

The effects of hematological parameters and anticoagulant/antiaggregant use on surgical outcomes in acute subdural hematoma

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ABSTRACT

Objective: A subdural hematoma is an abnormal collection of blood beneath the dura mater. The most common cause is head trauma. Small hemorrhages often resolve spontaneously and may not lead to complications. However, significant subdural hemorrhages can result in brain compression and herniation, necessitating emergency surgery due to their life-threatening nature. Given that mortality rates of 50-80% have been reported in cases of acute subdural hematomas (ASDH) resulting from severe head trauma, it is crucial to identify the parameters that can predict the prognosis of ASDH. This study aims to investigate the effect of hematologic parameters, including International Normalized Ratio (INR), platelet (Plt), hemoglobin (Hb), hematocrit (Htc), mean corpuscular volume (MCV), leukocyte, neutrophil, lymphocyte, C-Reactive Protein (CRP) on the outcomes of surgical treatment of acute subdural hematoma.

Methods: The file data of 31 cases who underwent surgery with a diagnosis of ASDH at the Private Ankara Güven Hospital Neurosurgery Clinic between January 1, 2019, and December 31, 2021, were retrospectively analyzed. The ages, genders, history of anticoagulant/antiplatelet medication use, INR, platelet count, hemoglobin level, hematocrit level, leukocyte count, and CRP values of the patients were recorded. These parameters were then statistically evaluated for their associations with re-bleeding, the number of surgeries performed, and mortality.

Results: The study was conducted with a total of 31 cases (35.5% (n=11) female and 64.5% (n=20) male). The average age of the cases was 72 (45-93). A single surgery was performed in 23 cases (74.2%), 8 patients (25.8%) were operated on again because of re-bleeding, and 9 of the cases (29%) died following the surgery. Among the nine patients who died, 5 (55.5%) underwent single surgery and 4 (44.5%) underwent more than one surgery. The number of cases not using pre-operative anticoagulants/antiaggregants was 10 (32.3%), 9 (29%) patients were using anticoagulants, seven patients (22.6%) were using single antiaggregant, and five patients (16.1%) were using dual antiaggregants. It was detected as statistically significant that the pre-operative INR, leukocyte, and neutrophil counts of the patients who underwent multiple surgeries were detected to be higher than those of ASDH patients who underwent single surgery.

Conclusion: Although pre-operative INR, leukocyte, and neutrophil elevation are not associated with mortality, these parameters can be associated with the requirement for re-surgery because of re-bleeding.

Keywords: re-bleeding, subdural hematoma, mortality, leukocyte, neutrophil

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INTRODUCTION

A subdural hematoma is bleeding that occurs in the subdural space, typically at the point where cortical bridging veins enter the dural sinuses, and it represents an urgent neurological condition. Brain tissue may experience hypoperfusion due to the direct compression of the hematoma on the surface blood vessels of the brain or as a result of vasospasm triggered by the breakdown products of the blood following the hemorrhage. They can be seen in 10-20% of serious head traumas (1,2). The morbidity of acute subdural hematomas, whose mortality varies between 50-80%, is also quite elevated (3).

Subdural hematomas greater than 10 mm in thickness or greater than 5 mm and causing midline shift must be treated surgically. It has been reported that the earlier the operation is (especially in the first 4 hours) in subdural hematomas with surgical indications, the lower the mortality and morbidity rate (3-5). If parameters that are strongly associated with prognosis in patients operated for ASDH can be identified and optimized, it will be possible to reduce mortality and morbidity rates.

In our present day, in parallel with the increased prevalence of patients with atherosclerotic risk factors, cardiac arrhythmias, and a history of venous thromboembolism, the use of antiaggregant/anticoagulant drugs is increasing gradually⁶. It is an undeniable fact that these drugs prepare the ground for the development of subdural hemorrhage. It is reported in the literature that the use of Warfarin increases the risk of subdural hemorrhage by 7-fold, and the use of Dabigatran increases it by 2.4-fold (6-9).

Although parameters such as the Glasgow Coma Score (GCS) at presentation, patient's age, time between admission and surgery, and abnormalities in the pupillary reaction were defined in determining the prognosis of subdural hematomas, the requirement for more sensitive, specific, and easily applicable markers continues^{10,11}.

The current study aimed to examine whether the use of anticoagulants and hematological parameters had any impact on mortality and the need for multiple surgeries due to re-bleeding in patients who underwent surgery for ASDH.

MATERIAL and METHODS

The study was conducted as a retrospective cohort study in the Private Ankara Güven Hospital Neurosurgery Department, and its approval was obtained from the Private Ankara Güven Hospital Scientific Committee with the date and number of 05.04.2023/1274.

A total of 31 patients who underwent craniotomy and hematoma evacuation with the diagnosis of Acute Subdural Hematoma in Private Ankara Güven Hospital Neurosurgery Clinic between 01.01.2019 and 31.12.2021 were examined in terms of factors that might affect prognosis and mortality. Patients who were not considered for surgery due to the expectation of spontaneous resorption and patients with a Glasgow Coma Scale (GCS) score of 3 who did not undergo surgery were excluded from the study. The study involved the examination of hospital records and discharge summaries. Additionally, Computed Tomography (CT) scans taken both before and after surgery were assessed for all cases. The patients who were included in the re-operation group were those who required re-operation within 2 weeks following their first operation. The main determinants for the decision for re-operation were that the shift was not decreased or re-bleeding was detected in the post-operative CT and the patient's neurologic manifestation had a significant regression. The ages, genders, number of operations, use and type of anticoagulant/antiaggregant, laboratory parameters, INR, platelet, hemoglobin, hematocrit, leukocytes, C-Reactive Protein values studied 24 hours before the operation were evaluated for all cases.

Statistical analysis

Statistical analyses were made by using the SPSS Software (SPSS for Windows, Version 22.0 Chicago, Illinois, USA). The mean values were analyzed with their standard deviation.

Mann-Whitney U test was used to compare independent variables such as age, INR, platelet, hemoglobin, MCV, neutrophil, CRP, lymphocyte, hematocrit and leukocyte count in age, INR, platelet, hemoglobin, MCV, neutrophil, CRP, lymphocyte, hematocrit, and leukocyte count between single surgery and multiple surgeries subgroup. The logistic regression analysis was used to assess the factors with predominant prognostic value of the in-hospital mortality in multivariate analysis. The data was accepted as statistically significant if the P value was <0.005.

RESULTS

The study was conducted with a total of 31 cases (35.5% (n=11) female and 64.5% (n=20) male). The mean age of the cases was 72 (45-93). The distribution of descriptive data and patient characteristics are summarized in Table 1.

A total of 23 patients (74.2%) underwent a single surgery, 8 patients (25.8%) had to be operated again because of re-bleeding, 9 (29%) died before being discharged from the hospital following surgery or within 30 days of being discharged. Single surgery was conducted in 5 (55.5%) out of the 9 cases that resulted in mortality, while multiple surgeries were performed in the remaining 4 (44.5%) cases.

The number of patients who did not use pre-operative anticoagulant/antiaggregant was 10 (32.3%), 9 (29%) patients were using anticoagulants, 7 (22.6%) were using single antiaggregant, and 5 (16.1%) were using dual antiaggregants.

There was no statistically significant difference in median age, platelet, hemoglobin, hematocrit, MCV, lymphocyte and CRP values between single surgery and multiple surgery subgroups ($P>0.05$).

Pre-operative leukocyte count was statistically significantly higher in the multiple surgeries subgroup (Mean = 14.7 ± 1) than the single surgery subgroup (Mean = 8 ± 2.7), $U=66$ $Z=2.76$ $P=.001$. Pre-operative neutrophil count was statistically significantly higher in multiple surgeries subgroup (Mean = 11.9 ± 1.34) than single surgery subgroup (Mean = 6.01 ± 2.53), ($U=65$ $Z=2.67$ $P=.002$) INR value was statistically significantly higher in multiple surgeries subgroup (Mean = 1.50 ± 0.1) than single surgery subgroup (Mean = 1.2 ± 0.24), ($U=59$ $Z=2.17$ $P=.027$).

The mortality rate was higher in the multiple surgeries subgroup (57.1%) than the single surgery subgroup (20.8 %), but the difference between the two independent binominal proportions was not statistically significant ($P=.086$).

There was no statistically significant relationship between pre-operative anticoagulant and antiaggregant drug use and mortality rate ($P=.306$).

Similarly, there was no statistically significant relationship between pre-operative anticoagulant and antiaggregant drug use and the requirement for multiple operations because of re-bleeding ($P=.096$).

Table 1: Descriptive Statistics comparison of single surgery subgroup and multiple surgery subgroups

	Single Surgery		Multiple Surgeries		Total		P value
	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.	
Age (years)	74,27	11,76	60,67	9,81	72,64	12,23	0,089
INR	1,20	0,240	1,50	0,11	1,24	0,24	0,027
Platelet ($10^3/\mu\text{L}$)	240,81	150,366	236,33	20,55	240,28	140,78	0,353
Hemoglobin (g/dL)	12,80	1,962	12,36	1,19	12,75	1,87	0,783
MCV (fL)	87,33	5,125	86,33	1,96	87,21	4,83	0,906
Neutrophil ($10^3/\mu\text{L}$)	6,01	2,531	11,90	1,34	6,71	3,09	0,002
CRP (mg/l)	37,71	60,523	56,85	59,30	40,00	59,48	0,238
Lymphocyte ($10^3/\mu\text{L}$)	2,86	2,837	1,82	0,49	2,74	2,68	1,000
Hematocrit (%)	38,14	9,730	35,26	2,17	37,80	9,17	0,353
Leukocyte ($10^3/\mu\text{L}$)	8,04	2,749	14,70	1,04	8,84	3,401	0,001

INR: International Normalized Ratio MCV: Mean Corpuscular Volume CRP: C-Reactive Protein. fL: Fento Liter

DISCUSSION

Despite the advancements in modern medicine and the widespread availability of healthcare in the 21st century, the mortality and long-term neurocognitive morbidity rates for ASDHs remain high.

The average age of the patients assessed in the study was 72 years, with all but one patient being over 50 years old (96.7%). The literature reports that the mean age for ASDH cases is 64 years, with 80% of them being over 50 years old (12).

It is reported in the literature that subdural hemorrhages are more common in males, which can be explained by the fact that men are more open to trauma in social life (1,13). In our study, male predominance (64.5%) was detected in ASDH, consistent with the literature data.

The overall mortality is 48% in surgically treated ASDH. In the contemporary series (as of the year 2000), post-operative mortality in comatose patients GCS ≤ 8 was 41% and mortality following non-coma ASDH surgery was 12% (3,14). In the current study, the observed mortality rate was 29%, which aligns with the data reported in the general literature (3, 14, 15).

In the current study, it was observed that the leukocyte and neutrophil counts were higher in patients who underwent multiple surgeries for ASDH compared to those who had a single surgery. Similarly, Oliveira et al. detected that pre- and post-operative neutrophil counts were higher in SDH patients who required recurrent surgery in their study evaluating chronic subdural hematoma recurrence, but no correlation was detected between other pre-operative laboratory parameters or other baseline characteristics and recurrence of hematomas (16).

A correlation between platelet count and re-bleeding is expected, but the fact that there were no thrombocytopenic patients in our study and all patients had a pre-operative Plt value $>100.000/\mu\text{L}$ may explain the lack of correlation between the platelet count and requirement for re-operation.

Leukocyte-cytokine signalling and subsequent inflammation resulting from traumatic brain injury impair cellular repair, which is vital for restoring blood-brain barrier integrity (17).

When the blood-brain barrier cannot show normal functioning, the normal filtration process cannot occur, and uncontrolled cerebral edema and an increase in intracranial pressure occur. These changes cause the continuation of intracranial bleeding and the expansion of the hematoma (18).

Many studies were conducted to examine the relationship between neutrophils and tissue damage. In traumatic brain injury, in addition to the opportunistic infiltration provided by the trauma to the central nervous system, neural damage is also increased by "Neutrophil Extracellular Traps" (NETs), which are the structures released by neutrophils that aim to capture and neutralize/eliminate pathogens (19). NETs produce excessive amounts of cytotoxic proteins that impair cellular repair. The inflammatory origin for hematoma formation in traumatic brain injury is thought to be the membranous structure on the inner surface of the dura described by Virchow in 1857 in a case of "pachymeningitis hemorrhagic interna" (20) Histologic analysis shows the presence of this modified layer of connective tissue cells, termed "dural border cells", in the duramater of SDH patients. The cells involved here have two main roles, developing a fibro-cellular connective tissue and phagocytosis (21). This layer contains thin-walled, highly permeable capillaries with numerous gap junctions, allowing continuous leukocyte migration into the subdural hematoma cavity (22). Systemic repercussions occur following this local migration.

Neutrophils collect in the injury area during acute brain injury and increase tissue damage by causing the release of inflammatory cytokines, free radicals, and proteases that play roles in the pathogenesis of secondary damage (23). Unlike neutrophils, which respond first to acute brain injury, lymphocytes remain unresponsive within the first week of acute injury (24). Unlike neutrophils, which come to the scene in the acute stage and increase tissue damage, T-lymphocytes trigger the recovery process in the damaged brain (25). Elevated neutrophil counts and reduced lymphocyte counts, leading to a higher Neutrophil-to-Lymphocyte Ratio (NLR), may be indicative of worse outcomes in patients with acute brain injuries due to the differing functions of these cells. Supporting this hypothesis, many studies are reporting that elevated NLR is an independent prognostic factor for mortality in patients with severe brain injury (25,26).

Anticoagulant/anti-aggregant use is the most common predisposing factor for ASDH in patients without a history of trauma (27). Also, the use of pre-operative anticoagulant/antiaggregant makes surgery significantly more difficult. In the present study, 10 (32.3%) patients were not using pre-operative anticoagulant/antiaggregant drugs, but 21 (67.7%) patients used at least 1 drug. However, no statistically significant relationship was detected between the use of these drugs and mortality and the requirement for multiple surgeries. In the meta-analysis in which 24 studies were evaluated, Wang et al. reported that anticoagulant and antiaggregant agents increased the risk of chronic SDH recurrence but did not increase the risk of mortality (28). We think that the fact that the expected increased risk of SDH recurrence with the use of anticoagulants and antiaggregants could not be demonstrated in the present study was because of the large number of subgroups because of the small number of patients in the present study and the heterogeneity of the drugs used.

The therapeutic range of Warfarin, one of the most widely used anticoagulants, is controlled by INR. INR < 1.4 is safe for surgical procedures. If it is appropriate to stop the drug before the operation in patients using Warfarin, it is appropriate to stop it 5 days before and to check the INR one day before the surgery.

The risk of developing intracerebral hemorrhage approximately doubles with every 1-unit increase in INR level (29).

In the present study, the mean INR value detected in the patient group requiring multiple surgeries was detected to be statistically significantly higher compared to the mean INR values of the patient group who had been operated on once. These clinical results, consistent with theoretical knowledge, emphasized the importance of optimizing INR values before surgery to reduce re-bleeding and resulting repetitive surgeries. When INR <2, low/intermediate risk surgical procedures can be performed safely, but in high-risk surgeries or in patients who will undergo surgery with low/intermediate risk of bleeding but have INR>2, the risk of bleeding must be reduced by using prothrombin complex concentrates, fresh frozen plasma, cryoprecipitate, and vitamin K (30).

CONCLUSION

In conclusion, ASDH still has an elevated risk of mortality and morbidity in the present day. The requirement to identify more sensitive, specific, and easily applicable markers to be used to predict the results of surgical treatment continues. Pre-operative INR, Leukocyte, and Neutrophil elevation can be associated with the requirement for re-operation and morbidity, although not with mortality. If they are supported by studies involving a larger number of cases, it will be inevitable that these parameters will find a place in our daily practice.

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