Elevated Troponin Levels in Acute Stroke Patients Predict Long-term Mortality

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Background: Elevated plasma levels of troponin in acute stroke patients are common and have in several studies been shown to predict in-hospital and short-term mortality. Little is, however, known about the long-term prognosis of these patients. The aim of this study was to determine patient characteristics and 5-year mortality in patients with acute stroke and troponin elevation on admission. *Methods:* A retrospective cohort study of all consecutive patients with acute stroke and a plasma troponin I (TnI) analyzed on admission to Danderyd Hospital between January 1, 2005, and January 1, 2006 (n = 247). Patient characteristics were obtained from the Swedish National Stroke Register, Riksstroke, as well as hospital records. Mortality data were obtained from the Swedish Cause of Death Register. *Results:* There were 133 patients (54%) with TnI less than .03 μg/L (normal), 74 patients (30%) with TnI .03-.11 μg/L (low elevation), and 40 patients (16%) with TnI greater than .11 μg/L (high elevation). TnI elevations were associated with a higher age, prior ischemic stroke, chronic heart failure, renal insufficiency, stroke severity, and ST segment elevation or depression on admission. The rate of hyperlipidemia decreased with increasing TnI. Adjusted for age and comorbidity, elevated TnI values on admission had a significantly and sustained increased mortality over the 5-year follow-up, with a hazard ratio of 1.90 (95% confidence interval, 1.33-2.70). *Conclusions:* Troponin elevation in patients with acute stroke, even when adjusted for several possible confounders, is associated with an almost 2-fold increased risk of 5-year mortality. **Key Words:** Acute stroke—troponin elevation—myocardial damage—long-term prognosis.

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Elevated plasma levels of troponin in acute stroke patients are common and have been shown to predict in-hospital and short-term mortality.[1,2] Little is, however, known about cardiovascular morbidity and long-term mortality in these patients. Likewise, the underlying pathophysiology is largely unknown, and there are likely multiple mechanisms behind concomitant cerebral and cardiac pathophysiological events. Renal insufficiency (RI), congestive heart failure (CHF), and atrial fibrillation (AF) are recognized causes of troponin elevation[3-5] and may be important confounders contributing to troponin elevation in acute stroke patients. A number of other possible explanations have, however, been suggested, such as acute coronary syndrome with concomitant acute ischemic stroke[6] supported by the similar risk factors and the high prevalence of coronary atherosclerosis in patients with cerebral infarction.[7] Other studies suggest a neurologically induced myocardial injury due to sympathoadrenal activation.[8,9]

Large studies have shown that the main cause of long-term mortality in stroke patients, not taking troponin levels into account, is cardiovascular disease, and coronary artery disease in particular.[10] Biomarkers, such as troponins, may be a way to identify those at highest risk of mortality and morbidity. There are, however, no studies of long-term mortality of troponin elevation in stroke patients, the longest follow-up so far being 19 months.[11] The objective of this study was therefore to describe patient characteristics and the 5-year mortality and morbidity of troponin elevation in acute stroke.

Methods

Study Group

The study database was obtained retrospectively from the Swedish National Stroke Register, Riksstroke,[12] and comprised all consecutive patients diagnosed with acute ischemic stroke or intracerebral hemorrhage admitted to Danderyd Hospital within 7 days of symptom onset between January 1, 2005, and January 1, 2006 (n = 725). In the event of a recurrent stroke during the study period (n = 13), only the first event was included in the study. Cardiac troponin I (cTnI) values (Dade Behring's Stratus CS) were obtained from hospital records, and patients without a cTnI registered on admission (n = 464) were excluded. Patients were divided into 3 groups according to the cTnI value on admission: less than .03 μg/L, .03-.11 μg/L, and greater than .11 μg/L. These cut points were chosen on the basis of hospital guidelines at the time.

Patient Characteristics

Demographic data and prior diagnosis of ischemic stroke, transient ischemic attack (TIA), hemorrhagic stroke, CHF, coronary artery disease (CAD), hypertension, and diabetes mellitus (DM) were collected from Riksstroke as well as hospital records. A diagnosis of hyperlipidemia was considered present if patients received lipid-lowering medication on admission. AF was determined by history or electrocardiogram (ECG) during the hospital stay, and RI was defined as plasma creatinine greater than 120 μmol/L on admission. Prior cancer diagnosis was obtained from the Swedish Cancer Register[13] (Swedish Board of Health and Welfare). Medication on admission and at discharge was obtained from Riksstroke.

Stroke severity was determined using the National Institutes of Health Stroke Scale by certified raters. All patients received computed tomography of the brain, and stroke etiology was evaluated by a senior stroke physician according to criteria of the Trial of Org 10172 in Acute Stroke Treatment,[14] which includes large-artery atherosclerosis, cardioembolism, small-artery occlusion, other etiology, and undetermined etiology.

Chest pain on admission and referral to the department of cardiology were considered present if stated in hospital records.

Twelve-lead ECG on admission was interpreted by a senior cardiologist blinded to clinical data. ECG alterations were defined (according to the modified Minnesota code) as left or right bundle branch block, T-wave inversion of more than .1 mV, prolonged QTc (>.45 seconds), and ST segment depression or elevation of more than 1 mm, with the exception of ST elevation in V2 or V3, where more than 2 mm was required.

Laboratory data including hemoglobin, C-reactive protein, leukocyte count, platelet count, serum creatinine, and plasma glucose on admission were collected from hospital records.

Prognostic Data

Mortality data and cause of death were obtained from the Cause of Death Register[15] (Swedish Board of Health and Welfare). Causes of death were divided into 4 categories: stroke (ischemic stroke, hemorrhagic stroke, and stroke unspecified), cardiac (acute myocardial infarction, CHF, and other cardiac causes comprising valvular heart diseases and endocarditis), cancer, and other causes. Morbidity during the 5-year follow-up was obtained from the National Patient Register[16] (Swedish National Board of Health and Welfare) and was divided into 4 categories: recurrent stroke (ischemic stroke or intracerebral hemorrhage), cardiovascular event (CAD, CHF, and AF), cancer, and other events.

Excluded Group

A subanalysis was done comparing the excluded group of patients due to missing cTnI on admission with the study group. Age, sex, comorbidity (prior stroke, hypertension, AF, and DM), medication on admission and at