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The relationship of laboratory values with prognosis in acute stroke recanalization treatment applied patients

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ABSTRACT

Objectives: Many factors affect the results of acute recanalization treatment and prognosis of ischemic stroke patients. Some markers which has a role in inflammation process cause atherosclerosis that leads to ischemic stroke. We aimed to evaluate the relationship between admission laboratory findings and prognosis in patients to whom acute recanalization therapy were applied.

Methods: In our study, we evaluated 139 acute stroke patients to whom acute recanalization therapies had been applied. Demographic data, glomerular filtration rate, uric acid, albumin, lipid profile, C-reactive protein, fibrinogen values were evaluated. Admission and discharge National Institutes of Health Stroke Scale and modified Rankin Scale scores were recorded. The effect of laboratory parameters on prognosis was examined. $P < 0.05$ was considered significant.

Results: Tissue plasminogen activator (tPA) therapy was applied to 53 (38.1%) patients, thrombectomy to 62 (44.6%) patients, tPA bolus+thrombectomy to 3 (2.2%) patients, tPA full dose+thrombectomy to 19 (13.7%), and thrombectomy+stent to 2 (1.4%) patients. None of the laboratory were statistically related to prognosis except for lymphocytes count ($p = 0.012$) and albumin ($p = 0.01$). There was no relationship between laboratory findings with hemorrhagic transformation and acute recanalization treatment outcome.

Conclusions: In the etiology of ischemic stroke, there are many inflammatory processes that cause atherosclerosis such as hypertension, hyperlipidemia, diabetes mellitus. The effect of admission laboratory values on prognosis has not been clarified. In patients with acute recanalization therapies, admission laboratory findings has no effect on patient management. Consequently, laboratory parameters provide limited information about the prognosis of patients who underwent acute recanalization therapies.

Keywords: Acute stroke, thrombectomy, thrombolysis in cerebral infarction (TICI), laboratory findings

In the etiology of ischemic stroke, hypertension, hyperlipidemia, diabetes mellitus and smoking are major risk factors [1]. The role of C-reactive protein (CRP), fibrinogen, white blood cell (WBC), complement fragments, lipoprotein (a) and acute phase reactants (AFR) in the etiology of ischemic stroke is not clear [2]. There are multiple factors affecting the prognosis of stroke patients who underwent acute recanalization therapies such as perfusion grade of vessels after thrombolysis and hemorrhagic transformation of ischemic parenchyma. The perfusion grade of vessels after thrombolysis was stated as grade 0 is 'no perfu-

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sion'.Grade 1 means minimal perfusion and grade 2 means partial perfusion. Partial perfusion is divided into grade 2A and 2B. 2A means that only a portion of the vascular region (less than two-thirds) is visible. Grade 2B is indicated when the estimated vascular territory is completely filled, but the filling is slower than usual. Complete perfusion implies grade 3 [3]. There are limited satisfactory data on whether admission laboratory findings affect Thrombolysis in Cerebral Infarction (TICI) and the European Cooperative Acute Stroke Study II (ECASS II), which evaluated hemorrhagic transformation. ECASS II defines HI as petechial hyperdensities in the infarct region. If it is punctat petechiae, it is referred to as HI1, and if it is confluent petechiae, it is referred to as HI2. PH means for homogenously hyperdense hematoma, and it is referred to as PH1 if it covers less than 30% of the infarct region, and PH2 if it covers more than 30% of the infarct area with mass effect [4].

CRP, an inflammatory marker, reveals vascular inflammation caused by a cytokine-dependent inflammatory process in the vascular system, as well as arterial atherosclerosis caused by the inflammation. Decreased albumin levels are also linked to peripheral vascular disease. According to certain research, the CRP/albumin ratio (CAR) may be a factor influencing stroke mortality [5].

We aimed to evaluate the relationship between admission laboratory findings and prognosis of stroke patients who underwent acute recanalization treatments.

METHODS

Study Design and Patients

Total 139 patients who underwent acute recanalization treatment between 2019-2022 were evaluated retrospectively. All of the patients and their families signed written informed consent forms. Before receiving acute recanalization treatment, each patient was examined by a physician. Demographic data of the patients, CRP, albumin, uric asid, fibrinogen values, lipid profile, National Institutes of Health Stroke Scale (NIHSS) and modified Rankin Scale (mRS) scores, results of recanalization treatments according to TICI, consideration of 24th CT according to ECASS II were recorded. In the assessment of laboratory findings, patients with elevated CRP values secondary to infection were excluded from the study.

Study Outcomes

The relationship between the admission laboratory findings and the acute recanalization treatment results (TICI) or the 24th hour CT results (ECAS II) were evaluated. The effect of laboratory findings on prognosis was examined by comparing the NIHSS and mRS scores at admission and discharge. Among the laboratory measures, inflammation-related indicators were explicitly chosen. Simultaneously, the lipid profile was chosen since hyperlipidemia plays a role in the etiology of stroke.

Ethical Approval

Ethics committee approval was obtained with protocol number 2022/83 (Decision no.:2022-05, Date: 07.03.2022) from Bakırköy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethical Committee.

Statistical Analysis

Statistical analyzes were performed using IBM SPSS Statistics for Windows 20.0 (IBM Corp., Armonk, NY, USA). Shapiro-Wilk test was used to detect normal distribution of the data. ANOVA test (post hoc: Bonferroni test) or Kruskal Wallis H tests (post hoc: Dunn's test) were used to compare numerical variables in groups of three or more. Chi-square test, Yates correction and Fisher exact test were used for comparison of categorical data. The relationship between numerical variables was examined by Pearson or Spearman correlation analysis. $P < 0.05$ was considered statistically significant.

RESULTS

The mean age of 139 acute stroke patients who underwent recanalization treatment was 70.6 ± 14 years, 64 of the patients were female and 75 were male. Sixty (43.2%) patients had hypertension, 40 (28.9%) patients had diabetes mellitus, 42 (30.2%) patients had coroner artery disease, 22 (15.8%) of them had history of ischemic cerebrovascular disease, 9 (6.5%) patients had hyperlipidemia, 2 (1.4%) patients had malignancy, and 47 (33.8%) had other comorbidities. Thrombec-

Table 1. Comparison of TICI and laboratory findings

Variables	TICI (1) n = 13	(2A) n = 11	(2B) n = 15	(3) n = 45	*p value*
GFR (mL/min)	77.6 ± 21.8	87.6 ± 15.9	83.9 ± 19.9	83 ± 24.6	0.747
Uric acid (mg/dL)	5.9 ± 1.2	5.3 ± 0.9	5.4 ± 1.0	5.7 ± 1.5	0.701
CRP (mg/L)	10.9 (0-148.3)	7 (1-85)	3.4 (0-24)	6 (0-161)	0.244
Albumin (g/L)	36.4 ± 4.1	37.2 ± 3.7	38.8 ± 2.2	37.8 ± 3.9	0.383
HDL (mg/dL)	44.7 ± 12	35.4 ± 9.3	42.5 ± 12.5	41.8 ± 10.6	0.280
LDL (mg/dL)	137.1 ± 43.6	90.3 ± 30.5	127.1 ± 32.8	125.5 ± 62.8	0.227
TG (mg/dL)	99 (37-178)	95 (37-145)	92.5 (50-284)	92.5 (28-329)	0.949
Fibrinogen (mg/dL)	338 (338-338)	338 (338-338)	447 (447-447)	386 (317-457)	0.706
CAR	0.3 (0-5.2)	0.2 (0-2.1)	0.1 (0-0.6)	0.2 (0-5.4)	0.207

TICI = Thrombolysis in Cerebral Infarction, GFR = glomeruler filtration rate, CRP = C-reactive protein, HDL = high density lipoprotein, LDL = low density lipoprotein, TG = triglyceride, CAR = CRP-albumin ratio

TICI 0: no perfusion, **1**: antegrade reperfusion past the initial occlusion, but limited distal branch filling with little or slow distal reperfusion, **2a**: antegrade reperfusion of less than half of the occluded target artery previously ischemic territory, **2b:** antegrade reperfusion of more than half of the previously occluded target artery ischemic territory, **3:** complete antegrade reperfusion of the previously occluded target artery ischemic territory, with absence of visualized occlusion in all distal branches

Table 2. Comparison of ECASS II and laboratory findings

Variables	ECASS II HI1 n =2 5	HI2 n = 15	PH1 n = 21	PH2 n = 12	Hemorrhage (-) n = 61	*p value*
GFR (mL/min)	79.6 ± 22.9	82.8 ± 31	75.3 ± 20.9	79.3 ± 20.4	86.3 ± 19.7	0.319
Uric acid (mg/dL)	5.6 ± 1.1	5.9 ± 1.6	5.2 ± 1.6	5.9 ± 2.8	5.7 ± 1.5	0.639
CRP (mg/L)	8 (0-85)	3.1 (0-17.5)	5.1 (0.7-148.3)	5.1 (1-161)	6 (0.6-100.1)	0.244
Albumin (g/L)	38.2 ± 2.7	38.1 ± 3.5	37.9 ± 4.2	37 ± 3.2	37.6 ± 4.9	0.932
HDL (mg/dL)	41.9 ± 10.6	44 ± 14.4	57.6 ± 56.3	41.2 ± 9.7	41.7 ± 10.5	0.142
LDL (mg/dL)	134 ± 70.1	119.7 ± 53.2	125.6 ± 44.9	117.5 ± 44.3	128.8 ± 41.6	0.863
TG (mg/dL)	100 (37-329)	91.5 (45-275)	96 (37-284)	113 (28-161)	105 (50-436)	0.828
Fibrinogen (mg/dL)	338 (337-386)	317 (317-317)	-	372.5 (260-428)	384 (0.7-615)	0.711
CAR	0.2 (0-1.9)	0.1 (0-0.5)	0.1 (0-5.2)	0.1 (0-5.4)	0.2 (0-3.1)	0.268

ECASS II = European Cooperative Acute Stroke Study II, GFR = glomeruler filtration rate, CRP = C-reactive protein, HDL = high density lipoprotein, LDL = low density lipoprotein, TG = triglyceride, CAR = CRP-albumin ratio

Hemorrhagic infarction type 1 (HI1) indicates petechial hemorrhages at the infarct margins. Hemorrhagic infarction type 2 (HI2) shows petechial hemorrhages throughout the infarct and there is no mass-effect attributable to the hemorrhages. Parenchymal hematoma type 1 (PH1) defines less than 30% of the infarcted area has hemorrage and there's minor mass effect attributable to the hematoma. Parenchymal hematoma type 2 (PH2) if it covers more than 30% of the infarct area with mass effect

tomy was applied to 62 (44.6%) patients, 53 (38.1%) patients treated by full dose tissue plazminogen activator (tPA), 19 (13.7%) patients by full dose tPA with thrombectomy, 3 (2.2%) patients by bolus tPA with thrombectomy, and 2 (1.4%) patients underwent to thrombectomy with stent procedure. In the assessment of laboratory values, the mean glomeruler filtration rate (GFR) was 82.5 ± 21.7 mL/min, uric acid: 5.6 ± 1.6 mg/dL, CRP: 6 mg/L, albumin: 37.8 ± 4.1 g/L, high density lipoprotein (HDL): 44.3 ± 23.6 mg/dL, low density lipoprotein (LDL): 127 ± 9.2 mg/dL, triglyceride (TG): 101 mg/dL, and the CAR: 0.2. The laboratory findings were compared according to TICI grades and there was no statistical significance (Table 1). There was no significant difference between the laboratory findings according to the groups of hemorrhagic transformation (Table 2). Admission and discharge NIHSS and mRS scores were compared to laboratory findings but there was no significant difference (Table 3). There was a direct relationship between albumin level and admission mRS ($p = 0.001$). The same relationship between discharge mRS and albumin level was not discovered. At the same time, there was no significant difference in NIHSS and albumin levels.

DISCUSSION

Comorbid diseases, hemodynamic, metabolic or infectious status of patients at admission usually affect the success of the acute recanalization therapy process and the follow-up period. Prognosis of the patients may be affected by these multiple conditions. Systemic infections which caused endothelial damage, impaired hemostasis and clot formation have been shown to be associated with stroke [6]. It was considered that the CRP and fibrinogen values at admission may be ineffective regarding the outcome of the acute recanalization process. In a meta-analysis, it was stated that the logarithmic increase in CRP and fibrinogen values is associated with increased risk of recurrent major vascular events in stroke patients [7]. We don't know whether CRP and fibrinogen levels are effective in the acute, chronic, or both processes. In our study, CRP and fibrinogen values of the patients were compared according to the TICI results, there was no significant difference between the groups. It was considered that the CRP and fibrinogen values of admission may be ineffective for the outcome of the acute recanalization process. The limited influence of our study results on the acute process does not allow us to assess their ef-

Table 3. Comparison of laboratory findings with admission and discharge NIHSS and mRS scores

	Admission				Discharge			
Variables	**NIHHS**		**mRS**		**NIHHS**		**mRS**	
	r	*p*	r	*p*	r	*p*	r	*p*
GFR	-0.090	0.295	-0.115	0.188	-0.109	0.282	-0.139	0.109
Uric acid	0.022	0.805	0.012	0.890	-0.088	0.394	0.012	0.891
CRP	0.020	0.819	0.072	0.413	0.036	0.722	-0.007	0.940
Albumin	-0.055	0.524	-0.305	**0.001**	-0.124	0.220	-0.030	0.726
HDL	0.076	0.398	0.049	0.588	-0.074	0.468	-0.040	0.657
LDL	-0.055	0.546	-0.100	0.264	-0.027	0.796	0.025	0.781
TG	-0.039	0.671	-0.048	0.600	-0.077	0.453	0.104	0.249
Fibrinogen	0.040	0.854	0.041	0.851	0.022	0.927	0.078	0.716
CAR	0.013	0.878	0.094	0.279	0.034	0.735	-0.006	0.948

CAR: CRP albumin ratio.

NIHHS = National Institutes of Health Stroke Scale, mRS =modified Rankin Scale scores, GFR = glomeruler filtration rate, CRP = C-reactive protein, HDL = high density lipoprotein, LDL = low density lipoprotein, TG = triglyceride, CAR = CRP-albumin ratio

fect on the chronic process. Similarly, NIHSS and mRS scores (admission and discharge) and hemorrhagic transformation according to ECASS II were not affected by admission CRP and fibrinogen values. We suggest that, admission CRP and fibrinogen values do not affect the short-term prognosis.

Albumin values, a negative acute phase reactant was reported to be lower in patients with high level carotid artery stenosis compared to patients without stenosis [8]. On the contrary, in our study, the albumin, CRP and CRP albumin ratio did not affect the admission-discharge NIHSS, mRS scores, the results of the procedure (TICI) and the degree of hemorrhagic transformation (ECASS II). There was only a slight correlation between the admission albumin level and the admission mRS score. In general, the admission albumin level could be ignored in patients who will undergo acute recanalization treatment. Many hemodynamic alterations and systemic illnesses might affect albumin value. Although if it is difficult to assign meaning solely, it can be thought of as a factor when combined with other laboratory variables.

Serum uric acid level is strongly correlated with GFR and triglyceride level in diabetic patients and therefore there is a high risk for stroke in these hyperuricemic patients [9, 10]. Because of the common ethiology atherosclerosis, it is reasonable to assume that stroke patients may have high uric acid levels. However, in our study, we found that uric acid and GFR did not affect the outcome of the procedure, hemorrhagic transformation and short-term prognosis in patients treated with acute recanalization therapies. Since this presence largely correlates with chronic processes, it is difficult to take into account increased uric acid for stroke patients in the acute stage.

Dislipidemia is also a risk factor for acute stroke and TG < 100.2 mg/dL was found as an independent risk factor in the acute-term stroke mortality in a study [11]. A high LDL cholesterol concentration in acute stroke patients with large artery occlusion is independently associated with a favorable prognosis at 3 months [12]. On the other hand, there is a perplex effect of dyslipidemia on reperfusion therapies. According to our results the admission lipid profile did not effect the TICI score and short-term ECASS II results. Similarly admission and discharge NIHSS, mRS scores were not affected by the lipid profile. Although a positive correlation between ischemic stroke and LDL cholesterol and triglyceride levels and a negative correlation with HDL cholesterol were reported, we did not find any relationship in the acute period. Dyslipidemia clearly has an impact on stroke risk. Lack of long-term follow-up may be the cause of our study's inability to detect a significant difference. These findings also raise questions about how crucial it is to take into account the lipid profile when choosing a course of treatment for the acute phase of the disease.

Limitations

Lack of consideration of lipid subgroups in our study is a shortcoming. At the same time, there is insufficient data to provide information about the long-term prognosis.

CONCLUSION

Our study implies that the laboratory findings such as lipid profile, infectious markers at admission do not affect the outcome of the procedure and do not have an effect on the short term prognosis in the patients who underwent to acute stroke recanalization treatments.

Authors' Contribution

Study Conception: İA; Study Design: İA; Supervision: VAY; Funding: N/A; Materials: MS; Data Collection and/or Processing: MS, HOY; Statistical Analysis and/or Data Interpretation: İA, HOY; Literature Review: HAE; Manuscript Preparation: İA, HAE and Critical Review: HAE.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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