

Serum Troponin Level in Acute Ischemic Stroke Identifies Patients with Visceral Infarcts

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Background and Purpose: Patients with ischemic stroke of cardioembolic origin are at risk of visceral (renal or splenic) infarction. We hypothesized that serum troponin level at time of ischemic stroke would be associated with presence of visceral infarction. *Methods:* Data were abstracted from a single center prospective stroke database over 18 months and included all patients with ischemic stroke who underwent contrast-enhanced computerized tomography (CT) of the abdomen and pelvis for clinical purposes within 1 year of stroke. The primary predictor was troponin concentration $\geq .1$ ng/mL. The primary outcome was visceral infarct (renal and/or splenic) on CT abdomen and pelvis. Univariate and multivariable logistic regression models were used to estimate the odds ratio and 95% confidence intervals (OR, 95% CI) for the association of troponin with visceral infarction. *Results:* Of 1233 patients with ischemic stroke, 259 patients had a qualifying visceral CT. Serum troponin level on admission was measured in 237 of 259 patients (93.3%) and 41 of 237 (17.3%) had positive troponin. There were 25 patients with visceral infarcts: 16 renal, 7 splenic, and 2 both. In univariate models, patients with a positive troponin level (versus negative) were more likely to have visceral infarcts (39.1% [9/23] versus 15.0% [32/214], $P = .008$) and this association persisted in multivariable models (adjusted OR 3.83; 95% CI 1.42-10.31, $P = .006$). *Conclusions:* In ischemic stroke patients, elevated serum troponin levels may help identify patients with visceral infarcts. This suggests that troponin in the acute stroke setting is a biomarker of embolic risk. Larger studies with systematic visceral imaging are needed to confirm our findings.

Key Words: Stroke—visceral infarct—troponin—cardioembolic stroke—ESUS
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Background

Cardiac troponin level is a marker of cardiac injury and studies show that elevated troponin levels are associated with increased stroke risk, particularly those related to cardioembolism.^{1,2} In the acute ischemic stroke setting, a positive serum troponin level on admission has been independently associated with cardioembolic stroke subtypes.^{3,4}

Visceral (kidney or splenic) infarcts have been reported in the ischemic stroke setting and recently a study showed an association between visceral infarcts and cardioembolic and cryptogenic stroke subtypes.⁵

In this study, we aim to determine the association between positive admission serum troponin level and the presence of visceral infarction. We hypothesize that a positive serum troponin level in the acute ischemic stroke setting would be associated with the presence of visceral infarcts.

Methods

Patient Population

We abstracted data from a comprehensive stroke center prospective quality improvement REDCap (Vanderbilt University, Nashville, TN) registry and included consecutive patients with a discharge diagnosis of ischemic stroke between January 1, 2016 and June 30, 2017. We then cross matched the above patients during the study period with picture archiving and communication system and included only those patients who underwent a clinically indicated contrast-enhanced computerized tomography (CT) of the abdomen and pelvis within 1 year from the stroke (up to 1 year before and up to 1 year after). The study was approved by the institutional review board.

Primary Predictor

The primary predictor was serum troponin level on admission (cardiac troponin I) measured by a 3-site sandwich immunoassay (ADVIA Centaur TnI-Ultra Assay; Siemens Medical Solutions USA, Inc.; Malvern, PA). In general, all patients admitted with suspected ischemic stroke had a serum troponin level checked on admission as part of the diagnostic evaluation. According to our laboratory, a positive cardiac troponin I was defined as ≥ 0.1 ng/mL.³

Study Covariates

Study variables were abstracted from the database including:

1. Demographic variables: age, sex;
2. Clinical variables: history of hypertension, history of diabetes, history of hyperlipidemia, history of coronary heart disease, history of prior

stroke, history of atrial fibrillation, history of congestive heart failure, active smoking, and National Institute of Health Stroke Scale score on admission.

Abdomen and Pelvis CT

Abdominal and pelvic CTs were performed for clinical purposes. In general, contiguous axial images were obtained in the axial plane following the intravenous administration of iodinated contrast material; sagittal and coronal reconstructions were obtained from the axial data based on hospital protocol. All studies that included contrast-enhanced imaging were reviewed if obtained within 1 year before or after the ischemic stroke admission. The CT abdomen and pelvis was reviewed by a clinical provider blinded to clinical information and serum troponin level, for the presence of renal or splenic infarcts with excellent inter-rater reliability ($\kappa = .85$).

Outcome

The outcome was visceral infarction. Visceral infarctions in the kidneys or spleen were graded on a binary scale based on the characteristic imaging findings of 1 or more cortically based wedge-shaped areas of hypoattenuation directed at the hilum. A thin rim of cortical enhancement was required to delineate a renal infarction from other pathology such as pyelonephritis.

Statistical Analysis

Patients were divided into 2 groups: visceral infarct versus no visceral infarct. We compared demographic factors, clinical characteristics, and troponin positivity between the 2 groups. We used *t* tests for continuous variables and Fisher's test for categorical variables. We then performed multivariable regression analyses to determine the association between troponin positivity and visceral infarcts, adjusting for covariates according to 2 models: model 1, which adjusted for age and sex; model 2, which adjusted for age, sex, history of hypertension, diabetes, hyperlipidemia, coronary heart disease, atrial fibrillation, prior transient ischemic attack or stroke, congestive heart failure, and active smoking. Analysis was performed using SPSS version 20.0 (Chicago, IL) and $P < .05$ was considered statistically significant.

Results

Baseline Characteristics and Univariate Analyses

Of 1233 patients with ischemic stroke, 259 patients had a qualifying CT abdomen and pelvis. Reasons for obtaining a CT scan were abdominal symptoms ($n = 127$, 49.0%), cancer screening ($n = 61$, 23.6%), abdominal trauma ($n = 24$, 9.3%), abdominal infection ($n = 17$, 6.6%),

Table 1. Baseline characteristics of patients with and without CT abdomen and pelvis performed

	CT performed (n = 259)	CT not performed (n = 974)
Age (mean)	72.9	70.7
Sex (% men)	149 (57.5%)	510 (52.3%)
Hypertension (%)	217 (83.8%)	720 (73.9%)
Diabetes (%)	71 (27.4%)	273 (28.0%)
Hyperlipidemia (%)	136 (52.5%)	477 (49.0%)
Prior stroke (%)	69 (26.6%)	208 (21.4%)
Atrial fibrillation (%)	98 (37.8%)	250 (25.7%)
Congestive heart failure (%)	41 (15.8%)	94 (9.7%)
Coronary heart disease (%)	70 (27.0%)	195 (20.0%)
Active smoking (%)	54 (20.8%)	174 (17.9%)
Positive troponin (%)	41/237 (17.3%)	90/891 (10.1%)

Abbreviation: CT, computed tomography.

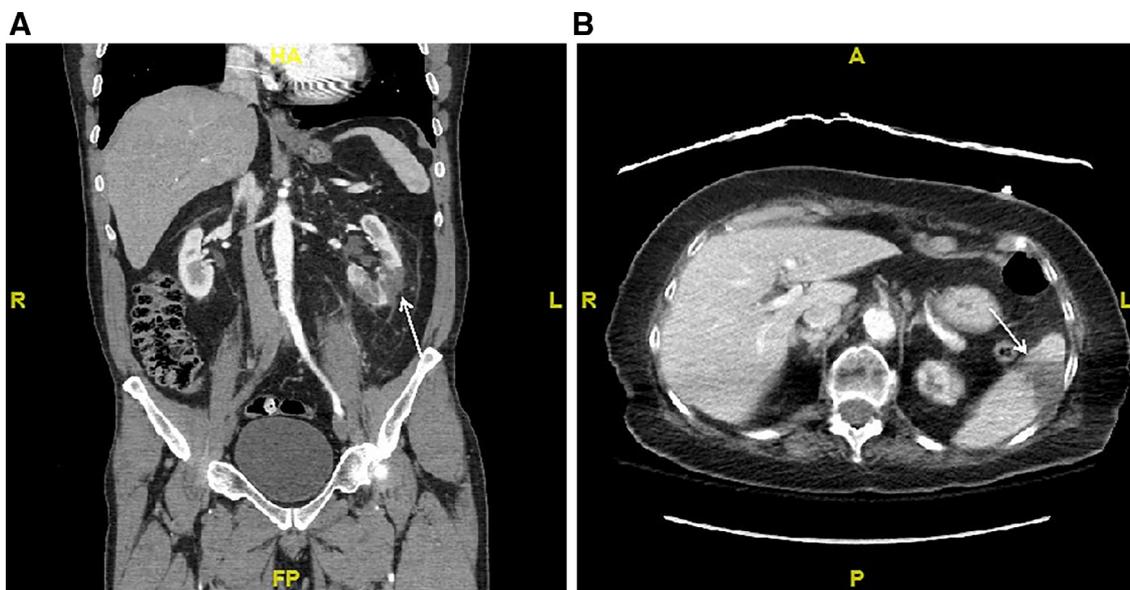


Figure 1. Computerized tomography scans of the abdomen of 2 patients with visceral infarcts (A). Left kidney infarct (white arrow). (B) Splenic infarct (white arrow).

genitourinary symptoms (n = 11, 4.3%), vascular evaluation (n = 9, 3.5%), and other (n = 10, 3.9%). The baseline characteristics between patients with and without a qualifying CT were similar (Table 1).

Serum troponin level on admission was measured in 237 of 259 patients (93.3%) and 41 of 237 (17.3%) had positive troponin. There were 25 patients with visceral infarcts: 16 renal, 7 splenic, and 2 both (Fig 1).

On univariate analysis, patients with a positive troponin level were more likely to have visceral infarcts (39.1% [9/23] versus 15.0% [32/214], P = .008; Table 2).

Association between Positive Troponin and Visceral Infarcts

In an unadjusted model, there was an association between positive troponin and visceral infarct (odds ratio

3.65, 95% confidence intervals 1.46-9.17, P = .006). After adjusting for potential confounders including atrial fibrillation, this association persisted (model 2; odds ratio 3.83, 95% confidence intervals 1.42-10.31, P = .008; Table 3).

Discussion

In this study, we show an association between a positive troponin level at the time of ischemic stroke and the presence of visceral infarcts, and this association persisted after adjusting for potential confounders.

Would include para here about what else is in literature on this or related topics (troponin in stroke, visceral infarcts in stroke) before getting into mechanism

There are several reasons that could possibly explain this association. First, serum troponin level is a biomarker of cardiac disease,² and therefore patients with elevated

Table 2. Baseline characteristics of patients with and without visceral infarcts

	Visceral infarct (n = 25)	No visceral infarct (n = 234)	P value
Age (mean \pm SD)	72.0 \pm 16.4	73.1 \pm 13.8	.705
Sex (% men)	14 (56.0%)	135 (57.7%)	1.000
Hypertension (%)	22 (88.0%)	195 (83.3%)	.776
Diabetes (%)	6 (24.0%)	65 (27.8%)	.816
Hyperlipidemia (%)	14 (56.0%)	122 (52.1%)	.834
Prior stroke (%)	9 (36.0%)	60 (25.6%)	.340
Atrial fibrillation (%)	13 (52.0%)	85 (36.3%)	.134
Congestive heart failure (%)	4 (16.0%)	37 (15.8%)	1.000
Coronary heart disease (%)	5 (20.0%)	65 (27.8%)	.485
Active smoking (%)	6 (24.0%)	48 (20.5%)	.615
NIHSS score (mean \pm SD)	13 \pm 9	11 \pm 9	.222
Positive troponin (%)	9/23 (39.1%)	32/214 (15.0%)	.008

Table 3. Multivariable models showing association between positive serum troponin level and visceral infarcts

	Odds ratio	95% Confidence interval	P value
Unadjusted	3.65	1.46-9.17	.006
Model 1	4.00	1.56-10.31	.004
Model 2	3.83	1.42-10.31	.008

Model 1: adjusted for age and sex; model 2: adjusted for age, sex, hypertension, diabetes, hyperlipidemia, coronary heart disease, congestive heart failure, atrial fibrillation, and smoking.

serum troponin levels may be at heightened risk for cardiac thrombi and embolism to the brain or viscera which is not uncommon in patients at risk for cardioembolism. For instance, one study showed that in patients with atrial fibrillation, nearly 12% of clinical thromboembolic events were classified as systemic embolism, out of which nearly 30% involved the viscera.⁶ Second, as previous studies suggested, troponin positivity in the setting of an acute stroke is associated with cardioembolic subtypes³ and therefore patients with a positive troponin are at risk of recurrent cardioembolic stroke that can involve the viscera. Third, it is also possible that cardiac troponin is a marker of systemic vascular disease and therefore patients with positive troponin level may be more likely to have systemic atherosclerosis and visceral infarcts. This is less likely since the association between troponin positivity and visceral infarcts persisted even after adjusting for a wide range of vascular risk factors. We cannot exclude residual confounding, however.

In addition, this study has clinical implications. The association between serum troponin positivity and visceral infarcts suggests that in patients with ischemic stroke, a positive troponin level may help identify a subgroup of patients at risk for developing visceral infarcts. This may be particularly useful in patients with cryptogenic stroke and positive admission troponin level in whom anticoagulation can be tested against antiplatelet therapy to reduce the risk of recurrent embolism. In fact, a post hoc analysis of the Warfarin Aspirin Stroke Study

showed that N-terminal pro b-type natriuretic peptide in the acute stroke setting may be useful to select patients with ischemic stroke who may benefit from anticoagulation.⁷ The ongoing ARCADIA trial is testing apixaban versus aspirin in patients with cryptogenic stroke and evidence of atrial cardiopathy⁸ (NCT03192215) and may provide further evidence on the role of anticoagulation for secondary stroke prevention in patients with cryptogenic stroke and elevated troponin concentrations.

Our study has several limitations including its retrospective nature and being single center therefore limiting generalizability. Furthermore, although patients with and without a CT abdomen and pelvis available shared similar baseline characteristics, less than one fourth of patients had abdomen and pelvis CT available, which may have introduced selection bias. In addition, the quality of a small proportion of CT scans may have precluded the reviewing physician from detecting visceral infarcts. Moreover, we did not account for infarcts involving other visceral organs such as the intestine. On the other hand, our study has several strengths including the prospective nature of our registry, a relatively large number of patients with admission troponin level available, and visceral infarcts adjudicated by a blinded reader.

Conclusions

In ischemic stroke patients, elevated serum troponin levels may help identify patients with visceral infarcts.

This suggests that troponin in the acute stroke setting is a biomarker of embolic risk. Larger studies with systematic visceral imaging are needed to confirm our findings and to test anticoagulation in patients with cryptogenic stroke and positive admission troponin level.

Supplementary Materials

Supplementary data to this article can be found online at doi:[10.1016/j.jstrokecerebrovasdis.2019.01.004](https://doi.org/10.1016/j.jstrokecerebrovasdis.2019.01.004).

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