Troponin Elevation Predicts Atrial Fibrillation in Patients with Stroke or Transient Ischemic Attack

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Background: Atrial fibrillation (AF) is a major cause of ischemic stroke. Cardiac troponin (cTnI) is a marker of myocardial damage and may predict arrhythmia. We sought to determine if increased cTnI levels were a predictor of new-onset AF in ischemic stroke or patients with transient ischemic attack (TIA). *Methods:* Consecutive patients who presented to Charles-Lemoyne Hospital between October 2006 and November 2010 with a diagnosis of acute ischemic stroke or TIA, without a history of AF, with a baseline measurement of cTnI were included in the study. The primary outcome was new-onset AF on 24-hour Holter measurement within 1 week of admission in patients without AF on the baseline electrocardiogram (ECG). Secondary outcomes included AF on Holter measurement, death, myocardial infarction (MI), and stroke within 3 months. *Results:* A total of 408 patients were included. Forty-six patients (11.3%) had elevated cTnI levels. These patients were older and had a higher prevalence of coronary artery disease and diabetes. AF on baseline ECG or 24-hour Holter measurement was present in 51 patients (12.5%) and was more frequent among patients with increased cTnI levels compared to patients with normal cTnI levels (34.7% vs 9.7%; $P = .004$ multivariate analysis). Elevated cTnI levels also predicted the composite outcome of stroke, MI, and death at 3 months (50.0% vs 16.1%; $P = .0001$). *Conclusions:* cTnI elevation predicts new-onset AF on 24-hour Holter measurement in patients with acute ischemic stroke or TIA and may indicate a poorer prognosis and a higher risk of stroke, MI, and death at 3 months. **Key Words:** Acute stroke—atrial fibrillation—cardiac emboli—cerebrovascular accident—transient ischemic attack.

Atrial fibrillation (AF) is a major cause of ischemic stroke in adults. The identification of AF is important in the secondary prevention of stroke or transient ischemic attack (TIA) because these patients may benefit from anticoagulation.[1] Testing for AF after a stroke or TIA usually includes serial electrocardiograms (ECGs) or Holter recording. Unfortunately, these tests are insensitive, and some studies suggest that prolonged monitoring may increase diagnostic yield,[2,3] but at a higher cost.

Cardiac troponin I (cTnI) and troponin T are recognized as sensitive and specific markers of cardiac injury.[4] Elevated levels of troponin have been described in about 18% of patients with acute ischemic stroke (AIS) in a systematic review.[5] Recently, major focus has been given to establish the possible mechanisms and clinical implications of troponin elevation in these patients. Multiple studies have found that high levels of troponin correlate with worse outcome after AIS.[5-7] Moreover, troponin elevation may be a marker of cardiac disease in stroke patients. Indeed, a recent retrospective study found that troponin elevation in AIS was related to new-onset AF on cardiac monitoring.[8]

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Given the low sensitivity of cardiac testing for AF, it would be helpful to have a marker that identifies patients at higher risk of AF. The aim of our study was to show that elevated cTnI levels are related to new-onset AF in AIS and TIA patients on 24-hour Holter monitoring.

Methods

Our study included all consecutive patients >18 years of age who presented with AIS or TIA at Charles-LeMoyne Hospital and who had a troponin measurement within 24 hours of symptom onset between October 4, 2006 and November 1, 2010. Patients were excluded if any of the following was present: hemorrhagic stroke on brain imaging, known AF, no baseline ECG performed, or a glomerular filtration rate (GFR) <60 mL/min/1.73 m^2. Most patients were seen in the emergency room and very few patients (8) were evaluated for a stroke or TIA occurring during hospitalization for another medical condition.

Demographics, medical history, GFR, medication, imaging data, stroke lateralization, baseline and 90-day follow-up National Institutes of Health Stroke Scale and modified Rankin Scale (mRS) scores, recurrent vascular events (stroke, myocardial infarction, and vascular death), and orientation at discharge were recorded.

The troponin assay available in our institution was cTnI. Despite slight biochemical differences between troponin T and I, they are found to be comparable in diagnostic and prognostic efficacy.[8] The minimum detectable concentration for cTnI was 0.01 μg/L. To avoid false-positive results, we used a cutoff value of 0.03 μg/L (ie, the value at which the coefficient of variation is 10%, as suggested by previous studies[9,10]). Patients were then dichotomized into 2 groups based on troponin levels: elevated (>0.03 μg/L) or normal (≤0.03 μg/L) cTnI.

All data were prospectively collected and entered into a standardized database. The analysis of the data and the design of the study, however, were retrospective. cTnI levels and Holter recordings were therefore ordered at the treating physician's discretion until mid-2009, when cTnI measurement became routine at our institution in patients with AIS and TIA. Acute ischemia on baseline ECG was defined as ST segment elevation or depression or T-wave inversion.

The primary outcome was new-onset AF on 24-hour Holter measurement. New-onset AF was defined as paroxysmal or permanent AF documented on 24-hour Holter monitoring during the first week of hospitalization in patients who had no history of previous AF and no AF on the baseline ECG. Baseline ECGs were done within minutes of the troponin sampling. ECGs and Holter monitoring were interpreted by cardiologists blinded to the patient's medical history. Secondary outcomes included AF on baseline ECG and recurrent stroke, MI, mRS at 90 days, and death from any cause.

Statistical analysis was performed with SPSS software (version 17.0; SPSS, Inc, Chicago, IL). Continuous variables were expressed in means with standard deviations or median values. Fisher exact and Pearson Chi-square tests were used to evaluate categorical variables. $P < .05$ was considered statistically significant. A multivariate analysis using multiple logistic regression was performed for all variables significant in the univariate analyses (age, diabetes, coronary artery disease [CAD], baseline blood glucose, and medication) and for gender, hyperlipemia, heart failure, and baseline ECG changes. The study protocol was approved by a local ethics committee.

Results

In the study period, a total of 587 consecutive patients were evaluated in our center for AIS or TIA and had a troponin measurement. During that period, 637 patients with AIS or TIA had no cTnI measurement available within 24 hours of symptom onset and were not included in our study. Because cTnI measurement did not become routine for AIS/TIA before mid-2009, most of the patients (482/587; 82.1%) included in this study were seen in 2009 to 2010. A vast majority of the patients seen in 2010 (264/280; 94.3%) or 2009 to 2010 (482/584; 82.5%) had cTnI levels verified in comparison to patients evaluated in 2006 to 2008 (105/640; 16.4%).

Patients were excluded for the following reasons: 83 had hemorrhagic strokes, 10 had a GFR of <60 mL/min/1.73 m^2, 79 patients had a history of AF, and 7 had no baseline ECG. Therefore, 408 patients were included in the analysis, of which 284 had a 24-hour Holter measurement performed. Reasons for not ordering Holter moitoring as judged by the treating physician were as follows: AF diagnosed on baseline ECG (28), other explanation or cause for the stroke or TIA already found (eg, carotid stenosis [52]), contraindication to anticoagulants (32), patient refusal (4), and not mentioned (8). Baseline characteristics (same variables as in Table 1) were similar between patients who did or did not have a cTnI measurement and between patients with and without a Holter measurement.

Troponin levels were assessed within 24 hours of symptom onset in all 408 patients (mean 9 hours 38 minutes). Charts of patients with cTnI assessment were also reviewed in order to determine the reason(s) for ordering cTnI measurement. Chest pain was mentioned in 10 cases, all with myocardial ischemia on baseline ECG (8 in the normal cTnI group and 2 in the elevated cTnI group). In all other cases, the troponin test was ordered as part of routine assessment.

Forty-six patients (11.3%) had elevated cTnI levels on presentation, with a similar proportion between patients with AIS and patients with TIA (11.5% vs 10.6%; $P = .971$). Patients with elevated cTnI levels were significantly older, had a higher prevalence of diabetes, CAD, had