

Risk Factors of Delayed Surgical Intervention after Conservatively Treated Acute Traumatic Subdural Hematoma

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Objective : Acute subdural hematoma (ASDH) is generally considered a condition that should be managed surgically. However, some patients initially receive conservative treatment, a subset of whom require surgical intervention later. This study aimed to evaluate the predictors of delayed surgical intervention in ASDH patients who are initially managed conservatively.

Methods : From January 2007 to December 2015, 842 patients diagnosed with ASDH were treated at our institution. Among them, 158 patients with convexity ASDH were initially treated conservatively. Patients were divided into a delayed surgery group and a conservative group. Demographic characteristics, past medication and medical histories, and radiological and laboratory data were collected by retrospective chart review. Independent risk factors were identified with univariate and multivariate analyses.

Results : Twenty-eight patients (17.7%) underwent delayed surgical intervention. Their mean age was 69.0 years, and 82.1% were male. Hypertension, diabetes mellitus, and heart disease prevalence and use of anti-platelet agents did not significantly differ from the conservative group. However, age ($p=0.024$), previous cerebral infarction history ($p=0.026$), increased maximal hematoma thickness ($p<0.001$), midline shifting ($p=0.001$) and accompanying subarachnoid hemorrhage ($p=0.022$) on initial brain computed tomography (CT) scan, low hemoglobin level ($p<0.001$), high leukocyte count ($p=0.004$), and low glucose level ($p=0.002$) were significantly associated with delayed surgical intervention. In multivariate analysis, increased maximal hematoma thickness (odds ratio [OR]=1.279, 95% confidence interval [CI] 1.075–1.521; $p=0.006$), low hemoglobin level (OR=0.673, 95% CI 0.467–0.970; $p=0.034$), and high leukocyte count (OR=1.142, 95% CI 1.024–1.272; $p=0.017$) were independent risk factors for delayed surgical intervention.

Conclusion : Due to the high likelihood of delayed surgical intervention among minimal ASDH patients with a thicker hematoma on initial brain CT, lower hemoglobin level, and higher leukocyte count, these patients should receive more careful observation.

Key Words : Hematoma, Subdural · Surgical procedure, Operative · Conservative treatment · Risk factors · Outcome.

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INTRODUCTION

Acute subdural hematoma (ASDH) generally considered a condition that should be managed surgically, but in some cases may be treated conservatively¹⁾. Minimally symptomatic ASDH patients do not always require early surgical evacuation³⁾. In minimal ASDH patients, initial treatment is typically determined according to surgical guidelines and the surgeon's experience²⁾. With advances of radiological diagnostic tools, the number of patients with minimal subdural hematoma (SDH) who are treated conservatively is increasing. However, some ASDH patients managed with conservative treatment require surgical intervention later²⁸⁾. Hemorrhage resulting from injury of the bridging veins is liquefied with micro-bleeding and progresses to symptomatic chronic subdural hematoma (CSDH) as expanding⁸⁾. Patients with progression to CSDH require surgical decompression such as craniotomy and Burr hole trephination with or without irrigation and drainage⁸⁾. Therefore, it is important to know the conditions when the SDH progresses and who will require surgical intervention. The purpose of this study was to identify predictable risk factors that are associated with ASDH patients who are initially managed conservatively undergoing delayed surgical intervention.

MATERIALS AND METHODS

We retrospectively collected data from 842 patients diagnosed with SDH who were treated at the neurosurgery department of our tertiary medical center between January 2007 and December 2015. Two hundred fifty-seven patients underwent emergency craniectomy and hematoma evacuation. Cases of minimal falx or subtentorial hemorrhage (n=280), which commonly does not require surgery, were not included. Patients younger than 15 years old (n=37) or who received surgical intervention within 7 days after diagnosis (n=47) were excluded. Sixty-three patients who died or refused treatment were also excluded (Fig. 1).

Finally, 158 patients were enrolled in the study. All patients were admitted to the neurosurgical department and initially treated conservatively. Anti-epileptic drugs were administered to all patients, and osmotic diuretics were given when needed. Anti-platelet agents and anticoagulation agents were halted at

the time of diagnosis. If patients demonstrated coagulopathy on initial laboratory findings, such as low platelet count or prolonged international normalized ratio (INR), the issue was corrected with platelet and fresh frozen plasma transfusion or IV administration of vitamin K.

Patients' medical histories were retrospectively collected by chart review. Past medical comorbidities, medication, and trauma histories were reviewed. Radiological and laboratory studies were performed at the time of diagnosis, and follow-up brain computed tomography (CT) scanning was performed routinely within the first 8 hours and every 1 week unless neurological deterioration was observed.

Radiological findings were obtained by chart review. All films were interpreted by a radiologist when the patient was admitted and confirmed by neurosurgeons. On the initial brain CT scan, intracranial injuries accompanying SDH, such as intraparenchymal hemorrhage or subarachnoid hemorrhage, were evaluated, and maximal hematoma thickness and midline shifting were measured.

Surgery was performed when follow-up brain CT scan revealed hematoma progression or a mass effect appeared such as headache aggravation or development of a neurological deficit. All such patients underwent Burr hole trephination and drainage with or without irrigation under general or local anesthesia.

Chi-square and Fisher's exact test were utilized to analyze

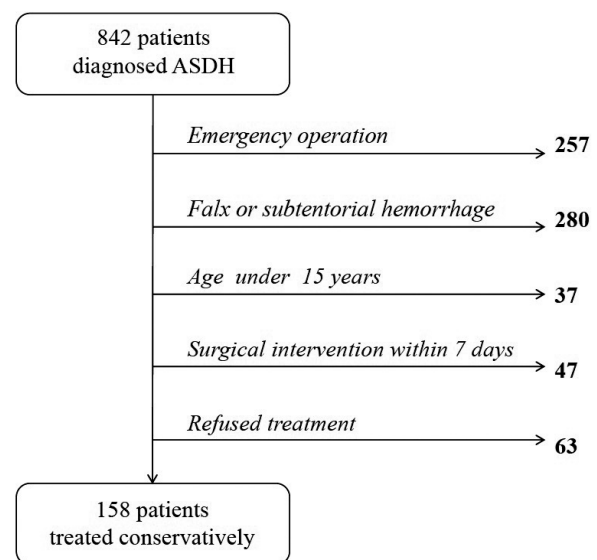


Fig. 1. Flow chart of eligible patients included in the study. ASDH, acute subdural hematoma.

categorical data, and numerical variables were compared with Student's t-test. Statistical differences were considered significant for *p* values less than 0.05. Finally, to adjust for relationships among various factors, multivariate logistic regression was used to identify independent risk factors.

RESULTS

The 158 patients enrolled in this study were all initially treated conservatively. They were divided into two groups according to follow-up treatment: the conservative treatment group (n=130) and surgical treatment group (n=28). Patient characteristics are listed in Tables 1 and 2. All patients presented minor symptoms, such as headache, dizziness, nausea, or vomiting. No definite neurologic deficit was observed. Patients' mean age was 62.93 years; 112 patients (70.9%) were male, 46 (29.1%) were female. Twenty-eight patients (17.7%) demonstrated progression of SDH on follow-up brain CT and underwent surgical intervention. The mean interval between initial diagnosis to operation was 13.9 days.

Patients in the surgical group were older than those in the conservative group (mean age 69.00 vs. 61.62 years, *p*=0.024). However, there was no significant difference in sex distribution, with 89 males and 41 females in the conservative group and 23 males and 5 females in the surgical group (*p*=0.229).

In total, 69 patients had hypertension : 53 in the conserva-

tive group and 16 in the surgical group, with no significant difference between groups (*p*=0.113). Rates of diabetes mellitus (DM) and cardiac disease history did not differ between the groups (*p*=0.966 and *p*=0.506), while history of cerebral infarction significantly more in surgical group (*p*=0.026). Medication rates did not differ between the two groups. Eighteen patients in the conservative group and 5 in surgical group were taking anti-platelet agents. Two patients were on anti-coagulant agents, one in each group.

The initial brain CT scans of patients in surgical group showed greater in maximal thickness (11.54 vs. 5.78 mm, *p*<0.001) and more midline shifting to the opposite hemisphere compared to the conservative group (3.32 vs. 1.08 mm, *p*=0.001).

On initial brain CT scan, 45 patients had subarachnoid hemorrhage, and 26 patients had intraparenchymal hemorrhage. The conservative group included a significantly higher proportion of patients with subarachnoid hemorrhage (42 vs. 3, *p*=0.022), but no difference was seen in intraparenchymal hemorrhage (22 vs. 4, *p*=1).

Among the initial laboratory findings, prothrombin time (INR) and platelet count did not differ between the two groups (*p*=0.522 and *p*=0.279). However, initial hemoglobin was negatively correlated with surgical intervention (12.25 vs.

Table 1. Characteristics, past medical and medication histories of conservative group and surgical group

Variable	Conservative (n=130)	Surgery (n=28)	<i>p</i> -value
Age	61.62±15.65	69.00±15.01	0.024
Sex (male)	89 : 41 (68.5)	23 : 5 (82.1)	0.148
Comorbidity			
HTN	53 (40.8)	16 (57.1)	0.113
DM	33 (25.4)	7 (25.0)	0.966
Heart disease	13 (10.0)	4 (14.3)	0.506
Prev. infarction	6 (4.6)	5 (17.9)	0.026
Anti-PLT	18 (13.8)	5 (17.9)	0.563
Anticoagulant	1 (0.8)	1 (3.6)	0.324

Values are presented as mean±standard deviation or number (%) unless otherwise indicated. HTN : hypertension, DM : diabetes mellitus, PLT : platelet

Table 2. Radiologic and laboratory findings of conservative group and surgical group

Variable	Conservative (n=130)	Surgery (n=28)	<i>p</i> -value
Radiology			
Thickness	5.78±3.27	11.54±5.16	<0.001
Midline shift	1.08±2.36	3.32±3.13	0.001
Bilaterality	23 (17.7)	6 (21.4)	0.643
SAH	42 (32.3)	3 (10.7)	0.022
ICH	22 (16.9)	4 (14.3)	1
Laboratory			
Leukocyte	5.82±5.63	9.00±4.83	0.004
Hemoglobin	13.56±1.78	12.18±2.07	<0.001
Platelet	216.87±186.78	175.00±63.91	0.244
Glucose	157.65±59.36	132.64±27.51	0.002
INR	1.14±1.08	1.00±0.01	0.52

Values are presented as mean±standard deviation or number (%). SAH : subarachnoid hemorrhage, ICH : intracerebral hemorrhage, INR : international normalized ratio

13.53, $p=0.001$). Leukocyte count was also higher in the surgical group than in the conservative group (89.0 vs. 58.6, $p=0.005$). By contrast, initial glucose was lower in the surgical group (134.6 vs. 157.3, $p=0.005$).

To correct for confounding factors, we performed a multivariate logistic regression analysis including possible risk factors with p values less than 0.01 on univariate analysis. Multi-

variate logistic regression analysis identified initial SDH thickness (odds ratio [OR]=1.279, 95% confidence interval [CI] 1.075–1.521; $p=0.006$) and leukocyte count (OR=1.142, 95% CI 1.024–1.272; $p=0.017$; Table 3) as independent risk factors for delayed surgical intervention. Additionally, initial hemoglobin was confirmed as an independent negative predictor of hematoma progression (OR=0.673, 95% CI 0.467–0.970; $p=0.034$). Age ($p=0.692$), history of cerebral infarction ($p=0.993$), midline shifting ($p=0.191$), accompanying SAH ($p=0.747$), and glucose level ($p=0.254$) were not significantly associated with surgical intervention.

Table 3. Result of multivariate analysis

Variable	p -value	Odds ratio	95% confidence interval
Thickness	0.006	1.279	1.075–1.521
Leukocyte	0.017	1.142	1.024–1.272
Hemoglobin	0.034	0.673	0.467–0.970

Table 4. Previous reports on progression of hematoma in initially conservatively treated ASDH patients

Study	Country	Study population	Surgical group	Country	Risk factors	Not risk factor
Laviv and Rappaport (2014) ¹⁰	Israel	95	43 (45.2)	Israel	IHD HTN ACE-inhibitor Anticoagulant Clopidogrel Size of SDH	DM Bilaterality
Lee et al. (2015) ¹¹	Korea	117	16 (13.7)	Korea	Age Midline shifting Hematoma depth Hounsfield Unit	HTN DM SAH H. contusion Bilaterality Midline shifting Aspirin, clopidogrel Warfarin
Kim et al. (2014) ⁹	Korea	98	34 (34.7)	Korea	Thickness Hematoma volume Midline shifting H. contusion SAH	Sex Combined hemorrhage Warfarin
Han et al. (2014) ⁷	Korea	277	20 (7.2)	Korea	HTN DM Cb. Infarction Anti-PLT Location (convexity) Encephalomalacia	Age Sex Gcs Anticoagulant Anti-PLT
Bajsarowicz et al. (2015) ¹	Canada USA	647	42 (6.5)	Canada USA	Prev. fall Alcohol Location (convexity) Thickness Midline shifting	Age Sex INR Thickness Midline shifting

Values are presented as number (%). ASDH : acute subdural hematoma, IHD : ischemic heart disease, HTN : hypertension, ACE : angiotensin-converting-enzyme, DM : diabetes mellitus, H. : hemorrhagic, Cb. : cerebral, PLT : platelet, GCS : Glasgow coma scale, Prev. : previous

DISCUSSION

A few previous reports have investigated the risk factors of delayed surgical intervention in initially conservatively treated traumatic ASDH patients (Table 4). According to previous studies, 12.6% of ASDH patients developed CSDH that required delayed surgical intervention. In this study, 28 patients (17.7%) showed progression of SDH and required surgical decompression. They presented aggravation of headache, dysarthria, gait disturbance, or subjective motor weakness. These patients underwent Burr hole trephination and drainage under general or local anesthesia an average of 13.9 days after admission, and none showed neurological deterioration after surgery.

Older patients with minimal ASDH in elderly were more likely to undergo delayed surgery than younger patients. Physiology factors in the brain, such as low elasticity, vulnerable bridging veins, and atrophy, makes older people more susceptible to head injury^{12,15}. In the present study, mean age was significantly higher in the surgical group than the conservative group (69.00 vs. 61.62 years) in univariate analysis ($p=0.024$) but not multivariate analysis. These findings suggest that aging is not an independent factor, but may be related to other co-morbidities or physiological factors^{2,5,6,12}.

Previous studies have reported conflicting results regarding whether hypertension influences the risk of delayed surgery. In the present study, hypertension demonstrated no significant correlation with delayed surgical intervention. These findings may suggest that hypertension is not an independent risk factor for SDH progression. But some previous studies showed the relationship between hypertension and delayed surgery, future research should focus on risk factors influenced by hypertension^{7,10}. Previous studies have also reported conflicting results on the association between DM and SDH progression^{7,9-11}. Han et al.⁷ suggested that DM vasculopathy may play a role in re-bleeding in SDH, while DM was found not to be a risk factor for the progression of ASDH to CSDH. In DM patients, it has been proposed that higher blood osmotic pressure induces hyperviscosity and increases platelet aggregation, thus potentially decreasing re-bleeding in SDH patients^{25,29}.

We expected that history of cardiovascular or cerebrovascular disease and usage of anti-coagulant or anti-platelet agents would influence delayed surgery. However, only history of

cerebrovascular disease significantly differed between the two groups. Cerebral infarction leads to a reduction in brain parenchyma volume, creating a larger subdural space. Consequently, patients are at greater risk of SDH progression¹⁹. Use of anti-platelet agents was shown to increase the risk of morbidity and mortality in ASDH patients²¹. Among the previous studies on SDH progression, Kim et al.⁹, Lee et al.¹¹, and Bajsarowicz et al.¹ reported that use of anti-platelet agents does not influence delayed surgery. By contrast, Laviv and Rappaport¹⁰ and Tseng et al.²⁶ reported that use of anti-platelet agents increases the risk of delayed surgery. Consistent with the former group, in the present study, use of anti-platelet agents did not increase the risk of delayed surgical intervention. Use of anti-platelet agents increases the risk of re-bleeding, is associated with liquefaction of SDH, and facilitates early redistribution of hematoma. Han et al.⁷ suggested that anti-platelet agents affect hematoma liquidity, allowing the hematoma to be more easily washed out by cerebrospinal fluid flow^{18,27}. Cessation and correction of coagulation abnormality could play a role in reducing the risk of delayed surgery. Additionally, it is possible that patients on anti-platelet agents might have had a much thicker SDH requiring emergency surgical decompression or refused intensive treatment, leading them to be excluded from this study.

We found that greater SDH thickness and midline shifting were associated with delayed surgical intervention, and SDH thickness was an independent risk factor for SDH progression. Midline shifting is influenced by SDH thickness, and smaller initial SDH thickness could be considered to reflect greater stability. A thicker hematoma can stress the bridging veins more severely and make them vulnerable to tearing¹³, resulting in hematoma expansion. Through a combination of persistent inflammatory reaction, neoangiogenesis, collection of subdural fluid, and repeated coagulation and fibrinolysis, the hematoma develops a neomembrane^{17,23,24}. Consequently, initially large SDH require more time to be washed out and have a greater risk of transforming to chronic SDH.

We analyzed the accompanying intracranial injuries on all patients' initial brain CT scan. Focal intraparenchymal hemorrhage was not associated with delayed surgery. However, concomitant subarachnoid hemorrhage was more frequently seen in the conservative group. Combined subarachnoid hemorrhage could make the parenchymal swelling. Brain swelling after head injury compresses the hematoma, leading to redis-

tribution⁶⁾. It is possible that an edematous cerebral condition might reduce the free subdural space between the skull and parenchyma, preventing the progression of SDH¹⁴⁾.

In addition, we collected initial laboratory findings for all patients. Among the initial complete blood cell count, hemoglobin demonstrated an independent negative correlation with delayed surgery, and leukocytes demonstrated an independent positive correlation with surgery. Low hemoglobin count could be considered to reflect the aging process, but also indicates low viscosity of the blood. Viscosity has an important role in coagulation pathways. Low hemoglobin indicates low viscosity of the blood, and these patients have tendency for micro-bleeds and progression to CSDH²⁰⁾. CSDH is also a consequence of inflammatory reactions in hematoma^{23,24)}. Previous reports suggested that eosinophil granulation is associated with SDH membrane formation^{16,22,30)}. Another previous study indicated that the inflammatory reaction is the key role in progression of the CSDH. Leukocytes, eosinophils, macrophages and inflammatory cytokines were elevated and play the important role of progression. At this point of view, an elevated leukocyte count could be interpreted as a marker of inflammatory processes. Pro- and anti-inflammatory cytokines encourage the neoangiogenesis⁴⁾. So patients with a high leukocyte count, more easily form a hematoma neomembrane. Moreover, leukocytes, especially neutrophils, are thought to mediate the exacerbation of secondary brain injury in intracerebral hemorrhage by releasing additional pro-inflammatory proteases that affect blood-brain barrier permeability^{31,32)}. Therefore, relieving the inflammatory condition might reduce the risk of delayed surgery and secondary brain injury⁴⁾, and further studies should focus on the association of CSDH progression and inflammatory markers including not only leukocyte count but also specific cell types (eosinophils, neutrophils, and basophils) and other markers such as erythrocyte sedimentation rate and C-reactive protein.

Initial low glucose was also a risk factor for surgical intervention, which could be considered from the same point of view as hemoglobin. High glucose indicates high viscosity of the blood, which could facilitate hemostasis. This phenomenon could in turn prevent additional bleeding and halt the SDH expansion.

CONCLUSION

In this study, 17.7% of initially conservatively treated ASDH patients developed CSDH and required delayed surgical intervention. Greater initial hematoma thickness, low hemoglobin, and high leukocyte count were identified as independent risk factors of hematoma progression. Therefore, patients with thicker hematomas on initial brain CT and low hemoglobin or high leukocyte count require more careful observation to prevent delayed surgical intervention.

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