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Risk Factors for the Recurrence of Chronic Subdural Hematoma

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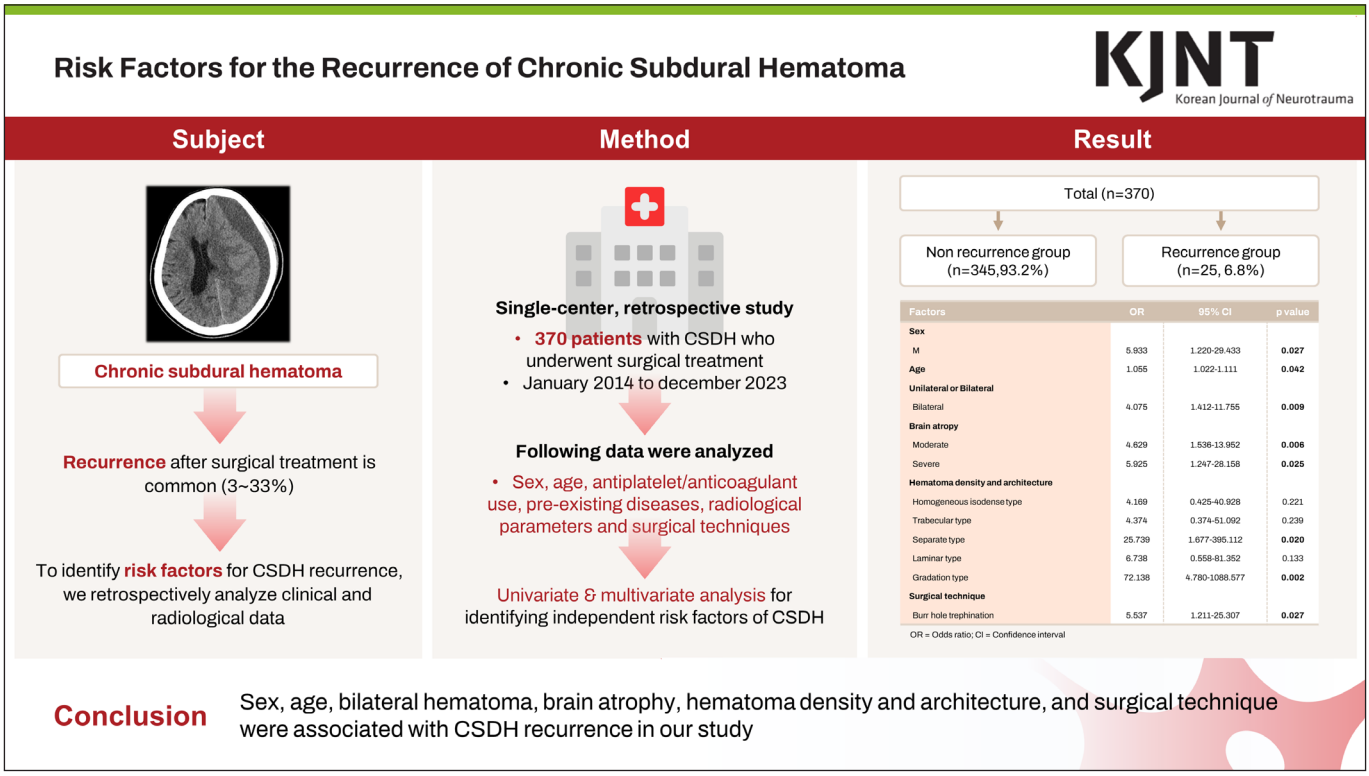
The authors have no financial conflicts of interest.

ABSTRACT

Objective: Chronic subdural hematoma (CSDH) is commonly encountered in neurosurgery, and often occurs in elderly patients following a head injury. Despite favorable postoperative prognosis, recurrence remains common. Herein, we retrospectively analyzed the clinical and radiological data of patients at our institute to identify the risk factors for CSDH recurrence.
Methods: We investigated 370 patients who underwent surgery for CSDH at our institute. The following data were analyzed: sex, age, antiplatelet/anticoagulant use, preexisting diseases, radiological parameters, and surgical techniques. A univariate analysis was subsequently performed to examine the association between these variables and CSDH recurrence. Variables with a *p*-value of <0.05 in univariate analysis were further subjected to a multivariate logistic regression model to identify independent risk factors of CSDH.
Results: Of the 370 patients, 345 (93.2%) had no recurrence and 25 (6.8%) had recurrence. Univariate and multivariate analyses revealed that male sex, advanced age, bilateral hematoma, moderate or severe brain atrophy, separation type, gradation type, and burr hole trephination were independent risk factors for CSDH recurrence.
Conclusion: Sex, age, bilateral hematoma, brain atrophy, hematoma density and architecture, and surgical techniques are all associated with CSDH recurrence.

Keywords: Chronic subdural hematoma; Trauma; Recurrence

GRAPHICAL ABSTRACT



Informed Consent

This study is a retrospective research and corresponds to the reason for consent exemption.

Ethics Approval

The study protocol was approved by Institutional Review Board of Konyang University Hospital. Konyang University Hospital (approval No. 2024-02-008).

INTRODUCTION

Chronic subdural hematoma (CSDH), which occurs among elderly patients after head trauma, presents with liquified hematoma and has a characteristic outer membrane.[1] Surgical treatments for CSDH typically comprise burr hole trephination or craniotomy combined with subdural drain placement.[27,31] Despite a favorable prognosis postoperatively, recurrence is commonly observed, with recurrence rates varying widely (ranging from 3% to 33%).[8] Factors such as age, sex, a bleeding tendency, diabetes mellitus (DM), a history of seizure, hematoma density, hematoma width, midline shift, postoperative pneumocephalus, bilateral CSDH, and a low Glasgow Coma Scale (GCS) score are associated with CSDH recurrence.[1,3,7,30,34] However, these results vary across individual studies, and differences in parameter definitions may result in statistical bias. Therefore, we aimed to retrospectively analyze the clinical and radiological data of patients with CSDH at our institute to identify risk factors for recurrence of CSDH.

MATERIALS AND METHODS

We retrospectively investigated 370 patients with CSDH who underwent surgical treatment in our institute, from January 2014 to December 2023. Sample size was not calculated and all the patients operated during study period were included. The following data were analyzed: sex, age, antiplatelet/anticoagulant use, pre-existing diseases, radiological parameters and surgical techniques. The study protocol was approved by our Institutional Review Board (approval No. 2024-02-008).

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Radiological parameters were assessed via brain computed tomography (CT) scans. All patients underwent a brain CT scan on admission, and postoperative brain CT scan was conducted within two days postoperatively. The following radiological data were assessed: unilateral hematoma or bilateral hematoma, brain atrophy, midline shift, hematoma density and architecture, maximum width of hematoma, and postoperative pneumocephalus. Brain atrophy was classified into three categories: no or mild atrophy, moderate atrophy (opening of sulci and mild ventricular enlargement), and severe atrophy (volume loss of gyri and severe ventricular enlargement).[20] Hematoma densities and architectures were classified into 6 types based on brain CT scan and illustrated in **FIGURE 1** (homogeneous hypodense type, homogeneous isodense type, trabecular type, separate type, laminar type, and gradation type). The trabecular type consisted of a hematoma with high-density septations, typically against a background of low or isointensity. The separate type comprised two components of different densities. High-density components were located at down the bottom, whereas low-density components were positioned above them, and a clear boundary between the 2 components was observed. Similarly, the gradation type was also composed of two components, but with an unclear boundary between them. The laminar type was defined as a hematoma with thin, high-density layers along the inner membrane.[16,17]

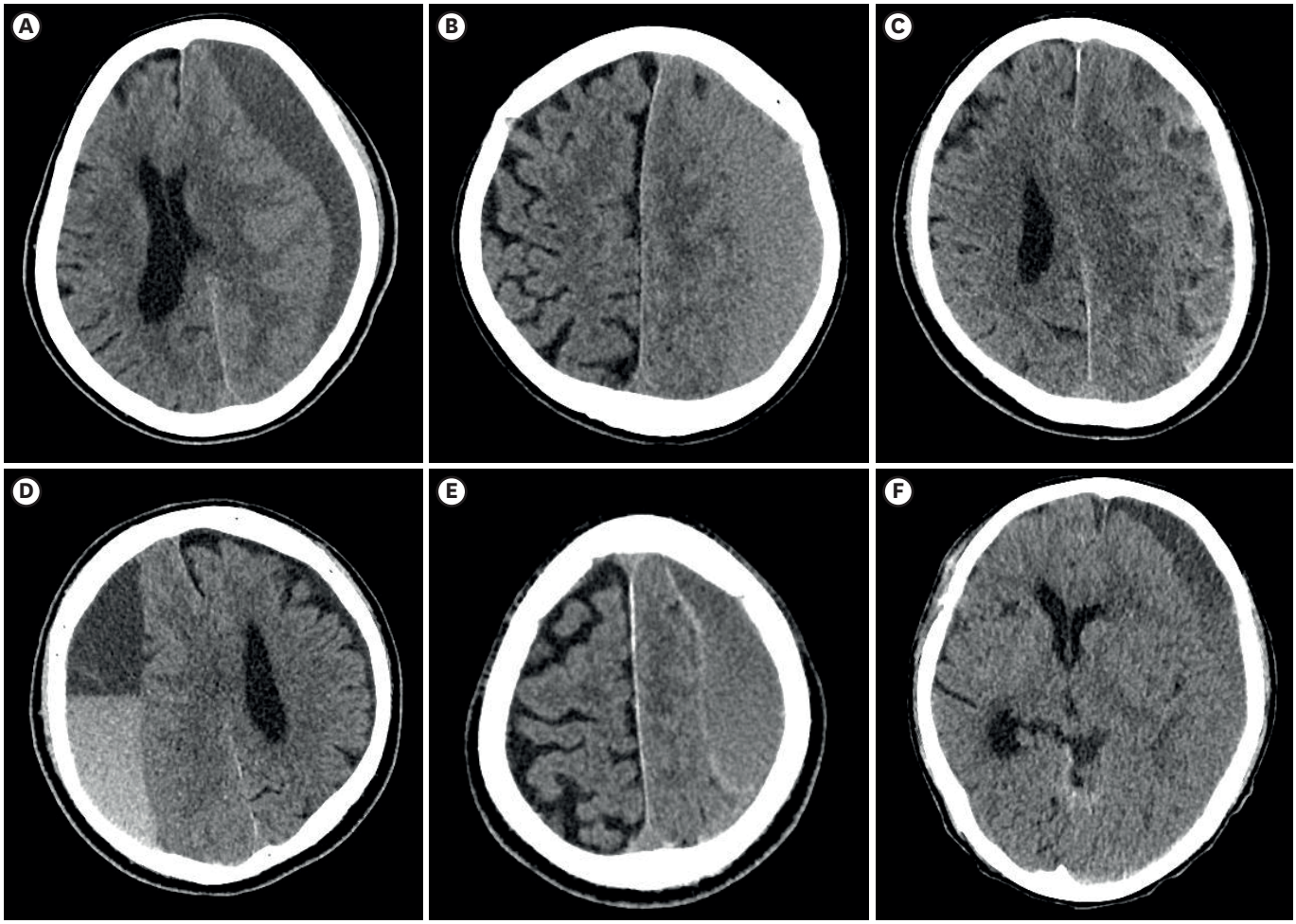

FIGURE 1. CT imaging of different types of CSDH. (A) Homogeneous hypodensetype, (B) Homogeneous isodense type, (C) Trabecular type, (D) Separate type, (E) Laminar type, and (F) Gradation type.
CT: computed tomography, CSDH: chronic subdural hematoma.

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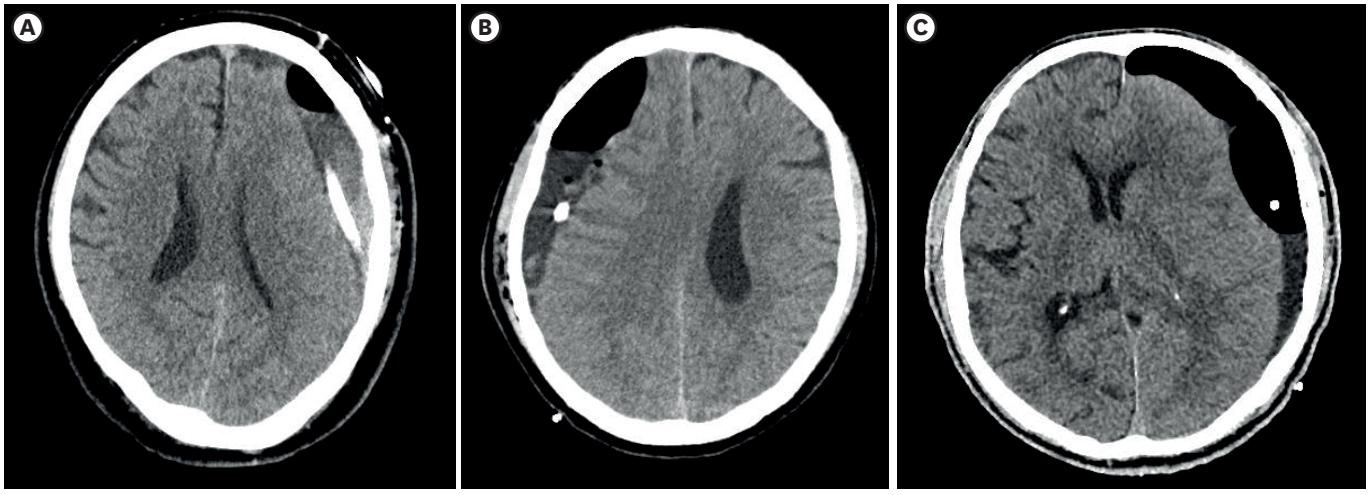

FIGURE 2. CT imaging of postoperative pneumocephalus categories. (A) No or mild, (B) Moderate, and (C) Severe.
CT: computed tomography.

Postoperative pneumocephalus was classified into 3 categories. If the volume of subdural air was less than one-third of the postoperative residual cavity, this was defined as no or mild pneumocephalus. If the volume of subdural air was more than one half of the postoperative residual cavity, this was defined as severe pneumocephalus. And when between one-third and one-half, this was defined as moderate pneumocephalus (**FIGURE 2**). For comparing recurrence, the maximum width of the hematoma was divided into 2 categories, based on a threshold of 20 mm (a width of ≥20 mm compared with a width of <20 mm). Preoperative midline shift was divided into two categories, based on a threshold of 10 mm (a width of ≥10 mm compared with a width of <10 mm).

Surgery was indicated if a brain CT scan showed a maximal hematoma thickness of approximately 1 cm or larger, accompanied by symptoms such as focal deficits, changes in mental status, or seizures caused by the hematoma. Surgery was routinely conducted upon admission but delayed if the results of routine coagulation tests were pathologic (international normalized ratio ≥1.3, activated partial thromboplastin time ≥45 seconds, platelet count ≤100,000/μL) or patients were taking antiplatelet/anticoagulant. The surgical technique was either burr hole trephination with placement of subdural drain or mini-craniotomy with placement of subdural drain, while considering the patient's age, general condition, coagulation tests, antiplatelet/anticoagulant use, and presence of a significant acute clot. The subdural drain catheter was inserted into either the frontal area or the temporoparietal area, depending on the location of the hematoma. After surgery, patients were advised to remain on bed rest until the catheter was removed. The catheter was drained at a level 5–10 cm below the tragus, and prophylactic antibiotics were administered for up to 5 days post-surgery. Postoperative brain CT was conducted on the day of or after surgery. Based on a postoperative brain CT scan, the drain was removed after confirming adequate hematoma evacuation. After discharge, the patients were followed up in an outpatient setting, and antiplatelet and anticoagulant therapies were discontinued until confirming the absence of recurrence. An increase in hematoma size in the ipsilateral subdural space within three months after surgery was defined as recurrence of CSDH and reoperation was indicated if the patient experienced recurrence of hematoma with neurological deterioration.

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Statistical analyses were performed using IBM SPSS Statistics for Windows, version 27.0 (IBM Corp., Armonk, NY, USA). Statistical significance was defined as a *p*-value <0.05. Univariate analysis was conducted for examining the association between patients' data and recurrence of CSDH. Categorical variables were compared using the χ^2 and Fisher's exact tests, and continuous variables were assessed using the *t*-test. Variables with a *p*-value of <0.05 in univariate analysis were subjected into a multivariate logistic regression model for identifying independent risk factors of CSDH. The relationship between variables and CSDH recurrence is presented using odds ratios (ORs) and 95% confidence intervals (CIs).

RESULTS

This study included a total of 370 patients with CSDH. Of the 370 patients, there were 345 cases (93.2%) with non-recurrence and 25 cases (6.8%) had recurrence. Among patients with recurrence, 20 patients (80.0%) underwent a second surgery, 5 patients (20.0%) underwent a third surgery, and no cases underwent surgery more than three times. There were 256 males (69.2%) and 114 females (30.8%), with recurrence rates of 9.0% and 1.8%, respectively, and a higher rate observed in males. The average age at diagnosis was 72.16 years (range, 22–96 years). The average ages were 71.83±12.12 years and 76.72±7.00 years for the non-recurrence and recurrence groups, respectively, indicating a higher average age in the recurrence group. Patients were categorized as follows: 222 (60.0%) with no or mild brain atrophy, 132 (35.7%) with mild brain atrophy, and 16 (4.3%) with moderate brain atrophy. Recurrence in the severe brain atrophy group was the highest at 25%. The 370 CSDH patients were classified into 6 types according to hematoma density and architecture on brain CT scans: homogeneous hypodense type (46 patients, 12.4%), homogeneous isodense type (113 patients, 30.5%), trabecular type (87 patients, 23.5%), separate type (13 patients, 3.5%), laminar type (96 patients, 25.9%), and gradation type (15 patients, 4.1%). Recurrence rate was lowest at 2.2% in the homogeneous hypodense type and highest at 33.3% in the gradation type. In postoperative pneumocephalus category, 155 (41.9%) patients had no or mild pneumocephalus, 158 (42.7%) patients had moderate pneumocephalus, and 57 (15.4%) patients had severe pneumocephalus. Recurrence rate was highest at 12.3% in the severe pneumocephalus group. 245 (66.2%) patients underwent burr hole trephination and 125 (33.8%) patients underwent mini-craniotomy, with recurrence rates of 9.0%, and 2.4%, respectively. The remaining clinical and radiological characteristics are summarized in **TABLE 1**.

Univariate analysis revealed that sex (*p*=0.012), age (*p*=0.003), unilateral or bilateral CSDH (*p*=0.007), brain atrophy (*p*=0.006), hematoma density and architecture (*p*=0.002), and surgical technique (*p*=0.016) were significantly associated with CSDH recurrence.

A multivariate logistic regression analysis was conducted (**TABLE 2**). Results demonstrated that male (OR, 5.933; 95% CI, 1.220–29.433; *p*=0.027), age (OR, 1.055; 95% CI, 1.022–1.111; *p*=0.042), bilateral hematoma (OR, 4.075; 95% CI, 1.412–11.755; *p*=0.009), moderate (OR, 4.629; 95% CI, 1.536–13.952; *p*=0.006; no or mild as reference) and severe (OR, 5.925; 95% CI, 1.247–28.158; *p*=0.025; no or mild as reference) brain atrophy, seperate type (OR, 25.739; 95% CI, 1.677–395.112; *p*=0.020; homogeneous hypo-dense type as reference), gradation type (OR, 72.138; 95% CI, 4.780–1088.577; *p*=0.002; homogeneous hypo-dense type as reference) and burr hole trephination (OR, 5.537; 95% CI, 1.211–25.307; *p*=0.027) were independent risk factors for CSDH recurrence.

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TABLE 1. Univariate analysis of factors related to recurrence of chronic subdural hematoma

Factors	Number of patients (%)		*p*-value
	No recurrence	Recurrence	
Total patients	345 (93.2)	25 (6.8)	
Sex			**0.012**
Male	233 (91.0)	23 (9.0)	
Female	112 (98.2)	2 (1.8)	
Age (year)	71.83±12.12	76.72±7.00	**0.003**
Hypertension			0.353
No	143 (94.7)	8 (5.3)	
Yes	202 (92.2)	17 (7.8)	
Diabetes mellitus			0.986
No	234 (93.2)	17 (6.8)	
Yes	111 (93.3)	8 (6.7)	
Stroke history			0.176
No	307 (93.9)	20 (6.1)	
Yes	38 (88.4)	5 (11.6)	
Antiplatelet use			0.702
No	250 (92.9)	19 (7.1)	
Yes	95 (94.1)	6 (5.9)	
Anticoagulant use			0.096
No	339 (93.6)	23 (6.4)	
Yes	6 (75.0)	2 (25.0)	
Unilateral or bilateral			**0.007**
Unilateral	281 (95.3)	14 (4.7)	
Bilateral	64 (85.3)	11 (14.7)	
Brain atrophy			**0.006**
No or mild	213 (95.9)	9 (4.1)	
Moderate	120 (90.9)	12 (9.1)	
Severe	12 (75.0)	4 (25.0)	
Hematoma density and architectures			**0.002**
Homogeneous hypodense type	45 (97.8)	1 (2.2)	
Homogeneous isodense type	105 (92.9)	8 (7.1)	
Trabecular type	83 (95.4)	4 (4.6)	
Separate type	10 (76.9)	3 (23.1)	
Laminar type	92 (95.8)	4 (4.2)	
Gradation type	10 (66.7)	5 (33.3)	
Midline shift			0.914
≥10 mm	148 (93.1)	11 (6.9)	
<10 mm	197 (93.4)	14 (6.6)	
Maximum width of the hematoma			0.278
≥20 mm	282 (92.5)	23 (7.5)	
<20 mm	63 (96.9)	2 (3.1)	
Postoperative pneumocephalus			0.135
No or mild	148 (95.5)	7 (4.5)	
Moderate	147 (93.0)	11 (7.0)	
Severe	50 (87.7)	7 (12.3)	
Surgical technique			**0.016**
Burr hole trephination	223 (91.0)	22 (9.0)	
Minicraniotomy	122 (97.6)	3 (2.4)	

Values are presented as mean ± standard deviation or number (%). Bold styled *p*-values indicate a *p*-value of less than 0.05.

DISCUSSION

CSDH is a common neurosurgical disease that typically occurs among elderly patients after trauma, with majority of patients having a good prognosis. However, in some patients, recurrence is observed following surgery. Various risk factors for CSDH recurrence, including age, sex, a bleeding tendency, DM, a history of seizure, hematoma density, hematoma width,

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TABLE 2. Multivariate logistic regression analysis of factors related to recurrence of chronic subdural hematoma

Factors	OR	95% CI	*p*-value
Sex			
Male	5.933	1.220–29.433	**0.027**
Age	1.055	1.022–1.111	**0.042**
Unilateral or Bilateral			
Bilateral	4.075	1.412–11.755	**0.009**
Brain atropy			
Moderate	4.629	1.536–13.952	**0.006**
Severe	5.925	1.247–28.158	**0.025**
Hematoma density and architecture			
Homogeneous isodense type	4.169	0.425–40.928	0.221
Trabecular type	4.374	0.374–51.092	0.239
Separate type	25.739	1.677–395.112	**0.020**
Laminar type	6.738	0.558–81.352	0.133
Gradation type	72.138	4.780–1,088.577	**0.002**
Surgical technique			
Burr hole trephination	5.537	1.211–25.307	**0.027**

Bold styled *p*-values indicate a *p*-value of less than 0.05.
OR: odds ratio, CI: confidence interval.

midline shift, postoperative pneumocephalus, bilateral CSDH, and a low GCS score have been proposed[1,3,7,30,34]; however, variations in research methods across individual studies have made it difficult to draw a clear conclusions. In this study, we found that male sex, advanced age, bilateral hematoma, moderate and severe brain atrophy, separation type, gradation type, and burr hole trephination were independent predictors of CSDH recurrence.

Using *t*-test and logistic regression analysis, age was revealed as an independent risk factor for recurrence of CSDH. According to previous studies, head trauma due to incidents such as falls is the most common cause of CSDH[26] and elderly patients are at a higher risk of falls after surgery, leading to CSDH recurrence.[4,6] Elderly patients are also at a higher risk of developing hypertension, DM, cardiovascular and cerebrovascular diseases. Moreover, the coexistence of these diseases may cause postoperative complications.[18,25] The most common postoperative complication in the recent study was acute subdural hematoma,[9,15] leading to CSDH recurrence. Advanced age was also associated with poor brain expansion after surgery and CSDH recurrence.[11,15,21,23,24]

A few studies have indicated significant differences in the recurrence rates according to sex. In a study presenting higher recurrence rates among males, males had a much higher chance of experiencing head trauma compared with females and were predisposed to developing CSDH.[2,13] Higher estrogen levels among females may have protective effects on capillaries and induce vascular repair and angiogenesis.[5,28] In our study, we found a significant relationship between sex and CSDH recurrence, with a tendency towards higher recurrence rates in males. Due to the small sample size of the recurrence group and possibility of selection bias, further research is warranted.

A statistical analysis was conducted for investigating the relationship between the patients' medical histories of hypertension, DM, stroke, and disease recurrence. However, none of these factors was significantly associated in our study. There are several studies investigating the relationship between DM and CSDH recurrence. In the study by Yamamoto et al.,[34] DM might decrease the rebleeding tendency because hyperglycemia can cause blood hyperviscosity, platelet aggregation and increased blood osmotic pressure. Meanwhile, in the

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study by Torihashi et al.,[30] capillary vasculopathy, such as retinal hemorrhage, was a major DM-related complication and that exudation from macrocapillaries in the outer membrane of the CSDH plays a crucial role in chronic CSDH enlargement.[12,29] Based on these findings, the authors considered that DM contributes to an increased recurrence rate of CSDH.[30]

As the population ages, the number of individuals with cardiovascular and cerebrovascular diseases increases, leading to an increase in the number of patients taking antiplatelet and anticoagulant medications. The relationship between antiplatelet and anticoagulant use and CSDH recurrence remains controversial. Some studies have suggested an association between antiplatelets/anticoagulant usage and CSDH recurrence,[7] whereas others have reported no such correlation.[14,30] Such differences could be attributed to the medication types that patients had taken, number of medications, drug resistance, and their adherence to medication regimens. In this study, we conducted a χ^2 test for assessing the relationship between antiplatelet medication use and disease recurrence and Fisher's exact test for examining the association between anticoagulant use and disease recurrence; however, neither revealed a significant correlation. A study on platelet counts and CSDH recurrence suggested that decreased platelet counts are associated with disease recurrence, and the risk gradually increases in parallel with a decrease in platelet counts.[33] Despite not being addressed in this study, further research is necessitated to explore this aspect.

In our study, bilateral hematoma, moderate and severe brain atrophy compared with no or mild brain atrophy, separate and gradation type compared with homogeneous hypodense type revealed higher recurrence rates. In some studies, bilateral CSDH was found to be a risk factor for CSDH recurrence.[22,24] There is a tendency for patients with bilateral CSDH to have previous brain atrophy, potentially causing poor brain re-expansion postoperatively. Poor brain re-expansion has been associated with CSDH recurrence and was considered to generate the subdural space for hematoma reaccumulation.[15,24] Several studies have investigated the relationships between hematoma density and hematoma recurrence; however, results remain variable.[7,19] Nakaguchi et al.[16] showed that fibrinolytic activity and a rebleeding tendency from the neomembrane were high in the laminar and separated types. One experimental study showed that in the separate type, inflammatory cytokine concentration was high and was associated with high recurrence rates; whereas, in the trabecular type, inflammatory cytokine concentration was low, and showed a low recurrence rate.[10] Considering the relationship between these types and rebleeding tendency, it is reasonable to assume that differences in hematoma density and architecture are associated with different recurrence rates. In this study, multivariate logistic regression analysis revealed that despite no significant results in the laminar type, recurrence rates were significantly higher for the separate and gradation types. Hence, unless severe symptoms are present, delaying surgery for separate, gradation, and laminar types may reduce recurrence rates.

Many studies have aimed at determining the optimal surgical techniques for CSDH, including burr hole trephination and mini-craniotomy. In our study, there was a significant difference in the recurrence rates between burr hole trephination and mini-craniotomy, with a lower recurrence rate observed in mini-craniotomy. Van Der Veken et al.[32] explained that mini-craniotomy could be an alternative to burr hole trephination due to better visualization of the subdural space and the possibility of opening more septae, constricting membranes, and cauterizing bleeding vessels. However, other studies suggest that there is no significant difference between burr hole trephination and mini-craniotomy regarding disease recurrence or complications or that burr hole trephination is superior.[35] Hence, follow-up randomized

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controlled trials incorporating various variables such as postoperative complications and mortality rates, in addition to disease recurrence rates, are necessary.

CONCLUSION

In conclusion, male sex, advanced age, bilateral hematoma, moderate and severe brain atrophy, hematoma density and architecture (separate and gradation types), and burr hole trephination were associated with CSDH recurrence in our study. We believe that these risk factors will contribute for a better understanding of CSDH.

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