

"It Was the Best of Times, It Was the Worst of Times": Cardiovascular Disease and Troponins

JANELLE M. CHIASERA, SAMANTHA GIORDANO, NEENA XAVIER, ANA OLIVEIRA,
ROBERT ESTES, REMO GEORGE, TOSI GILFORD, KRYSTLE GLASGOW,
HEATHER HALLMAN, FLOYD JOSEPHAT, WEI LI

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 United States Food and Drug Administration's clearance of the fifth-generation high-sensitivity cardiac troponin assays, a new history in diagnosing, treating, 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 highly sensitive troponin assays, and a third article presenting clinical implications of the new high-sensitivity troponin assays.

Janelle M. Chiasera, The University of Alabama at Birmingham

Samantha Giordano, The University of Alabama at Birmingham

Neena Xavier, The University of Alabama at Birmingham

Ana Oliveira, The University of Alabama at Birmingham

Robert Estes, The University of Alabama at Birmingham

Remo George, The University of Alabama at Birmingham

Tosi Gilford, The University of Alabama at Birmingham

Krystle Glasgow, The University of Alabama at Birmingham

Heather Hallman, The University of Alabama at Birmingham

Floyd Josephat, The University of Alabama at Birmingham

Wei Li, The University of Alabama at Birmingham

Address for Correspondence: *Janelle M. Chiasera*, The University of Alabama at Birmingham, chiasera@uab.edu

ABBREVIATIONS: AMI - acute myocardial infarction, CVD - cardiovascular disease, FDA - United States Food and Drug Administration, hs-cTn - high-sensitivity cardiac troponin.

INDEX TERMS: troponin, acute coronary syndrome, myocardial infarction, high-sensitivity troponins, cardiovascular disease.

Clin Lab Sci 2018;31(4):190–191

From the first description of cardiovascular disease (CVD) over 150 years ago, to the historic Framingham Heart Study of the 1950s, to the high-sensitivity cardiac troponins (hs-cTns) 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 United States Food and Drug Administration's (FDA's) 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 remained the number one cause of death globally, accounting for more deaths annually than from any other cause.^{1,2} One in every six healthcare dollars is spent on CVD, 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 FDA announced the clearance of a fifth-generation hs-cTn assay for use in the United States.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. Although 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 American College of Cardiology/American Heart Association guidelines, to the expanded definition of acute myocardial infarction (AMI), 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 AMI, we have "nothing before us." This FOCUS series represents our effort to shed some light on CVD 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*, in which 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 are yet to be seen. *A Tale of Two Cities* was a novel published in weekly installments, 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.

REFERENCES

1. Centers for Disease Control and Prevention. About underlying cause of death 1999–2016 on CDC WONDER online database. Centers for Disease Control and Prevention, National Center for Health Statistics. Accessed June 28, 2018. <http://wonder.cdc.gov/ucd-icd10.html>.
2. Mozaffarian D, Benjamin EJ, Go AS, et al; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2015 update: a report from the American Heart Association. *Circulation*. 2015;131(4):e29–e322.
3. Heidenreich PA, Trogdon JG, Khavjou OA, et al; American Heart Association Advocacy Coordinating Committee; Stroke Council; Council on Cardiovascular Radiology and Intervention; Council on Clinical Cardiology; Council on Epidemiology and Prevention; Council on Arteriosclerosis; Thrombosis and Vascular Biology; Council on Cardiopulmonary; Critical Care; Perioperative and Resuscitation; Council on Cardiovascular Nursing; Council on the Kidney in Cardiovascular Disease; Council on Cardiovascular Surgery and Anesthesia, and Interdisciplinary Council on Quality of Care and Outcomes Research. Forecasting the future of cardiovascular disease in the United States: a policy statement from the American Heart Association. *Circulation*. 2011;123(8):933–944.
4. Phend C. Next-generation troponin test cleared by FDA. Medpage Today. January 19, 2017. Updated January 23, 2017. Accessed August 6, 2018. <https://www.medpagetoday.com/cardiology/myocardialinfarction/62620>.