Assay of macrotroponin I not complexed with troponin T: effect on the performance of troponin T to predict myocardial infarction


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Funding Acknowledgements: Type of funding sources: Public grant(s) – National budget only. Main funding source(s): Health Research Council of New Zealand
Upstream Medical Technologies made FAST-TRAC samples available for analyses

Background: Cardiac troponin-immunoglobulin (Ig) complexes (macrotroponin) can interfere with cardiac troponin (cTn) test performance. However, the role of this interference has not been fully explored. We developed a specific, novel, 2-hour prototype immunoassay of monomer IgG-bound TnI (bTnI-IgG). Using this assay, our purpose was to examine the potential contribution of cTnT binding to macro-TnI, and report its effects on the clinical diagnostic and predictive performance of highly sensitive TnT (hs-TnT) and TnI (hs-TnI) assays.

Methods: Using the bTnI-IgG assay, we evaluated EDTA blood samples taken at presentation (t=0) from two ED acute chest pain studies; SPACE (n=1066) and FAST-TRAC (n=1440), with statistical analysis (logistic regression, ROC curves), to AMI and 1-year outcomes, alone and in combination, with hsTnT (Roche) and hsTnI (Abbott/Beckmann) tests. Pathway analysis was used to identify if single bTnI-IgG measurements improve risk stratification in low and high AMI risk.

Results: In individual and combined study datasets, bTnI-IgG concentrations in patients with adjudicated acute MI (n=336) were lower than all other diagnoses (p<0.001). Singularly, and in multivariable models containing hs-TnT or hs-TnI concentrations, bTnI-IgG was an independent predictor of MI. Amongst all patients with MI not ruled-out on presentation (hs-TnT >5ng/L) and not high-risk (hsTnT<14ng/L), the addition of bTnI-IgG to a model containing hs-TnT, HxMI and sex improved discrimination (AUC increase of 0.014 (95%CI: 0.004 to 0.025) from 0.788 to 0.802, p=0.009). Within a diagnostic pathway analyses of n=2126 matched patient data points, adding presentation bTnI-IgG measurement alone to an MI risk stratification model consisting of hs-TnT ≤URL, HxMI and sex yielded 14% more low risk patients identified (n=586 v 667 patients) through improved specificity (77% to 88%) whilst maintaining an overall sensitivity of >99%. bTnI-IgG also predicted 1-year mortality and new stroke in all patients (Odds Ratios 0.292 [95%CI 0.130 to 0.654] p=0.009) and 0.255 ([95%CI 0.078 to 0.834] p=0.024), respectively.

Conclusions: Measurement of bTnI-IgG that is free from cTnT could potentially improve ED presentation diagnostic test performance and risk stratification of MI patients using criteria that includes hs-TnT. No effects upon hs-TnI assays were observed. This data suggests current hs-TnT test design and measurements may be impacted by binding interactions between TnT and TnI. Finally, bTnI-IgG can independently predict mortality and stroke outcomes within 1 year of index presentation.