The Egyptian Heart Journal (2017) xxx, xxx–xxx

HOSTED BY

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Egyptian Society of Cardiology

The Egyptian Heart Journal

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REVIEW

Elevated troponin in patients with acute stroke – Is it a true heart attack?

George V. Dous [a,*], Angela C. Grigos [b], Richard Grodman [c]

[a] SUNY Downstate, Department of Cardiology, Brooklyn, New York, United States
[b] Richmond University Medical Center, Department of Medicine, Staten Island, New York, United States
[c] Richmond University Medical Center, Department of Cardiology, Staten Island, New York, United States

Received 9 July 2016; accepted 19 January 2017

KEYWORDS

Stroke;
Myocardial infarction;
Troponin;
Neurogenic heart syndrome

Abstract Although the prognostic value of a positive troponin in an acute stroke patient is still uncertain, it is a commonly encountered clinical situation given that Ischemic Heart Disease (IHD) and cerebrovascular disease (CVD) frequently co-exist in the same patient and share similar risk factors. Our objectives in this review are to (1) identify the biologic relationship between acute cerebrovascular stroke and elevated troponin levels, (2) determine the pathophysiologic differences between positive troponin in the setting of acute stroke versus acute myocardial infarction (AMI), and (3) examine whether positive troponin in the setting of acute stroke has prognostic significance. We also will provide an insight analysis of some of the available studies and will provide guidance for a management approach based on the available data according to the current guidelines.

Contents

Abbreviations: ACS, acute coronary syndrome; AMI, acute myocardial infarction; CVD, Cardiovascular Disease; CAST, Chinese Acute Stroke Trial; CT, computed tomography; CAD, Coronary Artery Disease; CK-MB, Creatine Kinase-MB; DAPT, dual antiplatelet therapy; ECG, electrocardiogram; IST, International Stroke Trial; ICH, intracranial hemorrhage; IHD, Ischemic Heart Disease; LV, left ventricular; LDL, low-density lipoprotein; MI, myocardial infarction; NHS, neurogenic heart syndrome; SAH, subarachnoid hemorrhage; TRELAS, The Troponin Elevation in Acute Ischemic Stroke; TIA, Transient Ischemic Attacks; cTnI, Troponin I; cTnT, Troponin T

* Corresponding author.

Peer review under responsibility of Egyptian Society of Cardiology.

http://dx.doi.org/10.1016/j.ehj.2017.01.005

Please cite this article in press as: Dous GV et al. Elevated troponin in patients with acute stroke – Is it a true heart attack?, *The Egypt Heart J* (2017), http://dx.doi.org/10.1016/j.ehj.2017.01.005

1. Introduction

Concurrent stroke and myocardial infarction (MI) are not uncommon, clinical, observational and experimental trials have pointed to the coexistence between neurological and myocardial injury. Interestingly, with the development of highly sensitive cardiac biomarkers, more patients with stroke are being tested for troponin. A strong association seems to exist between both conditions causing both a diagnostic and management dilemma to clinicians.

Several unanswered questions have emerged. What are the mechanisms and the pathophysiology behind an elevated troponin in the setting of acute stroke? How does an elevated troponin affect prognosis and mortality? Should an elevated troponin alter the management approach?

In this review article we will discuss the pathophysiologic mechanism of cardiac muscle regulatory protein troponin T (cTnT) elevation in a stroke patient, its prognostic significance and its effect on patient management decisions.

2. Method

Twenty-six articles were identified in the period between 1997 and 2015 through searches on PubMed, Medline and the Cochrane Library using the following keywords: stroke, cardiac enzymes, cerebrovascular, troponin, myocardial infarction, and neurogenic heart syndrome were searched systematically to obtain relevant literature.

3. Discussion

Several studies have evaluated the incidence of elevated troponin in the acute stroke patient, the incidence varying between 5% and 10% depending on the troponin cut off limit.[1] Data from the RANTTAS trial placebo cohort suggest that angina, MI, and cardiac ischemia complicate 6% of acute strokes.[2]

Comparing troponin to Creatine Kinase-MB (CK-MB), troponin T has superior sensitivity and specificity for revealing minor myocardial injury.[3] In a study by Hakan et al., 32 patients with large cerebral hemispheric infarctions and with no history of coronary heart disease were evaluated for elevation of cardiac of troponin T, CK-MB, myoglobin and total CK. The investigators concluded that only troponin T is a more specific biochemical marker of myocardial injury in a stroke patient.[3]

Forty percent of the patients with subarachnoid hemorrhage (SAH) have an elevated cardiac biomarker while 10% have demonstrated left ventricular (LV) systolic dysfunction on echocardiography. When compared to men, women with SAH tend to have more LV systolic dysfunction.[4] In addition, stroke severity, not its location, was associated with higher troponin levels.[5]

TRELAS study compared coronary vessel status in acute ischemic stroke (AIS) patients with elevated cardiac troponin (cTn), to patients presenting with non-ST-elevation acute coronary syndrome (NSTE-ACS), Patients with elevated cTn levels (>50 ng/L) on presentation or during the following day underwent diagnostic coronary angiography within 72 h. Patients with impaired kidney function (creatinine >1.20 mg/dl) were excluded, the study concluded that despite similar baseline cTn levels, coronary culprit lesions are significantly less frequent in AIS patients compared to age- and gender-matched patients with NSTE-ACS.

In the small study by Darki et al., statistically significant results found an association of positive troponin level with positive echocardiogram; with the most common results being in the inferior or septal wall motion abnormalities.[7] A lower ejection fraction was strongly associated with cTI release.[8] In addition Raza et al., reported that the ejection fraction of less than 50% did not predict adverse outcomes, and the likely cause is very different from newly diagnosed cardiomyopathy but that it is possibly due to sympathetic nervous system surge that occurs during an acute stroke.[9]

4. Pathophysiology of Neurogenic Heart Syndrome (NHS)

The phenomenon has been explained as a neurally mediated process due to increase in catecholamine release as a result of hypoperfusion of the posterior hypothalamus causing autonomic nervous system imbalance and increased sympathetic output.[4,8]

Increased troponin I level is associated with elevation of circulating epinephrine in acute ischemic stroke[10]; therefore, activation of the sympathoadrenal system could be an important contributor to myocardial damage in these patients.[10]

Myofibrillar degeneration (coagulative myocytolysis and contraction band necrosis) is a common microscopic and pathologic picture seen in myocardial necrosis in stroke patients. Whereby cells die in a hyper-contracted state with prominent contraction bands, which happens within minutes and is associated with early calcification and mononuclear infiltration. This is in contrast to myocardial lesions due to coronary heart disease where the cells die in a relaxed state without prominent contraction bands known as coagulation necrosis - a process that can take hours or even days, with late calcification.[11]

Elevated catecholamine levels are often noted in stroke patients, which may account for the cardiac arrhythmias and ECG changes. The toxicity from catecholamine then causes cardiac necrosis.[11] Autonomic imbalance with exaggerated sympathetic activity is evident after a stroke. Hence the exaggerated release of catecholamines, and so acute lesions within the central autonomic system may result in acute derangement in the sympathetic and parasympathetic activity (see Diagram 1).[12]

5. Prognosis

In a 1997 observational study by James et al., of the 181 patients admitted for acute stroke, troponin T concentration was raised (>0.1 microgram/l) in Thirty patients who died in hospital (12/30 (40%) patients with a raised troponin T con-

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