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# Acute Ischemic Stroke with Elevated Cardiac Troponin: A Case Report and Review of the Literature

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**Abstract**

Elevated cardiac troponin (cTn) signals myocardial necrosis and injury but does not specify the mechanism of that injury. The measurement of cardiac troponins is widely used to diagnose myocardial infarction and has become an important tool for the risk stratification and clinical management of patients with acute coronary syndrome

**Keywords**: Troponin; Acute ischemic stroke

## Introduction

Elevated cardiac troponin (cTn) signals myocardial necrosis and injury but does not specify the mechanism of that injury. The measurement of cardiac troponins is widely used to diagnose myocardial infarction and has become an important tool for the risk stratification and clinical management of patients with acute coronary syndrome (ACS) [1-4]. 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 (CAD), higher cTn levels were observed in patients with concomitant kidney disease or diabetes mellitus, and therefore interpretations of elevated troponin can be clinically challenging [5,6].

It is not uncommon to see elevated troponin in acute ischemic stroke. Several studies have described the prevalence of positive troponin in acute ischemic stroke from 10-18% [7-12]. However, the significance of an abnormal troponin in patients with acute ischemic stroke and how it should impact clinical management are not always clear. Here we describe a case of a patient who presented with an acute ischemic stroke with a suspected cardioembolic source due to reduced left ventricular function from a myocardial infarction.

## Case Report

In February 2016, an 85 year-old woman with a past medical history significant for hypertension was hospitalized for altered mental status. She was found unresponsive in her home at a senior living facility with right-sided weakness and transferred to the emergency department. She was last seen normal the evening prior to her admission. Initial vital signs revealed blood pressure 119/78 mmHg, heart rate 92 beats per minute, respiratory rate of 17 breaths per minute, and pulse oximetry 99%. Physical exam on presentation showed the patient was awake and alert with aphasia and dysarthria. She had 0/5 motor strength in the right upper extremity and 3/5 strength in the right lower extremity. Sensation to light touch was diminished on the right side. Right plantar reflex was extensor. She was not following commands. There was bruising on her extremities, and she had prominent suprasternal notch pulsations. She did not have any peripheral edema or an elevated jugular venous pulse. Initial basic laboratory values were notable for sodium 141 mmol/L, potassium 3.6 mmol/L, creatinine 1.1 mg/dL, total creatine kinase 317 U/L (reference range 9-185 U/L), white blood cells 13,000/microliter, hemoglobin 13.2 g/dL, and platelets 307,000/microliter. Coagulation studies noted an international normalized ratio (INR) 1.1, prothrombin time (PT) 14 seconds, and activated partial thromboplastin time (aPTT) 36.2 seconds (reference range 24-34 seconds). Additional notable laboratory values included total cholesterol 147 mg/dL, low density lipoprotein (LDL) 87 mg/dL, and hemoglobin A1c 6%.

Computed tomography (CT) of the head on admission showed a large recent parietal lobe infarct in left middle cerebral artery (MCA) territory with underlying stable moderate chronic small vessel ischemic changes and a questionable punctate lacunar infarct in left basal ganglia. Magnetic resonance imaging and angiography of the brain and cerebral vessels showed a subacute left parietal lobe infarction with suggestion of occlusions of left MCA branches. A repeat CT head 24 hours later showed interval expected evolution of the left MCA territory infarct. Initial electrocardiogram (ECG) obtained on presentation showed normal sinus rhythm with heart rate 91 beats per minute (bpm), poor R wave progression in leads V1-V3, nonspecific but non-diagnostic ST elevations in leads V2-V3, inverted T waves in inferior leads, and nonspecific T changes in the lateral precordial leads. No prior ECG was available for comparison. A repeat ECG one hour later showed normal sinus rhythm with heart rate 92 bpm, definite Q waves in leads V1-V2, nonspecific but non-diagnostic ST elevation in leads V2-V3, and inferolateral T wave abnormality.

Transthoracic echocardiogram was obtained as part of standard stroke workup on hospital day 2 and showed moderately reduced left ventricular function with an estimated ejection fraction of 43%. There were regional wall motion abnormalities with anterior, septal, and lateral hypokinesis as well as apical dyskinesis. No prior echocardiograms were available for comparison. The cardiology service was consulted for evaluation. After reviewing the data showing ECG abnormalities suggestive of prior myocardial injury, cardiac biomarkers were checked. Initial troponin T (TnT) obtained 48 hours after admission was 0.57 ng/dL (reference range <0.1 ng/dL). CK-MB and CK-MB relative index obtained at the same time were 3.4 ng/dL (reference range 0-9.9 ng/dL) and 3.3% (reference range 0-3.9%) respectively. Subsequent TnT on hospital day 3 was 0.4 ng/dL; CK-MB was 3.3 ng/dL. Telemetry monitoring showed normal sinus rhythm with few premature atrial and ventricular complexes (<1% of QRS complexes), no evidence of atrial fibrillation, and no ventricular tachycardia. In light of elevated troponin, left ventricular systolic dysfunction with segmental wall motion abnormalities, and ECG abnormalities consistent with Q-wave

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infarction, further risk stratification for CAD was initiated. Cardiac catheterization was deferred in setting of patient's recent stroke, limited functional status, no signs of hemodynamic compromise, and patient's inability to consent for coronary angiography. A regadenoson pharmacologic nuclear stress test showed typical response to regadenoson with no evidence of myocardial ischemia on the stress electrocardiogram. The myocardial perfusion scintigraphy was abnormal and showed a large-sized fixed defect in the left anterior descending artery territory consistent with infarction, a medium-sized mild defect in left circumflex artery territory that was reversible, and no resting or inducible defect in the right coronary artery territory. The summed stress score was 23 with a summed difference score of only 3. Gated perfusion images showed moderately diminished systolic performance with regional wall motion abnormalities. The patient was started on guideline-directed medical therapy for her CAD with subacute myocardial infarction and reduced left ventricular function, i.e. high dose statin, beta blocker, and ACE-inhibitor. Although no thrombus was visualized on transthoracic echocardiography, a cardioembolic source was suspected as a likely cause of the ischemic MCA stroke, possibly stemming from the left ventricle in the setting of apical dyskinesis and recent Q wave infarction. Therefore, the patient was started on therapeutic anticoagulation with warfarin with goal INR 2-3. Taken together, the ECG findings on presentation were suggestive of underlying CAD. However, no cardiac biomarkers were checked until the results of the echocardiography demonstrated abnormal left ventricular function. She most likely had a recent myocardial infarction, and the patient's presentation was felt to be consistent with cardio-embolic acute ischemic stroke possibly stemming from a thrombus of the left ventricular cavity after myocardial injury/infarction.

## Discussion

Multiple studies have been published documenting troponin elevation in acute ischemic stroke. Other neuro-cardiogenic abnormalities such as ECG changes and blood pressure changes have also been documented in that setting [8]. Despite the multitude of studies in the literature, the mechanism of troponin elevation in acute ischemic stroke is still not well understood. Increased catecholamine levels have been noted in stroke and a hypothesis of massive catecholamine resulting in myocardial injury has been posited but not proven. In general, the differential diagnosis for elevated troponins includes ischemia from obstructive epicardial CAD (e.g. myocardial infarction), non-ischemic cardiac conditions (e.g. heart failure, myocarditis, pericarditis, surgical or ablative trauma, stress cardiomyopathy), and non-cardiac conditions (e.g. pulmonary embolus, chemotherapy toxicity, renal failure, sepsis, stroke). Importantly, with increased sensitivity of troponin assays, clinical interpretation of elevated troponin has become more challenging [7].

A systematic review of 15 studies including 2,901 patients with acute stroke by Kerr et al. identified 18% of patients with positive troponin level within 7 days of symptom onset. These patients were more likely to have ECG change suggestive of myocardial ischemia, and elevated troponin was independently associated with mortality. However, this analysis did not investigate potential etiologies of ECG changes [8]. To address the role of cTn in predicting culprit or obstructive coronary lesions in patients with acute ischemic stroke and to ascertain if subsequent revascularization therapy could be potentially beneficial, Mochmann et al. prospectively screened 2,123 consecutive patients presenting with acute ischemic stroke at two tertiary referral hospitals in the troponin elevation in acute ischemic stroke (TRELAS) study [10,11]. The TRELAS study is an observational study designed to assess for possible coronary causes of troponin elevation in acute ischemic stroke with invasive coronary angiography evaluation for culprit lesions. Stroke patients presenting within 72 hours of symptoms onset and elevated troponin (>50 ng/L on a 5th generation high-sensitivity TnT assay; this corresponds to 0.03 micrograms/L on a 4th generation TnT assay) underwent coronary angiography within 72 hours. Patients who had renal insufficiency, severe disability, or ST elevations were excluded. Similar to previous studies, 14% of patients with confirmed acute ischemic stroke by neuroimaging had elevated cTn on hospital admission. A subset of 29 out of 291 stroke patients with elevated cTn (about 10% of the at-risk population) underwent diagnostic coronary angiography and their findings were compared to an age- and gender-matched control cohort of non-ST-elevation MI (NSTEMI)-ACS patients presenting with comparable cTn levels. Surprisingly, the prevalence of culprit coronary lesions in acute ischemic stroke patients with elevated cTn was only 24% compared to 79% in the NSTEMI-ACS patients. Given the low incidence of coronary culprit lesions in acute ischemic stroke patients with elevated cTn, only 21% of stroke patients with elevated cTn eventually underwent revascularization compared to 86% of NSTEMI-ACS patients. However, 12 of the 29 acute stroke patients had received intravenous tPA, which may have affected the findings upon angiography. Ejection fraction on left ventricular angiography did not differ between the two groups. Three patients with stroke had intervention to a culprit lesion, and 3 more were recommended for interventions once completing neurological rehabilitation. Only 1 stroke patient with a culprit lesion had chest pain; 3 had ECG changes. Six of 7 stroke patients with culprit lesions had a delta change in TnT of over 4 times the 99th percentile. Although patients with acute ischemic stroke were less likely to have a culprit lesion on angiography, a positive TnT was felt to be useful in this setting. The study authors proposed using TnT levels as a surrogate for concomitant silent CAD and as a useful tool to identify patients that need more intensive secondary prevention or workup for CAD.

The prognostic significance of troponin has been observed in other studied as well. Batal et al. studied a prospective cohort of 1718 patients at the University of Pittsburgh admitted with acute ischemic stroke [9]. 18% of patients had an elevated troponin I (≥ 0.1 microgram/L). Positive TnI patients had higher NIH stroke scale (NIHSS) scores, but NIHSS did not change with progressively higher TnI. 181 (59%) of these patients with elevated troponin had no chest pain or ECG abnormalities suggestive of MI, but 119 (39%) patients were classified into a separate MI group for analysis based on the presence of ischemic symptoms, ECG changes, or cardiac imaging evidence of new MI. Within one year after discharge for acute ischemic stroke, only 50 patients with positive TnI (16%) had evaluation for CAD. In the no-MI positive TnI group, 22% of patients had evidence of prior infarction and 56% had at least 50% luminal stenosis on angiography. 33% had at least 70% stenosis, and 22% had either left main stenosis or three-vessel CAD. Only 4 patients total (1%) underwent coronary revascularization, and only 1 of those patients was from the no-MI group despite the above-noted presence of coronary disease. Patients were followed up to 3 years and those in the positive troponin and MI group had significantly higher mortality than those with positive troponin and no MI, who in turn had worse survival than those patients with negative troponin (Figure 1). This finding was significant even after adjusting for age, comorbidities, stroke etiology, and NIHSS score. Although this study was unable to determine the precise etiology of troponin elevations, these results again suggest that cardiac troponin may be helpful in selecting patients with acute ischemic stroke who could benefit from additional risk stratification for CAD.

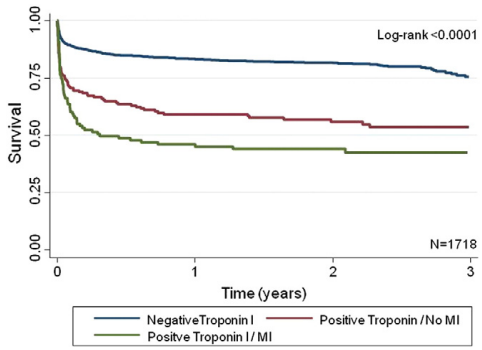


**Figure 1:** Survival analysis in patients with acute ischemic stroke comparing TnI negative patients vs positive TnI/no-MI group vs the MI group. There was a stepwise worse mortality outcome comparing TnI negative patients (n=1409) vs positive TnI/no-MI group (n=190) vs the MI group (n=119) (log rank <0.0001, test of trend <0.0001). Reprinted with permission from Reference 9.

CAD is commonly seen in patients with acute ischemic stroke due to shared risk factors. Thus, the ACCF 2012 expert consensus document on the clinical considerations in the interpretation of troponin recommends that stroke patients with positive troponin should be screened more carefully for CAD [7]. Regarding routine use of troponin for assessment, current UK acute stroke guidelines do not recommend routinely checking cardiac markers. However, current AHA/ASA treatment guidelines for acute ischemic stroke do recommend cardiovascular assessment and measurement of troponin in all stroke patients due to the close association between stroke and cardiac abnormalities, noting that ischemic stroke can be associated with elevated troponin and electrocardiographic abnormalities. The report notes that elevated troponin is associated with worse clinical outcomes, and cardiovascular evaluation is important to optimize both immediate and long-term management [13].

## Conclusions

It is not uncommon to see elevated troponin in the setting of acute ischemic stroke. Although the mechanism of this abnormality has not been fully defined, coexistence of CAD in patients with stroke is common due to the shared cardiovascular risk factors. However, based on recent findings in the TRELAS study, only approximately 24% of patients with acute ischemic stroke and troponin elevation have angiographic evidence of a "culprit lesion", and the rate of percutaneous vascularization was only 21% in this cohort. Nevertheless, elevated troponin portends worse prognosis in stroke patients and should prompt closer evaluation for ischemic heart disease. Although it can be challenging to interpret elevated troponin in the setting of acute ischemic stroke, signs such as ischemic symptoms, ECG abnormalities, or abnormalities on cardiac imaging can signal patients at an even higher risk.

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