Editorial

Relative Lack of Culprit and Obstructive Coronary Lesions in Patients With Acute Ischemic Stroke and Elevated Cardiac Troponin

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The measurement of cardiac troponins (cTn) is widely used to diagnose myocardial injury or necrosis, and has become an important tool for the risk stratification and clinical management of patients with acute coronary syndrome (ACS). However, elevated cTn levels are also found in non-ACS patients. For example, in a recent study of patients with chronic stable coronary artery disease, higher cTn levels were observed in patients with concomitant kidney disease or diabetes mellitus. Furthermore, 15% of patients with acute ischemic stroke have elevated cTn, many of whom have no other clinical manifestation of acute coronary ischemia. Because cTn still provides important prognostic information regarding mortality outcomes in patients who have had a stroke, current American Heart Association guidelines recommend its measurement in all patients presenting with acute ischemic stroke. However, the role of cTn in predicting culprit or obstructive coronary lesions in these patients remains unknown, but may be important to ascertain if subsequent revascularization therapy could be shown to be beneficial.

To address this issue, Mochmann et al in this issue of Circulation prospectively screened 2123 consecutive patients presenting with acute ischemic stroke at 2 tertiary referral hospitals in the Troponin Elevation in Acute Ischemic Stroke (TRELAS) study. Elevated cTn was defined by levels ≥50 ng/L as measured by the high-sensitivity troponin T assay, which corresponds to a value of 0.03 ng/mL on the cTnT assay that is commonly used to diagnose myocardial infarction. Patients with ST-segment-elevation myocardial infarction, renal insufficiency, severe premorbid disability, contraindication for coronary angiography, or refusal to consent were excluded from the study. Similar to previous studies, they found that 14% of patients with confirmed acute ischemic stroke by neuroimaging have elevated cTn on hospital admission. A subset of 29 of 291 patients who have had a stroke with elevated cTn (10% of the at-risk population) underwent diagnostic coronary angiography within 72 hours of admission, and was compared with an age- and sex-matched control cohort of non-ST-segment-elevation myocardial infarction (NSTEMI)-ACS patients with comparable cTn levels. Surprisingly, the prevalence of culprit coronary lesions in patients who have had an acute ischemic stroke with elevated cTn was 24% in comparison with 79% in NSTEMI-ACS patients. Given the low incidence of coronary culprit lesions in patients who have had an acute ischemic stroke with elevated cTn in comparison with NSTEMI-ACS patients, only 21% of patients who have had a stroke with elevated cTn eventually underwent revascularization in comparison with 86% of NSTEMI-ACS patients.

The low incidence of culprit or obstructive coronary lesions in patients who have had a stroke is unexpected given that there was no difference in median cTn between the 2 groups on admission. Possible explanations include relative lack of chest pain and ECG changes that are suggestive of coronary ischemia, higher use of thrombolytics (41% of patients who have had a stroke and 0% in NSTEMI patients), and the longer duration from cTn detection to coronary angiography (44 hours versus 2–4 hours) in patients who have had stroke in comparison with that of NSTEMI-ACS patients. However, among stroke patients with elevated cTn, the presence of culprit and obstructive coronary lesions occurred more frequently in older patients, and was associated with more frequent chest pains and ECG abnormalities (other than ST-segment elevation), higher baseline (170 versus 90 ng/L) and subsequent changes (74 versus 26 ng/L) in cTn, and higher Global Registry of Acute Coronary Events score (127 versus 102). These findings suggest that other clinical parameters associated with coronary ischemia may help identify culprit or obstructive coronary lesions in patients with acute ischemic stroke and elevated cTn.

In contrast to atherosclerotic coronary artery disease with plaque rupture, the etiology of acute ischemic stroke identified in this study through neuroimaging was entirely embolic in nature. Indeed, patients who have had an acute ischemic stroke had a higher incidence of atrial fibrillation than NSTEMI-ACS patients did. Despite this, oral anticoagulation therapy was grossly underused in this study in patients with known atrial fibrillation, a high CHADS2-VASc score of 6, and no documented contraindication for anticoagulation. Only 1 of 6 eligible patients in this study received anticoagulation therapy in the therapeutic range before presenting with acute ischemic stroke. This underscores the missed opportunities to reduce the incidence of ischemic stroke in patients with atrial fibrillation and the need to reinforce appropriate anticoagulation therapy to
prevent cardioembolic stroke in patients with atrial fibrillation. It is also possible that a subgroup of patients presenting with acute ischemic stroke may have had a silent or missed myocardial infarction before hospital admission, and a newly developed left ventricular thrombus could be the embolic source of the acute ischemic stroke.

Although ≈14% of patients with acute ischemic stroke have elevated cTn, the majority of these patients in this study do not have coincident acute coronary syndrome and approximately half of these patients do not have any evidence of obstructive coronary artery disease. What then could be the source of cTn elevation? Interestingly, patients who have had a stroke with elevated cTn tended to have worse renal function (higher creatinine level and lower glomerular filtration rate) and higher incidence of atrial fibrillation, severe heart failure, diabetes mellitus, and chronic total coronary occlusions. Many of these conditions, such as renal failure and diabetes mellitus, could be attributed to chronic myocyte injury from small-vessel ischemia, hypertension, metabolic abnormalities, and renal dysfunction.5,6 In addition, atrial fibrillation, heart failure, and chronic total coronary occlusion could lead to acute coronary demand ischemia, particularly during stressful conditions such as acute ischemic stroke. A large stroke could also precipitate a neurogenic heart syndrome through bursts of neurogenic sympathetic activity and catecholamine release, leading to coronary demand ischemia and myocardial necrosis.8 Indeed, among patients with acute ischemic stroke, higher baseline stroke severity (National Institutes of Health Stroke Scale 8 versus 4) was significantly correlated with elevated cTn levels.

Elevated troponins in patients with acute stroke not explained by ACS or obstructive coronary artery disease could also be attributable to acute nonischemic myocyte injury. Possible mechanisms include myocardial stretch, cytokine-mediated myocardial injury, catecholamine-mediated myocardial toxicity, microvascular spasms, and endothelial dysfunction.8 These factors may play a role in stress-induced cardiomyopathy, which in its extreme form presents as Takotsubo cardiomyopathy.15,16 This view is partially supported by a recent study,12 which demonstrated that of the patients with acute ischemic stroke and positive cardiac troponins diagnosed as “supply-demand mismatch” based on best clinical practice, including ECG, echocardiography, stress test, or coronary angiography, 45% of patients had a rise-and-fall pattern in cardiac troponin and 8% had new wall motion abnormalities on echocardiography. However, a mechanistic pathophysiologic explanation of how neurologically mediated stress leads to the release of troponins is not clear, and further studies are needed to identify the potential sources of elevated cTn in patients who have had an acute ischemic stroke with no obvious culprit lesions or obstructive coronary artery disease. Nevertheless, the study by Moehmann et al is an important first step by providing evidence that the majority of elevated cardiac troponins in patients who have had an acute ischemic stroke are not related to epicardial coronary artery disease.

**Disclosures**

None.

**References**

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