NEUROGENIC STUNNED MYOCARDIUM IN ACUTE ISCHEMIC STROKE

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Background and purpose – Neurogenic myocardial injury occurs as a result of dysregulation of autonomic nervous system. The aim of this study was to explore the frequency of elevated troponin and dynamic ST segment/T wave changes and their relation with left ventricular (LV) systolic functions in acute ischemic stroke patients.
Methods – One hundred and twenty-five patients (mean age: 65.1±15.2years, 76 male) presenting with acute ischemic stroke were consecutively included. 12-lead electrocardiogram was taken to assess dynamic ST segment/T wave changes, conventional transthoracic echocardiography to determine LV ejection fraction (LVEF). High-sensitive cardiac troponin I (hs-cTnI) level>0.04ng/mL was accepted as elevated.
Results – Twenty-seven patients (21.6%) had elevated hs-cTnI and 60 patients (48%) had dynamic ST segment/T wave changes. The stroke patients with elevated hs-cTnI had significantly higher NT-proBNP values (2302±3450pg/mL vs 799±2075pg/mL p<0.001) and higher frequency of ST segment/T wave changes (85.2% vs 37.8% p<0.001), and lower LVEF (52.2±13.6% vs 61.0±8.5% p=0.002) compared to patients with normal troponin levels. The patients with ST segment/T wave changes had significantly higher frequencies of hyperlipidemia (31.7% vs 15.4% p=0.031) and coronary artery disease (CAD) (43.3% vs 13.8% p<0.001), hs-cTnI (0.19±0.55ng/mL vs 0.02±0.01ng/mL p<0.001) and NT-proBNP levels (1430±2564pg/mL vs 842±2425pg/mL p=0.016), and lower LVEF (56.1±11.7% vs 61.9±8.3% p=0.009). Linear regression analysis revealed presence of CAD, but not ST segment/T wave changes as an independent predictor of hs-cTnI (p=0.034). LVEF was independently associated with hs-cTnI (p=0.003) and presence of CAD (p=0.009) when adjusted by age, sex and presence of ST segment/T wave changes.

NEUROGÉN SZÍVIZOMBÉNULÁS AKUT ISCHAEMIÁS STROKE-BAN

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Háttér és cél – A neurogén szívizombénulás az autonóm idegrendszer diszregulációjának eredményeképpen alakul ki. A jelen vizsgálat célja az volt, hogy feltárja az emelkedett troponinszint és a dinamikus ST-szakasz/T-hullám változások gyakoriságát és ezek összefüggését a bal kamrai szisztolés funkcióval akut ischaemiás stroke-ban szenvedő betegek körében.
Módszerek – Százhuszonöt akut ischaemiás stroke-kal felvett beteget (átlagos életkor: 65,1 ± 15,2 év, n = 76 férfi) vontunk be a vizsgálatba. 12 elvezetéses elektrokardiogrammal értékeltük a dinamikus ST-szakasz/T-hullám változásokat, és konvencionális transthoracalis szívultrahang-vizsgálattal határoztuk meg a bal kamrai ejekciós frakciót (LVEF). A nagy érzékenységű cardialis troponin I (hs-cTnI) szintjét akkor értékeltük emelkedettnek, ha meghaladta a 0,04 ng/ml értéket.
Eredmények – Huszonhét betegnek (21,6%) volt emelkedett hs-cTnI-szintje, és 60 betegnél (48%) figyeltünk meg dinamikus ST-szakasz/T-hullám változásokat. A normál troponinszintű betegekkel összehasonlítva, az emelkedett hs-cTnI-szintű stroke-betegek esetén szignifikánsan magasabbak voltak az NT-proBNP-értékek (2302 ± 3450 pg/ml vs 799 ± 2075 pg/ml; p<0,001) és nagyobb gyakorisággal fordult elő ST-szakasz/T-hullám változás (85,2% vs. 37,8%; p<0,001), továbbá alacsonyabb volt körükben az LVEF (52,2 ± 13,6% vs. 61,0 ± 8,5% p = 0,002). Az ST-szakasz/T-hullám változással rendelkező betegek körében szignifikánsan gyakrabban fordult elő hyperlipidaemia (31,7% vs. 15,4%; p = 0,031) és koszorúér-betegség (CAD) (43,3% vs. 13,8%; p<0,001), emelkedett hs-cTnI-szint (0,19 ± 0,55 ng/ml vs. 0,02 ± 0,01 ng/ml; p<0,001) és emelkedett NT-proBNP-érték (1430 ± 2564 pg/ml vs. 842 ± 2425 pg/ml; p = 0,016), valamint alacsonyabb LVEF-érték (56,1 ± 11,7% vs. 61,9 ± 8,3%; p = 0,009). A lineárisregresszió-analízis azt

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Conclusion – Troponin elevation and ST segment/T wave changes occurring in patients suffering acute ischemic stroke, especially in those with CAD, may be a sign of neurogenic stunned myocardium.

Keywords: *acute ischemic stroke, myocardial stunning, neurogenic cardiac injury, troponin*

mutatta, hogy a CAD jelenléte a hs-cTnI-szint független prediktora (p = 0,034), az ST-szakasz/T-hullám változás azonban nem. Az életkor, a nem és az ST-szakasz/T-hullám változás illesztése után az LVEF a hs-cTnI (p = 0,003) és a CAD (p = 0,009) független változójának bizonyult.
Következtetés – Az akut ischaemiás stroke-ban szenvedő betegnél, különösen CAD esetén, a troponinszint-növekedés és az ST-szakasz/T-hullám változások neurogén szívizombénulás jelei lehetnek.

Kulcsszavak: *akut ischaemiás stroke, szívizombénulás, neurogén szívizombénulás, troponin*

Stroke is the fifth leading cause of death and the first leading cause of disability[1]. There are two main types of strokes, namely ischemic stroke and hemorrhagic stroke. Ischemic stroke, accounting for 85% of all acute strokes, develops as a result of thrombotic or embolic event that causes partial or complete obstruction of cerebral blood flow and is classified into four groups as large vessel atherosclerosis, small vessel diseases (lacunar infarcts), cardioembolic strokes and cryptogenic strokes according to the TOAST classification[2].

Neurogenic stunned myocardium (NSM) is a new definition of cardiac injury occurring after various types of central neurological system disorders, at which cardiac complications such as arrhythmias, ventricular dysfunction, myocardial infarction and sudden death were seen[3, 4]. It is accepted as subgroup of the stress-related cardiomyopathies such as acute left ventricular failure in the critically ill, pheochromocytoma and exogenous catecholamine administration according to previous studies[5]. NSM met the criteria of myocardial infarction such as electrocardiography (ECG) changes, decreased left ventricular (LV) ejection fraction (LVEF), high troponin levels and transient regional wall motion abnormalities extending beyond a single epicardial vascular distribution[6, 7].

The majority of data of NSM comes from subarachnoid hemorrhage subgroup of stroke. Diastolic dysfunction was seen more frequently with a prevalence of 71% while a depressed LVEF (<50%) was detected in 15% of the patients suffering acute subarachnoid hemorrhage[8, 9]. On the contrary, little is known about NSM developed after acute ischemic stroke[10].

The aim of this study was to explore the frequency of elevated troponin and dynamic ST segment or T wave changes and their relation with left ventricular systolic functions in acute ischemic stroke patients.

Methods

The investigation conformed to the principles outlined in the Declaration of Helsinki. The study was approved by local ethics committee. All participants gave written informed consent.

One hundred and fifty consecutive patients aged ≥18 years admitted with acute ischemic stroke documented by neuroimaging were invited to participate in the study. TOAST classification system was used to define the stroke subtypes. After the exclusion of patients with cancer (9 patients), dementia (5 patients), hemodynamically unstable or disabling stroke (9 patients) and pregnancy (2 patients), the remaining 125 patients with large-artery atherosclerosis (84 patients), small-vessel occlusion (21 patients) and cardioembolic stroke (20 patients) were included. National Institutes of Health stroke scale (NIHSS) scores of the patients were calculated during neurologic assessment,

All patients underwent a complete cardiac evaluation including patient history, physical examination, and standard 12-lead electrocardiography (ECG). Dynamic ST segment changes and T wave abnormalities were determined by checking both the previous ECGs of the patients and ECGs taken during the hospital stay. Patients were evaluated for the presence of cardiovascular risk factors, including hypertension, hyperlipidemia, diabetes, renal dysfunction, and smoking status. Patients who had do-

cumented ischemia in noninvasive stress tests or coronary stenosis ≥50% in at least one of their coronary arteries were accepted as having coronary artery disease (CAD). Blood samples for plasma glucose, high sensitive (hs) C-reactive protein (CRP), hs-cardiac troponin I (hs-cTnI), creatine kinase-MB (CK-MB), N-terminal pro-brain natriuretic peptide (NT-proBNP), creatinine, and hemoglobin levels were noted and repeated as necessary with the highest measure taken into statistical analysis. troponin I tests were repeated when the initial hs-cTnI was elevated or dynamic ST segment/T wave abnormality was noticed. troponin I and NT-proBNP levels were also compared with the available previous laboratory data. Serum troponin I levels was analysed by the Siemens ADVIA Centaur hs-cTnI assay (Siemens Healthcare Diagnostics, Deerfield, IL, USA) and a hs-cTnI >0.04ng/mL was accepted as elevated in our laboratory.

Framingham risk score (FRS) and 10-year risk of myocardial infarction and cardiac death were calculated for each patient[11]. Risk was defined as low (<10%), intermediate (10-20%) or high (>20%) according to FRS.

All patients underwent a transthoracic echocardiographic study by a Philips iE33 echocardiography device (Philips Medical Systems, Andover, MA, USA) by an experienced cardiologist within the first three days following acute ischemic stroke. Conventional echocardiographic measurements were performed in accordance with the recommendations of the American Society of Echocardiography guidelines[12]. LVEF was assessed by biplane Simpson's method. The regional wall motion abnormalities and LVEF were compared with the available previous echocardiographic examinations in patients with CAD.

Carotid artery intima-media thickness (CIMT) and presence of plaque in carotid arteries were evaluated by carotid ultrasonography by a blinded cardiologist via a commercially available Vivid 7 (GE Healthcare, Horten, Norway) ultrasound system with a 10-MHz linear transducer. Each subject was examined in the supine position in a semi-dark room. The carotid artery was investigated bilaterally and scanned at the level of the bifurcation of common carotid arteries. The image was focused on the far wall of the artery. CIMT was measured on the longitudinal views of the far wall of bilateral distal common carotid arteries (1–3 cm proximal to the carotid bifurcation) at the diastolic phase. CIMT was taken as the distance from the leading edge of first echogenic line to the leading edge of second echogenic line and expressed as the mean of six measurements (three on each side)[13]. Plaque was defined as an intima-media thickness ≥1.5mm measured from media-adventitia interface to intima-lumen interface or a focal structure protruding into arterial lumen ≥0.5mm or 50% of the adjacent intima-media thickness[14].

STATISTICAL ANALYSIS

Statistical analyses were performed by statistical software (SPSS 11.0 for windows, Chicago, IL). Distribution of data was assessed by using one-sample Kolmogorov–Smirnov test. Continuous data were expressed as mean ± SD, while categorical data were presented as number of patients. Chi-squared test was used for comparison of categorical variables, while Student's t test was used to compare the normally distributed continuous variables and Mann-Whitney U test was used to compare the nonparametric continuous variables. Linear regression analyses were modelled in order to explore the independent predictors of hs-cTnI and LVEF. A p-value of <0.05 was considered as statistically significant.

Results

One hundred and twenty-five ischemic stroke patients with large-artery atherosclerosis (84 patients), small-vessel occlusion (21 patients) and cardioembolic stroke (20 patients) were included in the study. The mean age of the patients was 65.1 ± 15.2 years and 76 patients were male. Thirty five patients (28%) had CAD and based on the previous echocardiographic and laboratory data, only 3 patients with CAD had regional wall motion abnormality with a LVEF of 45-50% and slightly elevated NT-BNP levels (<500pg/mL) with normal troponin I levels.

Twenty-seven of the patients (21.6%) had elevated hs-cTnI. The general characteristics and laboratory parameters of the patients according to hs-cTnI levels are shown in **Table 1**. Although there were not any significant differences in the general characteristics and NIHSS scores of the patients, the stroke patients with elevated hs-cTnI had significantly higher NT-proBNP and higher frequency of ST segment/T wave changes compared to those with normal hs-cTnI.

Conventional transthoracic echocardiographic and carotid artery ultrasonographic measures of the patients according to hs-cTnI levels are shown in **Table 2**. Stroke patients with elevated hs-cTnI had significantly larger LV and lower LVEF compared to patients with normal hs-cTnI. There was

Table 1. *The general characteristics and laboratory parameters of the patients according to high sensitive cardiac troponin I levels*

	Stroke patients with elevated troponin (n=27)	Stroke patients with normal troponin (n=98)	p
Age (years)	68.7 ± 12.4	64.2 ± 15.8	0.174
Male sex (n – %)	17 (63.0%)	59 (60.2%)	0.795
Hypertension (n – %)	20 (74.1%)	66 (67.3%)	0.504
Diabetes (n – %)	12 (44.4%)	42 (42.9%)	0.883
Hyperlipidemia (n – %)	8 (29.6%)	21 (21.4%)	0.371
Coronary artery disease (n – %)	11 (40.7%)	24 (24.5%)	0.096
Chronic kidney failure (n – %)	5 (18.5%)	9 (9.2%)	0.181
Framingham Risk Score (%)	23.0 ± 8.4	21.2 ± 9.6	0.391
Framingham Risk Score >20% (n–%)	18 (66.7%)	62 (63.3%)	0.744
NIHSS scores	6.1 ± 2.0	5.5 ± 2.7	0.119
Glucose (mg/dL)	130 ± 69	124 ± 56	0.876
Creatinine (mg/dL)	1.18 ± 0.63	0.96 ± 0.52	0.068
Total cholesterol (mg/dL)	197 ± 52	205 ± 50	0.466
LDL cholesterol (mg/dL)	124 ± 48	132 ± 42	0.409
HDL cholesterol (mg/dL)	40 ± 9	43 ± 10	0.171
Triglyceride (mg/dL)	152 ± 45	164 ± 87	0.926
Hemoglobin (g/dL)	13.1 ± 2.2	13.0 ± 1.8	0.851
hs-cTnI (ng/mL)	0.41 ± 0.76	0.02 ± 0.01	*<0.001*
hs-CRP (mg/L)	22.9 ± 29.0	20.3 ± 26.9	0.235
NT-proBNP (pg/mL)	2302 ± 3450	799 ± 2075	*<0.001*
ST segment/T wave changes (n–%)	23 (85.2%)	37 (37.8%)	*<0.001*

NIHSS: National Institutes of Health stroke scale, LDL: Low density lipoprotein, HDL: High density lipoprotein, hs-cTnI: high sensitive cardiac troponin I, hs-CRP: High sensitive C reactive protein, NT-proBNP: N terminal pro-brain natriuretic peptide

not any significant difference in CIMT between the groups.

Sixty of the patients (48%) had dynamic ST segment (ST segment elevation in 6 patients and ST segment depression in 27 patients) and T wave changes (T wave inversion in 58 patients). The general characteristics, laboratory parameters and conventional transthoracic echocardiographic measures of the patients according to ST segment/T wave changes are shown in **Table 3**. The patients

Table 2. *Conventional transthoracic echocardiographic and carotid artery ultrasonographic measures of the patients according to hs-cTnI levels*

	Stroke patients with elevated troponin (n=27)	Stroke patients with normal troponin (n=98)	p
Left atrium (mm)	40.0 ± 5.3	38.1 ± 5.1	0.091
LVEDD (mm)	49.9 ± 7.3	46.3 ± 5.8	*0.024*
LVESD (mm)	35.0 ± 8.7	30.7 ± 5.9	*0.011*
IVS (mm)	13.0 ± 2.6	12.3 ± 1.6	0.621
PW (mm)	10.9 ± 1.2	10.3 ± 1.4	*0.024*
LVEF (%)	52.2 ± 13.6	61.0 ± 8.5	*0.002*
Mitral E velocity	0.61 ± 0.18	0.59 ± 0.18	0.622
Mitral A velocity	0.77 ± 0.25	0.80 ± 0.18	0.524
Deceleration time (ms)	168 ± 39	179 ± 27	0.186
Mitral lateral annular e' velocity (cm/s)	7.2 ± 3.2	7.5 ± 2.7	0.445
E/e'	9.7 ± 4.4	8.6 ± 3.1	0.195
CIMT (mm)	0.97 ± 0.16	0.93 ± 0.24	0.184
Carotid plaque (n – %)	19 (70.4%)	55 (56.1%)	0.182

hs-cTnI: high sensitive cardiac troponin I, LVEDD: Left ventricular end-diastolic diameter, LVESD: Left ventricular end-systolic diameter, IVS: interventricular septum thickness, PW: posterior wall thickness, LVEF: left ventricular ejection fraction, CIMT: carotid artery intima media thickness

Table 3. *The general characteristics, laboratory parameters and conventional transthoracic echocardiographic measures of the patients according to ST segment/T wave changes*

	Stroke patients with ST segment/ T wave changes (n=60)	Stroke patients without ST segment/ T wave changes (n=65)	p
Age (years)	67.2 ± 12.8	63.3 ± 17.0	0.193
Male sex (n – %)	39 (65.0%)	37 (56.9%)	0.355
Hypertension (n – %)	46 (76.7%)	40 (61.5%)	0.068
Diabetes (n – %)	28 (46.7%)	26 (40.0%)	0.452
Hyperlipidemia (n – %)	19 (31.7%)	10 (15.4%)	*0.031*
Coronary artery disease (n–%)	26 (43.3%)	9 (13.8%)	*<0.001*
NIHSS scores	5.5 ± 2.4	5.7 ± 2.8	0.765
Glucose (mg/dL)	126 ± 60	125 ± 59	0.876
Creatinine (mg/dL)	1.03 ± 0.52	0.99 ± 0.58	0.612
Total cholesterol (mg/dL)	213 ± 50	194 ± 49	*0.015*
LDL cholesterol (mg/dL)	139 ± 43	123 ± 43	*0.010*
HDL cholesterol (mg/dL)	42 ± 9	42 ± 10	0.947
Triglyceride (mg/dL)	164 ± 70	160 ± 88	0.379
Hemoglobin (g/dL)	13.4 ± 1.9	12.8 ± 1.8	0.078
hs-cTnI (ng/mL)	0.19 ± 0.55	0.02 ± 0.01	*<0.001*
Elevated hs-cTnI (n-%)	23 (38.3%)	4 (6.2%)	*<0.001*
hs-CRP (mg/L)	23.6 ± 29.6	18.4 ± 24.9	0.070
NT-proBNP (pg/mL)	1430 ± 2564	842 ± 2425	*0.016*
Left atrium (mm)	39.0 ± 5.0	38.0 ± 5.4	0.257
LVEDD (mm)	48.7 ± 5.9	45.6 ± 6.3	*0.001*
LVESD (mm)	33.5 ± 6.9	29.9 ± 6.3	*<0.001*
IVS (mm)	12.8 ± 2.0	12.1 ± 1.6	0.072
PW (mm)	10.5 ± 1.5	10.3 ± 1.3	0.119
LVEF (%)	56.1 ± 11.7	61.9 ± 8.3	*0.009*
E/e'	9.3 ± 3.7	8.4 ± 3.1	0.177
CIMT (mm)	0.97 ± 0.18	0.90 ± 0.26	*0.020*
Carotid plaque (n – %)	42 (70.0%)	32 (49.2%)	*0.018*

NIHSS: National Institutes of Health stroke scale, LDL: Low density lipoprotein, HDL: High density lipoprotein, hs-cTnI: high sensitive cardiac troponin I, hs-CRP: High sensitive C reactive protein, NT-proBNP: N terminal pro-brain natriuretic peptide, LVEDD: Left ventricular end-diastolic diameter, LVESD: Left ventricular end-systolic diameter, IVS: interventricular septum thickness, PW: posterior wall thickness, LVEF: left ventricular ejection fraction, CIMT: carotid artery intima media thickness

with dynamic ST segment/T wave changes had significantly higher frequencies of hyperlipidemia and CAD, higher total cholesterol, LDL cholesterol, hs-cTnI and NT-proBNP levels compared to those without ST segment/T wave changes. They had also larger LV with lower LVEF and higher CIMT with higher frequencies of carotid plaque.

Linear regression analysis was modelled in order to explore the independent predictors of hs-cTnI (**Table 4**). Presence of CAD, but not ST segment/T wave changes was found as an independent predictor of hs-cTnI when adjusted by age and sex. LVEF was significantly correlated with hs-cTnI (r= -0.367, p<0.001) and NIHSS scores (r= -0.211, p= 0.019). Linear regression analysis revealed that LVEF was independently associated with hs-cTnI and presence of CAD when adjusted by age, sex and presence of ST segment/T wave changes (**Table 5**).

Discussion

Several case series have reported NSM with an incidence of 8–30% in subarachnoid hemorrhage and 1.2% in ischemic stroke[15, 16]. It is a reversible, neurologically mediated cardiac injury characterizes with high troponin levels, new ECG changes, and wall motion abnormalities with a decrease in LVEF. In our study, we explored the frequency of troponin elevation and dynamic ST segment/T wave changes and their relation with LVEF; all of which might be a sign of NSM in acute ischemic stroke patients.

We found that 21.6% of the patients had elevated hs-cTnI, while 48% had dynamic ST segment/T wave changes. Similar to our study, troponin levels are elevated in about one fifth of ischemic stroke patients on admission with a relatively less frequency in ischemic stroke patients without overt ischemic heart

Table 4. *Linear regression analysis models to explore the independent predictors of hs-cTnI*

	Beta	t	p	95% confidence interval
Model 1 (Adjusted R^2: 0.048 p=0.029)				
ST segment/T wave changes	0.206	2.329	*0.022*	0.024 – 0.294
Age	0.047	0.535	0.594	-0.003 – 0.006
Male sex	0.136	1.543	0.125	-0.030 – 0.244
Model 2 (Adjusted R^2: 0.076 p=0.009)				
ST segment/T wave changes	0.142	1.538	0.127	-0.031 – 0.250
Age	0.057	0.650	0.517	-0.003 – 0.006
Male sex	0.114	1.300	0.196	-0.047 – 0.226
Coronary artery disease	0.198	2.150	*0.034*	0.013 – 0.326

hs-cTnI: high sensitive cardiac troponin I

Table 5. *Linear regression analysis models to explore the independent predictors of LVEF*

	Beta	t	p	95% confidence interval
Model 1 (Adjusted R^2: 0.172 p<0.001)				
hs-cTnI	-0.298	-3.515	*0.001*	-12.563 – -3.510
ST segment/T wave changes	-0.193	-2.282	*0.024*	-7.474 – -0.530
Age	-0.064	-0.777	0.439	-0.156 – 0.068
Male sex	-0.135	-1.623	0.107	-6.350 – 0.629
Model 2 (Adjusted R^2: 0.211 p<0.001)				
hs-cTnI	-0.255	-3.025	*0.003*	-11.382 – -2.377
ST segment/T wave changes	-0.127	-1.477	0.142	-6.180 – 0.899
Age	-0.077	-0.955	0.342	-0.163 – 0.057
Male sex	-0.115	-1.411	0.161	-5.858 – 0.984
Coronary artery disease	-0.229	-2.641	*0.009*	-9.258 – -1.325

LVEF: left ventricular ejection fraction, hs-cTnI: high sensitive cardiac troponin I

disease[17–20]. Abnormal ECG findings including prolonged QT interval, T-wave inversions and ST-depression can be observed in 60–90% of the stroke patients[21, 22]. *Murthy* et al.[10] noted T-wave inversions and ST-segment elevations in 84.6% and 69.2% of the patients after acute non-hemorrhagic stroke.

Ischemic stroke patients with elevated troponin values were reported to exhibit a significantly increased rate of hypertension, history of stroke, history of CAD, history of myocardial infarction, heart failure and atrial fibrillation[17]. In our study, there were no significant differences in atherosclerotic risk factors and history of CAD between patients with elevated hs-cTnI and those with normal hs-cTnI. However, the patients with dynamic ST segment/T wave changes had significantly higher frequencies of hyperlipidemia, CAD and carotid plaque with higher CIMT.

There are many factors that are independently related to increased troponins in stroke patients. These include age, previous CAD, congestive heart failure, diabetes, hypercholesterolemia, chronic kidney disease and insular involvement[21]. A recent study showed that ST segment depression and negative T waves on baseline ECG were associated with hsTnT elevation[19]. In our study, the patients with ST segment/T wave changes had significantly higher hs-cTnI. However; multivariate analysis showed that presence of CAD, but not ST segment/T wave changes as an independent predictor of hs-cTnI when adjusted by age and sex.

In our study, both the patients with elevated hs-cTnI and the patients with ST segment/T wave changes had significantly higher NT-proBNP and lower LVEF. The LVEF of the patients in our study were not as low as could be expected in patients with subarachnoid hemorrhage. Maximum hs-cTnI elevation was shown to be lower in ischemic stroke patients with NSM compared to patients with subarachnoid hemorrhage, which suggested milder myocardial injury and relatively higher LVEF in these patients[10]. We found a significant relation between LVEF and hs-cTnI, which persisted when adjusted by age, sex and presence of ST segment/T wave changes. *Darki* et al.[18] also showed a signifi-

cant association between troponin and brain natriuretic peptide elevation with segmental wall motion abnormality on echocardiogram.

While the pathophysiological mechanism of NSM is still unclear, the most widely accepted theory is metabolic myocardial stunning due to the cardiotoxic effects of high levels of circulating plasma catecholamines in relation to the affected cerebral area[23]. The differential diagnosis of NSM should include acute coronary syndrome (ACS) in most of the cases and no specific factor including troponin elevation and dynamic ECG changes have been found to be helpful to differentiate NSM and ACS in the clinical setting[19]. The observed segmental patterns of LV dysfunction often do not correlate with coronary artery distributions; which may be helpful in differential diagnosis[24]. It is also important to differentiate from type I ST segment elevation myocardial infarction, especially if the patient had ST segment elevation in the ECGs. Acute rise/fall pattern of an elevated troponin and demonstration of regional wall motion abnormalities compatible with the localization of ST segment elevations may help to differentiate from ST segment elevation myocardial infarction.

The most prominent feature of NSM is the reversibility of LV dysfunction, usually within two weeks, if the underlying acute neurological condition improves. Two studies showed 15-18% of the patients had depressed ejection fraction (<50-55%) with wall motion abnormalities in 13-15% of the patients and LV function was recovered in 66% of them[9, 25]. We did not repeat the echocardiography and did not evaluate the recovery of the LV functions in our study, which was a limitation. *Ermis* et al.[26] evaluated myocardial function in the early stages of acute ischemic stroke and they found an LVEF of 53.2%, similar to our study, which increased to 55.8% after 10 days. They also assessed the LV functions with "Speckle tracking" echocardiography and detected a more profound improvement.

Diastolic function is more sensitive to myocardial pathologies than the indicators of systolic function. Echocardiography shows both an impaired LV systolic and diastolic function in patients with NSM[27]. In our study, although the mitral lateral annular e' velocity was lower and E/e' ratio was higher in patients with elevated troponin and in patients with ST segment/T wave changes, the differences were not statistically significant, which might be because of the presence of comorbidities such as hypertension and diabetes in both groups which affect diastolic functions.

Stroke severity and location may be associated with NSM. *Wira* et al.[28] showed that patients with an NIHSS greater than 10 had higher rates of in-hospital mortality, serum troponin elevation, and ischemic changes on ECG compared to those with an NIHSS of 10 or less with a trend toward a higher rate of systolic dysfunction among patients with more severe strokes. Ermis et al.[26] evaluated the effects of NIHSS score changes with time on cardiac function and found that during the period in which NIHSS values improved, there were a slight but nonsignificant improvement in LVEF, and a significant improvement in strain variables with a significant negative correlation between NIHSS scores and LV global longitudinal strain values. In our study, patients with elevated troponin or patients with ST segment/T wave changes had similar NIHSS scores compared to those without troponin elevation or ST segment/T wave changes. However, there was a weak correlation between NIHSS scores and LVEF.

STUDY LIMITATIONS

The major limitations of our study were the small sample size and that the study was a single-center one. We did not repeat transthoracic echocardiography and did not evaluate reversibility of LV dysfunction or its relation with hs-cTnI and ECG in following of these patients. Furthermore, we did not evaluate LV functions by "Speckle Tracking" echocardiography, which is superior to conventional echocardiography in assessing subclinical LV dysfunction. Finally, coronary angiography was not performed and the diagnosis of ACS might be underestimated.

Conclusion

Troponin levels may be elevated and ST segment/T wave changes may develop in acute ischemic stroke, which may accompany LV wall motion abnormalities and decrease in LVEF. These may be a sign of neurogenic stunned myocardium and may be more prominent in patients with concomitant CAD.

DECLARATIONS OF INTEREST
None.

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