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Cite this as: *BMJ* 2023;383:p2741
http://dx.doi.org/10.1136/bmj.p2741
Published: 28 November 2023

Do high sensitivity cardiac troponin assays improve patient outcomes?

New study reports benefits for some patients with suspected acute coronary syndrome

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Cardiac troponins have replaced other blood biomarkers for the diagnosis of myocardial injury. They are widely used to risk stratify patients towards safe early discharge or further investigation of coronary anatomy when clinical and electrocardiographic features are suggestive of acute coronary syndrome.

High sensitivity assays can detect lower concentrations of cardiac troponin than older assays, improving test sensitivity and enabling earlier detection of myocardial injury. In practice, use of high sensitivity assays leads to earlier discharge from emergency departments[1] and improved detection of myocardial injury that may require further investigation. Although use of high sensitivity assays is increasing in line with guideline recommendations,[2,3] it remains unknown whether use in emergency departments improves long term clinical outcomes for patients with suspected acute coronary syndrome. The linked paper by Lee and colleagues (doi:10.1136/bmj-2023-075009) addresses this important knowledge gap by reporting a secondary observational analysis of the High-Sensitivity Troponin in the Evaluation of patients with suspected Acute Coronary Syndrome (High-STEACS) clinical trial.[4]

The original cluster randomised stepped wedged trial design included 48 282 patients presenting to emergency departments at 10 Scottish hospitals with suspected acute coronary syndrome.[5] All patients had both standard (contemporary) and high sensitivity troponin tests. Hospitals were randomly allocated to use one or the other test to guide care (through hospital level allocation to early or late implementation of high sensitivity assays), and clinicians were blinded to the results of the alternative non-allocated troponin assay.

Primary results are already published: Overall, 10 360 patients had concentrations above the 99th centile measured using the high sensitivity troponin assay. Nearly one in six of these patients had their diagnoses reclassified by the high sensitivity assay. Use of such an assay to guide care increased provision of coronary angiography and the initiation of preventive drugs,[5] but it had no effect on the primary outcome—the risk of subsequent myocardial infarction or cardiovascular related death at one year. The authors speculated that the lack of effect on clinical outcomes may be due to insufficient duration of follow-up, as the benefits of a correct diagnosis probably accumulate over time.

In their new observational analysis, Lee and colleagues report the risk of myocardial infarction or all cause death at five years for the entire High-STEACS trial population,[4] through linkage with the national morbidity and mortality database. Use of the high sensitivity assay at the original emergency presentation was not associated with lower risk of the primary outcome at five years (adjusted hazard ratio 0.97, 95% confidence interval 0.93 to 1.01). Event rates were, however, reduced in the subgroup most likely to benefit—those reclassified by the high sensitivity assay (0.82, 0.72 to 0.94). In the reclassified population, the observed 9% absolute risk reduction (63% among patients managed before hospital implementation of high sensitivity assays versus 54% among patients managed after implementation) suggests that use of high sensitivity assays may prevent one event for every 11 patients reclassified.

No effect on the primary outcome was observed in subgroup analyses by type of myocardial injury among patients with an original diagnosis of myocardial infarction, but the authors reported a 17% lower relative risk of myocardial infarction or all cause death among patients with an original diagnosis of non-ischaemic myocardial injury (0.83, 0.75 to 0.91). Interestingly, this risk reduction was limited to patients with a cardiac cause for their non-ischaemic myocardial injury (0.69, 0.60 to 0.80). An early divergence of the survival curve in the subpopulation with non-ischaemic injury suggests that implementation of the high sensitivity assay may have led to improved diagnosis, followed by management that altered prognosis.

This secondary observational analysis from a large trial is noteworthy as it is the first to report a reduction in risk for subsequent myocardial infarction or all cause death after use of a high sensitivity assay in clinically relevant subgroups presenting with suspected acute coronary syndrome. In particular, the apparent benefit for patients with non-ischaemic myocardial injury is both intriguing and plausible. This diagnostic category included cardiac causes such as heart failure, cardiomyopathy, and aortic dissection, for which effective treatments for improving prognosis exist. Reclassified patients spent on average two days longer in hospital after the high sensitivity assay was implemented, providing evidence of an opportunity for additional investigation and management. Nevertheless, these post hoc analyses should be considered hypothesis generating and require confirmation.

Study strengths include the pragmatic design, large sample size, comprehensive long term follow-up of patients with suspected acute coronary syndrome, and adjudicated causes of myocardial injury at initial presentation. Limitations include a predominantly white population from Scottish hospitals, reducing generalisability. Although the trial was large, subgroups in the secondary analysis were relatively

small. Extended follow-up may have also introduced unmeasured confounding factors resulting from gradual changes in clinical practice or lifestyle over time. Finally, the use of discharge diagnostic codes and lack of event adjudication for the myocardial infarction component of the primary outcome may have led to misclassification, which could have contributed to the null findings in the subgroup originally diagnosed as having myocardial infarction.

Confirmation of Lee and colleagues' new findings are needed, along with a better understanding of the benefits reported for patients with non-ischaemic myocardial injury of cardiac origin. Other evidence suggests that even small elevations in high sensitivity cardiac troponin I well below the sex specific 99th centiles are associated with cardiovascular events,[6 7] non-cardiovascular events,[8 9] and all cause mortality.[10] Notably, although lower cut-offs for high sensitivity assays are increasingly used in accelerated protocols to rule out acute coronary syndrome, the long term effects on clinical events remain unknown.[11]

Lee and colleagues' analyses[4] provide novel information that could facilitate the design and conduct of future clinical trials. But—as often happens with carefully executed research—this paper raises more questions than answers.

Competing interests: The BMJ has judged that there are no disqualifying financial ties to commercial companies. The authors declare the following other interests: None.

Further details of The BMJ policy on financial interests is here: https://www.bmj.com/sites/default/files/attachments/resources/2016/03/16-current-bmj-education-coi-form.pdf.

Provenance and peer review: Commissioned; not externally peer reviewed.

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