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

CARDIAC Q&A SERIES I:
THE USE OF TROPONIN IN THE DIAGNOSIS OF AMI

How can we use the 4th Universal Definition of Myocardial Infarction (UDMI) to diagnose a patient with acute myocardial infarction (AMI)?

An AMI may be diagnosed in the clinical setting of evidence of acute myocardial ischemia and myocardial injury with detection of a rise and/or fall of troponin with at least one value greater than the 99th percentile upper reference limit and at least one of: symptoms of myocardial ischemia; new ischemic ECG changes; development of pathological Q waves; imaging evidence consistent with new myocardial ischemia or identification of a coronary thrombus by angiography or at autopsy. Sex-specific 99th percentiles should be used. The finding of an elevated troponin concentration alone or even a pattern of rising or falling is not enough to diagnose an AMI as myocardial injury due to non-ischemic causes is common. Thus, additional clinical information is essential to define the cause of the injury and to diagnose AMI.

Key reference: *'Ten Commandments' for the Fourth Universal Definition of Myocardial Infarction 2018. European Heart Journal, Volume 40, Issue 3, 14 January 2019, Page 226, https://doi.org/10.1093/eurheartj/ehy856*

Additional references*: Fourth Universal Definition of Myocardial Infarction (2018). Circulation. Volume 138, Number 20. https://doi.org/10.1161/CIR.0000000000000617; J Am Coll Cardiol. 2018 Oct 30;72(18):2231-2264. doi: 10.1016/j.jacc.2018.08.1038; European Heart Journal, Volume 40, Issue 3, 14 January 2019, Pages 237–269, https://doi.org/10.1093/eurheartj/ehy462*

Can 0/1- and 0/2-hour algorithms be applied routinely for patients presenting with suspected AMI?

Yes! This strategy has been included in numerous guidelines and many Emergency Departments are using such strategies, around the world. It's essential that assay-specific metrics (including cut-offs and deltas), in the timeframes that have been shown to be safe are used. No strategy is perfect and understanding the caveats around these algorithms can be helpful.

Key reference: *2023 ESC Guidelines for the management of acute coronary syndromes: Developed by the task force on the management of acute coronary syndromes of the European Society of Cardiology (ESC). European Heart Journal, Volume 44, Issue 38, 7 October 2023, Pages 3720–3826. https://doi.org/10.1093/eurheartj/ehad19*

Additional references: *2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guideline for the Evaluation and Diagnosis of Chest Pain: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. Volume 144, Number 22. https://doi.org/10.1161/CIR.0000000000001029*

Ruling-In Myocardial Injury and Ruling-Out Myocardial Infarction With the European Society of Cardiology 1-Hour Algorithm. Circulation. Volume 134, Number 20. https://doi.org/10.1161/CIRCULATIONAHA.116.024687

High-Sensitivity Cardiac Troponin and the 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR Guidelines for the Evaluation and Diagnosis of Acute Chest Pain. Circulation. 2022 Aug 16;146(7):569-581. doi: 10.1161/CIRCULATIONAHA.122.059678

The above content was produced by leading cardiac opinion leaders serving on the IFCC CC-B.
More details on cardiac biomarkers including other educational Q&A guides can be found at www.IFCC.org.
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What is a significant rise or fall (delta) in cardiac troponin?

A specific value for change in troponin cannot be given that can be applied for all assays and all clinical presentations. Interpretation of changes in troponin concentration is complex, and many aspects need to be considered. For example, the time symptoms start to the time samples are taken will impact the changes detected. If patients with AMI delay their presentation, a significant change may not be seen, as troponin concentrations can plateau if measured a few days later. Other considerations are the actual values used, as these may also be assay specific. Guidelines differentiate acute from chronic myocardial injury with the criteria for acute myocardial injury being that cardiac troponin concentrations change by more than 20% on serial testing. When baseline values are normal or low, absolute values (the difference when subtracting two measurements) are preferrable. However, once values are increased above the 99th percentile, both absolute and relative values (a percent difference) have equal utility except at very high values where relative values are more accurate.

Key reference: *Page e634-e636. Figure 7. Fourth Universal Definition of Myocardial Infarction (2018). Circulation. Volume 138, Number 20. https://doi.org/10.1161/CIR.0000000000000617*

Additional references: *Rising and Falling High-Sensitivity Cardiac Troponin in Diagnostic Algorithms for Patients With Suspected Myocardial Infarction. Journal of the American Heart Association. Volume 12, Number 10. https://doi.org/10.1161/JAHA.122.027166.*

How can 'optimized' rule out cut-offs be determined, validated, and used in Emergency department settings?

'Rule-out' cut-offs are derived to identify patients at low risk for AMI (not myocardial injury). These approaches can use what is known as the 'single sample rule out' method which depends on a low initial value to exclude AMI. This is described in the question below. The other approach is to observe for changes over time. This approach depends on small changes that are assay dependent. Institutions have an obligation to be sure that whatever protocol and threshold values they seek to use is convivial to their local population. Assays used should have extensive validation to optimize the percentage of the population where this approach can be utilized (efficacy) while maintaining high sensitivity and negative predictive value (safety).

Key reference: *Single Troponin Measurement to Rule Out Myocardial Infarction: JACC Review Topic of the Week. J Am Coll Cardiol. 2023 Jul 4;82(1):60-69. doi: 10.1016/j.jacc.2023.04.040*

Additional references: *in search for the Holy Grail: suggestions for studies to define delta changes to diagnose or exclude acute myocardial infarction: a position paper from the study group on biomarkers of the Acute Cardiovascular Care Association. Eur Heart J Acute Cardiovasc Care. 2014 Dec; 3(4):313-6*

Are there groups of emergency patients that should not be discharged with a single value?

Yes! Troponin should always be used alongside clinical judgement and electrocardiogram findings. Importantly, single-value testing is not appropriate for patients with:

- Ischemic ECG changes
- Chest pain onset <2 hours from testing

It is essential that this strategy is only applied when there is a high sensitivity troponin assay that has been validated for single sample rule out of AMI. Within the US, reporting of troponin values below the limit of quantification is not permitted. Therefore, for some assays single testing strategies cannot be used in the US.

Key reference: *Single Troponin Measurement to Rule Out Myocardial Infarction: JACC Review Topic of the Week. J Am Coll Cardiol. 2023 Jul 4;82(1):60-69. doi: 10.1016/j.jacc.2023.04.040*

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Additional references: *Asburn NP, Snavely AC,.O'Neill JC, et al. Performance of the European Society of Cardiology 0/1-HourAlgorithm With High-Sensitivity Cardiac Troponin T Among Patients With Known Coronary Artery Disease JAMA Cardiology 2023;8:347-356*

Should we be using sex-specific cut points to define normal and elevated values?

Yes! We know healthy females and males have different 'normal' values of circulating troponin discernible with all high-sensitivity cardiac troponin assays. We also know that using sex-specific cut points will identify similar proportions of male and female patients with myocardial injury. The use of uniform cut points (and not sex-specific values) to define normal and elevated values mean that women must have a greater elevation in troponin (i.e., greater amount of injured myocardium) than men for their test to be considered abnormal. Thus, the use of a uniform threshold is more likely to miss an AMI in women.

Key reference: *Analytical Considerations in Deriving 99th Percentile Upper Reference Limits for High-Sensitivity Cardiac Troponin Assays: Educational Recommendations from the IFCC Committee on Clinical Application of Cardiac Bio-Markers. Clin Chem. 2022 Jul 27;68(8):1022-1030. doi: 10.1093/clinchem/hvac092*

Additional references*: Sex-Specific Thresholds of High-Sensitivity Troponin in Patients With Suspected Acute Coronary Syndrome. J Am Coll Cardiol. 2019 Oct 22; 74(16): 2032–2043. doi: 10.1016/j.jacc.2019.07.082*

Is a clinical decision tool necessary to help use guideline-recommended 0/1 and 0/2 hour algorithms in routine settings?

No! Although this may be helpful, many sites are using these rapid assessment algorithms without a clinical decision tool. A good understanding and ready access to the specific metrics for the local assay in use is crucial, and of course clinical judgement and evaluation of electrocardiograms is always essential.

Key reference*: Risk Scores for Clinical Risk Stratification of Emergency Department Patients With Chest Pain but No Acute Myocardial Infarction: A Systematic Review. Can J Cardiol. 2023 Mar;39(3):304-310. doi: 10.1016/j.cjca.2022.12.028.*

Additional references*: Implementing an early rule-out pathway for acute myocardial infarction in clinical practice. Heart. 2021 Dec; 107(23): 1912–1919. doi: 10.1136/heartjnl-2019-316242*

The information provided above is a brief summary of common questions and answers developed by consensus of the IFCC 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.

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