# Immature granulocyte and other markers in prediction of mortality in spontaneous intracerebral hemorrhage

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## ABSTRACT

**Aim**: This study aims to evaluate immature granulocyte count (IG#) and percentage (IG%) in the prediction of mortality in spontaneous intracerebral hemorrhage (SICH).

**Material and Method**: Demographic characteristics and laboratory test results of patients diagnosed with SICH and admitted to the neurology clinic in a tertiary hospital between January 1, 2020, and January 1, 2022, were recorded. One hundred ten patients were included in the study. While 80 of these patients constituted the group that recovered after treatment, 30 of them formed the group that died despite treatment. IG and other laboratory and clinic parameters were statistically compared in both groups.

**Results**: Of 110 patients, 45 (42.7%) were female, and 65 (57.3%) were male. IG counts were higher in the non-survival group than in the survival group (p=0.001). When the patients were divided according to low IG% (<0.6) and high IG% (>=0.6), 30 patients were in the high IG# group, and 80 patients were in the low IG% group. White blood cell (WBC), neutrophil count (NEUT#), monocyte count (MONO#), IG#, neutrophil-lymphocyte ratio (NLR), and hemorrhage volume (HV) values were statistically significantly higher in the high IG% group than in the low IG% group; Glasgow coma score (GCS) and percentage of lymphocytes (LYMPH%) values were significantly lower too. In addition, the mortality rate in the high IG# group was significantly higher than the mortality rate in the low IG% group (53.23% vs. 17.5%).

**Conclusion**: IG is a new, easily accessible, inexpensive, and promising marker for predicting in-hospital mortality in patients with SICH.

Keywords: Spontaneous intracerebral hemorrhage, inflammation, immature granulocyte, prognosis, mortality

# **INTRODUCTION**

Stroke is one of the leading causes of death worldwide. SICH is an acute brain injury caused by sensitive blood extravasation from a ruptured cerebral blood vessel to the brain parenchyma. It is a common emergency associated with high morbidity and mortality rates. SICH accounts for 10 to 15% of all strokes. Hospitalizations for SICH have increased by 18% over the past decade, possibly due to an increase in the elderly population and increased anticoagulant and antiplatelet therapy (1).

Studies on SICH have been conducted to reduce morbidity and mortality, and some of these studies focus on antiinflammatory treatments due to the pathophysiology of inflammation. The goal is to minimize neuron damage caused by brain tissue edema and reduce morbidity and mortality by suppressing acute inflammation. The role of inflammation in the pathophysiology of SICH has been well-established in some studies. SICH causes the release of proinflammatory cytokines and an increase of immune cells in brain tissue. Studies have also reported the relationship between NLR, lymphocyte-monocyte ratio (LMR), and platelet-lymphocyte ratio (PLR) obtained from white blood cell count as systemic inflammation markers and poor prognosis in patients (2).

IG is a new inflammatory parameter measured using an automated blood cell analyzer. Recently, it has been discovered that the number and percentage of IG in peripheral blood help to predict complications and mortality in many diseases, such as sepsis, septic shock, local infection, coronary artery disease, acute appendicitis, and pancreatitis (3,4). Moreover, in one study, IG was associated with 30-day mortality in acute ischemic stroke (5). However, there is only one study on

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IG in the literature to predict mortality in patients with SICH, and the relationship between 30-day mortality and IG has been investigated (6). Therefore, in this study, we aimed to investigate the role of IG obtained at admission in predicting in-hospital mortality in patients with SICH.

### MATERIAL AND METHOD

The study was carried out with the permission of Kastamonu University Medical Faculty Clinical Researches Ethics Committee (Date: 05.10.2022, Decision No: 2022-KAEK-85). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

#### Patients

Data records from a tertiary hospital's laboratory information system were used for this retrospective study between January 1, 2020, and January 1, 2022. The diagnosis of intracerebral hemorrhage (ICH) was made after obtaining the patient's history, examination, and detecting the hemorrhagic lesion in computed tomography (CT). One hundred ten patients who applied to the emergency department and applied to the neurology clinic with the diagnosis of ICH were included in the study. While 80 individuals formed the post-treatment survival group, 30 died despite the treatment, creating the non-survival group (Table 1). Moreover, when the patients were divided (according to the literature, 4-7) low IG% (<0.6) and high IG% (>=0.6) (Table 2), 30 patients were in the high IG# group, and 80 patients were in the low IG% group. Patients without hemogram data, those under 18, pregnant women, trauma patients, those with a diagnosis of Covid-19, or those with PCR positivity were excluded from the study.

#### Materials

Age, gender, comorbidity, hemogram parameters, using drugs, ICH hemorrhage regions, and physical examination findings were compared. In addition, IG and other hemogram parameters routinely measured in the Sysmex XN 1000 (Hematology-Analyzer-Sysmex Corporation, Japan) were statistically compared in both groups. With these parameters, the rate of predicting the death of the patients from the hemogram results on the first day of admission to the hospital was investigated. Ethical rules and the principles of the Declaration of Helsinki carried out all procedures.

We retrospectively reviewed admission head CT scans of SICH patients. We assessed ICH volume on the admission with the ABC/2 method. The ABC/2 method identified the CT image with the largest hemorrhage area. Next, the largest diameter (A) of the hemorrhage on this image was measured. The largest diameter 90° to A on the same image was measured next (B). Finally, the approximate

number of 10-mm images on which the ICH was seen was calculated (C)-comparing each CT image with hemorrhage to the CT image with the largest hemorrhage on that scan calculated C. If the hemorrhage area for a particular image was greater than 75% of the size seen on the image where the hemorrhage was most significant, the image was considered one hemorrhage image for determining C. If the area was approximately 25% to 75%, the image was considered half a hemorrhage image; if the area was less than 25% of the largest hemorrhage, the image was not considered a hemorrhage image. These CT hemorrhage image values were then added to determine the value for C. All measurements for A and B were made using the centimeter scale on the CT scan to the nearest 0.5 cm. A, B, and C were then multiplied, and the product was divided by 2, which yielded the volume of hemorrhage in cubic centimeters. The degree of shift and herniation developed in patients didn't measure in the radiological images because these images were admission cranial CT, and herniation was not an expected finding in the first images. In addition, patients who died due to secondary causes were not included in the study.

#### **Statistical Analysis**

Statistical Package for Social Sciences 18.0 for Windows (SPSS Inc., Chicago, USA) program was used for statistical analysis of the data. Descriptive statistics of the obtained data were given as percentage (%) and number for categorical variables, and median (25 Percentiles, 75 Percentiles) for numerical variables. When the data between the survival and non-survival groups; high (>=0,6) and low (<0,6) IG% groups were compared, the Student's t-test and the Mann-Whitney U test were used for normally and non-normally distributed variables, respectively. Pearson Chi-square test was performed to determine whether there was a significant difference between conditions with a nominal distribution, such as: gender, diabetes mellitus (DM), hypertension (HT), hyperlipidemia (HL), atrial fibrillation (AF), coronary artery disease (CAD), prior stroke, GCS, antiplatelet agent (APA) use, oral anticoagulant (OAC) use, antihypertensive (AH) use, statin use, brainstem hemorrhage (BH), lober hemorrhage (LH), basal ganglia hemorrhage (BGH), cerebellum hemorrhage (CH), intraventricular hemorrhage (IVH), and surgical operation. Receiver Operating Characteristic (ROC) analysis was performed and Youden's index was used to determine Area Under Curve (AUC), sensitivity, specificity and cut-off values. A p value of <0.05 was considered statistically significant. For the multivariate analysis, the possible factors identified with univariate analyses were further entered into the logistic regression analysis to determine independent predictors of patient outcome.

### RESULTS

A total of 110 SICH patients who met the inclusion criteria were included in the study. 45 (42.7%) patients were female, and 65 (57.3%) were male. The median and interquartile range IQR ages of the patients were 70.5 and 65-77.2, respectively. Some of the patients also had comorbidities. 36 (32.7%) patients with DM, 101 (91.8%) patients with HT, 19 (17.2%) patients with HL, 14 (12.7%) patients with AF, 36 (32.7%) patients with CAD, and 21 (19.1%) ) patients with a previous stroke. Some of the patients were using drugs. 22 (20.0%) patients used APA, 16 (14.5%) patients used OAC, 95 (86.4%) patients used AH, and 9 (8.2%) patients used statins. When we classify patients according to ICH regions: 9 (8.3%) patients with bleeding into the brain stem, 39 (35.5%) patients with bleeding into the lober, 57 (51.8%) patients with bleeding into the basal ganglia, 6 (5.5%) patients with bleeding into the cerebellum, 39 (35.5%) patients with IVH, and 9 (8.2%) patients with who had a surgical operation.

When the demographic and hemogram data of nonsurvival and survival patients were classified according to hospital mortality (Table 1), it was observed that 30 patients were in the non-survival group and 80 patients were in the survivor group. There was no statistical difference between the ages of the non-survival and survival groups. Hyperlipidemia was higher in the survival group (p=0.018). On the other hand, atrial fibrillation (p=0.018), oral anticoagulant use (p=0.001), systolic (<0.001), and diastolic blood pressure (0.001) were statistically significantly higher in a non-survival group compared to the survival group. Furthermore, IVH, HV, pulse, WBC, PLT, PCT, NRBC#, NRBC%, NEUT#, IG#, and IG% values of the non-survival group were significantly higher in the non-survival group compared to the survival group. GCS values were substantially lower in the non-survival group compared to the survival group.

When the patients were classified according to low IG% (<0.6) and high IG% (>=0.6), (**Table 2**) 30 patients were in the high IG# group, and 80 patients were in the low IG% group. There was no statistically significant difference between the two groups regarding age and gender (p>0.05). WBC, NEUT#, MONO#, IG#, NLR, and HV values were significantly elevated in the high IG% group compared to the low IG% group; GCS and LYMPH% values were decreased in the high IG% group compared to the low IG% group. In addition, the mortality rate in the high IG# group was significantly increased compared to the mortality rate in the low IG% group (p=<0.001).

Table 1. Comparison of demographic, clinical and hemogram data of deceased and surviving patients with SICH				
	Non-Survival (30)	Survival (80)	р	
Age (Years)	72 (68;78)	70 (64;77)	0.119	
Male Gender n(%)	18 (60.0)	45 (56.3)	0.723	
<b>Clinical History</b>				
DM	10 (33.3)	26 (32.5)	0.934	
HL	1 (3.3)	18 (22.5)	0.018	
HT	29 (96.7)	72 (90.0)	0.256	
AF	9 (30.0)	5 (6.3)	0.001	
CAD	15 (50.0)	21 (26.3)	0.018	
Prior Stroke	7 (23.3)	14 (17.5)	0.488	
Vital Signs at ED pro	esentation			
SBP (mmHg)	190 (177; 205)	155 (140; 180)	< 0.001	
DBP (mmHg)	100 (97;110)	80 (70; 100)	0.001	
Heart Rate (BPM)	75 (69; 85)	70 (68; 74)	0.033	
GCS	5 (3; 12)	14 (13; 15)	< 0.001	
Prestroke Medicatio	ns			
APA	6 (20.0)	16 (20.0)	1.000	
OAC	10 (33.3)	6 (7.5)	0.001	
AH	28 (93.3)	67 (83.8)	0.192	
Statin	1 (3.3)	8 (10.0)	0.256	
<b>Brain Imaging ICH</b>	Parameters			
HV (mL)	33 (13; 51)	7.5 (1.3; 22.7)	< 0.001	
Location				
BH	5 (16.7)	4 (5.1)	0.111	
LH	8 (26.7)	31 (38.8)	0.238	
BGH	15 (50.0)	42 (52.5)	0.815	
CH	2 (6.7)	4 (5.0)	0.732	
Presence of IVH	17 (56.7)	22 (27.5)	0.005	
Surgery	5 (16.7)	4 (5.0)	0.061	
Laboratory Features	<b>i</b>			
WBC (×10 <sup>9</sup> /L)	11.1 (8.8; 14.5)	9.2 (7.1; 11.3)	0.006	
PLT (×10 <sup>9</sup> /L)	255 (257; 300)	205 (170; 248)	0.002	
PCT (%)	0.26 (0.21; 0.30)	0.20 (0.17; 0.25)	0.002	
NRBC# (×10 <sup>9</sup> /L)	0.00 (0.00; 0.00)	0.00 (0.00; 0.00)	0.012	
NRBC%	0.00 (0.00; 0.00)	$0.00\ (0.00;\ 0.00)$	0.045	
NEUT# (×10 <sup>9</sup> /L)	8.72 (6.07; 12.5)	7.05 (4.82; 8.97)	0.009	
LYMPH% (×10 <sup>9</sup> /L)	12.8 (6.5; 17.8)	15.4 (10.5; 23.3)	0.044	
MONO# (×10 <sup>9</sup> /L)	0.72 (0.40; 0.88)	0.57 (0.43; 0.69)	0.080	
IG# (×10 <sup>9</sup> /L)	0.06 (0.03; 0.12)	0.04 (0.02; 0.05)	0.001	
IG (%)	0.6 (0.4; 0.8)	0.4 (0.2; 0.5)	0.002	
NLR	6.4 (4.3; 9.8)	4.6 (2.9; 8.9)	0.116	
PLR	169 (109; 292)	146 (97; 206)	0.254	

Abbrevations: DM, diabetes mellitus; HL, hyperlipidemia; HT, hypertension; AF, atrial fibrillation; CAD, coronary artery disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; GCS, Glasgow coma score; APA, antiplatelet agent; OAC, oral anticoagulant; AH, antihypertensive; HV, hemorrhage volume; BH, brainstem hemorrhage; LH, lober hemorrhage; BGH, basal ganglia hemorrhage; CH, cerebellum hemorrhage; IVH, intraventricular hemorrhage; WBC, white blood cell, PLT, platelet; PCT, Plateletcrit; NRBC#, Nucleated red blood cell count; NRBC%, Nucleated red blood cells percentage; NEUT#, neutrophil count; LYMPH#, lymphocyte percentage; MONO#, monocyte count; IG%, immature granulocyte percentage; NLR, neutrophillymphocyte ratio; PLR, platelet-lymphocyte ratio

Referans Interval: WBC(×10<sup>9</sup>/L): (3.39 - 8.86), PLT (×10<sup>9</sup>/L): (171 - 388), PCT (%): (0.19 - 0.41), NRBC(×10<sup>9</sup>/L): (0.000 - 0.015), NRBC (%): (0.000 - 0.030), NEUT# (×10<sup>9</sup>/L): (1.50 - 5.00), LYMPH (%): (21.6 - 49.0), MONO#(×10<sup>9</sup>/L): (0.22 - 0.63), IG#(×10<sup>9</sup>/L): (0.01 - 0.04), IG (%): (0.16 - 0.62)

The Student's t-test and the Mann-Whitney U test were used for normally and nonnormally distributed variables respectively.

Pearson Chi-square test was performed to determine whether there was a significant difference between conditions with a nominal distribution.

<b>Table 2.</b> Comparison of demographic, clinical and hemogram data of SICH patients with high ( $>=0.6$ ) and low ( $<0.6$ ) IG%						
	High IG% Group (30)	Low IG% Group (80)	р			
Age (Years)	73 (67;77)	70 (64;78)	0.325			
Male Gender n(%)	21 (58.3)	42 (56.8)	0.875			
Clinical History						
DM	12 (40)	24 (30)	0.320			
HL	5 (16.7)	14 (17.5)	0.918			
HT	30 (100)	71 (88.8)	0.055			
AF	4 (13.3)	10 (12.5)	0.907			
CAD	14 (46.7)	22 (27.5)	0.056			
Prior Stroke	8 (26.7)	13 (16.3)	0.216			
Vital Signs at ED presentation						
SBP (mmHg)	175 (150; 193)	170 (150; 190)	0.360			
DBP (mmHg)	100 (88; 110)	100 (80; 100)	0.166			
Heart Rate (BPM)	73 (69; 79)	73 (70; 76)	0.860			
GCS	13 (7.7; 14.2)	14 (13;15)	0.021			
Prestroke Medications						
APA	9 (30.0)	13 (16.3)	0.108			
OAC	4 (13.3)	12 (15.0)	0.825			
AH	29 (96.7)	66 (82.5)	0.064			
Statin	4 (13.3)	5 (6.3)	0.227			
<b>Brain Imaging ICH</b>	Parameters					
HV (mL)	17.0 (4.8; 32.3)	5.1 (1.8; 20.7)	0.025			
Location						
BV	3 (10.3)	6 (7.5)	0.663			
LV	13 (43.3)	26 (32.5)	0.290			
BGV	12 (40.0)	45 (56.3)	0.129			
CV	2 (6.7)	4 (5.0)	0.663			
Presence of IVH	12 (40.0)	27 (33.8)	0.542			
Surgery	3 (10.0)	6 (7.5)	0.702			
Laboratory Feature	s					
WBC (×10 <sup>9</sup> /L)	11.1 (8.9; 17.1)	9.1 (7.2; 11.2)	0.002			
PLT (×10 <sup>9</sup> /L)	218 (260; 270)	205 (170; 248)	0.444			
PCT (%)	0.23 (0.18; 0.30)	0.22 (0.18; 0.26)	0.164			
NRBC# (×10 <sup>9</sup> /L)	0.00 (0.00; 0.00)	0.00 (0.00; 0.00)	0.326			
NRBC (%)	0.00 (0.00; 0.00)	0.00 (0.00; 0.00)	0.687			
NEUT# (×10 <sup>9</sup> /L)	8.9 (6.1; 14.8)	6.9 (4.8; 8.8)	0.002			
MONO# (×10 <sup>9</sup> /L)	0.73 (0.54; 1.00)	0.56 (0.40; 0.69)	0.001			
LYMPH (%)	12.8 (6.5; 17.8)	15.4 (10.5; 23.3)	0.044			
IG (%)	0.09 (0.06; 0.15)	0.03 (0.02; 0.05)	< 0.001			
NLR	6.3 (4.2; 13.1)	5.0 (2.9; 7.6)	0.048			
Mortality (%)	16 (53.23)	14 (17.5)	< 0.001			

Abbrevations: DM, diabetes mellitus; HL, hyperlipidemia; HT, hypertension; AF, atrial fibrillation; CAD, coronary artery disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; GCS, Glasgow coma score; APA, antiplatelet agent; OAC, oral anticoagulant; AH, antihypertensive; HV, hemorrhage volume; BH, brainstem hemorrhage; LH, lober hemorrhage; BGH, basal ganglia hemorrhage; CH, cerebellum hemorrhage; IVH, intraventricular hemorrhage; WBC, white blood cell, PLT, platelet; PCT, Plateletcrit; NRBC#, Nucleated red blood cell count; NRBC%, Nucleated red blood cells percentage; NEUT#, neutrophil count; LYMPH#, lymphocyte percentage; MONO#, monocyte count; IG%, immature granulocyte percentage; NLR, neutrophillymphocyte ratio; PLR, platelet-lymphocyte ratio

Referans Interval: WBC(x109/L): (3.39 - 8.86), PLT (x109/L): (171 - 388), PCT (%): (0.19 - 0.41), NRBC(×10<sup>9</sup>/L): (0.000 - 0.015), NRBC (%): (0.000 - 0.030), NEUT# (×10<sup>9</sup>/L): (1.50 - 5.00), LYMPH (%): (21.6 - 49.0), MONO#(×10<sup>9</sup>/L): (0.22 - 0.63), IG#(×10<sup>9</sup>/L): (0.01 - 0.04), IG (%): (0.16 - 0.62)

The Student's t-test and the Mann-Whitney U test were used for normally and nonnormally distributed variables respectively. Pearson Chi-square test was performed to determine whether there was a significant difference between conditions with a nominal distribution. In the ROC analysis (**Table 3**), IG# (cut off: 0.055, AUC: 0.703), IG% (cut off: 0.55, AUC: 0.693), HV (cut off: 0.693) off: 12.1, AUC: 0.801), and PCT (cut off: 0.255, AUC: 0.692), tests showed moderate-high predictive properties.

Table 3. ROC analysis values of some hematological data in SICH patients						
	Cut-off	AUC	95%CI	р	Sensivite %	Spesifite %
IG#	0.055	0.703	0.59-0.82	0.001	57	77
IG (%)	0.55	0.693	0.58-0.81	0.002	53	84
HV (mL)	12.1	0.801	0.71-0.89	< 0.001	80	72
Abbrevations: IG#, immature granulocyte count; IG%, immature granulocyte percentage; HV, hemorrhage volume						

In the univariate logistic regression analyses performed, IG% (OR:4.488, 95% CI:1.342-12.017, p=0.020), OAC (OR: 6.167, 95% CI: 2.000-19.018, p=0.002), HV (OR: 1.039, 95% CI: 1.1019-1.059 p<0.001), and IVH (OR: 3.448, 95) %CI: 1.440-8.255 p=0.005) were found to be independent predictors of hospital mortality. In multivariate logistic regression analysis, IG% OR: 11.218, 95% CI: 1.637-76.867, p=0.014), OAC (OR: 9.090, 95% CI: 2.124-38.905, p=0.003), HV (OR: 1.030, 95% CI: 1.1009-1.051 p=0.005), and IVH (OR: 3.922, 95 % CI: 1.180-13.032 p=0.026) were independent predictors of hospital mortality. Interestingly, IG% has a very high OR (**Table 4**).

Table 4. Logistic regression analysis of independent markers of hospital mortality in SICH patients						
	Univariate OR (95% CI)	р	Multivariate OR (95% CI)	р		
Age (Years)	1.030 (0.989-1.073)	0.152	1.066 (0.998-1.138)	0.056		
OAC	6.167 (2.000-19.018)	0.002	9.090 (2.124-38.905)	0.003		
HV (mL)	1.039 (1.019-1.059)	< 0.001	1.030 (1.009-1.051)	0.005		
Presence of IVH	3.448 (1.440-8.255)	0.005	3.922 (1.180-13.032)	0.026		
PLT (×10 <sup>9</sup> /L)	1.011 (1.003-1.018)	0.005	1.015 (1.005-1.025)	0.004		
IG (%)	6.488 (1.342-12.017)	0.020	11.218 (1.637-76.867)	0.014		
Abbrevations: OAC, oral anticoagulant; HV, hemorrhage volume; IVH, intraventricular hemorrhage: PLT platelet: IG% immature granulocyte percentage						

# DISCUSSION

The most important result of our study is that IG is an inexpensive, easily accessible, and important prognostic marker in predicting mortality in patients with SICH. Furthermore, in many studies (3-7) IG, is an important biomarker in predicting mortality and disease severity in patient groups, is also promising in patients with SICH.

Previous studies have associated white blood cells and NEUT#, NLR, PLR, and other inflammatory parameters with poor prognosis in SICH patients. For example, Lattanzi et al. (8) associated higher WBC in peripheral blood with hematoma early deterioration and enlargement. In addition, in previous studies, high WBC were found to be a strong predictor of poor prognosis in the prognosis of SICH and subarachnoid hemorrhage (SAH) patients (9). In a study by Walsh et al. (10), the MONO# was independently associated with the 30-day case fatality rate in 240 adults SICH patients. Another study reported that a high PLR value was a significant predictor for short-term prognosis in SICH patients (11). In our research, WBC, PLT, NEUT#, and were significantly higher in the non-survival group than survival group but for NLR and PLR was no significant difference between groups.

The early mortality of SICH has been reported to be approximately 30% to 40%. In our study, the mortality rate was determined as 37.5%. Consistent with other previously published studies, neither gender nor age was a significant predictor of outcome (10). In addition, for hypertension, diabetes, coronary artery disease, and the use of antiplatelet agents parameters there was not a significant difference between the survival and nonsurvival groups. However, similar to the literature, the mortality rate was significantly higher in patients with atrial fibrillation and using oral anticoagulants (11). It was thought that it might be due to their bleeding-increasing effects. However, hyperlipidemia was significantly higher in surviving patients. Roquer et al. (12) also found that low lipid serum levels are associated with poor prognosis in SICH. Iso et al. (13) also showed an inverse relationship between serum cholesterol levels and mortality in SICH. Moreover, our study confirmed that initial judgment status and ICH volume, as defined in previous studies, are significant predictors of mortality (14). Initial hemorrhage volume and associated cerebral edema are a sequential delayed effect on the medical course. It causes an increase in intracranial pressure and increases the risk of mortality. In addition, we found intraventricular hemorrhage is significantly associated with mortality, similar to the literature (15). The primary treatment is antiedema and general supportive therapy by keeping the systemic arterial blood pressure at the desired level. In our study, there was no statistical difference in mortality between patients who received and non received surgical treatment. The location of hemorrhage was not identified as a risk factor for mortality. While the infratentorial location was significant for mortality in some studies, it was not consistent in others (16).

IG is an early marker of bone marrow activation that can be easily and quickly measured from peripheral blood without needing additional equipment. In recent years, with technological developments, simple and easily measurable biomarkers such as IG have been used for diagnostic and prognostic purposes in many diseases. Immature granulocytes in the circulation are generally not released into the peripheral blood in healthy individuals, and elevation of immature granulocytes is an essential feature of early inflammation. Studies conducted in recent years have shown that IGC and IG% increase in cases of infection and sepsis (17). In such cases, an increase in the IGC may help indicate the presence of acute inflammation. In addition, studies have revealed that IG are significantly higher in the early period in many inflammatory conditions such as acute appendicitis, acute pancreatitis, and after cardiac surgery (16-20). In addition, it has been shown that IGC at admission can significantly predict mortality in cardiovascular diseases (21). Moreover, one study showed that IG alone effectively predicted 30-day mortality in ischemic stroke. Korkut et al. (6) also showed that a higher IG number at admission in SICH was an independent predictor of 1-month mortality. To the best of our knowledge, there has yet to be a study in the literature examining the relationship between the IG and the in-hospital mortality of SICH. Only one study examined 30-day mortality. Our study found that the IGC and IG% was significantly higher in non-survival group than in survival group. Patients with an IG% of 0.6 and above had a considerably worse prognosis in-hospital mortality. In addition, the high IG% in our study was determined to be an independent risk factor for mortality in SICH patients.

Our study had some limitations. First, it is a single-center and retrospective study. Second, serial IG measurements were kept a secret. Another limitation is the absence of tumor necrosis factor and interleukin-6 levels, which we could not test in the emergency department. Finally, prospective studies of the made larger patient population are needed to understand the mortality relationship between IG and SICH.

#### **CONCLUSION**

This study showed that IG is a new, easily accessible, inexpensive, meaningful, and promising marker for predicting mortality in patients with SICH. In addition, in centers where CT is not available, it can be useful and even life-saving in differential diagnosis and early referral of the patient to an advanced center.

### ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was carried out with the permission of Kastamonu University Medical Faculty Clinical Researches Ethics Committee (Date: 05.10.2022, Decision No: 2022-KAEK-85).

**Informed Consent:** Because the study was designed retrospectively, no written informed consent form was obtained from patients.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

#### REFERENCES

- 1. Broderick JP, Adams Jr HP, Barsan W, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: a statement for healthcare professionals from a special writing group of the Stroke Council. Am Heart Assoc Stroke 1999; 30: 905-15.
- 2. Tao C, Hu X, Wang J, et al. Admission neutrophil count and neutrophil to lymphocyte ratio predict 90-day outcome in intracerebral hemorrhage. Biomarkers Med 2017; 11: 33-42.
- 3. Ünal Y, Barlas AM. Role of increased immature granulocyte percentage in the early prediction of acute necrotizing pancreatitis. Turk J Trauma Emerg Surg 2019; 25: 177-82.
- 4. Bedel C, Korkut M, Aksoy F, Kuş G. Usefulness of immature granulocytes to predict high coronary SYNTAX score in acute coronary syndrome; a cross-sectional study. Arch Acad Emerg Med 2020: 8.
- 5. Korkut M, Bedel C, Zortuk Ö, Selvi F. Can immature granulocytes indicate mortality in patients with acute ischemic stroke? Neurol Asia 2021; 26: 665-70.
- Bedel C, Korkut M, Selvi F, Zortuk Ö. The immature granulocyte count is a new predictor of the 30-day mortality in intracerebral haemorrhage patients: preliminary study. Indian J Neurosurg 2021; 10: 114-20.
- Korkut M, Bedel C, Sivil R, et al. Usefulness of immature granulocytes as a prognostic factor in st-elevation myocardial infarction. Brazilian J Cardiovasc Surg 2022; 37: 6.
- Lattanzi S, Cagnetti C, Provinciali L, Silvestrini M. Neutrophilto-lymphocyte ratio predicts the outcome of acute intracerebral hemorrhage. Stroke 2016; 47: 1654-7.
- Al-Mufti F, Amuluru K, Damodara N, et al. Admission neutrophillymphocyte ratio predicts delayed cerebral ischemia following aneurysmal subarachnoid hemorrhage. J Neurointerventional Surg 2019; 11: 1135-40.
- 10. Walsh KB, Sekar P, Langefeld CD, et al. Monocyte count and 30day case fatality in intracerebral hemorrhage. Stroke 2015; 46: 2302-4.
- 11.Zhang W, Shen Y. Platelet-to-lymphocyte ratio as a new predictive index of neurological outcomes in patients with acute intracranial hemorrhage: a retrospective study. Medical Science Monitor: Int Med J Experiment Clin Res 2018; 24: 4413.
- 12. Bhatia R, Singh H, Singh S, et al. A prospective study of in-hospital mortality and discharge outcome in spontaneous intracerebral hemorrhage. Neurol India 2013; 61: 244.
- 13. Iso H, Jacobs Jr DR, Wentworth D, et al. Serum cholesterol levels and six-year mortality from stroke in 350,977 men screened for the multiple risk factor intervention trial. New Engl J Med 1989; 320: 904-10.

- 14. Takahashi O, Cook EF, Nakamura T, et al. Risk stratification for in-hospital mortality in spontaneous intracerebral haemorrhage: a Classification and Regression Tree analysis. J Assoc Physicians 2006; 99: 743-50.
- 15. Hwang BY, Bruce SS, Appelboom G, et al. Evaluation of intraventricular hemorrhage assessment methods for predicting outcome following intracerebral hemorrhage. J Neurosurg 2012; 116: 185-92.
- 16.Godoy DA, Pinero G, Di Napoli M. Predicting mortality in spontaneous intracerebral hemorrhage: can modification to original score improve the prediction? Stroke 2006; 37: 1038-44.
- 17.Lima LR, Cunha GS, Nogueira KS, Comar SR. Automated immature granulocyte count in patients of the intensive care unit with suspected infection. J Brasileiro de Patologia e Medicina Laboratorial 2019; 55: 267-80.
- 18. Ünal Y. A new and early marker in the diagnosis of acute complicated appendicitis: immature granulocytes. Ulus Travma Acil Cerrahi Derg 2018; 24: 434-9.
- 19. Daix T, Guérin E, Tavernier E, et al. Immature granulocytes: a risk factor of infection after cardiac surgery. Cytometry Part B: Clinical Cytometry 2018; 94: 887-94.
- 20.Karakulak S, Narcı H, Ayrık C, Erdoğan S, Üçbilek, E. The prognostic value of immature granulocyte in patients with acute pancreatitis. Am J Emerg Med 2021; 44: 203-7.
- 21. Monteiro Júnior JGDM, de Oliveira Cipriano Torres D. Hematological parameters as prognostic biomarkers in patients with cardiovascular diseases. Curr Cardiol Rev 2019; 15: 274-82.