



## CLINICAL APPLICATIONS OF HIGHLY SENSITIVE TROPONINS

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### Annotation

The article reports on the role of troponins in the laboratory diagnosis of myocardial infarction. Cardiospecific troponin isoforms are the most sensitive and specific biomarkers for the diagnosis of acute myocardial infarction.

**Keywords:** Biomarkers, troponins, laboratory diagnostics, highly sensitive troponins, myocardial infarction.

### Introduction

Troponin is the preferred biomarker for the diagnosis of acute myocardial infarction [1,3,5]. It is recognized that laboratory methods for testing troponin have improved markedly over the past two decades, resulting in lower detection limits and improved assay accuracy [9, 10,11]. Laboratory achievements in troponin testing have been outstanding, but optimal use of the test also requires good clinical arguments on the part of practitioners who use troponin testing in clinical practice. For optimal use of the troponin test in clinical practice, 3 critical elements are necessary:

- 1) the analytical performance of the test;
- 2) clinical sensitivity and specificity of the test result;





3) the clinical rationale for the order and the appropriate clinical context for interpreting the test result [12, 13, 14, 15].

All 3 elements are integral to ensure optimal clinical applicability. Most clinicians rely on their clinical laboratories to decide the analytical characteristics of the assay and are not familiar with the laboratory science of troponin testing [16, 17, 18]. The clinical sensitivity and specificity of troponin testing has been a source of confusion for clinicians because definitions have changed as the test has evolved, and because many different tests are available [19, 20, 21]. In addition, due to clinical considerations, little attention is usually paid to how to combine these test results with other clinical information. Review articles explain the performance and correct use of the troponin test [24, 25], but further explanation may be helpful.

The paper provides additional explanations to assist clinicians in making clinical decisions and interpreting troponin test results. Schematic visual explanations are provided to help clinicians develop a more intuitive understanding of troponin testing. Improving our understanding of troponin testing is especially important now because highly sensitive assays are already being used in practice in many countries.

### **Troponins**

The troponin complex consists of three subunits - T, I, C, which regulate the contractile activity of the myocardium. Cardiac troponin T, the tropomyosin-binding subunit, anchors the troponin complex to thin actin filaments. Troponin C, a calcium-binding subunit, binds calcium ions entering the cytoplasm from the sarcoplasmic reticulum upon contraction stimulation. Troponin I, an inhibitory subunit, blocks the hydrolysis of adenosine triphosphate, which is necessary for the interaction of actin and myosin [1, 2]. In the late 1980s, researchers developed immunoassays for troponin I and troponin T. Improvements in antibodies, reagents, and automation have made today's commercial troponin assays extremely sensitive and accurate.

Newest, the most sensitive assays are able to detect troponin in the circulation of patients without myocardial injury, possibly due to normal turnover of myocardial cells or the formation of exosomes that release small amounts of free troponin into the circulation [6, 7, 8].

Assay manufacturers measure and report the analytical performance of each assay. Analytical sensitivity is the lowest concentration of an analyte that can be consistently detected. The accuracy of the analysis is determined by the coefficient of variation (CV). Because CV is a measure of assay variability relative to analyte concentration, CV increases at lower concentrations. Ideally, the CV of the assay is 10% or less at the level chosen as the diagnostic cut-off point. Automated analyzers performed at central





laboratories have better accuracy and lower 10% CV levels than point-of-care troponin analyzes. Point-of-care analysis can have a CV-level of 10%, which is an order of magnitude higher than that of a central laboratory analysis. Point-of-care tests are not used for serial measurements of troponin, because the inaccuracy of these tests can lead to the false appearance of an increase or decrease in troponin levels [4, 5, 22, 23]. Due to the exclusive patent, there is only 1 commercially available troponin T test. The fourth generation of this assay is currently in use in the United States, and the new generation troponin T test, which is more analytically sensitive, is now in use in Europe. There are many commercially available troponin I tests. These tests have also undergone several generations of improvements over the years. Each of the various commercial troponin I assays recognizes a unique amino acid sequence (epitope) of the troponin I molecule, resulting in each assay having different analytical characteristics. These differences have created problems for researchers and regulators who are trying to develop industry standardization for troponin tests. The differences also pose challenges for physicians who are trying to understand published medical reports of troponin testing and apply the research findings to practice.

## Conclusion

As the analytical capabilities of troponin testing have improved over the years, the term sensitivity has become a source of confusion for clinicians. Laboratory experts commonly use the word "sensitivity" to describe analytical sensitivity, or the ability of an assay to detect low concentrations of an analyte. Clinicians, in contrast, use the word to describe clinical sensitivity, the performance characteristic of a test.

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