Original investigation

Are Monocyte/HDL, Lymphocyte/Monocyte and Neutrophil/Lymphocyte Ratios Prognostic or Follow-up Markers in Ischemic Cerebrovascular Patients?

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ABSTRACT

Background: We investigated the association of monocyte to high-density lipoprotein cholesterol (HDL) ratio (MHR), neutrophil to lymphocyte ratio (NLR) and lymphocyte to monocyte ratio (LMR) with prognostic value and infarct types in patients with acute ischemic cerebrovascular disease (CVD).

Matherial and Methods: The study was carried out retrospectively in 223 patients, but after the exclusion criterion, 150 patients with acute ischemic CVD were included to the study. The complete blood count and lipid profile were examined at the admission of the patients. For initial neurologic status, National Institutes of Health Stroke Scale (NIHSS) score and for following-up, modified Rankin Scale (mRS) score were evaluated. After the etiological investigations and neuroimaging, infarct types were defined.

Results: We found that as the NIHSS score increased, LMR values decreased and NLR values increased statistically (p=0.02, p=0.013). Additionally, statistical significant differences were determined between MHR values and mRS scores (p=0.045). According to the results of regression analysis, it was observed that the increase of MHR was statistically significant on the MRS of people with cardioembolic infarction (p=0.004, StB=0.383).

Conclusion: Our study provides, LMR and NLR values are related with the initial neurologic state, and they would be prognostic markers for the neurological deficit of acute cerebrovascular disease. MHR can be a follow-up marker for CVD and also a predictable marker for cardioembolic infarct type.

Key words: Acute ischemic cerebrovascular disease, monocyte to high-density lipoprotein cholesterol ratio, neutrophil to lymphocyte ratio, lymphocyte to monocyte ratio, prognosis.

INTRODUCTION

Ischemic cerebrovascular disease is a disorder which can be fatal or physically dysfunctional affecting both the person and the environment. According to the infarct types and related factors prognosis can be variable. Therefore, it is important to determine the prognostic factors in these patients.

Monocytes play an important role as pro-inflammatory and pro-oxidant cytokines in the immune system. In addition, monocytes are an important component of the atherosclerotic plaque structure. Therefore, high monocyte levels have been reported as an independent risk factor for coronary artery disease (1, 2). The protective effect of high-density lipoprotein (HDL) against low-density lipoprotein and monocyte oxidation is known (3). In recent years studies have shown that the ratio of monocyte/HDL (MHR) is a prognostic factor for coronary artery disease (4). In patients with

intracerebral hemorrhage, the relationship between MHR value and mortality and disability has been examined and it has been shown that high MHR values play a prognostic role for mortality and disability after intracerebral hemorrhage (5). There is one study available in the literature that examines the MHR value and mortality in acute ischemic cerebrovascular disease. In this study, high MHR values have been shown to be independent predictors of mortality after acute CVD (6). However, the relationship between infarct subtypes and MHR has not been studied yet.

Moreover, lymphocytes, like monocytes, are important immunocytes in the development of atherosclerosis. It has been shown that low lymphocyte levels and high monocyte levels have important prognostic value in the development of acute myocardial infarction in cardiovascular diseases (7, 8).

J Basic Clin Health Sci 2020; 1:38-43

Tekin et al. Prognostic ratios in acute CVD.

The lymphocyte-to-monocyte ratio (LMR) was a strong and independent predictor of long-term cardiac and cerebrovascular disease risk in patients with S-T elevated myocardial infarction (9). The relationship between LMR and acute cerebrovascular disease was examined and it was concluded that LMR may be a prognostic marker poor outcome (10).

In the present study, we aimed to investigate the prognostic value with simple and costless measurable indices like MHR, LMR and NLR in acute cerebrovascular disease. To the best of our knowledge this is the first study to evaluate the possible relationship between these indices and infarct subtypes.

MATERIALS AND METHODS

Study Group
We retrospectively investigated 223 patients with acute ischemic cerebrovascular disease who were hospitalized at Pamukkale University Neurology Department and intensive care unit in the first 24 hours of the CVD between the years 2014 and 2018. Ischemic stroke subtypes were classified according to the Trial of 10172 in Acute Stroke Treatment criterion (11). After the evaluation with exclusion criterion, 150 patients (81 males, 69 females were included to the study (Figure 1). The exclusion criterions were severe renal, liver, heart failure, malignancy, hematological disorder, systematic acute/chronic inflammatory/autoimmune or infectious diseases. Because of our study was a retrospective study, we did not take any written consent form from the patients. This study was approved by the Ethics Committee of Pamukkale University with the number of 60116787–020/32209.

Data Collection

Patients hospitalised with acute CVD in the first 72 hours between 2014 and 2018 at Pamukkale University Neurology Depertment (n=223)

Excluded

Exclusion Criterion
Hematological disorder n=5
Severe renal failure n=13
Severe congestive heart failure n=21
Malignancy n=4
Severe liver failure n=9
Autoimmun disorders n=11

Acute CVD patients with avaliable criterion n=160

Excluded

Patients died within 72 hours n=10

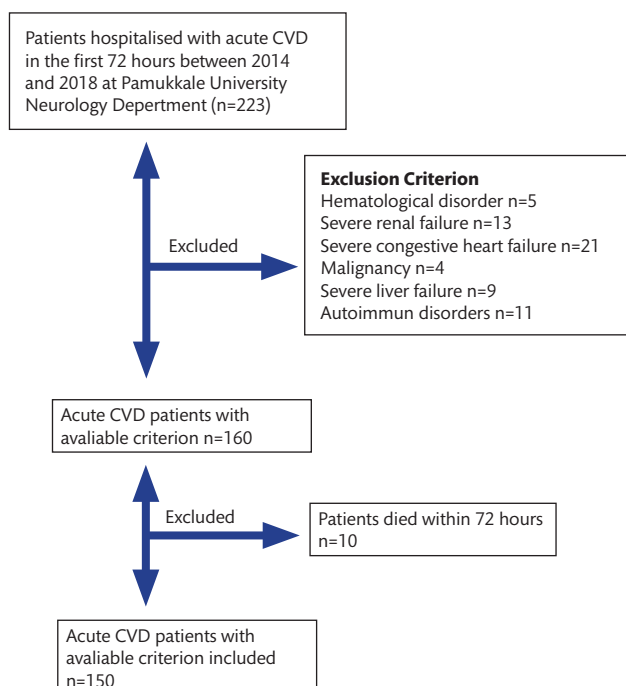Acute CVD patients with avaliable criterion included n=150

Figure 1. Features of included patients

Clinical data were collected for all patients, including demographic data (age, gender) and risk factors (hypertension, diabetes mellitus, hyperlipidemia, atrial fibrillation [AF], smoking, and heart disease). Cranial magnetic resonance (MR), or computed tomography (CT) imaging findings were used to show acute ischemic lesions.

Blood samples were taken within the 24 hours after the acute ischemic CVD. From each patient, approximately 8 ml venous blood sample were drawn into serum separating and hemogram tubes.

Serum total cholesterol, LDL-cholesterol, HDL-cholesterol, creatinine, uric acid and ALT, AST levels were analyzed in Cobas e702 biochemistry auto-analyzer (Roche Diagnostics GmbH, Mannheim, Germany). Complete blood counts were measured within 1 h of collection on a Siemens ADVIA 2120i hematology analyzer (Siemens Healthcare Diagnostics, Erlangen, Germany). MHR was calculated as the ratio of monocyte and HDL, LMR was calculated as the ratio of lymphocyte and monocyte lastly NLR was calculated as the ratio of neutrophil and lymphocyte, both obtained from the same automated blood sample at the same time.

Stroke Severity and prognosis
The patients' National Institutes of Health Stroke Scale scores (NIHSS) were measured on first admission. Stroke severity classified into 2 groups according to NIHSS values (NIHSS scores of 0–6 was defined as mild stroke and NIHSS scores >6 was defined as moderate to severe). After follow-up examinations stroke severity were measured with modified Rankin scale (mRS, scores range from 0 to 6, when numbers increase, clinical outcome worsens.) before discharging.

Statistical analysis
Continuous variables were expressed as mean ± standard deviation (SD), median (minimum-maximum values) and categorical variables as number and percent. Kolmogorov-Smirnov and Shapiro-Wilk tests were used for testing normality. If parametric test conditions were satisfied, Independent Samples t test was used for comparisons among groups. If parametric test conditions were not satisfied, Mann Whitney U test was used for comparisons among groups. In addition, the relationships between continuous variables were analyzed by Spearman or Pearson correlation analysis and the differences between categorical variables were examined by Chi-square analysis. All statistical analyses analyzed by SPSS 24.0 (SPSS 24 for Windows, Armonk, NY: IBM Corp) and p value less than 0.05 was considered statistically significant.

RESULTS

Out of 223 patients, 150 patients were included in this study, after exclusion of 73 patients according to the exclusion criterion. The mean age was 67.69±13.44 years. 81 of the patients (54%) were male and 69 were female (46%). Demographic and laboratory findings of the patients are shown in Table 1 and 2.

Moderate to severe strokes on admission were found in 34 patients (22.7%), and the other 116 patients (77.3%) were found to have mild stroke according to NIHSS scores.

J Basic Clin Health Sci 2020; 1:38-43

Tekin et al. Prognostic ratios in acute CVD.

Table 1. Demographic-clinical findings and risk factors of patients

		NIHSS Score			P value
		≤6	>6	Total	
Gender	male/female	64 (% 55.17)/52 (% 44.83)	17 (% 50)/17 (% 50)	81 (% 54)/69 (% 46)	0.595
Smoking	-/+	87 (% 75)/29 (% 25)	25 (% 73.53)/9 (% 26.47)	112 (% 74.67)/38 (% 25.33)	0.862
Diabetes Mellitus	-/+	82 (% 70.69)/34 (% 29.31)	21 (% 61.76)/13 (% 38.24)	103 (% 68.67)/47 (% 31.33)	0.324
Hypertension	-/+	40 (% 34.48)/76 (% 65.52)	14 (% 41.18)/20 (% 58.82)	54 (% 36)/96 (% 64)	0.475
Hyperlipidemia	-/+	90 (% 77.59)/26 (% 22.41)	29 (% 85.29)/5 (% 14.71)	119 (% 79.33)/31 (% 20.67)	0.329
Myocardial Infarction	-/+	93 (% 80.17)/23 (% 19.83)	28 (% 82.35)/6 (% 17.65)	121 (% 80.67)/29 (% 19.33)	0.777
Congestive Heart Failure	-/+	103 (% 88.79)/13 (% 11.21)	26 (% 76.47)/8 (% 23.53)	129 (% 86)/21 (% 14)	0.09
Atrial fibrillation	-/+	93 (% 80.17)/23 (% 19.83)	21 (% 61.76)/13 (% 38.24)	114 (% 76)/36 (% 24)	**0.027***
Stroke etiologic subtype	Atherosclerotic	31 (% 26.72)	15 (% 44.12)	46 (% 30.67)	**0.0001***
	Cardioembolic	37 (% 31.9)	18 (% 52.94)	55 (% 36.67)	
	Lacunar	21 (% 18.1)	1 (% 2.94)	22 (% 14.67)	
	Cyriptogenic	15 (% 12.93)	0 (% 0)	15 (% 10)	
	TIA	12 (% 10.34)	0 (% 0)	12 (% 8)	

NIHHS: National Institues of Health Stroke Scale scores; **TIA:** Transient ischemic attack.
*Significant

Table 2. The quantative features of patients

	NIHSS Score ≤6 (n=116)		NIHSS Score >6 (n=34)		P value
	Mean ± SD	Med (min-max)	Mean ± Sd	Med (min-max)	
Age	67.58±13.95	72 (23–91)	68.09±11.69	70.5 (43–92)	0.708
MRS	1.21±1.25	1 (0–6)	3.59±1.78	4 (1–6)	**0.0001***
Total Cholesterol (mmol/L)	177.14±40.68	173 (82–263)	170.56±47.49	161 (100–319)	0.184
LDL Cholesterol (mmol/L)	104.14±35.25	105 (0–186)	102.82±37.57	95 (51–207)	0.569
HDL Cholesterol (mmol/L)	44.05±12.95	41 (19–89)	43.94±13.56	40.5 (23–80)	0.807
VLDL Cholesterol (mmol/L)	27.79±14.05	25.5 (0–72)	22.91±13.36	21 (0–77)	**0.04***
Triglycerides (mmol/L)	145.04±79.2	132 (45–583)	117.85±63.17	105 (47–386)	**0.035***
Total WBC (10^9/L)	9.7±11.5	8.1 (4.2–13.0)	9.0±3.5	8.7 (3.2–21.7)	0.836
RBC (10^9/L)	4.72±0.62	4.69 (3.34–6.25)	4.65±0.68	4.59 (2.82–6.52)	0.586
Hemoglobin (g/L)	13.71±1.71	13.6 (8.9–18.6)	13.22±1.67	13.25 (9.4–16.4)	0.144
Hematocrit%	41.61±5.01	41.35 (26.3–55.8)	40.26±5.09	39.95 (28.8–50.7)	0.171
MCV (fl)	88.66±7.65	89.1 (59.7–123.2)	87.2±7.13	87.7 (64.9–103)	0.213
MCH (phg)	29.21±2.74	29.55 (19–39.8)	28.63±2.57	28.75 (21.6–34.5)	0.094
MCHC (g/L)	32.94±1.06	33 (30.4–35.5)	32.85±1.46	32.7 (30.1–37.4)	0.671
RDW%	14.46±1.86	14.1 (12.2–25.1)	15.2±2.46	14.75 (12.8–25.5)	**0.028***
Platelet count, (10^9/L)	234.74±59.89	226 (96–460)	269.24±150.21	236.5 (125–1012)	0.308
Lymphocyte (10^9/L)	1.9±0.8	1.9 (0.2–6.1)	1.6±0.8	1.4 (0.6–3.7)	**0.033***
Monocyte (10^9/L)	0.46±0.15	0.45 (0.08–0.85)	0.52±0.23	0.51 (0.07–1.16)	0.14
Neutrophils (10^9/L)	5.8±2.5	5.3 (0.23–14.3)	6.5±3.2	6.1 (2.2–19.2)	0.333
Monocyte to HDL ratio	11.64±5.73	10.87 (2–34.74)	13.29±6.81	11.85 (1.32–30)	0.16
Lymphocyte to monocyte ratio	4.51±1.77	4.5 (0.39–9.38)	3.89±2.77	3.46 (0.58–15.71)	**0.02***
Neutrophil to Lymphocyte ratio	4.46±6.29	2.68 (0.09–47.19)	5.4±5.46	3.63 (1–28.69)	**0.013***

NIHSS: National Institues of Health Stroke Scale scores; **MRS:** modified Rankin scale; **LDL:** low-density cholesterol; **WBC:** white blood cell; **RBC:** red blood cell; **MCV:** mean corpuscular volume; **MCH:** mean corpuscular volume; **MCHC:** mean corpuscular hemoglobin concentration; **RDW:** red blood cell distribution width.
*Significant

J Basic Clin Health Sci 2020; 1:38-43

Tekin et al. Prognostic ratios in acute CVD.

Table 3. Patients' prognostic and biochemichal parameters according to infarct subtypes

	Atherosclerotic (1)	Cardioembolic (2)	Lacunar (3)	Cyriptogenic (4)	TIA (5)	P value
Age	68±11.46	71.4±12.32	66.18±12.32	53.93±17.44	69.5±12.32	**0.005* (2–4)**
NIHSS	5.46±3.37	5.78±3.9	3.14±1.52	2.67±1.76	2.08±1.62	**0.0001* (1–5, 2–5, 1–4, 2–4, 2–3)**
MRS	2.04±1.71	2.22±1.82	1.55±1.47	0.8±0.86	0±0	**0.0001* (1–5, 2–5, 3–5, 2–4)**
Total Cholesterol (mmol/L)	173.2±40.68	168.44±42.31	201.77±46.89	170.93±36.98	176.08±31.5	**0.033* (2–3)**
LDL-cholesterol (mmol/L)	104.24±32.91	99.91±35.39	115.09±47.31	99.93±32	104.58±26.8	0.555
HDL-cholesterol (mmol/L)	43.39±11.61	44.53±15.26	46.59±14.18	39.07±7.28	45.67±10.22	0.562
VLDL-cholesterol (mmol/L)	25.39±11.03	23.28±11.1	34.85±21.14	31.93±12.76	25.75±15.87	**0.036* (2–4, 2–3)**
Triglyceride (mmol/L)	127.37±55.28	120.15±50.29	200.68±130.21	159.93±63.44	129.25±79.1	**0.013* (2–3)**
Total WBC (10⁹/L)	11.4±18.0	8.8±3.3	8.5±2.6	9.1±2.2	8.2±2.2	0.885
RBC (10⁹/L)	4.78±0.68	4.53±0.55	5.03±0.71	4.64±0.53	4.64±0.58	**0.025* (2–3)**
Hemoglobin (g/L)	13.76±1.84	13.23±1.56	14.25±1.83	13.51±1.55	13.53±1.6	0.183

TIA: transient ischemic attack; NIHSS: National Institues of Health Stroke Scale scores; MRS: modified Rankin scale; LDL: low-density cholesterol; HDL: high-density cholesterol; WBC: white blood cell; RBC: red blood cell; HGB: hemoglobine. *Significant

Table 4. The significant correlation between NIHSS and serum lipid, hematological markers

	NIHSS
VLDL	p=0.042*; r=-0.167
TG	p=0.03*; r=-0.178
MCV	p=0.05*; r=-0.16
MCH	p=0.009*; r=-0.214
RDW	p=0.0001*; r=0.305

NIHSS: National Institues of Health Stroke Scale scores; LDL: low-density cholesterol; MCV: mean corpuscular volume; MCH: mean corpuscular volume; RDW: red blood cell distribution width. * Significant

Table 5. The significant correlation between MRS and biochemical parameters

	MRS
MCH	p=0.021*; r=-0.189
RDW	p=0.001*; r=0.261
VLDL	p=0.010*; r=-0.212
TG	p=0.003*; r=-0.238

MRS: modified Rankin scale; MCH: mean corpuscular volume; RDW: red blood cell distribution width; VLDL: very low-density cholesterol; TG: trigyceride *Significant

The infarct sub-types were as follows: Atherosclerotic 46 (30.7%); cardio embolic 55 (33.7%); lacunar infarct 22 (14.7%); cryptogenic 15 (10%) and 12 patients (8%) without infarct were included in the transient ischemic attack (TIA) group.

The initial NIHSS scores were significantly higher in cardio embolic infarct group than the lacunar and cryptogenic infarct group (p=0.0001) (Table 3). Total cholesterol, VLDL, triglyceride, and RBC levels were found statistically higher in patients with lacunar infarcts than the other infarct subtypes (p=0.03, p=0.03, p=0.01, p=0.02) (Table 3).

VLDL, TG and lymphocyte values were significantly higher in mild strokes than the moderate to severe strokes. (p=0.04, p=0.035, p=0.033). But RDW values were significantly lower in mild strokes than the other group (p=0.028) (Table 2). There was positive correlation between NIHSS scores and RDW values (p=0.0001, r=0.305) and also there was a negative correlation between VLDL, TG values with NIHSS scores (p=0.042; r=-0.167, p=0.03; r=-0.178) (Table 4).

There was significant negative correlation between VLDL and TG values with mRS scores (p=0.01; r=-0.212, p=0.003; r=-0.238). In addition, we showed that poor outcome patients had lower VLDL and TG values. And there was significant positive correlation between RDW and mRS scores. The patients with good prognosis had lower RDW values (p=0.001; r=0.261) (Table 5).

There was significant negative correlation between MCV, MCH and NIHSS scores (p=0.05*; r=-0.16, p=0.009*; r=-0.214). Statistical

Table 6. The comparisons of infarct types according to relation between MRS and MHR

Dependent: MRS		Std. Beta	t	Sig.	% 95 C. I. Lower Bound	% 95 C. I. Upper Bound
Sub group model 1	Atherosclerotic	0.090	0.620	0.540	-0.050	0.100
Sub group model 2	Cardioembolic	0.380	3.020	0.004*	0.040	0.190
Sub group model 3	Lacunar	-0.300	-1.430	0.170	-0.250	0.050
Sub group model 4	Cyriptogenic	0.120	0.440	0.660	-0.090	0.140
Independent: Monocyte/HDL ratio (MHR)						

significant difference was determined between monocytes and mRS values (p=0.017). The patients who had bad outcome, had higher monocyte levels. There was significant difference between lymphocyte/monocyte (LMR) ratio, neutrophil/lymphocyte ratio (NLR) and NIHSS scores (p=0.02, p=0.013). As the NIHSS score increased, LMR and NLR values decreased statistically.

Statistical significant differences were determined between MHR values and mRS scores (p=0.045). According to the results of regression analysis, it was observed that the increase of MHR was statistically significant on the MRS of people with cardioembolic infarction (p=0.004, StB=0.383). This effect was not significant in other infarct types (Table 6).

J Basic Clin Health Sci 2020; 1:38-43

Tekin et al. Prognostic ratios in acute CVD.

DISCUSSION

Stroke is a disorder that can result with severe situations. If prognosis is predicted by the biomarkers, disability can be prevented earlier. There were many studies which evaluated stroke and the prognostic markers by the various hematological and biochemical parameters like the ratios; monocyte to high-density lipoprotein (HDL) ratio (MHR), lymphocyte to monocyte ratio (LMR), neutrophil to lymphocyte ratio (NLR). Nevertheless, there is no study which shows the relationship between MHR, LMR, NLR and infarct types. In this study, we investigated the relationship between LMR, NLR and MHR values and prognosis in patients with ischemic stroke, and this is the first study to examine the relationship between these ratios and infarction subtypes.

In our study, cardio embolic infarct group (33.7%) was more common than the atherosclerotic group in contrast to the common literature knowledge. Higher concentrations of plasma lipids can cause plaque formation, promoting artery stenosis and resulting ischemia. We found that statistical significant higher total cholesterol, VLDL, TG in patients with lacunar infarcts. These results were similar with the other studies in the literature (11, 12). VLDL and TG values were also higher in the patients with good prognosis. It may be related with the lacunar infarcts who have higher VLDL and TG and smaller infarct size, hence prognosis can be better than the patients who have larger infarcts. But some of the studies found that total cholesterol levels were not associated with lacunar infarcts (13, 14).

Our study demonstrates that patients with cardio embolic infarcts had lower RBC levels than the patients with lacunar infarcts. Hatamian et al. showed that RBC count could be used for to predict short term mortality in ischemic stroke (15). In our cardio embolic patients' population, initial neurologic examination was worse than the patient population of lacunar infarcts. According to this result we can conclude that lower RBC count may be a risk factor for poor prognosis in patients with cardio embolic infarcts than the patients with lacunar infarcts.

In our study, we found that RDW levels were correlated with NIHSS scores; higher RDW levels were associated with poor prognosis. Recent studies showed that elevated RDW values may cause stroke severity and independently predict future cardiovascular and all-cause mortality (16, 17). Our data confirmed the results of these studies and RDW levels were significantly higher in moderate to severe stroke group.

We observed that MCV, MCH values had negative correlation with NIHSS scores, hence lower MCV, MCH values were related with poor outcome. A. R Nayak et al. didn't find any significant alteration with these hematological parameters in acute ischemic stroke (18). Tzy-Haw et al. found that elevated MCV levels can be a predictor for the mortality of CVD and cardiovascular disease (19). But Hatamian et al. showed that lower MCV levels can be the predictors of short term mortality in ischemic stroke patients (15).

After ischemic brain damage, inflammatory response appears in damaged tissue. By the ischemia, oxygen-glucose deprivation causes releasing reactive oxygen species, complement factors and activated protease from the necrotic tissue (20). Experimental studies showed that after ischemia of the brain, pro-inflammatory cells like monocytes, T cells, neutrophils are activated and over time they decrease while anti-inflammatory monocytes increase. By the way inhibiting the inflammatory response, infarct size begins to be smaller (21, 22). Bolayir et al. showed that higher monocyte counts' prognosis in acute CVD was worse than lower monocyte counts (6). In our study we also found that higher monocyte levels were related with poor prognosis too.

Leucocytes; predominantly neutrophils but also monocytes migrate within several hours to ischemic area. Infiltration of leucocytes occlude cerebral micro vessels and perfusion may be affected. Lymphocytes infiltrates later, macrophages are visible within 24 hours and decreasing of neutrophils are seen within 48 hours (20). The role of lymphocytes in the pathogenesis of ischemic stroke is unclear. Some studies claim that lymphocytes have a therapeutic effect on inflammation (23) but some of the other studies shows that lymphocytes have a pro-inflammatory effect and worsen the ischemic area. Kim et al. reported that lower lymphocyte levels are associated with poor prognosis (23).

However, to evaluate prognosis with more sensitive biomarkers, some ratios were calculated and investigated about inflammatory cells. For example, recent studies showed that neutrophil to lymphocyte ratio can be used as a predictor of prognosis for cardiovasculer disease, cancer, stroke and TIA (24–26). In our study, we also found that LMR and NLR values are lower in patients with worse neurological status. We thought that it was associated with stroke-induced immunosuppression which is related with the activation of the hypothalamus-pituitary axis and sympathetic nervous system (27). Stroke induced immunosuppression was defined by Liesz et al. with the effect of high mobility group box 1 (HMGB1) which is a nuclear protein synthesed from damaged brain tissue. This protein induces proliferation of immature monocytes from bone marrow through a receptor of advanced glycation end product (RAGE) signaling. And then immature monocytes secrete arginase-1 which is a marker of myeloid-derived suppressor cells and causes lymphocyte reduction by inducing lymphocyte apoptosis (28). Park et al. found that LMR was significantly lower in stroke patients with infections and LMR may be useful for assessing the stroke induced immunosuppression (29).

We showed that MHR values were statistically higher in the patient with higher mRS scores. And this is the first study which showed that the increase of MHR was statistically significant on the MRS of patients who had cardioembolic stroke, this effect was not significant in other infarct types. Higher HDL cholesterol levels are found to be associated with lower NIHSS score and good outcome (modified Rankin Scale score 0–1) in the literature (30–32). Lower HDL levels are risk factor for cardioembolic diseases. However, Hindy et al. found that elevated HDL levels lowered the risk of lacunar infarcts (33). According to the results of regression analysis, it was observed that the increase of MHR was statistically significant on the MRS of people with cardioembolic infarction (p=0.004, StB=0.383). This effect was not significant in other infarct types.

J Basic Clin Health Sci 2020; 1:38-43

Tekin et al. Prognostic ratios in acute CVD.

Our study has some limitations like relatively small patient population, because our study is a one-center-retrospective study. In addition, because of the study design the patients' follow-up period is too short, new prospectively with longer follow-up period would be helpful to predict long time disability in such patients.

In conclusion, this study provides, LMR and NLR values are related with the initial neurologic state, LMR and NLR are lower in patients with worse neurological status and they can be prognostic markers for the acute state of cerebrovascular disease. MHR can be a follow-up marker for CVD and also a predictable marker for cardioembolic infarct type.

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