ISSN 2458-8865 E-ISSN 2459-1505
www.fppc.com.tr
Family Practice and Palliative Care
https://doi.org/10.22391/fppc.817258

Research Article

Evaluation of the relation of Platelet Volume Index, MPV and RDW values with mortality in spontaneous intraparenchymal hemorrhages

Spontan intraparankimal kanamalarda Platelet Volüm İndex, MPV ve RDW değerlerinin mortalite ile ilişkisinin değerlendirilmesi

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Abstract

Introduction: Intracerebral Spontaneous Hemorrhage (ISH) is a sudden hemorrhage into the brain parenchyma as a result of a rupture of the cerebral vessels that are not related to traumas. The purpose of the present study was to evaluate the relation of mortality with Platelet Volume Index (PVI) scoring systems, which have been reported in a small number of studies in terms of blood RDW, MPV, platelet and intracranial hemorrhages in patients diagnosed with intraparenchymal hemorrhage in Emergency Departments.

Methods: This study was performed retrospectively by examining patient files of patients who came to Emergency Medicine Clinic between 01.01.2019-31.12.2019. As a control group for comparison of blood parameters, blood parameters of 72 patients suitable for the same age population, without intraparenchymal haemorrhage.

Results: A total of 54.10% (n=85) intraparenchymal bleeding patients (IPC) and 45.90% (n=72) healthy control groups (HCG) were included in the study. There was no statistically significant difference between the clinical results of IPC groups in terms of mortality of RDW parameter and MPV parameter (p=0.930; p=0.118). When PVI ratio was evaluated in IPC group and HCG; the mean PVI (MPV/Platelet ratio) in the IPC group was 4.37±1.66, and the PVI (MPV/Platelet ratio) in the HCG was 3.89±1.02.A statistically significant difference was found between the PVI in the patient group and the HCG.A statistically significant difference was found between the PVI ratio clinical results of the patients with IPC (p=0.043).

Conclusion: Spontaneous Intraparenchymal hemorrhage are among the leading causes of stroke-induced mortality and disability. The Hemphill Score and hemorrhage volume are important factors in mortality evaluation in intraparenchymal hemorrhage. There are not many studied conducted on Platelet Volume Index, and it is an important marker in predicting mortality, especially in these patients.

Keywords: Intraparenchymal haemorrhage, Mean platelet volume, Red cell distribution width

Öz

Giriş: Spontan İntraserebral hemoraji (İSH), aniden oluşan ,travmaya bağlı olmayan beyin damarları rüptürü sonucu beyin parankimi içine kanamalardır. Bu çalışma ile intraparankimal kanama tanısı alan hastalarında kan RDW, MPV, platelet ve şu ana kadar intrakraniyal hemorajilerde az sayıda çalışma bildirilen platelet volüm indexinin (PVI) skorlama sistemleri ile birlikte mortalite ilişkisini değerlendirmesini amaçladık.

Yöntem: Bu çalışma 01.01.2019-31.12.2019 tarihleri arasında Acil Tıp Kliniğine gelen hastaların hasta dosyaları incelenerek retrospektif olarak yapıldı. Kan parametrelerinin karşılaştırılması için kontrol grubu olarak, intraparankimal kanama olmayan aynı yaş popülasyonuna uygun 72 hastanın kan parametreleri değerlendirildi. Klinik sonuçlara göre RDW, MPV, Platelet ve PVI kan parametreleri değerlendirildi.

Bulgular: Çalışmaya toplam %54,10 (n = 85) intraparankimal kanama hastası (IPK) ve %45,90 (n = 72) sağlıklı kontrol grubu (SKG) dahil edildi. IPK gruplarının klinik sonuçları arasında RDW parametresi ve MPV parametresinin mortalitesi açısından istatistiksel olarak anlamlı bir fark yoktu (p=0,930;p=0,118). IPK grubu ve SKG'de PVI oranı değerlendirildiğinde; ortalama PVI (MPV/Trombosit oranı) IPK grubu 4,37± 1,66 ve SKG'deki PVI (MPV/Trombosit oranı) 3,89 ± 1,02 idi. Hasta grubundaki PVI oranı ile SKG arasında istatistiksel olarak anlamlı bir fark bulundu. IPC'li hastaların PVI oranı klinik sonuçları değerlendirildi; mortalite açısından gruplar arasında istatistiksel olarak anlamlı fark vardı (p=0,043).

Sonuç: Spontan intraparankimal kanama, inmeye bağlı mortalite ve özürlülüğün önde gelen nedenleri arasındadır. Hemphill Score ve kanama hacmi intraparankimal kanamada mortalite değerlendirmesinde önemli faktörlerdir. Platelet Hacim İndeksi üzerine yapılmış çok fazla çalışma yoktur ve özellikle bu hastalarda mortaliteyi öngörmede önemli bir belirteçtir.

Anahtar Kelimeler: İntraparankimal kanama, Ortalama trombosit hacmi, Kırmızı hücre dağılım genişliği

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Introduction

Cerebrovascular diseases rank the third in terms of disability, in the second as the cause of mortality [1] and cerebrovascular diseases are basically classified into two groups as ischemic and hemorrhagic. Intracerebral Spontaneous Hemorrhage (ISH) is a sudden hemorrhage into the brain parenchyma as a result of a rupture of the cerebral vessels that are not related to traumas [2]. Intraparenchymal Hemorrhages are one of the diseases that have limited mortality, morbidity and treatment options [3]. Many parameters and scoring systems were reported to predict mortality in cerebrovascular diseases [4]. It was reported in some studies that the prognosis of intracerebral hemorrhage is determined by factors such as hematoma size, age, interventricular hemorrhage, and the activation of the inflammation process in intraparenchymal hemorrhages [6-8].

The RDW laboratory parameter, which is associated with inflammation in the light of the literature information, is called as the distribution width of the red blood cell [9]. RDW is the blood parameter that determines the mortality in many chronic diseases and vascular diseases regardless of hemoglobin and hematocrit [10-12]. It was reported in studies in the literature that there were increased RDW levels in the formation of clinically inflammatory conditions [9].

The platelet cells that were included in the scope of this study are responsible for cellular inflammation as well as chemokine, cytokine production and inflammatory process. Also, platelets play important roles in the migration of progenitor cells and leukocyte to vascular damage areas, and in the circulation of anti-inflammatory, proinflammatory, angiogenic factors and micro particles [13,14]. The Mean Platelet Volume (MPV), which is a marker of the functions of platelet cells, indicates platelet activation. In general, large platelets are considered to be more reactive [15,16]. It is reported in the literature that the MPV values increase in acute ischemic diseases and MPV values decrease in activation periods of chronic inflammatory diseases [17,18]. The change in the MPV value in acute and chronic diseases remains uncertain in terms of its association with mortality, especially in intracranial hemorrhage [19]. The PVI (Platelet Volume Index) plays roles specially to evaluate the activities of platelets that play roles in inflammation more clearly [20]. In some previous studies, it was reported that PVI is one of the thromboembolism markers and may be an important marker in evaluating the risk of cardiovascular disease in diabetes and hypertension [21, 22].

The purpose of the present study was to evaluate the relation of mortality with Platelet Volume Index (PVI) scoring systems, which have been reported in a small number of studies in terms of blood RDW, MPV, platelet and intracranial hemorrhages in patients diagnosed with intraparenchymal hemorrhage in Emergency Departments.

Method

Study Design

The present study was conducted retrospectively by examining the Hospital Automation System and patient files admitting to Yozgat Bozok University and Istanbul Health Sciences University Kanuni Sultan Suleyman Education and Research Hospital Emergency Medicine Clinic between 01.01.2019 and 31.12.2019 with intraparenchymal hemorrhage. Patients who were over the age of 18 were included in the study. The approval of the study was obtained from the Local Ethics Committee. In the records, 85 patients who had complete files among the total 105 patients were included in the study. As the Control Group to compare the blood parameters, the blood parameters of 72 patients of the same age group with nonspecific complaints and no additional diseases were evaluated. According to the clinical results of the patient data, they were divided into patients with healthy discharge and those who died. The 30-day mortality of the patients was evaluated. The Hemphill Score was used as the index in intraparenchymal hemorrhage. The Hemphill Score consists of the volume of hemorrhage, age, basal Glasgow Coma Scale (GKS) scores, and the presence of intraventricular and infratentorial hemorrhage [23].

Those with Glasgow Coma Scale 13-15 were included in Group 1, GKS 5-12 in Group 2, GKS 3-4 Group 3. In the first 24 hours of hospital admissions of the patients with intracerebral hemorrhage, full blood count values were recorded from venous blood samples placed in tubes with EDTA. In blood analysis, the MPV, RDW, Platelet (PLT) blood parameters were recorded from the files of each patient and for the control group. Platelet Volume Index was calculated as PVI = MPV value (fl)/PLT per 1000 x100 [24], and the calculated PVI values were then recorded. The hemorrhage size of the patients with intraparenchymal hemorrhage was recorded. The elimination of the causes that might lead to similar clinical and imaging findings (i.e., hemorrhage into the intracranial mass or trauma-related intracranial hemorrhage, and hemorrhagic transformation into the ischemic area) was excluded from the study. The hemorrhage volume of the patients who were included in the study was calculated by using the ABC/2 Formula [17]. The volume of the hematoma mass was calculated in approximately milliliters (ml) as a result of multiplying the widest diameter in CT section. Intraparenchymal hematoma locations were classified according to residential areas as lobber, deep parenchymal, and infratentorial. There were two groups according to the way it was opened to the ventricle and not.

Ethical approval

The ethical approval was obtained from the Ethics Committee of Yozgat Bozok University (IRB Number: 2019-10-218, Date: 30.10.2019)

Statistical Analysis

SPSS statistical software (version 20.0; SPSS, Chicago, IL) was used to complete all analyses. Descriptive statistics were used in the demographic examination of the patients. In the study, the Chi-Square Test was applied if the data were qualitative. When the study data were evaluated, numerical values were expressed as mean ± standard deviation. In the context of clinical research, the Mann-Whitney U-test were used in statistical evaluations according to the categorical (nominal or ordinal) and numerical independent groups of nonparametrically related variables. Spearman Rank Correlation Method was used in nonparametric data for correlations between data. According to the clinical results, the efficiency of RDW, MPV, PVI, and hemorrhage size was evaluated in terms of mortality with ROC curve (Receiver-Operating Characteristics Curve). The results were evaluated at a significance level of $p < 0.05$.

Results

A total of 54.10% (n=85) patients with intraparenchymal hemorrhage (IPK) and 45.90% (n=72) healthy control group (HCG) between 01.01.2019 -31.12.2019 were included in the study. In our study, data of 85 patients who were admitted to the hospital due to IPK (Intraparenchymal Hemorrhage) and with complete file data were analyzed. The results of the analysis are shown in Table 1 (Table 1). No significant differences were detected in median age between 85 patients with IPK and 72 control group (z:-0.338; p=0.735). A total of 34.10% (n=29) of the IPK patients were female, and 65.90% (n=56) were male. The healthy control group consisted of 51.49% (n=37) female, and 48.51% (n=35) male individuals, and no significant differences were detected in terms of gender between the two groups (χ^2:2.423; p=0.120).

Table 1. The Demographic characteristics of the study groups

Demographic Characteristics - Independent Variables (IVs)	Name of Characteristics	Number	Percent (%)	Mean±SD	p
Patients, Gender	Female	29	34.10		
	Male	56	65.90		
Control, Gender	Female	37	51.49		
	Male	35	48.51		
Statistical Analysis (Chi-Square Test)					
Patients, Age				60.09± 15.06	0.120*
Control, Age				60.27±10.35	
Statistical Analysis (Mann-Whitney U-test)					
Clinical results of patients	Discharged with Health	66	77.64		0.735*
	Exitus	19	22.36		

Chi-Square Test item was used as statistical analysis.
Mann-Whitney U-test were used in statistical evaluations according to numerical independent groups of nonparametrically related variables. .* Not significant.

Clinical findings of patients with intraparenchymal hemorrhage

The clinical findings of the intraparenchymal patients and the hemorrhage characteristics parameters that made up the Hemphill Score are shown in Table 2. In this respect, when the Glasgow Coma Scale (GCS) scores of the patients were evaluated, patients had 68.20% (n=58%) GCS 13-15, 25.91% (n=22) GCS 5-12, and GCS <5 5.89 % (n=5). The mean hematoma volume of the patients was 12.26±13.37 cc (min: 0.18; max: 60). The hematoma locations of the patients were recorded as 45% (39) lobber, 35% (n=29) deep parenchymal, and 20% (n=17) infratentorial. In the mortality evaluation according to hematoma regions, infratentorial hemorrhage had the highest mortality rates, and 47.1% of the patients died. There were statistically significant differences in mortality between the groups (p<0.05).

Table 2. Distribution of patients according to their clinical results

Clinical final results	Discharged with Cure n(%)	Died	P value
Total	66(77.6)	19(22.4)	
Glasgow Coma Score			
GCS 13-15	57(98.3)	1(1.7)	
GCS 5-12	9(40.9)	13(59.1)	<0.001[a]
GCS <5	-	5(100)	
Hematoma Location			
Lobar	37(94.9)	2(5.1)	
Deep parenchymal	20(69)	9(31)	0.001[a]
Infratentorial	9(52.9)	8(47.1)	

Chi-Square Test item was used as statistical analysis. a: Significant at the 0.05 level (p<0.05). GCS: Glasgow Coma Score

A total of 80% (n=68) hemorrhages were not opened to intraventricular area, and hematoma hemorrhages in 20% (n=17) opened to intraventricular area. The Hemphill Mean Score was 1.07±1.13. A total of 77.60% (n=66) of the patients were discharged with cure, and 22.40% (n=19) patients died. Hemphill Index Parameters are shown in Table 2. When the relation between the clinical final results of the patients was evaluated, GCS score was significantly lower in patients who died (p<0.05). However, mean hematoma volume and Hemphill Index mean were significantly higher in patients who died (p<0.05).

Laboratory features of patient who had intraparenchymal hemorrhage and healthy control group

The differences in the laboratory findings between the patients who had intraparenchymal hemorrhage and the control group are shown in Table 3. The RDW-CV level values were higher in the patient group than in the control group (z;-3.036; p=0.002). The PVI (MPV/Platelet) ratios were significantly higher in IPK patient group than healthy control group (z:-2.191; p=0.028). Platelet laboratory parameter was significantly lower in the patient group than in the healthy group (z:-3.239; p=0.001). However, as seen in the table, the difference in the MPV laboratory parameter was not statistically significant in the patient and healthy group (z:-0.190; p=0.985).

Table 3. Laboratory characteristics of the patient with intraparenchymal hemorrhage and the healthy control group

Blood Parameters	Groups	Mean±SD	p
RDW Blood Parameter(%)	Patients	14.22±2.41	0.002[a]
	Control	13.23±1.33	
MPV Blood Parameter(fL)	Patients	10.47±2.63	0.985[b]
	Control	10.11±0.95	
Platelet Blood Parameter(u/L)	Patients	259.71±76.7x10^3	0.001[a]
	Control	288.69±96.6x10^3	
PVI (MPV/Platelet) Ratio	Patients	4.37±1.66	0.028[a]
	Control	3.89±1.02	

Mann-Whitney U-test item was used as statistical analysis. a: Significant at the 0.05 level (p<0.05), b: Not significant.

Evaluation of laboratory parameters, clinical features and mortality relationship of intraparenchymal patient group

The laboratory parameter evaluations according to the clinical results of the patients are shown in Table 4. In this respect, no significant differences were detected between the groups in the mortality assessment of patients with intraparenchymal hemorrhage of RDW-CV, MPV and platelet laboratory parameters (z:-0.878; p=0.930, z:-1.563; p=0.118, z:-0.047; p=0.962). However, the group of patients who died with PVI (MPV/PLT) had higher values in terms of clinical results and the PVI mean was significantly higher than the living patient group (z:-2.010; p=0.043). When the correlation between the Hemphill Index and PVI value was evaluated, a moderately positive and significant relation was detected (r_s:0.423; p=0.010). The relation between intraparenchymal hematoma volume and laboratory parameters indirectly affects the Hemphill Index. When the hematoma volume parameter that is used in Hemphill Index calculation and RDW, MPV, Platelet and PVI relations were evaluated together, a positive and moderate relation was detected between PVI index and hematoma size; and a weak and negative relation was detected between platelet laboratory parameter (r_s:-0.217; p=0.046). However, no positive or negative s were detected in terms of the correlation of RDW and MPV blood parameters regarding hematoma size (r_s:0.182; p=0.095, r_s:0.183; p=0.094).

Table 4. Comparison of blood parameters according to the clinical course of the patients

Blood Parameters	Groups	Mean±SD	p
RDW Blood Parameter(%)	Healthy Discharge Patients With IPC	14.34±2.51	0.930[b]
	Ex Patients With IPC	13.94±1.97	
MPV Blood Parameter(fL)	Healthy Discharge Patients With IPC	10.04±1.07	0.118[b]
	Ex Patients With IPC	10.61±2.93	
Platelet Blood Parameter(u/L)	Healthy Discharge Patients With IPC	261.26±69.02 x10^3	0.962[b]
	Ex Patients With IPC	252.89±69 x10^3	
PVI (MPV/Platelet) Ratio	Healthy Discharge Patients With IPC	4.47±2.29	0.043[a]
	Ex Patients With IPC	5.37±1.70	

Mann-Whitney U-test item was used as statistical analysis.a: Significant at the 0.05 level (p<0.05), b: Not significant.

ROC analysis for Hemphill Index, hematoma size, MPV/PLT parameters

The Hemphill Index, PVI and hematoma size, which are statistically significant for using to predict the mortality of IPK patients, and the EAA, cut-off, sensitivity and specificity were analyzed with the ROC curve for distinguishing the diagnostic efficacy and patient follow-up to guide the clinician about the patient's condition. The AUC, cut-off, sensitivity, specificity of the PVI were 0.708, 5.13, 68.42% and 81%, respectively for predicting mortality. The Hemphill Score, AUC, cut-off, sensitivity, and specificity were 0.903 1.54%, 84.83% and 78%, respectively. The ROC analysis results of the Hematoma Size in predicting mortality, AUC, cut-off, sensitivity, and specificity were 0.807 19.51 cc, 83.32% and 68%, respectively (Figure 1).

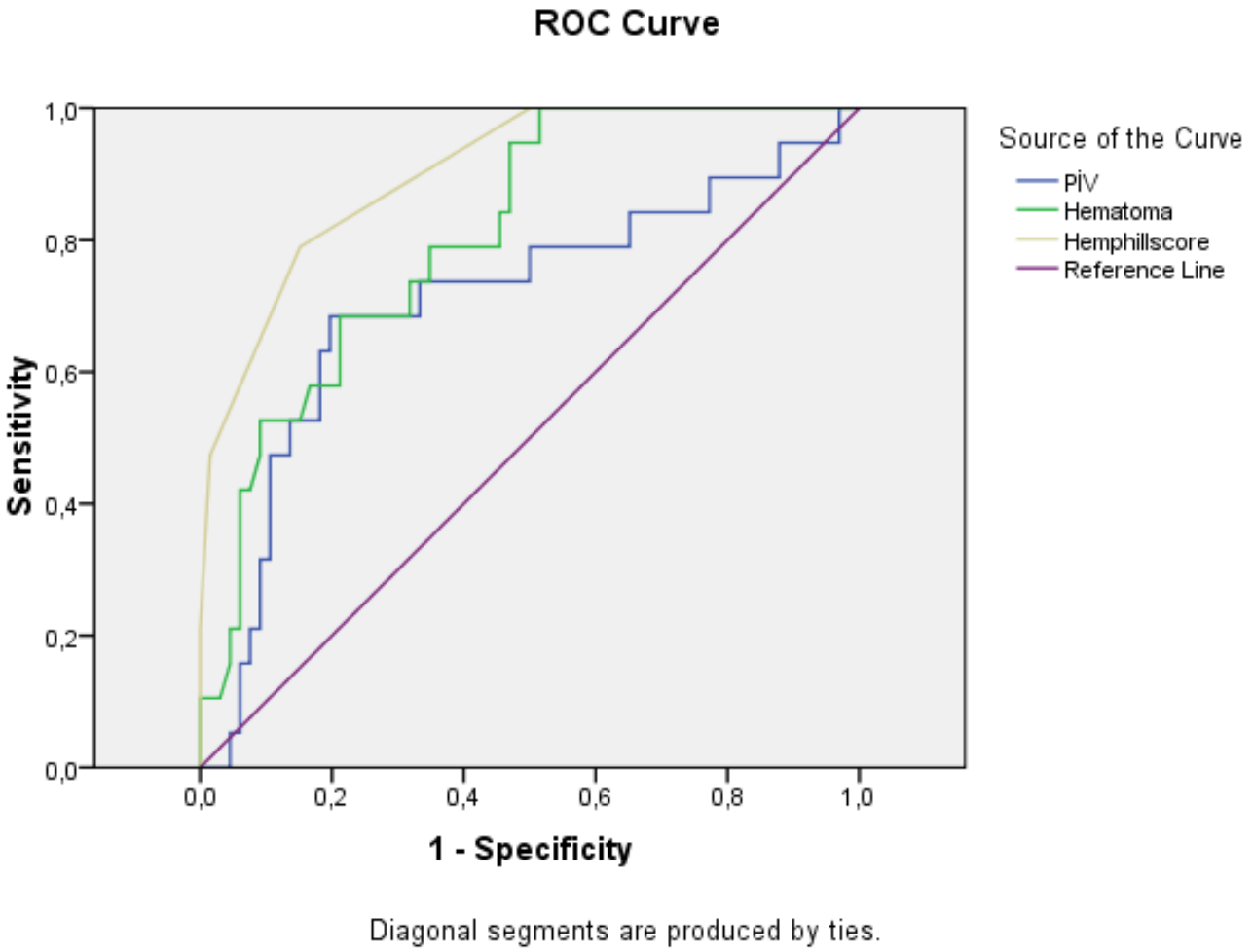

Figure 1. The Roc analysis Platelet volume index, Hematoma and Hemphill score point in predicting mortality in patients with IPC. The AUC, cut-off, of the PVI were 0.708, 5.13, respectively for predicting mortality. The Hemphill Score, AUC, cut-off was 0.903 1.54%, respectively. The ROC analysis results of the Hematoma Size in predicting mortality, AUC, cut-off was 0.807 19.51 cc.

Discussion

Although intraparenchymal hemorrhages are seen at a rate of 10-20% among all stroke types, their mortality and morbidity are higher than ischemic stroke and subarachnoid hemorrhage [25, 26]. Early detection of the disease during the diagnosis stage and effective treatment plans may reduce sequelae and mortality rates. The Hemphill Index is used to predict mortality especially in intraparenchymal hemorrhages [5]. In addition to this index, cheap and easily accessible prognostic markers are needed especially starting from 1st line healthcare facilities. In the present study, we evaluated RDW-CV, MPV, and platelet laboratory parameters, which are effective with full blood count, and which are easily available anywhere. The RDW-CV, PIV Index, and Platelet values differed compared to the healthy Control Group.

In the scope of the study, the RDW-CV parameter differed in the patient group compared to the healthy Control Group. The studies in the literature report that the RDW-CV laboratory parameter is increased during inflammation, chronic diseases, and hemorrhage-related diseases [27, 28, 29]. Inflammatory mechanisms are activated because of the damage done to nerve cells in intraparenchymal hemorrhages. In this respect, compensatory hyperplasia of the erythroid cell line is activated. Also, many immature red blood cells are released, and an increase occurs in the RDW-CV parameter [30]. Although they have different mechanisms than our study, some studies conducted on subarachnoid hemorrhage reported an increase in RDW [31,32]. In a study conducted on intensive care patients in the literature, it was reported that RDW might be a marker in predicting mortality [33]. According to our study findings, although we believe that the RDW-CV blood parameters are higher in patients with intraparenchymal hematoma than in healthy patients, it cannot be used as a prognostic marker in mortality evaluation even though we think it may be a marker in intraparenchymal hemorrhages.

The low platelet laboratory parameter levels in the scope of the study compared to the healthy Control Group may be because of the effect of the neuro-inflammatory mechanism and the migration of platelets. A study in the literature supported the results of our study, reporting that low platelet levels are concurrent especially during cerebral hemorrhages [34]. We think that low platelet levels cause clotting disorder, and it might be an element triggering intracerebral hemorrhage. According to the results of our study, it cannot be used as the predictor of mortality, but we think it may be a parameter to be considered in patients with suspected intracerebral hemorrhage. Although platelet levels were found to be low in patients with intracerebral hemorrhage in the study of Arikanoglu et al., which is similar to our study, it was not significant in terms of mortality

[16]. In a study conducted in the literature, they emphasized that especially the growth in intracerebral hematoma volume was associated with decreased platelet activity and caused a worse prognosis[35].

The Mean Platelet Volume (MPV), which is a laboratory parameter used to evaluate platelet functions, is reported to be a prognostic parameter indicating thromboembolism in ischemic cerebrovascular diseases [36]. In other studies of the literature, increases were reported in MPV levels, especially in thromboembolisms diseases such as Coronary Artery Disease and cerebrovascular disease [37]. The MPV value shows platelet activation. Cytokine, chemokine and clotting factors are activated and released from platelets, which increase in terms of volume in neural inflammation [36]. This occurs because of the increase in MPV values simultaneously with ischemia. Although the MPV value increased in embolism, it was not clear in terms of being a prognostic marker in intracranial hemorrhage. In some previous studies, it was reported that the MPV laboratory parameter remained uncertain in hemorrhagic strokes [38,39]. Although MPV value was low especially in the patient group of our study compared to the healthy Control Group, this difference was not at a statistically significant level. The volume and amount of granulation are definite since the first development of platelets, and although they are a predictive parameter for ischemic cerebrovascular disease, we cannot argue that low MPV levels in hemorrhagic cerebrovascular disease are predictive with these results in our study. In another study conducted on subdural hemorrhages in the literature, it was reported that there were no differences in patients with subdural hemorrhage in MPV value, which is similar to our study [40].

When the PVI results, which was another parameter in our study, were evaluated, Ray et al. reported that PVI value was an important marker in the course of the disease in the study conducted on patients with subarachnoid hemorrhage [41]. Dündar et al. emphasized that the platelet volume and platelet medium changed in response to intra-cranial vasospasm especially in patients with subarachnoid hemorrhage [24]. This occurs especially to limit the neuron damage in the subarachnoid or intra-parenchymal area [42]. As far as we know, studies especially on intraparenchymal hemorrhage and PVI index are limited in the literature. According to the results of our study, significant results were obtained especially in terms of the diagnosis and clinical prognosis evaluation of patients with intraparenchymal hemorrhage. Our study supports the results of previous studies conducted on patients with diseases that proceed with intracranial hemorrhage. In addition, in our study, the value of PVI was associated with the size of the hematoma, which has important sensitivity and specificity in evaluating mortality. As a result, we conclude that PVI Index may be an important marker in early diagnosis and mortality evaluation in patients with intraparenchymal hemorrhage.

According to the results of our study, the Hemphill Index, hematoma size, and PVI Index are important in mortality evaluation. However, MPV, RDW and Platelet are not directly significant in mortality evaluation. However, a correlation was detected between hematoma size and platelet laboratory parameter among blood parameters, and we believe that there may be parameters that may be useful in evaluating mortality.

Limitations

The biggest limitation of our study was that it was conducted with a limited number of patients. We believe that prognosis will be better evaluated with prospective studies in which more patients and longer-term mortality follow-ups are done.

Conclusion

Spontaneous Intraparenchymal hemorrhage are among the leading causes of stroke-induced mortality and disability. For this reason, revealing the controllable or not-yet-known risk factors, determining their effects on mortality will give clues regarding the course of treatment and estimation of the prognosis. The Hemphill Score and hemorrhage volume are important factors in mortality evaluation in intraparenchymal hemorrhage. There are not many studied conducted on Platelet Volume Index, and it is an important marker in predicting mortality especially in these patients. Platelet values, on the other hand, affect the volume of hemorrhage; and therefore, we believe that more studies are needed to show that it is a marker in predicting mortality.

Financial support: This study was not funded by any organization.
Conflict of interest: The authors have no conflict of interest in this study.

Author Contributions		Author Initials
SCD	Study Conception and Design	DA, BB,ES
AD	Acquisition of Data	DA,RY,RU
AID	Analysis and Interpretation of Data	DA,BC,RY,BB,ES
DM	Drafting of Manuscript	DA,BC,RY,BB,RU
CR	Critical Revision	DA,BC,RU,ES

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