Letter by Conti and Volpe Regarding Article, "Cardiac Troponin I but Not Cardiac Troponin T Induces Severe Autoimmune Inflammation in the Myocardium"

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Circulation. 2007;115:e383
doi: 10.1161/CIRCULATIONAHA.106.674598
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7322. Online ISSN: 1524-4539

Correspondence

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To the Editor:

The intriguing observations by Göser et al[1] on autoimmunity to segregated myocardial autoantigens open new areas for understanding "cardiovascular inflammatory disease." At the same time, the authors do not fully use the opportunity to discuss the implications of their finding on acute development of atherothrombosis. A previous contact with troponin I—a largely used, sensitive marker of even small myocardial damage—is shown to induce an autoimmune reaction that, after left anterior descending coronary artery ligation, leads to increased ischemia-induced infarct size, severely increased myocardial inflammation, and dysfunction in infarct-remote regions.[1]

In acute coronary syndromes, increased troponin levels can occur independently of epicardial coronary artery stenosis,[2] reflecting a transient mural embolized, or a microvascular distal thrombosis, which produces focal necrosis of myocardiocytes. This pathophysiological condition clinically features acute myocardial infarction (according to the recent redefinition) and prognostically identifies a state with worse brief and midterm outcomes compared with acute chest pain without troponin elevation.[2]

Increased/normal troponin levels, which are correlated to 10-year mortality, also have been described in healthy subjects, suggesting that increased/normal troponin levels are present earlier than and beyond acute coronary syndromes and significantly predict outcomes.[3] In these subjects, serum autoantibodies to cardiac troponins, already shown for patients with acute coronary syndromes,[4] have not yet been studied.

The simple short- or long-term exposure to classical risk factors would determine transient waxing and waning of a thrombophylic milieu, through increased levels of apoptotic exfoliated endothelial microparticles exposing modified phosphatidylserine,[5] and eventually realize transient increases in troponin, and subsequent autoimmunization.

Moreover, a higher necrosis susceptibility of myocardium to different insults (infective, hypoanoxic, inflammatory) in frailty or high-risk conditions (aging, chronic renal failure, diabetes) could, through troponin release, autoimmune–inflammatory activation, and reduced tolerance, influence progression of disease.

Thus, autoimmune troponin-directed response, also priming autoimmunity toward other myocardial[1] (and vascular?) autoantigens, could represent an early player not only of myocardial but also vascular inflammation in acute coronary syndromes. Autoimmune pathways may thus contribute to destabilizing both the patient and the plaque and participate in incompletely understood phenomena, such as no reflow in myocardial infarction or slow coronary flow with normal coronary arteries.

Whether an imbalance between autoimmunity and tolerance to troponins is an early event in the natural history of atherothrombosis, and whether it is potentially linked to the timing and size of clinical manifestations of ischemic heart disease, is an interesting issue that needs to be elucidated.

Disclosures

None.

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(*Circulation*. 2007;115:e383.)

Circulation is available at http://www.circulationaha.org DOI: 10.1161/CIRCULATIONAHA.106.674598