity 30 day MACE for a range of rounded and unrounded high-sensitivity troponin T concentrations at presentation.

Error bars: 95% Confidence Intervals