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ORIGINAL ARTICLE

The relationship between infarct volume and high sensitivity troponin I level in patients diagnosed with ischemic stroke

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Abstract

Background Various biomarkers and clinical variables are used to determine the probability risk, diagnosis, and the prognosis of acute ischemic stroke, but effective markers are still warranted.

Aim We aimed to determine the effectiveness of Hs-cTnI levels to predict the prognosis of AIS.

Methods This study was planned as a retrospective observational study. Patients with available data and over 18 years old were included in the study. Diffusion magnetic resonance images were evaluated by a senior radiologist and the infarct size was calculated.

Results We included 110 (54.2%) males and 93 (45.8%) females; a total of 203 patients with a mean age of 68.9 were included in the present study. Patients were divided into two groups according to the cut-off level of Hs-troponin-I (group I: lower than 8.5 mg/dL; group 2: higher than 8.5 mg/dL). These two groups were compared for mortality and infarct volume. Infarct volume and the mortality ratio of the group 2 was significantly higher [$p = 0.041$, $U = 4294.5$, LV = 6.5 (IQR = 1.8–25.4)].

Conclusions Hs-troponin I may be an effective biomarker in predicting the prognosis of patients with acute ischemic stroke. Multicenter comprehensive prospective studies are warranted to obtain stronger results.

Keywords Acute ischemic stroke · Emergency · GKS · High sensitive troponin I · Mortality

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Introduction

Acute stroke is the second death reason with a ratio of 11% on earth [1]. Besides this high mortality ratio, it causes chronic sequel in survivors and a common cause of disability [1–3]. An immediate diagnosis and treatment should be administered when this high mortality and disability ratio is considered. It is also important to predict the prognosis to determine the requirement of aggressive treatment in selected patients.

Troponin protein complex is consisted of troponin C, I, and T subunits and contributes to striated muscle contraction modulation. Cardiac troponin C is similar to skeletal muscle isoform but troponin I and T are defined as cardiac specific isoforms. Recently, new generation high sensitive troponin (hs-cTns) provides measuring 5–10 times lower concentrations than conventional troponins and also provides to detect smaller ischemic areas of heart muscle [4]. By this way, besides the routinely use of cardiac troponins (cTns) in the diagnosis of acute myocardial infarction (AMI), they also show an increment in cardiac muscle diseases such as rapid response ventricular atrial fibrillation, congestive heart failure, cardiomyopathy and pulmonary embolism, severe sepsis, acute ischemic stroke (AIS), and chronic renal failure (CRF) [5, 6].

Nowadays, various biomarkers and clinical variables (elder age, AF existence, severity of the symptoms etc.) are used to determine the probability risk, diagnosis, and the prognosis of AIS, but effective markers are still warranted. In this study, we aimed to determine the effectiveness of Hs-cTnI levels to predict the prognosis of AIS.

Materials and methods

Study design

After the ethics committee approval (Health Science University, Adana City Research and Training Hospital, Ethics Committee, Meeting Number: 80, Decision Number: 1395, Date: 06/May/2021), we included patients diagnosed with AIS in the emergency department (ED) between 1 Jan 2020 and 31 Dec 2020 in this retrospective observational study. Patient data was obtained from hospital automation system.

Diffusion magnetic resonance images were evaluated by a senior radiologist and the infarct size was calculated. Demographic data, Glasgow Coma Scale (GCS), CBC, AST, ALT, BUN, Cr, coagulation parameters, BNP, CK-MB, and Hs-cTn-I levels were noted.

Patients with available data and over 18 years old were included in the study. Patients with hemorrhagic stroke, mass, and lesions apart from AIS were excluded. We also excluded patients under 18 years old, patients with missed data, patients diagnosed with acute coronary syndrome, cardiac arrest patients (inhospital-out of hospital) who were not return to spontaneous circulation, patients with rheumatologic and oncologic diagnosis, and patients who underwent chemotherapy/radiotherapy.

Laboratory analyses

WBC, Hb, Hct, platelet, monocyte count, neutrophil count, BUN, Cr, AST, ALT PTZ, INR, Aptt, CK-MB, and Hs-troponin I levels were noted. CBC was analyzed via Sysmex XN 10 (Automated Hematology Analyzer XN series, Sysmex Corporation, 1–5-1 Wakinnohama-Kaigandori, Chuo-ku, Kobe 651–0073, Japan) and biochemical parameters were measured with Beucher Coulter AU5800 (Beckman Coulter GmbH, Europark Fichtenhain B 13, 47,807 Krefeld, Germany) device.

Calculation of infarct volume

The brain diffusion MR images of the patients were screened via 1.5 T and 3 T Philips Ingenia. Acute infarct volume was measured with tumor tracking method via Philips İntelliSpace Workstation (Fig. 1). Apparent diffusion coefficient (ADC) mapping was used in the diffusion weighted images. Diffusion limited areas were manually drawn with 3D-ROI (region-of-interest). The volume of diffusion limitation signals was noted as cm^3.

Statistical analyses

Statistical comparisons were performed using the statistical software package SPSS 25.0 (SPSS Inc., Chicago, IL, USA). The Shapiro–Wilk test was used to control for normal distribution. The normally distributed variables were evaluated with independent sample *t*-test and for three or more groups we used one-way ANOVA test. Non-normally distributed variables were analyzed using the Mann–Whitney *U* test and Kruskal–Wallis. Post hoc tests (Bonferroni for

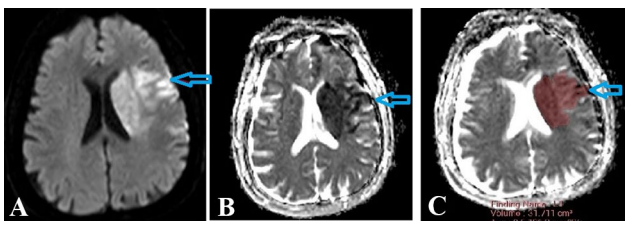

Fig. 1 Infarct volume by diffusion magnetic resonance. (the blue arrow indicates the infarct area)

Table 1 Demographic data, presentation symptoms, comorbidities, GCS, and Hs-troponin-I levels of the patients

		Frequency (*n*)	Percent (%)
Sex	Male	110	54.2
	Female	93	45.8
Arrhythmia	No	187	92.1
	Yes	16	7.9
Cerebrovascular disease	No	166	81.8
	Yes	37	18.2
Ischemic heart disease	No	136	67.0
	Yes	67	33.0
Diabetes mellitus	No	138	68.0
	Yes	65	32.0
Hypertension	No	85	41.9
	Yes	118	58.1
Symptoms	Hemiparesis/hemiplegia	112	55.2
	Dysarthria	22	10.8
	Syncope	9	4.4
	Altered mental status	36	17.7
	Dizziness	14	6.9
	Loss of feeling	5	2.5
	Weakness	1	0.5
	Defect of vision	4	2.0
Glasgow Coma Scale	13–15	184	90.6
	9–12	13	6.4
	3–8	6	2.95
Disposition	Discharge	169	83.3
	Exitus	34	16.7
Hs-troponin I (ng/L) (normal range: 0–16)	Discharge/high	169/34	20.1
	Exitus/high	34/14	41.2
	Minimum	**Maximum**	**Mean ± Std**
Age	33.00	95.00	68.9655 ± 12.41700
Hs-troponin I (ng/L)	0.00	4150.00	65.3867 ± 319.77446
Lesion size (cm^3) (discharge)	0.10	238.4	18.4895 ± 32.5717
Lesion size (cm^3) (exitus)	0.01	250.1	34.4847 ± 57.9482

normally distributed groups and Tamhane's T2 test for non-normally distributed groups) were used to determine the source of the difference between groups. The categorical variables are expressed in frequencies and percentages. Chi-square test was used to compare the categorical data. Definitive statistics were expressed as mean ± SD and median (interquartile range, IQR). A p value < 0.05 was considered significant. Cut-off values were determined via ROC curve.

Results

We included 110 (54.2%) males and 93 (45.8%) females; a total of 203 patients with a mean age of 68.9 were included in the present study. Demographic data, presentation symptoms, comorbidities, GCS, and Hs-Trop-I levels are given in Table 1.

Table 2 Analyses of categorical variables according to the outcome

Parameter	Disposition	N	(No/yes)^{X2}	p
Sex	Discharge	169	93/76	0.592
	Exitus	34	17/17	
Hypertension	Discharge	169	68/101	0.292
	Exitus	34	17/17	
Diabetes mellitus	Discharge	169	110/59	**0.049**
	Exitus	34	28/6	
Ischemic heart disease	Discharge	169	113/56	0.929
	Exitus	34	23/11	
Cerebrovascular disease	Discharge	169	139/39	0.696
	Exitus	34	27/7	
Arrhythmia	Discharge	169	155/14	0.635
	Exitus	34	32/2	
	Exitus	34	67/17	
Thrombolytic therapy	Discharge	169	22/102	0.543
	Exitus	34	8/21	

Pearson chi-square test

Table 3 Outcome of the patients according to main parameters

Parameter	Disposition				
	Disposition	N	Median (IQR)	U	p
Age (years)	Discharge	169	70 (61–77)	1765.500	**0.000**
	Exitus	34			
Glasgow Coma Scale	Discharge	169	15 (14–15)	2070.500	**0.003**
	Exitus	34			
Lesion size (cm3)	Discharge	169	6.5 (1.8–25.4)	2321.500	0.078
	Exitus	34			
Hs-troponin I (ng/L)	Discharge	169	8 (5–17)	2136.500	**0.018**
	Exitus	34			

Mann–Whitney *U* test

According to categorical variable analyses, mortality ratio of the patients with diabetes mellitus is significantly higher both in survivor and the non-survivor group (Table 2).

When we considered the patients according to the outcome (discharged/ex), mortality increased with age and high hs-troponin I level; similarly, GSC was negatively related with mortality (Table 3).

Cut-off level of Hs-troponin-I level for mortality prediction was 8.5 mg/dL according to ROC curve (Fig. 2, Table 4).

Patients were divided into two groups according to the cut-off level of Hs-troponin-I (group I: lower than 8.5 mg/dL; group 2: higher than 8.5 mg/dL). These two groups were compared for mortality and infarct volume (Table 6). Infarct volume and the mortality ratio of the group 2 was significantly higher [$p = 0.041$, $U = 4294.5$, LV = 6.5 (IQR = 1.8–25.4)] (Tables 5 and 6).

Patients were categorized according to GCS (mild-GCS: 13–15, moderate-GCS: 9–12, and severe-GCS: 3–8) and these groups were compared for mortality and infarct volume. Hs-troponin-I levels and infarct volume increased with low GCS. Hs-troponin-I levels were higher in moderate GCS than mild GCS. Infarct volume was higher in severe GCS than mild GCS (Fig. 3).

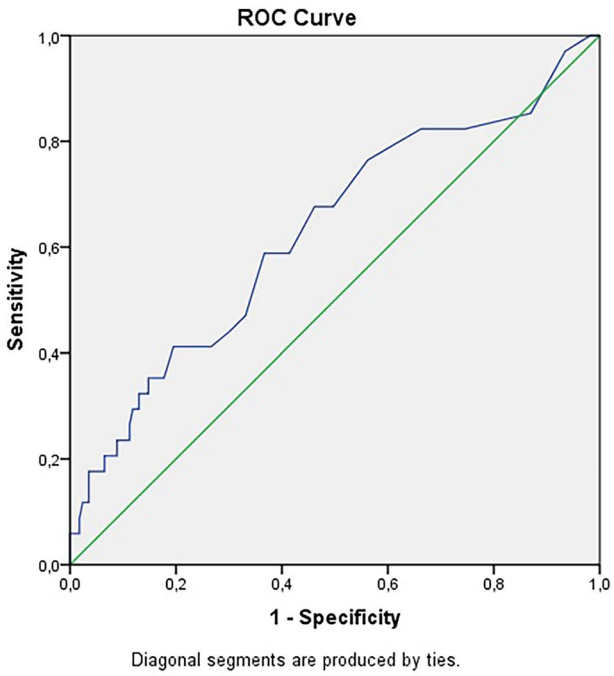

Fig. 2 ROC analyses of Hs-troponin-I level according to mortality

Discussion

Cardiac complication risk of ischemic stroke patients are correlated with severity of the stroke and neurologic dysfunction [7]. So, besides the administration of immediate and appropriate treatment of stroke patients in the ED, we also carefully observe the cardiac biomarkers [8]. Troponin levels were high in 48 (23.26%) patients in our study. Hs-trop levels higher than 8.5 mg/dL were 68% sensitive and 54% specific. Mortality ratios were significantly higher in patients whose Hs-troponin levels higher than 8.5 mg/dL. Infarct volume and GCS which are very important for prognosis in stroke were significantly correlated with hs-trop I level.

Although the etiology of high troponin levels in stroke patients is not clear, various theories have been suggested.

Table 4 ROC analyses of Hs-troponin-I levels according to mortality

Area under the curve = according to disposition 2							
Test result variable	**Area (AUC)**	**95% CI**		***p***	**Cut-off**	**Sensitivity (%)**	**Specificity (%)**
		Lower	**Upper**				
Hs-troponin I (ng/L)	0.628	0.519	0.737	0.018	8.5	68	54

Table 5 Mortality ratio analyses of Hs-troponin-I by groups

		Outcome				Odds ratio (95%CI)
		N	Discharge	Exitus		
Hs-troponin I (ng/L)	Group 1 < 8.5	102	91	11	**0.022**	2.439 (1.119–5.319)
	Group 2 ≥ 8.5	101	78	23		

Pearson chi-square test

The first one is the incidental existence of acute coronary syndrome [9]. The second and the commonly accepted theory includes activation of sympathoadrenal system with increased intracranial pressure due to acute cerebral lesions. Serum troponin level increase with the activation of this system and myocyte degeneration (myocytolysis) because of high catecholamine secretion. Recently, incidence of high hs-trop levels is common in AIS because of usual measurement of hs-trop levels. According to a systemic review published in 2009, this high ratio of hs-trop is 5–34% [10]. In Scheitz et al.'s study [11], this ratio was 50%. In our study, 23.6% patients' hs-trop levels were high and this ratio was 41.17% among non-survivors.

Infarct area size is an important parameter to determine the severity, ability after recovery, and the prediction of prognosis in AIS [12]. Kimura et al. suggested that wide lesion volume in diffusion weighted screening was associated with poor clinical outcome [13]. Similarly, Pop et al. showed that the poor prognosis was related with lesion volume and hs-trop was correlated with lesion volume [14]. In our study, lesion volume and mortality were not directly correlated but mean lesion volume was larger in non-survivors. Besides, hs-trop levels increased with the increment in lesion volume. This correlation made us think that increased intracranial pressure caused a sympathoadrenal discharge and myocyte damage.

Table 6 Lesion size analyses of Hs-troponin-I by groups

		n	Lesion size (IQR)	*U*	*p*
Hs-troponin I (ng/L)	Group 1	102	6.5 (1.8–25.4)	4294.500	0.041
	Group 2	101			

Hypertension is a potential risk factor for AIS with a ratio of 54% [15, 16]. Similarly, DM is also an important risk factor for AIS. According to literature, existence of DM in the patient with AIS is related with rehospitalization, poor prognosis, and high mortality rates (including all reasons) within next 3 years [17]. The prognosis of AIS patients with DM was poor when compared with non-diabetics in Pop et al.'s study [14]. In our study, 58.1% of the patients had DM and hypertension and mortality ratio was higher in patients with DM.

Limitations

This retrospective study was a single-center study and included limited count of patients. And our patient group was not constituted of follow-up study population. One of the limitations of our study is that the duration of symptoms could not be determined exactly. For this reason, the relationship between the hs-troponin I levels studied from the blood sample taken at the time of admission to the emergency department could not be examined.

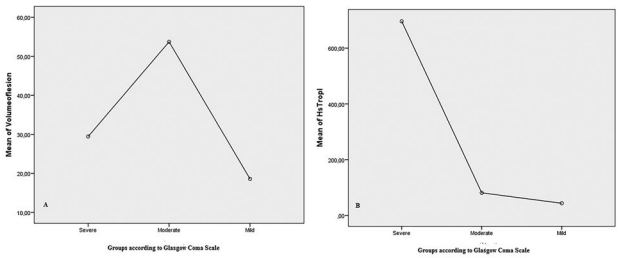

Fig. 3 Mean value of volume lesion and Hs-troponin I level according to Glasgow Coma Scale

Conclusion

Clinicians have been struggling to determine a biomarker for diagnosis and prediction of prognosis in AIS. Among these biomarkers, Hs-Trop-I may be an effective biomarker in predicting the prognosis of these patients. Multicenter comprehensive prospective studies are warranted to obtain stronger results.

Author contribution Dr. Aksu Arif, Dr. Icme Ferhat, Dr. Avci Akkan, Dr. Yolcu Sadiye, Dr. Sumbul Hilmi Erdem, Dr. Kaya Adem, and Dr. Avci Begum Seyda: conceptualization, methodology, investigation, and writing—original draft. Dr. Tugcan Mustafa Oguz, Dr. Demir Ozan, Dr. Arici Fatih Necip, Dr. Ozturk Huseyin Ali, and Dr. Dilek Okan: resources, formal analysis, and writing—review and editing. Dr. Sumbul, Dr. Avci A, and Dr. Yolcu: conceptualization, methodology, and writing—review and editing. All authors read and approved the final version of the manuscript.

Availability of data and materials Data and materials are reachable from hospital automation information systems.

Declarations

Ethics approval The ethics committee of Health Science University, Adana City Research and Training Hospital approved the study. The study was performed according to the recommendations set by the Declaration of Helsinki on medical research involving human subjects.

Consent to participate Informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors declare no competing interests.

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