The role of high-sensitivity C-reactive protein in predicting mortality beyond troponin in over 100,000 patients with suspected acute coronary syndrome (NIHR Health Informatics Collaborative CRP-risk study)

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Background The incremental long-term prognostic value of high-sensitivity C-reactive protein (hsCRP) above troponin in a large real-world cohort of unselected patients presenting with suspected acute coronary syndromes (ACS) is unknown. We hypothesised that a mildly elevated hsCRP is associated with mortality risk in patients with suspected ACS, independent of troponin level.

Methods We used the National Institute for Health Research Health Informatics Collaborative data of 257,948 patients who had a troponin measured at 5 cardiac centres. We excluded patients with clinically abnormal white cell counts and hsCRP >15 mg/L to try limiting the population to those without overt infections, malignancies or systemic inflammatory conditions that may confound our analyses. Patients were divided into four hsCRP groups (<2, 2–4.9, 5–9.9 and 10–15 mg/L) and the association between hsCRP levels and all-cause mortality assessed.

Results There were 102,337 patients included in the analysis (hsCRP <2 mg/L (n=38,390), 2–4.9 mg/L (n=27,397), 5–9.9 mg/L (n=26,957) and 10–15 mg/L (n=9,593)). Figure 1A displays cumulative mortality per hsCRP group, revealing increasing mortality with each consecutive group. Figure 1B further stratifies the groups according to dichotomised peak troponin level as positive or negative. This shows the greatest mortality for patients in the highest hsCRP group who also had a positive troponin assay (36.0% at 3 years).

In Cox regression analysis with time-dependent covariates, even mildly raised hsCRP was an independent predictor of mortality over time, after adjusting for age, gender, haemoglobin, white cell count, platelet count, creatinine and troponin positivity. There was a positive and graded relationship between hsCRP level and mortality at baseline, which remained at 3-years (hazard ratio (95% CI) of 1.32 (1.18–1.48) for those with hsCRP 2.0–4.9 mg/L, and 1.40 (1.26–1.57), and 2.00 (1.75–2.28) for those with hsCRP 5–9.9 mg/L and 10–15 mg/L, respectively.

We explored whether inclusion of hsCRP could better reclassify the population into at-risk mortality groups. The association with 30-day, 1-year and 3-year mortality was assessed using three different risk models (model 1: age, gender, haemoglobin, white cell count, platelet count, creatinine and troponin positivity; model 2: model 1 plus troponin positivity versus negativity; model 3: model 2 plus hsCRP groups. For cumulative mortality at each time point, each
successive model was better able to discriminate risk than its precursor ($p<0.0001$); such that inclusion of troponin and hsCRP gave the most robust risk discrimination. Model 3 achieved an AUROC $>0.8$ at 30 days, 1-year and 3-year mortality, surpassing the use of troponin on its own. Conclusion These multi-centre, real-world data from a large cohort of patients with suspected ACS identify hsCRP as a clinically meaningful prognostic marker in addition to troponin levels and point to its potential utility in selecting patients for novel treatments targeting inflammation.

Conflict of Interest No conflicts of interest

THE PROGNOSTIC IMPLICATION OF A POSITIVE TROPNONIN ACROSS THE AGE SPECTRUM IN A QUARTER OF A MILLION PATIENTS WITH SUSPECTED ACUTE CORONARY SYNDROME (NIHR HEALTH INFORMATICS COLLABORATIVE TROP-RISK STUDY)

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Background In the past two decades, assays for troponin have undergone vast improvements, allowing fast detection of troponin with increased precision. With improved sensitivity of current troponin assays, more patients end up with a positive troponin result. There is limited data to help inform the implications of a positive troponin test across the age spectrum, in clinical practice. The aim of this study was to investigate the overall prognostic impact of a positive troponin result on all-cause mortality in patients in whom troponin testing has been done for clinical purposes.

Methods The NIHR Health Informatics Collaborative (NHIC) project was established to enable the sharing and repurposing of routinely captured clinical data for re-use in research. All troponin values measured during the study period (generally 2010 to 2017) were assembled from five contributing cardiovascular centres. The results were dichotomised as being positive or negative based on the 99th percentile of the upper limit of normal for all relevant troponin assays. All patients were followed up on the National Health Service Spine Application, Summary Care Record until death or censoring on 1st April 2017. Statistical analyses were performed using SPSS software version 24.0 (SPSS Inc., Chicago, Illinois, United States).

Results 257948 patients underwent troponin assessment during the study period. The median age was 65 (IQR 50–79) and 55.3% were men. During a median follow-up of 1198 (IQR 514–1866) days, there were 55850 (21.7%) deaths. The proportion of troponins that were positive progressively rose with age from 9.1% in the 18–29 band to 50.0% in the over 90s. The median positive troponin was 2280 times higher than the median negative troponin, and this relationship was largely invariant with age. A positive troponin was associated with an overall 3.2-fold higher mortality hazard (95% CI 3.1–3.2) than a negative troponin over 3 years. For young patients (18–29 years) this was a particularly strong effect, with a mortality hazard of 10.6 (95% CI 8.5–13.3). The effect declined progressively with age to a mortality hazard of 1.5-