Evaluating Pediatric High-Sensitivity Troponin Thresholds and Testing Trends: A Multicenter Retrospective Cohort Study

Alexander J F Thurston[1*], Eirik Å. Røys[2,3*], Ragnhild Røysland[4,5], Øyvind Skadberg[6], Dorien M Kimenai[7], Nicholas L Mills[7,8], Kristin M Aakre[2,3,9]

[1] Centre for Cardiovascular Science, The University of Edinburgh, Edinburgh, UK
[2] Department of clinical science, University of Bergen, Bergen, Norway
[3] Department of Medical Biochemistry and Pharmacology, Haukeland University Hospital, Bergen, Norway
[4] Multidisciplinary Laboratory Medicine and Medical Biochemistry, Division of Diagnostics and Technology, Akershus University Hospital, Lørenskog, Norway
[5] Institute of Clinical Medicine, Faculty of Medicine, University of Oslo, Oslo, Norway
[6] Laboratory of Medical Biochemistry, Stavanger University Hospital, Stavanger, Norway
[7] BHF Centre of Research Excellence, University of Edinburgh, Edinburgh, UK
[8] Usher Institute, University of Edinburgh, Edinburgh, UK
[9] Department of Heart Disease, Haukeland University Hospital, Bergen, Norway

[*]Both authors contributed equally to this paper

Background: There are no clear clinical recommendations regarding use of high-sensitivity cardiac troponin (hs-cTn) measurements in children and young adults. Upper reference limits (URL) are known to be age dependent in pediatric patients but there is an ongoing debate if the 97.5 or 99th percentile should be recommended as URL. This retrospective cohort study, conducted across four hospitals in Norway and the United Kingdom from 2013 to 2023, aimed to; 1) analyze trends in hs-cTn testing, 2) compare pediatric- and adult-derived cutoffs including the 97.5th and 99th percentile URL and 3) assess associations with clinical outcomes such as myocarditis and pericarditis.

Methods: We identified 9,669 pediatric patients (≤18 years) who underwent hs-cTn testing, retaining only the first measurement per individual. Troponin assays included high-sensitivity cardiac troponin T (Roche) and I (Abbott), with values below detection limits assigned half the reporting threshold. The proportion of patients with elevated troponin levels was evaluated using the local URL, adult sex-specific 99th percentiles, and pediatric-derived URLs (99th and 97.5th percentiles). Trends in hs-cTn test volumes were normalized towards concurrent creatinine measurements, while clinical diagnoses of myocarditis and pericarditis were retrieved from hospital records (United Kingdom) or health care registers (Norway).

Results: Troponin testing increased at some sites while remaining stable at others, with the most marked rise occurring during the COVID-19 pandemic. Overall, 18.1% of patients had troponin levels exceeding the adult sex-specific 99th percentile, compared with 18.0% using the pediatric 99th percentile. By contrast, the sex-specific pediatric 97.5th percentile identified 23.2% of patients as having elevated troponin (relative increase of 28%). Infants (<1 year) had notably higher rates of elevated hs-cTn, in line with recognized physiological elevations in early life. Despite increased testing at select locations, the incidence of myocarditis and pericarditis remained low, and no clear link emerged between testing volume and disease prevalence.

Conclusions: In this multicenter retrospective cohort, pediatric-specific reference intervals had minimal impact on the proportion of patients identified with elevated hs-cTn levels compared to adult thresholds, except when using the paediatric sex-specific 97.5th percentile, which

significantly increased the classification of myocardial injury. The variability in testing trends suggests that local clinical practices influence hs-cTn utilization, but increased troponin testing did not lead to a corresponding rise in myocarditis or pericarditis diagnoses.

Keywords: multi-site retrospective study, pediatric, high-sensitivity cardiac troponin

Disclosure Statement:

N.L.M reports receiving honoraria or consultancy with Roche Diagnostics, Abbott Laboratories and Siemens Healthineers.

K.M.A. has served on advisory board for Roche Diagnostics, Siemens Healthineers, Radiometer and SpinChip, consultant honoraria form CardiNor, lecturing honorarium from Siemens Healthineers, Roche Diagnostics, Mindray and Snibe Diagnostics and research grants from Siemens Healthineers and Roche Diagnostics, she is Associate Editor of Clinical Biochemistry and Chair of the IFCC Committee of Clinical Application of Cardiac Biomarkers.

The remaining authors report that they have no competing interests to declare.