



# Effect of Antithrombotic Therapy on Development of Acute Subdural Hematoma After Burr Hole Drainage of Chronic Subdural Hematoma

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## ABSTRACT

**AIM:** To evaluate the relationship between the time from cessation of anticoagulant/antiplatelet medication to surgery and risk of postoperative acute subdural hematoma (ASDH) after burr hole drainage of chronic subdural hematoma (CSDH).

**MATERIAL and METHODS:** A retrospective study of patients who underwent burr hole drainage of CSDH between December 2014 and December 2019 was performed. Demographic and clinical data regarding age, gender, medication (antithrombotic therapy), smoking, daily alcohol consumption, history of head trauma, presenting symptoms, and neurological examination were collected from the medical records. Patients were divided into 3 groups based on time from referral to surgery: <24 hours, 24–72 hours, and >72 hours.

**RESULTS:** One hundred seventeen patients underwent burr hole drainage of CSDH during the 5-year study period. Seventy-two patients were male (61.5%) and 45 were female (38.5%). Mean age was  $70.5 \pm 7.2$  years. Postoperative ASDH occurred in 2 of the 32 patients (6.3%) who were not taking antithrombotic medication and 6 of the 85 patients (7.1%) who were taking antithrombotic medication. The difference was not significant ( $p=0.797$ ).

**CONCLUSION:** The risk of ASDH after burr hole drainage of CSDH was not affected by antithrombotic medication. Although the literature suggests that antiplatelet and anticoagulant drugs be discontinued between 5 and 7 days before surgery, our results showed that acute hemorrhage was not detected in any patient who underwent surgery more than 72 hours after referral.

**KEYWORDS:** Anticoagulant, Antiplatelet, Antithrombotic therapy, Chronic subdural hematoma, Complications

**ABBREVIATIONS:** **ASDH:** Acute subdural hematoma, **COPD:** Chronic obstructive pulmonary disease, **CSDH:** Chronic subdural hematoma, **CT:** Computed tomography, **CVA:** Cerebrovascular accident, **DM:** Diabetes mellitus, **HT:** Hypertension, **ND:** Neurodegenerative disease, **RF:** Renal failure

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## ■ INTRODUCTION

Chronic subdural hematoma (CSDH) is common and predominantly seen in the elderly. The annual incidence in the population under the age of 60 years is 3.4 per 100,000 persons; in those over age 65 years, the annual incidence is 58–80 per 100,000 (2). Comorbidities in CSDH patients may increase the risk of postoperative complications. Many studies have reported that use of antithrombotic (anticoagulant or antiplatelet) agents in the elderly is associated with the development of CSDH as well as postoperative recurrence (2,18,20). Studies have also shown that antithrombotic agents may also cause complications that result in mortality during or after surgery, such as acute subdural hematoma (ASDH) (14,16). In our clinical experience, any form of acute intracranial hemorrhage may occur after surgery and is associated with poor clinical outcomes. Therefore, it is important to identify perioperative risk factors, early symptoms, and clinical findings of postoperative acute intracranial bleeding.

Surgical intervention is the primary treatment of CSDH but the timing of surgery and its early complications in patients using antithrombotic agents have not been well investigated. In addition, the timing of surgery after cessation of antithrombotic agents remains controversial. This study aimed to evaluate the relationship between the time from cessation of anticoagulant/antiplatelet medication to surgery and risk of acute postoperative hemorrhage in CSDH patients undergoing burr hole drainage.

## ■ MATERIAL and METHODS

Approval for this study was obtained from the Namık Kemal University Research Ethics Board (Date: 25.02.2020; No: 2020.30.02.04). The patients or their relatives provided written informed consent before treatment. Data of 117 patients who underwent burr hole drainage for CSDH between December 2014 and December 2019 in our hospital were reviewed. Demographic and clinical data, including age, gender, medication (antithrombotic therapy), smoking, daily alcohol consumption, history of head trauma, presenting symptoms, and neurological examination were collected from the medical records. In addition, comorbidities such as arterial hypertension (HT), diabetes mellitus (DM), renal failure (RF), chronic obstructive pulmonary disease (COPD), neurodegenerative disease (ND), and previous cerebrovascular accident (CVA) were recorded. Patients with a CSDH due to ventriculoperitoneal shunt overdrainage were excluded. A neurosurgeon evaluated all preoperative computed tomography (CT) scans and determined surgical indications and timing of surgery.

### Surgical Procedure and Clinical Management

Surgeries were performed as early as safely possible. Patients not receiving antithrombotic medication who had normal coagulation study results and completed any necessary preoperative preparation were operated on the day of admission. Neurologically intact patients taking antithrombotic agents underwent surgery 72 hours after cessation of antithrombotic

medication; however, if neurological deterioration occurred during the waiting period, urgent surgical evacuation was performed. All patients underwent frontal and/or parietal burr hole drainage with irrigation and insertion of a subdural drainage catheter. A baseline CT scan was performed within 24 hours of CSDH surgery, followed by routine scans approximately 1, 4, 12, and 24 weeks later. Patients were no longer followed once the hemorrhage completely resolved. Patients who developed postoperative neurological deterioration underwent urgent CT; if an ASDH was detected, craniotomy for evacuation was performed. Hemorrhagic complication was defined as new onset intracranial hemorrhage (intracerebral, subdural, epidural, or subarachnoid) identified on CT.

Patients were divided into 3 groups based on time from referral to surgery: <24 hours, 24–72 hours, and >72 hours. The groups were analyzed using SPSS software version 19.0 (IBM Corp., Armonk, NY, USA). Data are presented as means with standard deviation. Comparisons were performed using the Student's t-test for continuous variables and the chi-square test for categorical variables.  $P < 0.05$  was considered significant.

## ■ RESULTS

In the 5-year study period, 117 patients underwent burr hole drainage of CSDH. Seventy-two patients were male (61.5%) and 45 were female (38.5%). Mean patient age was  $70.5 \pm 7.2$  years (range, 43–88). At least one medical comorbidity was present in 100 patients (85.4%). HT was present in 84 patients, DM in 31, COPD in 12, CVA in 11, ND in 6, and RF in 6. Forty-nine patients (41.9%) were taking antiplatelet medication (acetylsalicylic acid or clopidogrel) and 36 patients (30.8%) were taking anticoagulant medication (warfarin) at the time of presentation (Table I).

Presenting symptoms were as follows: headache in 73 (62.4%) patients, motor deficit in 42 (25.9%), mental status change in 18 (15.4%), slurred speech in 11 (9.4%), and seizure in 5 (4.3%). CT assessment showed right hemispheric CSDH in 65 (55.6%) patients, left hemispheric CSDH in 46 (39.3%), and bilateral CSDH in 6 (5.1%) (Table I).

Thirty-seven patients underwent surgery within the first 24 hours of admission, 49 underwent surgery between 24 and 72 hours, and 31 underwent surgery after 72 hours. The medication data according to timing of surgery are summarized in Table II. Regarding postoperative complications, ASDH developed in 5 patients who underwent surgery within the first 24 hours and 3 patients who underwent surgery between 24 and 72 hours; no ASDH was observed in the patients who underwent surgery after 72 hours.

Postoperative ASDH occurred in 2 of 32 patients (6.3%) not taking antithrombotic medication and 6 of 85 patients (7.1%) who were taking antithrombotic medication (Table III). The difference was not significant ( $p = 0.797$ ). However, among the patients who underwent surgery within the first 24 hours, ASDH development occurred in 1 of 17 patients (5.9%) not taking antithrombotic medication, 3 of 11 patients (27.3%) taking antiplatelet agents, and 1 of 9 patients (11.1%) taking

anticoagulant medication. Although the incidence of ASDH development was highest in patients taking antiplatelet medication, the difference was not significant (Table III). No

significant difference was found in postoperative ASDH incidence between the 24–72 hours and >72 hours surgical groups as well.

**Table I:** Clinical Characteristics of the 117 Patients with Chronic Subdural Hematoma (CSDH)

	No antithrombotic therapy	Antiplatelet therapy	Anticoagulant therapy
Age (Year)	62.9 ± 5.8	73.6 ± 5.5	72.9 ± 6.7
Female/male	14/18	23/26	8/28
Preoperative symptom	n(%)	n(%)	n(%)
Headache	17 (53.1)	35 (71.4)	21 (58.3)
Hemiparesis	13 (40.6)	17 (34.7)	12 (27.8)
Cognitive impairment	6 (18.8)	8 (16.3)	4 (11.1)
Dysphasia	2 (6.3)	5 (10.2)	4 (11.1)
Seizure	0 (0.0)	4 (8.2)	1 (2.8)
Comorbidity	n(%)	n(%)	n(%)
HT	1 (3.1)	49 (100)	34 (94.4)
DM	8 (25)	14 (28.6)	9 (25)
COPD	4 (12.5)	2 (4.1)	6 (16.7)
CVA	0 (0.0)	7 (14.3)	4 (11.1)
NR	0 (0.0)	3 (6.1)	3 (8.3)
RF	3 (9.4)	2 (4.1)	1 (2.8)
HT+DM	0 (0.0)	12 (24.5)	6 (16.7)
HT+COPD	0 (0.0)	1 (2)	6 (16.7)
HT+ CVA	0 (0.0)	6 (12.2)	2 (5.6)
Mixed	1 (3.1)	3 (6.1)	2 (5.6)
Location	n()	n(%)	n(%)
Right	17 (53.1)	29 (59.2)	19 (52.8)
Left	15 (46.9)	16 (32.7)	15 (41.7)
Bilateral	0 (0.0)	4 (8.2)	2 (5.6)
Acute subdural hematoma complication	2 (6.3)	4 (8.2)	2 (5.6)

**COPD:** Chronic obstructive pulmonary disease, **CVA:** Cerebrovascular accident, **DM:** Diabetes mellitus, **HT:** Hypertension, **ND:** Neurodegenerative disease, **RF:** Renal failure.

**Table II:** Distribution of Patients according to Medication History and Time to Surgery

	<24 hours	24-72 hours	>72 hours
No Antithrombotic Therapy n=32	17	15	0
Antiplatelet Therapy n=49	11	21	17
Anticoagulant Therapy n=36	9	13	14
<b>Total</b>	<b>37</b>	<b>49</b>	<b>31</b>

**Table III:** Acute Subdural Hematoma Development according to Timing of Surgery n(%)

Preoperative medication	Postoperative complications n (%)			Total
	<24 hours	24-72 hours	>72 hours	
No Antithrombotic Therapy	1 (5.9)	1 (6.7)	0 (0)	2 (6.3)
Antiplatelet Therapy	3 (27.3)	1 (4.8)	0 (0)	4 (8.2)
Anticoagulant Therapy	1 (11.1)	1 (7.7)	0 (0)	2 (5.6)
<b>Total</b>	5 (13.5)	3 (6.1)	0 (0)	

## ■ DISCUSSION

CSDH, a disease with increasing incidence in developed countries, mostly affects the elderly and is one of the most common pathologies encountered in daily neurosurgical practice (12,17,22-24). Predictors of CSDH development include frequent falls (10), and long-term use of antithrombotic agents due to comorbidities such as cardiac disease or previous CVA (6). Many CSDHs begin as an ASDH, possibly after minor trauma, with disruption of subdural venous structures. The blood in the subdural space evokes an inflammatory response, which interferes with absorption of the subdural blood and causes expansion over time (7,13). The exact mechanisms underlying expansion have not been elucidated, but several different mechanisms have been proposed. The new vessels formed in the membrane wall by angiogenesis are fragile and the fibrinolytic process is thought to cause continued bleeding due to the inhibition of clot formation. Growth of the membrane and fluid accumulation then ensue, which is thought to be caused by a response that stimulates the inflammatory process (4). Antithrombotic and fibrinolytic substances secreted by the outer membrane are thought to liquefy the hematoma and cause it to expand over time (7-9).

Hemostasis usually begins within seconds of vessel damage. The endothelial response is followed by vascular spasm, formation of a platelet plug, and fibrin clot formation. Aspirin inhibits the enzyme cyclooxygenase-1 (COX-1), resulting in an antiplatelet effect. Oral anticoagulants and heparin delay the formation of fibrin clots by inhibiting coagulation factors (15,21). Thus, antithrombotic agents are known to increase the risk of developing CSDH. In addition, these effects are thought to be a cause of postoperative ASDH, a complication associated with high morbidity and mortality.

In our study of CSDH, the mean overall patient age was 70.4 years. However, the mean age was significantly lower in patients who were not taking antithrombotic medication (62.9 years) when compared to patients taking long-term antithrombotic medication. In addition, most of the patients were male (61.5%). These findings are similar to those of previous studies and confirm that CSDH predominantly occurs in the seventh decade of life and in male patients (2,24).

Comorbidities in CSDH patients increase the risk of postoperative complications. For instance, the use of antiplatelet and anticoagulant drugs is a risk factor for acute hemorrhage in

the elderly (14,16). Therefore, it is an accepted fact that these drugs should be discontinued during the perioperative period (3,5,11). However, waiting for the antithrombotic effect of these agents to wear off is sometimes not possible due to the development of potentially life-threatening neurological conditions. In this study, due to development of life-threatening neurological conditions, 20 patients (23.5%) taking antithrombotic medication underwent surgery within the first 24 hours of referral and 34 (40%) underwent surgery between 24 and 72 hours. ASDH development occurred in 5 patients of the group operated on within the first 24 hours. Three of these patients were taking antiplatelet medication, 1 was taking anticoagulant medication, and 1 was not taking any antithrombotic medication. The risk of ASDH development was higher in the antiplatelet group compared to the two other groups. However, antithrombotic medication did not increase the risk of acute hemorrhage in patients operated on between 24 and 72 hours (Table II). In a recent study of 323 patients conducted by Amano et al., acute hemorrhage was detected in only 6 patients (1.9%) (1), which is quite low compared to our study. However, surgical intervention was performed one week after cessation of antithrombotic medication in their study. In our study, no complications developed in the group who underwent surgery after 72 hours. Pang et al. evaluated 303 patients and reported 14 patients (4.6%) with postoperative acute hemorrhage; 7 of these were using antithrombotic agents and 7 were not (19). They concluded that the use of antiplatelet or anticoagulant drugs was not associated with postoperative acute hemorrhage, similar to our results (19).

This study is limited by its retrospective nature, which exposes it to potential sources of bias. However, we attempted to avoid selection bias by including all consecutive patients in a 5-year-period. In addition, the relatively large sample size gave us enough power to identify the risk of postoperative acute intracranial hemorrhage.

## ■ CONCLUSION

The risk of ASDH after burr hole drainage of CSDH was not affected by antithrombotic medication. Although the literature suggests that antiplatelet and anticoagulant drugs be discontinued between 5 and 7 days before surgery, our results showed that acute hemorrhage was not detected in any patient who underwent surgery more than 72 hours after referral.

## ■ REFERENCES

- Amano T, Matsuo S, Miyamatsu Y, Yamashita S, Nakamizo A: Impact of antithrombotic therapy on surgical treatment in patients with chronic subdural hematoma. *J Clin Neurosci* 74:55-60, 2020
- Baechli H, Nordmann A, Bucher HC, Gratzl O: Demographics and prevalent risk factors of chronic subdural haematoma: Results of a large single-center cohort study. *Neurosurg Rev* 27:263-266, 2004
- Ducruet AF, Grobelny BT, Zacharia BE, Hickman ZL, DeRosa PL, Andersen KN, Sussman E, Carpenter A, Connolly ES Jr: The surgical management of chronic subdural hematoma. *Neurosurg Rev* 35:155-169; discussion 169, 2012
- Edlmann E, Giorgi-Coll S, Whitfield PC, Carpenter KLH, Hutchinson PJ: Pathophysiology of chronic subdural haematoma: Inflammation, angiogenesis and implications for pharmacotherapy. *J Neuroinflammation* 14:108, 2017
- Gonugunta V, Buxton N: Warfarin and chronic subdural haematomas. *Br J Neurosurg* 15:514-517, 2001
- Guha D, Coyne S, Macdonald RL: Timing of the resumption of antithrombotic agents following surgical evacuation of chronic subdural hematomas: A retrospective cohort study. *J Neurosurg* 124:750-759, 2016
- Huang KT, Bi WL, Abd-El-Barr M, Yan SC, Tafel IJ, Dunn IF, Gormley WB: The neurocritical and neurosurgical care of subdural hematomas. *Neurocrit Care* 24:294-307, 2016
- Ito H, Komai T, Yamamoto S: Fibrinolytic enzyme in the lining walls of chronic subdural hematoma. *J Neurosurg* 48:197-200, 1978
- Ito H, Yamamoto S, Komai T, Mizukoshi H: Role of local hyperfibrinolysis in the etiology of chronic subdural hematoma. *J Neurosurg* 45:26-31, 1976
- Javadi SA, Naderi F, Javadi AM: The optimal surgical approach for treatment of chronic subdural hematoma: Questionnaire assessment of practice in iran and review of literature. *Acta Med Iran* 53:617-621, 2015
- Kawamata T, Takeshita M, Kubo O, Izawa M, Kagawa M, Takakura K: Management of intracranial hemorrhage associated with anticoagulant therapy. *Surg Neurol* 44:438-442; discussion 443, 1995
- Lee KS: Natural history of chronic subdural haematoma. *Brain Inj* 18:351-358, 2004
- Markwalder TM: Chronic subdural hematomas: A review. *J Neurosurg* 54:637-645, 1981
- McMillian WD, Rogers FB: Management of prehospital antiplatelet and anticoagulant therapy in traumatic head injury: A review. *J Trauma* 66:942-950, 2009
- Mega JL, Simon T: Pharmacology of antithrombotic drugs: An assessment of oral antiplatelet and anticoagulant treatments. *Lancet* 386:281-291, 2015
- Moore MM, Pasquale MD, Badellino M: Impact of age and anticoagulation: Need for neurosurgical intervention in trauma patients with mild traumatic brain injury. *J Trauma Acute Care Surg* 73:126-130, 2012
- Mori K, Maeda M: Surgical treatment of chronic subdural hematoma in 500 consecutive cases: Clinical characteristics, surgical outcome, complications, and recurrence rate. *Neurol Med Chir (Tokyo)* 41:371-381, 2001
- Nakaguchi H, Tanishima T, Yoshimasu N: Factors in the natural history of chronic subdural hematomas that influence their postoperative recurrence. *J Neurosurg* 95:256-262, 2001
- Pang CH, Lee SE, Kim CH, Kim JE, Kang HS, Park CK, Paek SH, Kim CH, Jahng TA, Kim JW, Kim YH, Kim DG, Chung CK, Jung HW, Yoo H: Acute intracranial bleeding and recurrence after bur hole craniostomy for chronic subdural hematoma. *J Neurosurg* 123:65-74, 2015
- Potdar NV, Suresh KS, B. K: Effect of antiplatelet/anticoagulant agents in elderly patients of chronic subdural hematoma: A case control study from a tertiary care centre. *Int J Res Med Sci* 5:2947-2951, 2017
- Sere KM, Hackeng TM: Basic mechanisms of hemostasis. *Semin Vasc Med* 3:3-12, 2003
- Spallone A, Giuffre R, Gagliardi FM, Vagnozzi R: Chronic subdural hematoma in extremely aged patients. *Eur Neurol* 29:18-22, 1989
- Tabuchi S, Kadowaki M: Chronic subdural hematoma in patients over 90 years old in a super-aged society. *J Clin Med Res* 6:379-383, 2014
- Toi H, Kinoshita K, Hirai S, Takai H, Hara K, Matsushita N, Matsubara S, Otani M, Muramatsu K, Matsuda S, Fushimi K, Uno M: Present epidemiology of chronic subdural hematoma in Japan: Analysis of 63,358 cases recorded in a national administrative database. *J Neurosurg* 128: 222-228, 2018