

**“It Was the Best of Times, It was The Worst of Times”
Cardiovascular Disease and Troponins**

Abstract

There have been significant changes in the diagnosis and definition of acute myocardial infarction over the years. From its first description and definition over 150 years ago to the high sensitivity cardiac troponin assays of today, we have come a long way in the diagnosis, management, and treatment of those with cardiovascular disease. With the recent Food and Drug Administration's (FDA) clearance of the fifth generation high-sensitivity cardiac troponin assays, a new history in diagnosing, treatment and managing those with heart disease is just beginning. The three articles associated with this focus series described advances in diagnosis and definition of acute myocardial infarction (AMI) with the first article presenting an in-depth description into the structure and function of troponin in health and disease, a second article presenting a description of AMI and how its diagnosis and definition has changed over the years culminating with a description of the high sensitive troponin assays, and a third article that presents clinical implications of the new high sensitivity troponin assays.

Index Terms

Troponin, Acute Coronary Syndrome, Myocardial Infarction, High-Sensitivity Troponins, Cardiovascular Disease

Abbreviations

ACC/AHA - American College of Cardiology/American Heart Association, AMI-Acute Myocardial Infarction, CVD-Cardiovascular Disease, FDA-Food and Drug Administration, hs-cTn-High-sensitivity Cardiac Troponins

From the first description of cardiovascular disease (CVD) over 150 years ago, to the historic Framingham Heart Study of the 1950's, to the high-sensitivity cardiac troponins (hs-cTn) of today, there is no doubt we have come a long way in the diagnosis, management, and treatment of those with CVD. Similar to the way Charles Dickens paired contrasting concepts to reflect the mirror images of good and evil that recur in characters and situations throughout the novel *A Tale of Two Cities*, the discovery and FDA clearance of the fifth generation hs-cTn assays presents a sweeping backdrop of forces and events that will forever shape the way we diagnose, treat, and manage those with myocardial damage. It was the “best of times” in that never before have we been presented with such rapid advances in imaging studies, medications, interventions, and laboratory testing that have enhanced our ability to quickly and more accurately identify, treat and manage those with CVD. It was the “worst of times” in that despite these advances heart disease remains as the number one cause of death globally, accounting for more deaths annually than from any other cause.¹⁻² One in every six health care dollars is spent on cardiovascular disease and if things remain as they are today, costs associated with heart disease are projected to triple in 20 years from \$555 billion in 2016 to a whopping \$1.1 trillion in 2035.³ It was “the season of light” in January of 2017 when the Food and Drug Administration (FDA) announced the clearance of a fifth generation hs-cTn assay for use in the U.S.⁴ With sex-specific 99th percentile cutoffs, rule-out capability, new reporting units, and the potential to provide risk assessment in asymptomatic patients, this new assay is proving to be significantly different from its fourth generation counterpart. While this new assay carries significant advantages over the fourth generation assays, it is also “the season of darkness” as there is much more potential for this assay to be clinically misunderstood and results misinterpreted, leading to an increase in testing, inappropriate therapies, and increased resource utilization not due to CVD. From the

Framingham Heart Study to the new ACC/AHA guidelines to the expanded definition of acute myocardial infarction to the development of acute coronary syndrome algorithms, we have “everything before us.” With the advancement in troponin testing with its increased sensitivity and lack of specificity for acute myocardial infarction, we have “nothing before us.” This FOCUS series represents our effort to shed some light on cardiovascular disease from history to hs-cTn.

We decided to approach this topic in a more comprehensive fashion. The first article, *Troponin Structure and Function in Health and Disease*, provides the reader with just that, an in-depth review of the troponin molecule from discovery to its basic biology to its structure and function in health and disease. This article literally takes a back to the basics approach to a description of the troponin molecule. The second article, *Acute Myocardial Infarction: Definition, Diagnosis, and the Evolution of Cardiac Markers*, takes you on a historical ride through the years as the diagnosis and definition of AMI has changed resulting in updates to the guidelines for the management of those with AMI. The third article, *Clinical Considerations of High Sensitivity Troponins*, takes you to the present day describing the impact of hs-cTn on the diagnosis, management, and treatment of those with CVD.

Another aspect worthy of mentioning is the makeup of the authors included in developing this FOCUS series. Because this topic is so comprehensive, we felt it would be best developed from a comprehensive and multidisciplinary basis. As a result, we have engaged authors across various disciplines to contribute their content expertise to the development of these articles. This multidisciplinary team of authors was put together using faculty from various disciplines including clinical laboratory science, nuclear medicine technology, physician assistant studies, and biomedical sciences.

Just as with *A Tale of Two Cities* where the differences between London and Paris become more pronounced, I believe that the totality of differences between the fourth and fifth generation troponin assays and the impact on CVD is yet to be seen. *A Tale of Two Cities* was a novel published in weekly installments and, so too, I believe that the hs-cTn novel and its full impact on CVD is currently being developed and will be released in regular installments over the next few years.

We hope that you enjoy this FOCUS series.

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