

COVID-19 infection and possible vaccine reactions continue to impose on healthcare systems around the world. Acute presentations of potential acute coronary syndrome or myocarditis related to, or in the context of, COVID-19 infection or vaccination should, as suggested, consider assay interference when increased troponin levels are discordant with clinical or other investigations. Given that many emerging clinical guidance protocols may also suggest the use of tests such as troponin or natriuretic peptides in the assessment of patients with long COVID following the acute sequelae SARS-CoV-2 infection, then caution should also be observed in interpreting such test results in these patients.

Further work is now indicated to improve the knowledge surrounding interfering factors including prevalence in different clinical scenarios, clinical significance, and development of consistent, standardized approaches for identification and interpretation. Clarity around the prevalence and nature of immunoassay

interference in these patient groups is crucial for their future management.

**Author Contributions:** *All authors confirmed they have contributed to the intellectual content of this paper and have met the following 4 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; (c) final approval of the published article; and (d) agreement to be accountable for all aspects of the article thus ensuring that questions related to the accuracy or integrity of any part of the article are appropriately investigated and resolved.*

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## References

1. Michielsen ECHJ, Bisschops PGT, Janssen MJW. False positive troponin result caused by a true macrotroponin. *Clin Chem Lab Med* 2011;49:923–5.
2. Warner JV, Marshall GA. High incidence of macrotroponin I with a high-sensitivity troponin I assay. *Clin Chem Lab Med* 2016;54:1821–9.

## Commentary on Macro-troponin Complex as a Cause for Cardiac Troponin Increase after COVID-19 Vaccination and Infection

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During the coronavirus disease 2019 (COVID-19) pandemic, there was renewed interest in infection, inflammation, and myocardial injury. Intriguingly, a publication from a decade ago looking at high-sensitivity cardiac troponin T (hs-cTnT) testing at 3 different biennial collection intervals in healthy children revealed that transient increases in hs-cTnT were more suggestive of an infective etiology as opposed to any cardiac disease (1). With the findings from Bularga and colleagues' clinical case study on macro-troponin following COVID-19 vaccination or infection, another possible explanation, in hindsight, for the previous hs-cTn elevations in children may be due to macrocomplexes.

There are several analytical causes for increased cTn concentrations that are incongruent with ongoing

myocardial injury (2), with one being immunoglobulin bound cTn, often called "macro-troponin." Biochemical detection of macrocomplexes can be performed by either polyethylene glycol precipitation or immunoglobulin removal, as was performed in this case study. However, prior to performing such biochemical procedures, it is often helpful to assess whether the cTn elevations in serial sampling represent stable levels, where <20% change in concentrations is used for this stable designation. Intriguingly, 1 of the 3 patients in the case study exhibited a major decrease in hs-cTnI over 3–6 hours, from 280 000 ng/L to 180 000 ng/L (–36%), yet the paired hs-cTnT concentrations in these same samples were normal/unchanged at 8 ng/L and 6 ng/L, respectively.

When investigating possible macrocomplexes, testing with another hs-cTnI method may be beneficial, and here testing with hs-cTnT (another protein) further suggested an interference. However, macrocomplexes may yield different hs-cTn results on different manufacturer platforms and assay versions, with the findings from this case study also indicating that samples requiring dilutions (i.e., Abbott hs-cTnI >50 000 ng/L requires dilution) may also yield discrepant results. Careful collaboration between the

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clinical care and laboratory team is a necessity for these complex investigations.

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## References

1. Potter JM, Koerbin G, Abhayaratna WP, Cunningham RD, Telford RD, Hickman PE. Transient troponin elevations in the blood of healthy young children. *Clin Chim Acta* 2012;413:702–6.
2. Kavsak PA, Clark L, Martin J, Mark CT, Paré G, Mondoux S, et al. Acute phase response and non-reproducible elevated concentrations with a high-sensitivity cardiac troponin I Assay. *J Clin Med* 2021;10:1014.