Threshold and Kinetic Differences Between Fifth- and Sixth-Generation High-Sensitivity Cardiac Troponin T in Routine Clinical Care Testing

Megan Palacio[1*], Lori B. Daniels[2,] Nolan R. Martin[2], Spencer Seely[1], Ronald W. McLawhon[1], Robert L. Fitzgerald[1], Raymond T. Suhandynata[1,3]

[1]Department of Pathology, University of California San Diego, San Diego, CA, USA

[2]Division of Cardiovascular Medicine, University of California San Diego, San Diego, CA, USA

[3]Skaggs School of Pharmacy and Pharmaceutical Sciences, University of California San Diego, San Diego, CA, USA

*Author for correspondence
Center for Advanced Laboratory Medicine
University of California San Diego
10300 Campus Point Dr.
San Diego, CA 92121
mepalacio@health.ucsd.edu

Background: High-sensitivity cardiac troponin T (hs-cTnT) assays are central to the evaluation of myocardial injury, with clinical interpretation directed by the assay-specific 99th percentile upper reference limit (URL). Transition from the fifth-generation (Gen5) to sixth-generation (Gen6) hs-cTnT assays may introduce analytical differences that impact threshold-based interpretation, particularly near the 99th percentile URL where small concentrations changes may alter classification. Data describing the real-world clinical implications of this assay transition remain limited.

Methods: Residual clinical specimens from patients undergoing routine hs-cTnT testing were analyzed in parallel using Roche Gen5 and Gen6 assays in a retrospective paired study design. Longitudinal paired measurements (n=3,617) from 1,847 encounters representing 1,737 unique patients were evaluated. Comparative analyses included time to first elevation above the assay-specific 99th percentile URL, peak hs-cTnT values, simulated 0/1/3-hour clinical pathway categorization, and temporal kinetic characteristics.

Results: Gen5 and Gen6 assays demonstrated strong concordance overall for paired measurements and encounter-level peak classification. Observed differences were concentrated near the 99th percentile URL rather than across the full analytical measurement range. Gen6 crossed the 99th percentile URL earlier than Gen5 more frequently than the reverse scenario (2.6% vs 0.1%; p=0.0001). Simulated application of a 0/1/3-hour clinical pathway showed high overall agreement between assays, though select encounters were reassigned among rule-out, indeterminate, and abnormal categories. Compared with Gen5, Gen6 exhibited larger relative changes during early rising phase and more rapid decline following peak concentration, with decay characteristics more closely approximating CK-MB kinetics.

Conclusion: Gen5 and Gen6 hs-cTnT assays show high overall analytical concordance yet modest differences near clinical decision thresholds can alter timing of 99th percentile URL crossing and downstream modeled pathway classification. These findings

underscore the need for careful assay-specific validation and interpretation when adopting newer hs-cTnT assay generations.

Keywords: high-sensitivity cardiac troponin T, myocardial injury, assay comparison

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