

Expert Answers

From the IFCC Committee on Clinical Applications of Cardiac Bio-Markers

CARDIAC Q&A SERIES V: ANALYTICAL, PHYSIOLOGICAL, AND CLINICAL FACTORS AFFECTING TROPONIN PERFORMANCE

How worried should I be about skeletal muscle disorder, renal dysfunction and biotin affecting high sensitivity troponin assays?

Clinical diagnosis should never rely on a single laboratory finding. To avoid misinterpreting cardiac troponin (cTn) increases in patients with comorbidities, healthcare providers must use the totality of evidence, integrating assay trends with clinical signs, symptoms, ECG results, and imaging and rely on monitoring acute changes of cTn in serial sampling in accordance with international guidelines

Skeletal muscle disorder: In some types of skeletal muscle diseases, such as noninflammatory myopathies, neuromuscular disorders and myositis, stable increased concentrations of cTnT may be detected. High-sensitivity (hs) cTnI assays can be used to evaluate possible cardiac involvement, as these assays are not affected by skeletal muscle disorders without myocardial involvement. However, hs-cTnI may not always be increased in some of these patients despite documented myocardial disease so these cases must always be reviewed in light of all clinical, imaging and biochemical data.

Renal dysfunction: In renal disease increases above the assay-specific 99th percentile, are more common for cTnT than cTnI. Although there are multiple factors behind this, one part is related to the way cleavage products of cTnT and cTnI are produced in patients with renal failure. The cTnT assay selects epitopes within the stable region of cTnT which allows detection of even very small troponin fragments.

Biotin: Interference due to biotin intake has become less common during the last years. All present commercial hs-cTn assays listed in the reference table of the IFCC Committee on Clinical Applications of Cardiac Bio-Markers claim an interference threshold of at least 100 ng/mL of biotin. For biotin regimens of ≤ 10 mg q.d. (10 mg is >300 -times the adequate daily intake), serum biotin concentrations will be below 30 ng/mL after 8 hours.

Key reference: The IFCC Biomarker Reference Tables. Current Interference: Cardiac Troponin Assays.
<https://ifcc.org/ifcc-education-division/emd-committees/committee-on-clinical-applications-of-cardiac-bio-markers-c-cb/biomarkers-reference-tables/>

Additional reading: du Fay de Lavallaz J, Prepoudis A, Wendebourg MJ, et al. Skeletal Muscle Disorders: A Noncardiac Source of Cardiac Troponin T. *Circulation*. 2022;145:1764-1779.

Fridén V, Starnberg K, Muslimovic A, et al. Clearance of cardiac troponin T with and without kidney function. *Clin Biochem*. 2017;50:468-474.

Harley K, Bissonnette S, Inzitari R, et al. Independent and combined effects of biotin and hemolysis on high-sensitivity cardiac troponin assays. *Clin Chem Lab Med*. 2021;59:1431-1443.

🔍 How should clinicians interpret cardiac troponin in the context of dialysis patients (both hemodialysis and peritoneal dialysis)?

Cardiac troponin concentrations are typically increased in patients with end-stage renal disease, patients on hemodialysis or peritoneal dialysis. cTn concentrations are similar in hemodialysis and peritoneal dialysis patients although interindividual and intraindividual variation is high. The chronically increased concentrations in dialysis patients can be distinguished from acute cTn release in acute myocardial infarction by monitoring the change in cTn concentrations in serial sampling. Relative changes of >20% have been suggested for the detection of AMI, but the variation of the assay may affect the performance of this approach. It has been suggested that higher percentage changes may improve the specificity of the diagnosis of AMI. All increased cTn concentrations in dialysis patients have prognostic value in predicting cardiac events and death.

Key reference: Snaedal S, Bárány P, Lund et al. High-sensitivity troponins in dialysis patients: variation and prognostic value. *Clin Kidney J.* 2020;14:1789-1797.

Additional reading: Aakre KM, Røraas T, Petersen PH et al. Weekly and 90-minute biological variations in cardiac troponin T and cardiac troponin I in hemodialysis patients and healthy controls. *Clin Chem.* 2014;60:838-47.

Knott JD, Ola O, De Michieli L, et al. Major adverse cardiovascular events after diagnosis of myocardial injury and types 1 and 2 myocardial infarction. *EHJACC.* 2022;11:546-557

Sandoval Y, Herzog CA, Love SA, et al. Prognostic value of serial changes in high-sensitivity cardiac troponin I and T over 3 months using reference change values in hemodialysis patients. *Clin Chem* 2016; 62:4631-638.

🔍 What are the reasons for increased cardiac troponins that are not AMI, clinically and analytically?

As cardiac troponins are biomarkers of myocardial injury, increased concentrations may be detected in pathophysiological conditions with myocardial injury, such as heart failure, myocarditis, cardiomyopathy, Takotsubo syndrome, cardiac procedures, kidney disease, stroke, pulmonary embolism, use of chemotherapeutic agents or strenuous exercise, in addition to MI. Commonly, there are good explanations for increases but clinicians can at times forget that increases in cTn are not unique to coronary artery disease. Better education about the multiplicity of causes for increases in cTn in the absence of coronary heart disease are needed.

Analytically false cTn increases should only be considered when repeated cTn measurements are roughly unchanged and the clinical situation suggests myocardial injury is unlikely. The most prevalent forms of analytical interference that cause increased cTn results are fliers due to poor sample quality (likely fibrin plug-related errors in the analysis), heterophilic antibodies and macrotroponin. Fliers can be mitigated by repeated analysis on the same sample after centrifugation. Once fliers have been eliminated as a cause, the use of an alternative assay can be helpful as many interferences are unique for specific assays. Some have suggested the use of PEG precipitation to remove macrotroponin but the data in regard to this use is controversial and assay dependent.

Key reference: Agewall S, Giannitsis E, Jernberg T, et al. Troponin elevation in coronary vs. non-coronary disease. *Eur Heart J.* 2011;32:404-11.

Additional reading: Hammarsten O, Warner JV, Lam et al. Antibody-mediated interferences affecting cardiac troponin assays: recommendations from the IFCC Committee on Clinical Applications of Cardiac Biomarkers. *Clin Chem Lab Med.* 2023;61:1411-1419.

Strandkjær N., Hansen MB, Afzal S et al. Influence of Macro-troponin on the 99th Percentile Threshold in 2 High-Sensitivity Cardiac Troponin Assays. *Clin Chem.* 2025;71:884-895

Donato LJ, Wockenfus AM, Katzman BM. Analytical and Clinical Considerations in Implementing the Roche Elecsys Troponin T Gen 5 STAT Assay Purchased. *AJCP* 2021;156:1121-1129.

🧐 How do the differences in antibodies used by cardiac troponin assays affect test result concentration and sample storage stability?

Result Concentrations: Cardiac troponin from different manufacturers use different antibody combinations targeting different parts of the cardiac troponin molecules and accordingly will produce different concentrations when measuring the same sample.

Sample Storage: Sample storage may affect the assay results, especially if it is not conducted as advised by the assay manufacturer. The use of different antibodies targeting different epitopes on the troponin molecule may lead to differences between assays in sample stability

Key reference: Katrukha IA, Katrukha AG. Myocardial Injury and the Release of Troponins I and T in the Blood of Patients. *Clin Chem.* 2021;67:124-130.

Additional reading: Salonen SM, Kristensen JH, Simonen S et al. Exploring the Role of Cardiac Troponin-Specific Autoantibodies: Prolonged Cardiac Troponin Elimination, Reduced Clearance, and Variable Interference across 5 Commercial Assays. *Clin Chem.* 2025;71:970-979.

The information provided above is a brief summary of common questions and answers developed by consensus of the IFCC C-CB committee, however it is important to recognise that greater knowledge and understanding is recommended and can be sourced from the referenced resources and <https://ifcc.org/ifcc-education-division/emd-committees/committee-on-clinical-applications-of-cardiac-bio-markers-c-cb/> including links to detailed papers, podcasts and presentations.