

## Troponin Serum Level in Ischemic Stroke Patients and its Prognostic Value

Farhad Iranmanesh, M.D.<sup>1</sup>, Akbar Hamzei-Moghadam, M.D.<sup>2</sup>, Mahbobeh Dehghan, M.D.<sup>3</sup>

1- Professor of Neurology, Stroke fellowship, Neurology Research Center, Kerman, Iran (Corresponding author; E-mail: fpp\_farhad@yahoo.com)

2- Professor of Neurology, Neurology Research Center, Kerman, Iran

3- Neurologist, Neurology Research Center, Kerman, Iran

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### Abstract

**Background:** Some recent studies have shown that troponin may have a Prognostic value in patients with ischemic stroke. This study seeks to evaluate the prognostic value of troponin on 3 months mortality and recurrence in patients with ischemic stroke.

**Method:** In this study 63 patients with ischemic stroke were evaluated. Embolic and lacunar stroke were excluded from the study. In the first 24 hours, serum troponin levels were measured. Patients were evaluated for a three-month period in terms of death and recurrence of stroke, and the results were analyzed using independent t-test and logistic regression.

**Results:** In this study, 32 (50.8%) were male and the rest were female. Of the 63 patients studied, 8 (12.7%) had an abnormal troponin level. The mean serum level of troponin in patients who had died was 75.52 and patients who did not die was 38.2. This difference was statistically significant ( $p = 0.013$ ). However, in the regression analysis, this result was not significant. Age ( $P=0.04$ ) and NIHSS ( $P = 0.001$ ) had a meaningful relationship with mortality. Of the 53 patients who were discharged, 5 (9.4%) had recurrence after 3 months. The mean serum level of troponin in patients with recurrence was  $43.36 \pm 55.23$  and mean serum troponin level in patients who did not relapse was  $40.52 \pm 93.20$ . This difference was statistically significant ( $p = 0.54$ ).

**Conclusion:** Troponin has no prognostic value on three months mortality and recurrence rate in ischemic stroke patients.

### Introduction

Stroke is the second leading cause of death in the world and one of the most important causes of disability in developing countries (1). Stroke can be divided into two categories: Hemorrhagic and ischemic infarction (2). Ischemic stroke is the most common type of cerebrovascular accident and, based on TOAST calcification, is divided into 5 subcategories: 1) large vessel atherosclerosis; 2) Cardioembolism; 3) Small vessels occlusion; 4) stroke of other determined etiology and 5) stroke of undetermined etiology (3). Twenty five percent of ischemic strokes are cardioembolic and recent MI, AF, mechanical valve

and mitral stenosis are the most common cardiac disorders (1,3,4). Symptomatic and asymptomatic ischemic heart diseases are reported in about 40% of ischemic stroke patients (5). It is necessary to find a simple, easy, accessible and non-invasive method to determine prognosis and help selecting high-risk individuals so as to provide appropriate therapeutic measures. Troponin is a high-molecular-weight protein which is found specifically in muscle tissues. Troponin is found in three subunits I, T, C, and is produced by various genes. Subunit I attaches to F-actin, subunit C connects with calcium ions, and subunit T attaches to thropomyosin. Troponin is the

gold standard method for acute coronary ischemia diagnosis (6). Some recent studies have shown that ischemic stroke is associated with change in troponin serum level. For example, in a study by Su et al., on 871 patients with ischemic stroke, it was found that 146 patients had high troponin serum level and these patients were older than the others and had higher HR, WBC, NIHSS, MRS and Cr and lower Hb and HCT. It was also concluded that the high level of troponin during acute stroke is a predictive and independent factor for poor prognosis and hospital mortality (5). In a study conducted by Lasek et al., troponin serum level was found to be high in 10% of ischemic stroke patients, with a marked disability and lower independency in their daily function (7). In 2015, another study was conducted by Thalini et al., They wanted to determine the 5-year mortality rate of patients with acute stroke. Out of 218 patients, 85 had high troponin level which showed that high troponin is associated with double risk of death (8). In a study by Bayir et al., whose purpose was to detect the relationship between troponin and prognosis in ischemic stroke patients, out of 151 patients, 81 patients had troponin abnormality and the study findings showed that high troponin was associated with high mortality and troponin serum level was a predictive factor in ischemic stroke (9). In contrast to the above mentioned studies, there are several studies that show different findings. For example, Barter et al. in their evaluation of patients with ischemic stroke demonstrated that 20% of patients had high serum level of troponin. However this increase didn't correlate with mortality (10). Etagen and his colleagues also achieved the same results (11). According to such controversies and the lack of a final conclusion as well as the lack of studies about the predictive value of troponin on recurrence, this study aims to evaluate serum troponin level and its prognostic value on 3-

month mortality and recurrence in patients with acute ischemic stroke.

## Method

This study was conducted on 63 patients in 2017 in Shafa Hospital in Kerman. The patients were suffering from ischemic stroke for the first time, and had been hospitalized within the first 12 hours of the onset of symptoms. Diagnosis of ischemic stroke was based on CT-scan and MRI (DWI, T1, and T2). All patients had supratentorial ischemic stroke and others were excluded from the study. A cardiologist visited all patients and the patients underwent transthoracic echocardiography (if necessary, TEE) and ECG monitoring for 24 hours and cardioembolic stroke was excluded. Lacunar infarctions were also excluded from the study by brain MRI. Patients with diseases other than diabetes, hypertension, ischemic heart disease and hyperlipidemia and patients with acute myocardial ischemia and pulmonary embolism were excluded from the study (confirmed by internist and cardiologist). Further, patients receiving r-TPA were also excluded. Serum troponin level was measured at 8:00 AM on the day after admission by radioimmunoassay method. Serum troponin I level higher than 0.1 ng / mL was considered abnormal (12). In this study, those patients undergoing drug therapy or having systolic blood pressure higher than 140 or diastolic higher than 90 mmHg were considered as having HTN. Patients were also treated diabetic if they were under drug therapy or had fasting blood glucose > 126 mg/ml or random blood sugar over 200 mg/dl with the symptoms of diabetes. Those who used five cigarettes per day were regarded as smokers. Hyperlipidemia was defined as total fasting, total cholesterol (200 mg / dL), LDL above 100 mg / dl, or triglyceride levels greater than 150 mg / dl, or history

of using lipid lowering drugs (13). Then, the patients were followed for 3 months for death and recurrence. Recurrence was defined as a new neurological symptom with new DWI abnormality. The power of study was 80% and  $P \leq 0.050$  was considered statistically significant. Demographic information and other findings were analyzed using t-test and logistic regression. The study was approved by the Ethic Committee of Kerman University of Medical Sciences.

## Results

In this study, 63 patients with the age range of 27-95 were studied. Thirty two (50.8%) were male and the rest were female. Of all patients, 15 (23.8%) had DM, 48 (76.2%) had HTN, 18 (28.6%) had HLP, and 8 (12.7%) were cigarette smokers (Table 1).

Twenty-two (34.9%) patients died at the end of 3th month, of which 10 were due to their stroke, 5 died due to stroke recurrence and 6 died due to fever and sepsis (pulmonary and urinary tract infections), and the death of one patient had an unknown cause. Of the 53 patients who had been discharged out of hospital, 5 (9.4%) had recurrence after 3 months.

Mean NIHSS was 14.26 in all patients,  $17.54 \pm 2.78$  in death patients and  $12.51 \pm 3.80$  in alive Patients. Mean NIHSS in patients with recurrence was  $16.6 \pm 2.07$  and in non-recurrent patients was  $13.2 \pm 3.97$ . Of the 63 patients, 8 (12.7%) had abnormal serum troponin level and 55 (87.3%) had normal level. Five (22.7%) death patients and three (7.3%) alive patients had abnormal troponin. This difference was not statistically significant ( $P=0.090$ ). One of the patients with recurrence and 4 patients who did not recurrence, had abnormal troponin. This difference was not statistically significant. ( $P = 0.039$ ). The mean serum level of troponin was  $75.25 \pm 114.54$  in death patients and  $38.2 \pm 97.98$  in alive patients, a difference which was statistically significant ( $p = 0.013$ ). In the regression analysis, however, this result was not significant. The results showed that the age is an independent risk factor for mortality in ischemic stroke patients ( $P\text{-value} = 0.04$ ) (Table 2). Also, NIHSS had a significant relationship with mortality ( $P = 0.001$ ). The mean serum level of troponin in patients with recurrence was  $43.36 \pm 55.23$  and the mean serum troponin level in others was  $40.52 \pm 93.20$ . This difference was not statistically significant ( $p = 0.54$ ).

**Table 1.** Frequency of risk factors in terms of recurrence and mortality

Risk factor	Alive	Death	Non-recurrence	Recurrence
male	20	11	24	4
female	21	11	24	1
65>	25	3	27	0
65<	16	19	21	5
DM	10	5	11	1
HTN	29	19	36	4
HLP	12	6	15	1
smoking	6	2	7	1
Mean NIHSS	12.51	17.54	13.2	16.6

**Table 2.** The Relation between Mortality and Variables

Variable	Exp(B)	P-value	95% C.I.for EXP(B)	
			Lower	Upper
Sex	2.021	.381	.418	9.763
Age	.223	.040	.053	.936
Diabetes	.540	.500	.090	3.230
Hypertension	1.774	.540	.283	11.113
Hyperlipidemia	1.660	.550	.315	8.736
Smoking	2.250	.464	.257	19.727
Troponin	2.786	.689	.018	420.632
NIHSS	.706	.001	.578	.863

## Discussion

The study at hand sought to evaluate serum troponin level in patients with ischemic stroke. The results showed that 12.7% of the patients had abnormal serum troponin level. This finding was in tune with some previous studies. In a number of studies, the frequency of the increased level of troponin = is reported from 5 to 10 percent (14). However, this number reached up to 20 % in some other studies (10). This difference is due to cut-off point of the studies level, but it is also dependent on the study population (14). Also, the study results showed that at the end of the three-month follow-up, the mean serum troponin level in patients who died is more than alive patients; but after logistic regression analysis the difference was not statistically significant. Only age ( $P = 0.04$ ) and NIHSS ( $P = 0.001$ ) had a significant relationship with mortality. These findings suggest that troponin cannot have prognostic value on 3 -month mortality rate. Our findings are consistent with some other studies. For example, Barber and colleagues in a cross-sectional study on patients with ischemic stroke showed that 20% of patients had high troponin levels, but troponin was not an

independent prognostic factor (10). Etagen et al. in another Prospective study found that about 8% of patients had abnormal levels of troponin but showed that there isn't any relation between troponin and mortality (11). Reza et al., in a two-year follow-up study, showed that in case of higher level of troponin, there was a higher incidence of myocardial infarction in people with ischemic strokes (15). Contrary to the findings of the present study and the above studies, there are some studies that show troponin has prognostic value. For example, Jensen et al. observed that troponin levels had a direct relationship with mortality in stroke patients (16). Thalin et al., in a retrospective study, showed that high troponin in ischemic stroke patients was associated with twofold increase in the risk of mortality (8). Undoubtedly, the follow-up period impacts on the results and should be taken into account (14). In a study by Maoz and his colleagues on 212 patients who had ischemic stroke, 35 had high troponin level and high troponin level was related to age, kidney dysfunction, and high NIHSS (17). Batal et al. also found that high troponin is associated with hypertension, high Cr and low HR (18). Etagen et al also found

that high troponin level is higher in patients with anterior circulation stenosis and high NIHSS (11). Abdi and colleagues also found that high troponin is associated with high age, high Cr and ECG abnormality (19). Miller et al. concluded that high troponin was associated with insular cortex infarction (20). In a study by Mitaias et al., troponin was measured in the first 24 hours after acute ischemic stroke. Also the volume of several brain regions including temporal, parietal, frontal, occipital, insular and brain stem, was calculated. It was concluded that patients with high troponin level had a higher risk of stroke. Additionally, the high level of troponin was related to the left parietal and right frontal lesions and these were associated with more myocardium damage (21). Von Rennenberg et al. showed that high-sensitivity cardiac troponin T levels were

associated with extent of white matter lesions in acute stroke patients and maybe cognitive decline (22).

We did not find any significant differences between the mean serum troponin level and the recurrence of stroke in our study. No studies has been conducted on this subject so far. Thus, we could not compare the findings with them. Our study had several limitations, including a relatively short follow-up period. Obviously, if the follow-up period becomes longer in future studies, the results will be more valuable especially for recurrence. Our next limitation was single measurement of troponin on the first day. Measuring the serial troponin level may affect the results and should be considered in future studies. In conclusion, our findings showed that ischemic stroke is associated with change in serum troponin level but this change has no prognostic value.

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