Diagnosing myocardial infarction: a highly sensitive issue

The advent of high-sensitivity troponin assays to enable the quantification of troponin concentration in up to 95% of the general population is thought to improve clinical care in patients presenting with suspected infarction.1,2 The application of high-sensitivity troponin assays could be beneficial by enabling the early ruling out of myocardial infarction on the basis of very low troponin concentrations;3–7 precise and rapid diagnosis of myocardial infarction on the basis of troponin-based algorithms8,9 followed by early treatment initiation; and improved risk stratification on the basis of low troponin concentrations that are only detectable by high-sensitivity assays.1

In The Lancet, the High-STEACS Investigators10 present an innovative and impressive strategy to compare a truly high-sensitivity troponin assay with previous contemporary troponin testing by use of a cluster-randomised controlled trial design. This design allows the comparison of outcomes 1 year after patient presentation at the emergency department, before and after implementation of this high-sensitivity assay across ten hospitals in Scotland.

The trial is large, with almost 50,000 patients included. Among the study population, 10,360 (21%) patients had troponin concentrations greater than those of the 99th percentile. Notably, 1771 (17%) of these 10,360 patients were reclassified by the high-sensitivity strategy, resulting in additional patients who had not been identified by the contemporary assay being identified by the high-sensitivity assay. These patients would have been missed if we were only to use the conventional assay.

How did this high-sensitivity approach affect cardiovascular outcomes, and what was the net benefit of identifying these reclassified patients? Within 1 year, 2586 (5%) patients had a subsequent myocardial infarction or death from cardiovascular causes, and these outcomes were more common in patients who had been reclassified. However, use of a high-sensitivity assay to diagnose those at risk did not significantly affect the risk of the combined endpoint of subsequent myocardial infarction or cardiovascular death (which occurred in 15% of reclassified patients during the validation phase vs 12% of these patients during the implementation phase). Therefore, Anoop Shah and colleagues10 report no benefit to the high-sensitivity strategy investigated.

This nationwide approach represents an intelligent approach to make clinical routine data accessible within the frame of a clinical trial. However, there still might be some crucial points to consider. It is a self-fulfilling conundrum that application of a high-sensitivity assay leads to a higher number of diagnoses of myocardial infarction when lower thresholds are applied. Ideally, earlier and more sensitive detection of myocardial infarction should lead to better therapeutic strategies and should also translate into better outcome. Obviously, this result is not observed in Scotland during and after the implementation phase. The application of high-sensitivity assays is not associated with a difference in outcome at 1 year in the study by Shah and colleagues. This finding might be explained by various factors. First, strong evidence proves the association between troponin concentration and outcome in disease-based and population-based studies, even at low concentrations. This association becomes stronger over time and is most likely not apparent after 1 year. A follow-up of 1 year is not sufficient to determine the benefit of clinical decision making that is based on more sensitive troponin assays. Second, although the use of coronary angiographies in reclassified patients was more common, the number of patients that received percutaneous coronary intervention was unchanged. Medical therapy was moderately improved in the reclassified patients, but the absolute numbers were small (new single or double antiplatelet drugs were used in 171 patients and new statins in 47 patients). These slight changes in medical treatment do not affect outcome after 1 year. Finally, and most importantly, the adoption of the 99th percentile as a threshold for the high-sensitivity assays largely ignores their potential. The 99th percentile of the high-sensitivity troponin assay is almost completely recognisable by the contemporary sensitive test (only 17% of those identified by which were reclassified). Hence, the use of the high-sensitivity assays in the implementation phase did not take advantage of the highly sensitive nature of the test.
Although this trial focused on the effects of high-sensitivity troponin assays for diagnosing myocardial infarction and progresses our understanding, additional questions remain. First, can the application of the high-sensitivity troponin assay safely rule out myocardial infarction by use of a baseline and 1-h protocol without affecting outcome? And second, could the application of troponin cutoff concentrations far below the 99th percentile lead to an improvement of clinical outcomes due to changes in treatment strategies in a longer follow-up? Both aspects need to be addressed in future.

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SB reports receiving honoraria from Abbott Diagnostics, Siemens, Thermo Fisher and Roche Diagnostics, outside the area of work commented on here. JTN and DW declare no competing interests.

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Imaging of coronary inflammation for cardiovascular risk prediction

Inflammation plays an important part in the development of atherosclerosis and is a predictor of cardiovascular disease manifestation. Although circulating biomarkers of inflammation—eg, high sensitivity C-reactive protein—are associated with cardiovascular risk, they might not adequately reflect inflammatory activity in the coronary arteries at the individual patient level. Epicardial and perivascular adipose tissue—surrounding the heart and coronary arteries—secretes proinflammatory and anti-inflammatory cytokines and chemokines locally, and these tissues are associated with the extent and progression of coronary atherosclerosis and hard coronary events. However, a link between imaging-based signs of local inflammation within the fat depot and subsequent events has not been established.

In The Lancet, Evangelos Oikonomou and colleagues report findings of a post-hoc analysis of prospectively obtained outcome data from two independent clinical cohorts in Erlangen, Germany (derivation cohort) and Cleveland, OH, USA (validation cohort). 3912 participants underwent coronary angiography (CT) to measure perivascular fat attenuation around the right coronary artery. The authors note a strong and independent association of the pericoronary fat attenuation index (FAI) with all-cause mortality (hazard ratio [HR] 1.49, 95% CI 1.20–1.85, p=0.0003 in the derivation cohort; 1.84, 1.45–2.33, p=0.0001 in the validation cohort) and cardiac mortality (HR 2.15, 95% CI 1.33–3.48, p=0.0017 in the derivation cohort; 2.06, 1.50–2.83, p=0.0001 in the validation cohort). To our knowledge, this is the first large and prospective study to show that a non-invasive imaging-based measure of local coronary inflammation can predict cardiovascular risk.

Currently, non-contrast cardiac CT is done routinely for risk stratification in primary prevention, to quantify