EDITORIAL

Relevance of Troponin I Elevation among Individuals with Hypertensive Emergency

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Hypertensive emergency is defined as the symptomatic elevation of blood pressure (>180/120 mm Hg) with evidence of acute or ongoing end-organ damage. It is considered as a medical emergency and requires rapid reduction in blood pressure within minutes to minimize hypertension-mediated organ damage (HMOD) unlike hypertensive urgency wherein blood pressure may be reduced slowly over hours.[1,2] Hypertension-mediated organ damage includes hypertensive encephalopathy, intracerebral hemorrhage, cerebral infarction, hypertensive retinopathy, acute heart failure, acute coronary syndrome, acute renal failure, and aortic dissection.[3] It is usually seen in patients who are noncompliant with their anti-hypertensive medications. Hypertensive emergency and urgency together constitute a clinical entity termed as hypertensive crisis. Hypertension is a major cause of premature death worldwide. According to the World Health Organization, approximately less than half of adults with hypertension are diagnosed and being treated. Physicians should perform detailed evaluations of patients who present with a hypertensive crisis to effectively reverse, intervene, and correct the underlying trigger aiming to improve long-term outcomes after the episode.

Cardiac troponin I (cTnI) is a cardiac-specific protein that is a component of the contractile apparatus of cardiac myocytes. Troponin assays have undergone vast improvements over the past two decades, allowing faster detection of troponin at low levels with increased precision. Cardiac troponin is an American and European guideline-recommended biomarker used for the evaluation of myocardial injury which is highly sensitive and specific in acute coronary syndrome.[4,5] Cardiac troponin I (cTnI) is not disease-specific and may be elevated in various ischemic, non-ischemic, and extra-cardiac conditions.[6] Extra-cardiac conditions causing rise in troponin levels include infection, sepsis, kidney, pulmonary, neurological disorders, and critically ill patients. In real-life clinical practice, interpretation of troponin results outside the confines of clinical trials is often challenging. High-sensitivity cardiac troponin assays are more widely adopted, and an improved understanding of the prevalence, determinants, and clinical associations of cardiac troponin in patients without acute coronary syndrome is required to ensure that test results are interpreted correctly and, thereby, subsequent clinical management is performed appropriately. Troponin levels are measured in patients presenting to the emergency department, not only for chest pain but often for a wide range of clinical presentations. There are good evidences to highlight specific cut-offs for troponin assay as per the age, sex, and comorbidities.[7] Cardiac troponin is used as a screening test, irrespective of the clinical presentation in many centers. In the vast, majority of these cases, raised cardiac troponin I concentration reflects myocardial injury rather than myocardial infarction. In coronary artery disease patients, cardiac troponin is a useful indicator of hospitalization and is strongly associated with an increased risk of heart failure.[8,9] It has been reported that cardiac troponin can predict major adverse cardiovascular events not only in patients with cardiovascular disease but also in the general population.[4] In the setting of hypertensive emergency, the increased left ventricular wall stress due to an increase in afterload and associated catecholamine surge leads to sub-endocardial ischemia resulting in elevated cardiac troponin levels, even in the absence of coronary artery disease.[4,6] Therefore, the rise in cTnI levels is attributed to myocardial supply-demand mismatch. The existing data also suggests that the endothelial dysfunction due to extremely high blood pressure causes inflammation and pro-thrombotic effects leading to tissue ischemia and subsequent rise in cardiac troponin.[10,11] About one-third of admissions for hypertensive emergency were found to have elevated cardiac troponin I levels despite of absence of apparent myocardial infarction.[12] There are only a few studies exploring the prevalence, clinical determinants, and prognostic significance of cardiac troponin I release in patients presenting with the hypertensive emergency.[12–14] Most of these studies used retrospective data, however, there is one prospective observation study currently available to determine the prevalence, clinical determinants, and prognostic significance of cardiac troponin I release in patients presenting with the hypertensive emergency.[14]

Cardiac troponin level is elevated as age advances in patients with the hypertensive emergency.[12,14] Existing data suggests

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no predilection to gender with regard to the rise in troponin. Despite obesity being an independent risk factor for developing heart disease, obese individuals have better short- and long-term prognoses compared to normal or low-weight individuals with coronary artery disease and heart failure, which is referred to as "obesity paradox".[15] "Obesity paradox" is also seen in patients with hypertensive crisis, but the mechanism behind this paradox is unclear. There exists an inverse association between body mass index and cardiac troponin level as per available evidence. This paradox is strongly associated in older individuals and female patients with hypertensive emergencies.[7] Clinical parameters like heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure were independently associated with elevated troponin levels.[14] An elevation of blood urea nitrogen (BUN) levels is seen in the setting of hypertensive emergency, which occurs due to vasomotor alterations in renal blood flow and activation of the renin-angiotensin-aldosterone system (RAAS).[16] Cardiac troponin I (cTnI) level elevation is directly correlated with an increase in BUN and creatinine in patients with hypertensive emergency.[9,14] Other predictors of cardiac troponin I elevation in hypertensive emergency include comorbidities like diabetes mellitus, chronic obstructive lung disease, hypercholesterolemia, and thyroid disease.[12] History of smoking and alcohol intake was also associated with high troponin I level in hypertensive emergency.[14] The highest elevation of cardiac troponin in patients with hypertensive emergency was associated with respiratory failure, pulmonary edema, and need for mechanical intubation.[12]

The risk of major adverse cardiovascular events was higher in patients with elevated cardiac troponin I levels than in patients with normal levels in patients with hypertensive emergency.[17] The patients with higher cardiac troponin I value on presentation are at increased risk for long-term cardiac events, including myocardial infarction and pulmonary edema, but they were not found to have a high risk for cerebrovascular accidents.[18] The rate of hospital admission was higher in patients with elevated and detectable cardiac troponin I level compared to an undetectable levels. The duration of hospitalization was also longer in patients presenting with hypertensive emergency with elevated troponin I levels.[14] The proportion of patients requiring to revisit to the emergency department and readmission was also higher in patients with elevated and detectable cardiac troponin I.[19] Elevated levels of cardiac troponin I are considered as an independent prognostic marker for mortality in patients with hypertensive emergency.[14] Normal but detectable range cardiac troponin I, which is considered clinically insignificant, also had a prognostic impact on all-cause mortality.[19] The long-term mortality after hospitalization with hypertensive emergencies is as high as 12% per year after 3.1 years of follow-up.[20]

To conclude, cardiac troponin I released during hypertensive emergency is regarded as an epiphenomenon that may confound or complicate its management. The pitfalls of elevated cardiac troponin I in individuals presenting with hypertensive emergency is that it is influenced by a variety of clinical factors. However higher association of mortality is highlighted with elevated cardiac troponin in patients with hypertensive emergency and therefore carries good prognostic significance in this setting despite of the limitations. It is noteworthy that with increasing awareness and better control of blood pressure, mortality due to hypertensive emergency has significantly decreased in the past three decades.

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