

Elevation of troponin I in acute ischemic stroke

Yu-Chin Su, Kuo-Feng Huang, Fu-Yi Yang, Shinn-Kuang Lin

Background. Cardiac morbidities account for 20% of deaths after ischemic stroke. Elevation of cardiac troponin has been regarded as a prognostic biomarker of poor outcome in patients with acute stroke. **Methods.** This retrospective study enrolled 871 in-patients with acute ischemic stroke from August 2010 to March 2015. Data included vital signs and laboratory parameters collected in the emergency department. National Institutes of Health Stroke Scale (NIHSS), Barthel index, and modified Rankin Scale (mRS) were used to assess stroke severity and outcome. **Results.** Elevated troponin I (TnI) $> 0.01 \mu\text{g/L}$ was observed in 146 (16.8%) patients. Patients with elevated TnI were older ($p < 0.001$), had higher heart rates ($p = 0.018$), higher blood urea nitrogen and creatinine levels ($p < 0.001$), lower hemoglobin ($p = 0.009$) and hematocrit ($p = 0.027$) levels, higher NIHSS scores on admission and at discharge, higher mRS scores but lower Barthel index scores at discharge ($p < 0.001$). Multivariate analysis revealed that female gender (OR 1.50, CI 1.05-2.13, $p = 0.025$), age ≥ 76 years (OR 2.24, CI 1.58-3.16, $p < 0.001$), heart rate ≥ 83 bpm (OR 1.77, CI 1.25-2.50, $p = 0.001$), blood urea nitrogen level ≥ 24.5 mg/dL (OR 1.94, CI 1.18-3.19, $p = 0.009$), evidence of clinical deterioration (OR 7.60, CI 3.70-15.4, $p < 0.001$), NIHSS score ≥ 14 on admission (OR 27.22, CI 12.81-54.87, $p < 0.001$), and abnormal TnI (OR 2.29, CI 1.42-3.69, $p < 0.001$) were associated with poor outcome. Significant factors for in-hospital mortality included evidence of clinical deterioration (OR 7.37, CI 3.04-17.84, $p < 0.001$), NIHSS score ≥ 14 on admission (OR 5.49, CI 2.09-14.45, $p < 0.001$), and elevated TnI level (OR 6.30, CI 2.60-15.25, $p < 0.001$). **Discussion.** Elevation of TnI during acute stroke is a strong independent predictor for both poor outcome and in-hospital mortality, particularly for a TnI level $> 0.1 \mu\text{g/L}$. Careful investigation of possible concomitant cardiac disorders is warranted for patients with abnormal troponin levels.

Elevation of Troponin I in Acute Ischemic Stroke

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Abstract

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of possible concomitant cardiac disorders is warranted for patients with abnormal troponin levels.

Key words: troponin I; acute ischemic stroke; cardiac enzyme; poor outcome; in-hospital mortality

Introduction

Heart disease and stroke are the second and third leading causes of death after cancer in Taiwan. Cerebrovascular and coronary arterial diseases share many of the same risk factors. Cardiac morbidities account for 20% of deaths after ischemic stroke (Bounds et al., 1981). Cardiac troponins are important biomarkers of acute myocardial infarction and are routinely studied in the setting of ischemic heart disease. Abnormal levels of cardiac troponins have also been reported to be associated with poor clinical outcome of patients with acute cerebrovascular diseases, including ischemic stroke (Di Angelantonio et al., 2005; Scheitz et al., 2012; Provide^ncia, Barra & Paiva, 2013; Faiz et al., 2014) , intracerebral hemorrhage (Hays & Diringer, 2006), and spontaneous subarachnoid hemorrhage (Deibert et al., 2003).

Common risk factors for vascular diseases, such as hypertension, diabetes, heart disease, and hyperlipidemia, are well known comorbidities of stroke. Most previous studies emphasized the correlation of these comorbidities with stroke and clinical outcomes. However, the definition of each risk factor is usually not identical and duration of these risk factors is not well described. The impact of a poorly controlled risk factor on the severity and outcome of stroke is dissimilar to that of a well-controlled one. Available laboratory parameters, clinical features, as well as biomarkers during acute stroke provide valuable information when investigating the clinical outcomes after stroke. In this study, we investigated whether certain clinical features and laboratory parameters including troponin I (TnI) that are commonly measured on admittance to the emergency department are predictive of outcome in patients with acute stroke.

Materials & Methods

Study Population and Data Collection

Patients who were treated for stroke in the neurological ward during the period August 2010 to March 2015 were retrospectively selected from the stroke registry database. Inclusion criteria included a diagnosis of acute ischemic stroke that was confirmed by clinical presentation and brain computed tomography or magnetic resonance study, and an available serum TnI study conducted at the emergency department within 48 hours of symptom onset. Data integrated for analysis in this study included sex and age of patients, clinical data such as blood pressure and heart rate, and hematological parameters including white blood cell count, hemoglobin, hematocrit, blood urea nitrogen, creatinine and TnI on arrival at the emergency department, and the severity of stroke evaluated on admission.

Definitions

TnI was measured using a Biomerieux Vidas Troponin I ultra system in the hospital's central laboratory. The analytical limit of detection and the 99th percentile upper reference limit was 0.01 $\mu\text{g/L}$. Abnormal elevation of TnI was defined as a TnI level in blood $> 0.01 \mu\text{g/L}$. Patients were stratified into two groups according to TnI level: a normal group ($\leq 0.01 \mu\text{g/L}$) and an abnormal group ($> 0.01 \mu\text{g/L}$). Patients with abnormal TnI were further stratified into two groups: a high-positive group ($> 0.1 \mu\text{g/L}$) and a low-positive group ($> 0.01 \mu\text{g/L}$). Stroke severity was assessed on admission according to the National Institutes of Health Stroke Scale (NIHSS). The etiology of stroke was classified according to the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) criteria (Adams et al., 1993). Clinical deterioration was defined in patients who demonstrated a greater than two point increase in NIHSS score during the acute stage of

stroke. Outcomes were evaluated using the NIHSS, the Barthel index and the modified Rankin Scale (mRS) at discharge. A mRS score > 3 was considered to indicate poor outcome. All causes of death during hospitalization were registered as in-hospital mortality.

Statistical Analysis

Continuous variables are presented as mean \pm standard deviation. TnI values and mRS scores were analyzed as continuous and dichotomous variables. The chi-square test and Fisher's exact test were used for categorical comparisons of data. Differences in means of continuous measurements were tested by the unpaired t-test and analysis of variance (ANOVA). Significant predictors in the univariate analyses were transferred to dichotomous variables with the cut-off level according to the mean values of poor outcome, and were included in a multiple logistic-regression model to identify the most important factors associated with poor outcome and in-hospital death. A *P* value of less than 0.05 was considered to indicate statistical significance. All statistical analyses were performed with the statistical package SPSS (Version 17, SPSS Inc, Chicago, IL). This study was approved by the Institutional Review Board of the Taipei Tzu Chi Hospital 00-IRB-027-XD. Written informed consent was obtained from the patient or from the next of kin of patients with decreased consciousness.

Results

During the study period, a total of 2,307 patients presented to our emergency department with acute ischemic stroke. Only 871 of those patients had valid data on TnI levels because during that period, measurement of TnI level was not routinely performed in the emergency department for patients with acute stroke. The mean age of the 871 patients enrolled in the study was 72.3 ± 13.6 years and 46.8% of them were women. Table 1 shows the comparison of clinical features, laboratory data, severity of stroke, and outcomes of patients of different genders. Women were significantly older and had lower diastolic blood pressure, hemoglobin levels and hematocrit levels. There was no significant difference in NIHSS score and TnI levels on admission between men and women. Although women had higher NIHSS and mRS scores as well as lower Barthel index scores at discharge, indicating poor outcome, the mortality rate was significantly higher in men. Elevated TnI was observed in 146 of the 871 patients (16.8%). Of them, 78 (8.9%) had high-positive levels and 68 (7.8%) had low-positive levels. Table 2 shows the comparison of clinical features, laboratory data, severity of stroke, and outcomes of patients with different levels of TnI. Abnormal TnI levels were more common in patients due to large artery atherosclerosis ($54/232 = 23\%$), cardioembolism ($38/131 = 29\%$), and undetermined etiology ($5/17 = 29\%$) than in patients due to small vessel occlusion ($48/482 = 10\%$) and other determined etiology ($1/9 = 11\%$) according to TOAST classification. Compared with patients with normal TnI levels, patients with abnormal TnI levels were significantly older ($P < 0.001$) and had significantly higher heart rate ($P = 0.018$), blood urea nitrogen levels ($P < 0.001$) and creatinine levels ($P < 0.001$) and significantly lower hemoglobin ($P = 0.009$) and hematocrit levels ($P = 0.027$). In addition, patients with abnormal TnI levels had higher NIHSS scores on admission (13.8 ± 10.8) and at discharge (10.2 ± 10.5) than patients with normal TnI levels

(7.3 ± 7.8 and 5.5 ± 7.5 , respectively) ($P < 0.001$). The Barthel index was lower (43.5 ± 38.3) and the mRS was higher (3.9 ± 1.7) in patients with abnormal TnI than in patients with normal TnI (64.9 ± 36.2 and 2.7 ± 1.7 , respectively) ($P < 0.001$). Of the total 871 patients, poor outcomes were observed in 421 (48%) patients and death occurred in 31 (3.6%) patients. Compared with patients with normal TnI levels, patients with abnormal TnI levels had higher rates of clinical deterioration (18% vs 9%, $P = 0.005$), poor outcome (71% vs 44%, $P < 0.001$), and death (14% vs 2%, $P < 0.001$).

The univariate analyses of continuous variables revealed that patients with poor outcome were older, had higher heart rates, TnI levels, white blood cell counts, blood urea nitrogen levels, creatinine levels, and NIHSS scores on admission and at discharge, higher mRS scores at discharge but lower hemoglobin levels, hematocrit levels, and Barthel index scores (Table 3). Analysis of dichotomous variables revealed that female gender, abnormal TnI levels, and evidence of clinical deterioration were associated with poor outcome. In-hospital death was found to be associated with high heart rate, high TnI level, high white blood cell count, and high NIHSS score on admission. Age was not associated with in-hospital death.

As shown in Table 4, multivariate analysis revealed that female gender ($p = 0.025$), age ≥ 76 years ($p < 0.001$), heart rate ≥ 83 bpm ($p = 0.001$), blood urea nitrogen level ≥ 24.5 mg/dL ($p = 0.009$), evidence of clinical deterioration ($p < 0.001$), NIHSS score ≥ 14 on admission ($p < 0.001$), and abnormal TnI level (odds ratio [OR]: 2.29; 95% confidence interval [CI]: 1.42-3.69; $p < 0.001$) were significant predictors of poor outcome. Evidence of clinical deterioration ($p < 0.001$), NIHSS score ≥ 14 on admission ($p < 0.001$), and abnormal TnI level (OR: 6.30; 95% CI: 2.60-15.25; $P < 0.001$) were significant predictors of in-hospital mortality. Comparison of patients with low-positive TnI levels and those with high-positive levels revealed that a TnI level

in the range of 0.02-0.1 $\mu\text{g/L}$ (OR: 2.05; 95% CI: 1.10-3.84; $p = 0.025$) and a TnI level > 0.1
 $\mu\text{g/L}$ (OR: 2.62; 95% CI: 1.32-5.19; $p = 0.006$) were independently associated with poor
outcome. Only a TnI level > 0.1 $\mu\text{g/L}$ was a strong independent predictor of in-hospital death
(OR: 11.59; 95% CI: 4.33-31.08; $p < 0.001$).

Discussion

Previous studies have shown that women were older with higher stroke severity at stroke onset, have higher prevalence of cardioembolism, poorer clinical outcomes and are at increased risk of death (Santalucia et al., 2013; Arboix et al., 2014). Different risk factors, stroke severity and the subtype of stroke have been proposed as being responsible for worse outcome in women. In this study, we found that NIHSS scores and laboratory parameters on admission did not differ between women and men. Female gender was associated with worse short-term outcome and male gender was associated with higher in-hospital mortality. The findings in this study are consistent with those reported elsewhere with the exception that initial stroke severity and death were not higher in women (Santalucia et al., 2013; Arboix et al., 2014). Advanced age, lower hemoglobin levels and lower hematocrit values contributed to the gender difference in poorer short-term outcome.

TnI is a highly sensitive and specific marker of acute myocardial infarction. Elevated TnI is characteristic of a number of cardiac diseases as well such as heart failure, pericarditis, myocarditis, atrial fibrillation and tachycardia (Tanindi & Cemri, 2011). Elevated TnI has also been found in patients with chronic renal failure, sepsis, critical illness, pulmonary embolism, chronic obstructive pulmonary disease, and stroke (Tanindi & Cemri, 2011; Mannu, 2014). Elevated levels of cardiac troponin has been reported in 10–34% of patients with acute stroke. Kerr et al conducted a systematic review of studies measuring troponin within 7 days of symptom onset in acute stroke patients and found that more than 18% of patients had a high troponin level (Kerr et al., 2009). Some studies reported that elevated troponin levels were more common in patients with stroke due to cardioembolism who also had evidence of atrial fibrillation, ischemic heart or heart failure (Etgen et al., 2005; Faiz et al., 2014). Abnormal TnI

was observed in 16.8% patients in our study. We found that patients with abnormal TnI were more likely to have large artery atherosclerosis, cardioembolism and undetermined etiology. Patients who had risks from both atrial fibrillation and stenotic cerebral arteries were grouped into undetermined etiology with conflict data when categorizing the subtype of stroke. This could explain why there was a similarly higher percentage of elevated TnI in patients with undetermined etiology. Patients with elevated TnI were older and had higher heart rate, blood urea nitrogen and creatinine but lower hemoglobin and hematocrit than patients with normal TnI. Patients with elevated TnI presented with more severe initial stroke severity and showed a greater degree of clinical deterioration during hospitalization. Worse outcome and higher in-hospital mortality were observed in patients with abnormal TnI as well. All of the above differences were most prominent in patients with high-positive TnI levels. These findings are similar to those reported by Angelantonio et al, who found that there was a dose-response relationship between the three TnI groups (normal, low-positive, and high-positive) and clinical features (Di Angelantonio et al., 2005).

Mechanisms for elevated TnI during acute ischemic stroke include primary myocardial damage with secondary cardioembolic stroke, primary cerebral ischemia with secondary myocardial injury owing to central activation of the sympathetic nervous system, and coexisting heart failure (Etgen et al., 2005). Myocytolysis surrounding patches of subendocardial hemorrhage or swollen myocytes surrounding epicardial nerves during early acute stroke has been suggested to be the cause of cardiac injury (Oppenheimer & Hachinski, 1992). Barber et al found that raised TnI was associated with elevation of circulating epinephrine in patients with acute ischemic stroke (Barber et al., 2007). Involvement of the parietal lobe or insular cortex has also been reported to be associated with elevated cardiac troponin levels due to the imbalance of

sympathetic and parasympathetic autonomic control (Ay et al., 2006; Rincon et al., 2008). Not all patients in our study underwent brain magnetic resonance imaging to indentify the precise location of stroke; therefore, we were not able to analyze the involvement of the insular or parietal cortex in this study. Cardiac cell damage with elevated troponins in acute stroke may be enhanced by the stress-related inflammatory response as well as the cytokine response pathways (Christensen et al., 2004). The etiologies of elevated troponin levels other than acute coronary syndrome in renal failure include subclinical myocardial damage (micro-infarctions) and decreased renal troponin excretion (Freda et al., 2002; Jensen et al., 2007; Faiz et al., 2014). Serum troponin T is increased more frequently than TnI in patients with renal failure, and TnI has been reported to be a more sensitive and specific biomarker of cardiac damage than Troponin T in patients with end-stage renal failure (Freda et al., 2002; Mannu, 2014).

There is no doubt that advanced age, higher NIHSS score on admission, and evidence of clinical deterioration during hospitalization are associated with worse outcome and higher rate of death at discharge. The average age of patients with abnormal TnI, patients with poor outcome, and patients who died in hospital in this study was approximately 76 years. Faiz et al also reported that age ≥ 76 years was independently associated with elevated troponin levels in patients with acute ischemic stroke (Faiz et al., 2014). Higher heart rate has been reported to be associated with worse outcomes, in particular death, in long-term follow-up of patients with vascular diseases (Erdur et al., 2014). In our study, higher heart rate was observed in patients with abnormal TnI, in those with poor outcome, and in those who died before discharge. Interestingly, the average heart rate (83 bpm) was the same in those three different groups of patients. Multivariate analysis revealed that heart rate ≥ 83 bpm was also an independent risk factor for poor outcome. Erdur et al reported that heart rate ≥ 83 bpm on admission was

independently associated with in-hospital mortality in acute ischemic stroke patients, suggesting early negative effects of autonomic imbalance (Erdur et al., 2014).

With the exception of NIHSS score on admission and the subsequent deterioration during hospitalization, only elevated TnI was a strong independent predictor of poor outcome and death, particularly for patients with TnI levels $> 0.1 \mu\text{g/L}$. Abnormal TnI had an OR of 2.29 for poor outcome and an OR of 6.30 for in-hospital mortality. In patients with a TnI level $> 0.1 \mu\text{g/L}$, the OR increased to 11.59 for in-hospital mortality. A meta-analysis of 2901 patients from 15 studies with different definitions and sampling times of troponin by Kerr et al revealed that elevated troponin is associated with poor outcome; however, they did not fully establish whether elevated troponin is an independent prognostic factor (Kerr et al., 2009). Recent studies with multivariate models including age and some measures of stroke severity have concluded that a positive level of troponin is associated with an overall increased risk of both death and disability (Jensen et al., 2007; Faiz et al., 2014a; Faiz et al., 2014b). The American Stroke Association recommended the routine checking of markers of cardiac ischemia during acute stroke (Adams et al., 2007). Whether troponin should be routinely checked is still under deliberation. However, recognition and careful investigation of possible concomitant cardiac disorders in patients with acute ischemic stroke is warranted for patients with elevated troponin levels.

This study has a number of limitations. First, this study was retrospective in nature and troponin I was checked only once in each patient in the emergency room. Second, we did not exclude patients who had concomitant myocardial infarction or severely impaired renal function. Finally, we did not perform a follow-up study after discharge. Notwithstanding these limitations, our data extend the current understanding of the implications of troponin positivity in acute ischemic stroke.

Conclusions

Elevation of TnI during acute stroke is a strong independent predictor for both poor outcome and in-hospital mortality, particularly for a TnI level $> 0.1 \mu\text{g/L}$. Both neurologists and cardiologists need to pay more attention to the possible concomitant cardiac disorders in patients with abnormal troponin levels during acute stroke.

References

Adams HP Jr, Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, Marsh EE 3rd. 1993.

Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. *Stroke* 24:35-41. DOI: [10.1161/01.STR.24.1.35](https://doi.org/10.1161/01.STR.24.1.35).

Adams HP Jr, del Zoppo G, Alberts MJ, Bhatt DL, Brass L, Furlan A, Grubb RL, Higashida

RT, Jauch EC, Kidwell C, Lyden PD, Morgenstern LB, Qureshi AI, Rosenwasser RH, Scott

PA, Wijedicks EF; American Heart Association; American Stroke Association Stroke Council;

Clinical Cardiology Council; Cardiovascular Radiology and Intervention Council;

Atherosclerotic Peripheral Vascular Disease and Quality of Care Outcomes in Research

Interdisciplinary Working Groups. 2007. Guidelines for the early management of adults with

ischemic stroke: a guideline from the American Heart Association/ American Stroke

Association Stroke Council, Clinical Cardiology Council, Cardiovascular Radiology and

Intervention Council, and the Atherosclerotic Peripheral Vascular Disease and Quality of Care

Outcomes in Research Interdisciplinary Working Groups: the American Academy of

Neurology affirms the value of this guideline as an educational tool for neurologists. *Stroke* 38:

1655-1711. DOI: [10.1161/STROKEAHA.107.181486](https://doi.org/10.1161/STROKEAHA.107.181486).

Arboix A, Cartanyà A, Lowak M, García-Eroles L, Parra O, Oliveres M, Massons J. 2014.

Gender differences and woman-specific trends in acute stroke:Results from a hospital-based

326 registry (1986–2009). *Clin Neurol Neurosurg* 127:19-24. DOI:10.1016/j.clineuro.2014.09. 024.

327 Ay H, Koroshetz WJ, Benner T, Vangel MG, Melinosky C, Arsava EM, Ayata C, Zhu

328 M, Schwamm LH, Sorensen AG. 2006. Neuroanatomic correlates of stroke-related myocardial

329 injury. *Neurology* 66:1325-1329. DOI: [http://dx.doi.org/10.1212/01.wnl.0000206077.13705.](http://dx.doi.org/10.1212/01.wnl.0000206077.13705.6d)

330 6d.

331 Barber M, Morton JJ, Macfarlane PW, Barlow N, Roditi G, Stott DJ. 2007. Elevated troponin

332 levels are associated with sympathoadrenal activation in acute ischaemic stroke. *Cerebrovasc*

333 *Dis* 23:260-266. DOI:10.1159/000098325.

334 Bounds JV, Wiebers DO, Whisnant JP, Okazaki H. 1981. Mechanisms and timing of deaths from

335 cerebral infarction. *Stroke* 12:474-477. DOI: 10.1161/01.STR.12.4.474.

336 Christensen H, Johannesen HH, Christensen AF, Bendtzen K, Boysen G. 2004. Serum cardiac

337 troponin I in acute stroke is related to serum cortisol and TNF- α . *Cerebrovasc Dis* 18: 194-199.

338 DOI:10.1159/000079941.

339 Deibert E, Barzilai B, Braverman AC, Edwards DF, Aiyagari V, Dacey R, Diringer M. 2003.

340 Clinical significance of elevated troponin I in patients with nontraumatic subarachnoid

341 hemorrhage. *J Neurosurg* 98:741-746. DOI: 10.3171/jns.2003.98.4.0741.

342 Di Angelantonio E, Fiorelli M, Toni D, Sacchetti ML, Lorenzano S, Falcou A, Ciarla MV, Suppa

343 M, Bonanni L, Bertazzoni G, Aguglia F, Argentino C. 2005. Prognostic significance of

admission levels of troponin I in patients with acute ischaemic stroke. *J Neurol Neurosurg Psychiatry* 76:76-81. DOI: 10.1136/jnnp.2004.041491.

Erdur H, Scheitz JF, Grittner U, Laufs U, Endres M, Nolte CH. 2014. Heart rate on admission independently predicts in-hospital mortality in acute ischemic stroke patients. *Int J Cardiol* 176:206-210. DOI: 10.1016/j.ijcard.2014.07.001.

Etgen T, Baum H, Sander K, Sander D. 2005. Cardiac Troponins and N-terminal Pro-brain natriuretic peptide in acute ischemic stroke do not relate to clinical prognosis. *Stroke* 36: 270-275. DOI: 10.1161/01.STR.0000151364.19066.a1.

Faiz KW, Thommessen B, Einvik G, Brekke PH, Omland T, Rønning OM. 2014. Determinants of high sensitivity cardiac troponin T elevation in acute ischemic stroke. *BMC Neurol* 14:96. DOI: 10.1186/1471-2377-14-96.

Faiz KW, Thommessen B, Einvik G, Omland T, Rønning OM. 2014. Prognostic value of high-sensitivity cardiac Troponin T in acute ischemic stroke. *J Stroke Cerebrovasc Dis* 23: 241-248. DOI: 10.1016/j.jstrokecerebrovasdis.2013.01.005.

Freda BJ, Tang WH, van Lente F, Peacock WF, Francis GS. 2002. Cardiac troponins in renal insufficiency: review and clinical implications. *J Am Coll Cardiol* 40:2065-2071. DOI: 10.1016/S0735-1097(02)02608-6.

Hays A, Diring MN. 2006. Elevated troponin levels are associated with higher mortality

362 following intracerebral hemorrhage. *Neurology* 66:1330-1334. DOI: <http://dx.doi.org/10.1212/>
363 01.wnl.0000210523.22944.9b.

364 Jensen JK, Kristensen SR, Bak S, Atar D, Høilund-Carlsen PF, Mickley H. 2007. Frequency and
365 significance of troponin T elevation in acute ischemic stroke. *Am J Cardiol* 99:108-112. DOI:
366 <http://dx.doi.org/10.1016/j.amjcard.2006.07.071>.

367 Kerr G, Ray G, Wu O, Stott DJ, Langhorne P. 2009. Elevated troponin after stroke: a systematic
368 review. *Cerebrovasc Dis* 28:220-226. DOI: 10.1159/000226773.

369 Mannu GS. 2014. The non-cardiac use and significance of cardiac troponins. *Scot Med J* 59:
370 172-178. DOI: 10.1177/0036933014540090.

371 Oppenheimer SM, Hachinski VC. 1992. The cardiac consequences of stroke. *Neurol Clin* 10:
372 167-176.

373 Provide^ncia R, Barra S, Paiva L. 2013. Atrial fibrillation, elevated troponin, ischemic stroke and
374 adverse outcomes: understanding the connection. *Clin Res Cardiol* 102:701-711. DOI:
375 10.1007/s00392-013-0591-0.

376 Rincon F, Dhamoon M, Moon Y, Paik MC, Boden-Albala B, Homma S, Di Tullio MR, Sacco
377 RL, Elkind MS. 2008. Stroke location and association with fatal cardiac outcomes: Northern
378 Manhattan Study (NOMAS). *Stroke* 39:2425-2431. DOI: 10.1161/STROKEAHA.107.50605 5.

379 Santalucia P, Pezzella FR, Sessa M, Monaco S, Torgano G, Anticoli S, Zanolli E, Maimone

Baronello M, Paciaroni M, Caso V, Women Stroke Association (WSA). 2013. Sex differences in clinical presentation, severity and outcome of stroke: Results from a hospital-based registry. *Eur J Intern Med* 24:167-171. DOI: 10.1016/j.ejim.2012.10.004.

Scheitz JF, Endres M, Mochmann HC, Audebert HJ, Nolte CH. 2012. Frequency, determinants and outcome of elevated troponin in acute ischemic stroke patients. *Int J Cardiol* 157:239-242. DOI: 10.1016/j.ijcard.2012.01.055.

Tanindi A, Cemri M. 2011. Troponin elevation in conditions other than acute coronary syndromes. *Vasc Health Risk Manag* 7:597-603. DOI: 10.2147/VHRM.S24509.

Table 1. Correlation of clinical features and gender in 871 patients with acute ischemic stroke

Characteristics	Gender		<i>P</i> value
	Men (n = 463)	Women (n = 408)	
<i>Unpaired-t test</i>			
Mean age (years)	69.5±13.9	75.4±12.5	<0.001
Systolic pressure (mmHg)	166±82	166±31	0.888
Diastolic pressure (mmHg)	92±19	89±17	0.004
Heart rate (bpm)	80±17	80±17	0.823
Troponin I (ug/L)	0.067±0.655	0.092±0.329	0.476
White blood cells (1000/mm ³)	8.27±3.01	8.01±2.81	0.187
Hemoglobin (g/dL)	14.2±2.0	12.6±1.9	<0.001
Hematocrite (%)	41.2±5.5	37.5±5.3	<0.001
Glucose (mg/dL)	166±81	168±92	0.719
Blood urea nitrogen (mg/dL)	22.6±12.6	22.8±15.4	0.592
Creatinine (mg/dL)	1.53±1.34	1.37±1.41	0.088
NIHSS score (on admission)	7.9±8.8	8.8±8.5	0.171
NIHSS score (at discharge)	5.6±7.9	6.9±8.4	0.024
Barthel index score	67.4±36.4	55.2±37.3	<0.001
modified Rankin Scale	2.7±1.8	3.1±1.7	<0.001
<i>Chi-square test</i>			
Abnormal troponin I	78 (17%)	68 (17%)	0.943
Deteriotaion	53 (11%)	41 (10%)	0.514
mRS > 3	196 (40%)	225 (55%)	<0.001
Death	23 (5%)	8 (2%)	0.017

Notes

NIHSS, National Institute of health Stroke Scale; mRS, modified Rankin Scale.

Data are expressed as mean±SD or n (%)

Table 2. Correlation of clinical features and troponin I level in 871 patients with acute ischemic stroke

Characteristics	Troponin I test			Troponin I level (ug/L)			<i>P</i> value
	Abnormal	Normal	<i>P</i>	> 0.1	0.02-0.1	≤0.01	
	(n = 146)	(n = 725)	value	(n =78)	(n =68)	(n =725)	
<i>Unpaired-t test</i>				<i>ANOVA</i> <i>test</i>			
Mean age (years)	75.8±12.8	71.6±13.6	<0.001	75.8±12.8	75.8±12.9	71.6±13.6	0.003
Systolic pressure (mmHg)	165±34	166±68	0.836	162±33	168±35	166±68	0.831
Diastolic pressure (mmHg)	90±21	91±17	0.652	90±22	90±20	91±17	0.901
Heart rate (bpm)	83±17	79±17	0.018	84±16	82±17	79±17	0.040
White blood cells (1000/mm ³)	8.52±3.02	8.04±2.85	0.064	9.26±3.29	7.68±2.44	8.04±2.85	<0.001
Hemoglobin (g/dL)	13.0±2.4	13.5±2.1	0.009	13.1±2.6	12.8±2.2	13.5±2.1	0.025
Hematocrite (%)	38.5±6.5	39.7±5.5	0.027	38.8±7.0	38.2±5.9	39.7±5.5	0.069
Glucose (mg/dL)	174±109	166±81	0.598	191±137	146±52	166±81	0.009
Blood urea nitrogen (mg/dL)	29.1±18.8	20.8±12.0	<0.001	31.5±21.9	26.3±13.9	20.8±12.0	<0.001
Creatinine (mg/dL)	2.22±2.34	1.29±1.01	<0.001	2.46±2.71	1.94±1.79	1.29±1.01	<0.001
NIHSS score (on admission)	13.8±10.8	7.3±7.8	<0.001	14.9±10.8	12.3±10.7	7.3±7.8	<0.001
NIHSS score (at discharge)	10.2±10.5	5.5±7.5	<0.001	10.6±10.2	9.8±10.9	5.5±7.5	<0.001
Barthel index score	43.5±38.3	64.9±36.2	<0.001	40.8±36.6	46.2±40.1	64.9±36.2	<0.001
modified Rankin Scale	3.9±1.7	2.7±1.7	<0.001	4.2±1.6	3.5±1.8	2.7±1.4	<0.001
<i>Chi-square test</i>							
Deteriotaion	26 (18%)	68 (9%)	0.005	16 (21%)	10 (15%)	68 (9%)	0.006
mRS > 3	103 (71%)	318 (44%)	<0.001	60 (77%)	43 (63%)	318 (44%)	<0.001
Death	20 (14%)	11 /(2%)	<0.001	16 (21%)	4 (6%)	11 (2%)	<0.001

Notes.

NIHSS, National Institute of health Stroke Scale; mRS, modified Rankin Scale.

Data are expressed as mean±SD or n (%)

Table 3. Correlation of clinical features and outcomes in 871 patients with acute ischemic stroke

Characteristics	Poor outcome (mRS > 3)			Death		
	Y (n = 421)	N (n = 450)	P value	Y (n = 31)	N (n = 840)	P value
<i>Unpaired-t test</i>						
Mean age (years)	76.6±12.4	68.2±13.4	<0.001	76.2±11.2	72.1±13.6	0.097
Systolic pressure (mmHg)	168±85	164±30	0.302	175±41	166±64	0.428
Diastolic pressure (mmHg)	89±18	92±18	0.122	91±26	91±18	0.877
Heart rate (bpm)	83±17	77±17	<0.001	83±17	77±17	<0.001
Troponin I (ug/L)	0.136±0.719	0.025±0.100	0.001	0.526±1.093	0.062±0.466	<0.001
White blood cells (1000/mm ³)	8.38±2.99	7.88±2.77	0.011	9.54±4.09	8.07±2.82	0.005
Hemoglobin (g/dL)	13.1±2.2	13.8±2.0	<0.001	13.3±2.5	13.4±2.1	0.673
Hematocrite (%)	38.6±5.8	40.3±5.5	<0.001	39.1±6.7	39.5±5.7	0.696
Glucose (mg/dL)	169±88	165±84	0.559	173±66	167±87	0.684
Blood urea nitrogen (mg/dL)	24.5±16.3	19.9±10.2	<0.001	25.7±11.7	22.3±14.0	0.218
Creatinine (mg/dL)	1.55±1.51	1.35±1.21	0.031	1.69±0.93	1.44±1.39	0.311
NIHSS score (on admission)	13.9±9.3	3.3±3.1	<0.001	25.3±10.9	7.7±7.9	<0.001
NIHSS score (at discharge)	11.7±9.5	1.7±1.8	<0.001	-	-	
Barthel index score	26.9±23.7	91.2±13.8	<0.001	-	-	
modified Rankin Scale	4.5±0.6	1.3±0.9	<0.001	-	-	
<i>Chi-square test</i>						
Women	225 (53%)	183 (41%)	<0.001	8 (26%)	400 (48%)	0.017
Abnormal troponin I	103 (24%)	43 (10%)	<0.001	20 (65%)	126 (15%)	<0.001
Deterioration	82 (19%)	12 (3%)	<0.001	18 (58%)	76 (9%)	<0.001

Notes.

NIHSS, National Institute of health Stroke Scale; mRS, modified Rankin Scale.

Data are expressed as mean±SD or n (%)

Table 4. Logistic model of factors influencing outcomes and mortality in 871 patients with acute ischemic stroke

Characteristics	Poor outcome (mRS > 3)		Death	
	OD (95% CI)	<i>P</i> value	OD (95% CI)	<i>P</i> value
Women	1.50 (1.05-2.13)	0.025	0.40 (0.15-1.11)	0.078
Age \geq 76 years	2.24 (1.58-3.16)	<0.001	0.91 (0.37-2.25)	0.831
Heart rate \geq 83 bpm	1.77 (1.25-2.50)	0.001	1.15 (0.48-2.74)	0.749
White blood cells \geq 8380 uL	1.27 (0.89-1.80)	0.178	1.94 (0.77-4.87)	0.159
Hemoglobin \leq 13.1 g/dL	1.47 (0.79-2.72)	0.221	0.53 (0.11-2.48)	0.421
Hematocrite \leq 38.6 %	1.19 (0.66-2.17)	0.565	2.91 (0.68-12.54)	0.151
Blood urea nitrogen \geq 24.5 mg/dL	1.94 (1.18-3.19)	0.009	0.69 (0.22-2.16)	0.524
Creatinine \geq 1.55 mg/dL	0.91 (0.55-1.50)	0.704	2.37 (0.85-6.63)	0.099
Deterioration	7.60 (3.75-15.40)	<0.001	7.37 (3.04-17.84)	<0.001
NIHSS score (admission) \geq 14	27.22 (12.81-57.84)	<0.001	5.49 (2.09-14.45)	<0.001
Anbormal troponin I	2.29 (1.42-3.69)	<0.001	6.30 (2.60-15.25)	<0.001

Notes.

NIHSS, National Institute of Health Stroke Scale; mRS, modified Rankin Scale; OD, odds ratio; CI, confidence interval.