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Identification of Radiological and Clinical Factors that Increase the Risk of Chronic Subdural Hematoma Recurrence

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ABSTRACT

AIM: Chronic subdural hematoma (CSH) is a commen type of intracranial hemorrhage in elderly patients. Despite improved medical diagnosis and treatment, the reoperation rate remains high. Here we aimed to identify risk factors predict CSH recurrence.

MATERIAL and METHODS: A retrospective review of 291 CSH patients admitted to our department was performed. Clinical and radiological factors predictive for CSH recurrence were identified by univariable analyses; variables whose p-value was <0.05 underwent multivariate logistic regression analyses.

RESULTS: Univariate analyses revealed that preoperative midline shift (p=0.025), mix-density hematoma (p=0.023), internal architecture of hematoma (p=0.044), membranectomy (p=0.001), and ambient cistern compression (p=0.001) correlated with a significantly higher rate of recurrence. Multivariate analyses showed that separated architecture, membranectomy and ambient cistern compression were independent risk factors for CSH recurrence.

CONCLUSION: Among many factors, membranectomy, separated architecture, and ambient cistern compression were the strongest predictors for recurrence.

KEYWORDS: Recurrence, Chronic subdural hematoma, Risk factor

ABBREVIATIONS: CSH: Chronic subdural hematoma, **CT:** Computed tomography, **DM:** Diabetes mellitus, **HU:** Hounsfield units, **WBC:** White blood cell, **INR:** International normalized ratio, **OR:** Odds ratio, **CI:** Confidence interval

INTRODUCTION

Chronic subdural hematoma (CSH) is a commen neurosurgical disorder worldwide, especially prevalent among the elderly. Its incidence is 8.2-17.6 per 100,000 individuals annually and increases with the age of the population (23). CSH is typically treated with burr hole craniostomy followed by closed-system drainage, whose prognosis and outcome are generally satisfactory. However, up to 26.5% of patients suffer recurrence after their first surgical intervention. The recurrence rate also increases with age. (24).

Several factors can predict the recurrence of CSH: age, sex, antiplatelet and/or anticoagulant use, bilateral or unilateral hematoma, preoperative midline shift, computed tomography (CT) density, preoperative hematoma thickness, method of hematoma evacuation, patients with diabetes mellitus (DM), and hypertension (6,12,13,18). Although many studies have explored multiple factors, their results often conflict. Here, we examined the medical records of patients treated in our clinic to reveal the most important risk factors for recurrence of CSH.

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MATERIAL and METHODS

We retrospectively evaluated 291 patients who underwent surgical evacuation in the our hospital between 2015 and 2020; they were initially evaluated and diagnosed using CT.

Medical records were accessed from the electronic files available at our hospital. Age, sex, hypertension, DM, antiplatelet therapy, anticoagulant therapy, Markwalder grading score (Table I), midline shift (mm), the initial maximum thickness of the subdural hematoma (mm), cisterna ambiens compression, the density of hematoma (Hounsfield units, HU), surgical procedure (single burr hole, double burr hole or craniotomy), membranectomy and laboratory findings (levels of white blood cell (WBC), hemoglobin, platelet, international normalized ratio (INR), and albumin) were assessed. Hematoma density was classified according to CT as follows: hypo-density (<25 HU), iso-density (25-35 HU), and mixed-density. CSH was classified according to its internal architecture as described by Nakaguchi: homogeneous architecture, laminar architecture, separated architecture, and trabecular architecture (11) (Figure 1). Bilateral subdural hematoma cases were excluded from the study.

Surgery was initiated in cases of focal neurologic deficit and/or unconsciousness; the procedure was determined by the characteristics of the hematoma. In general, as all over the world, patients were operated by single or double burr hole craniostomy with irrigation and closed-system drainage under general anesthesia. However, a small (<4 cm) craniotomy was performed if a multilayer intrahematomal structure was detected by T2-weighted MRI or the CSH was organized, calcified, and had numerous thick membranes. In these cases, after dural opening, the outer membrane was opened and the subdural space irrigated with isotonic solution. A small opening was created in the inner membrane, and the space below the inner membrane was also irrigated. A wide membranectomy was performed if the brain did not expend or there were encapsulated hematoma or intralesional solid components. Membranectomy was performed such that all capsular membrane components (both outer and inner membranes) were resected as much as possible, and the membrane edges coagulated.

An external closed drainage system was maintained for two to three days and removed after a CT. However, CT was performed immediately in patients whose symptom such as low level of consciousness, weakness or headache worsened. A craniotomy was performed to evacuate the hematoma if new bleeding was observed in the early CT scan.

All patients who used anticoagulants or antiplatelets paused their usage for 10 days before surgery and were instructed to not use them until two weeks post-operation if if they did not have a neurological emergency. Low-molecular-weight heparin was used during this period. Patients whose neurological status deteriorated and were scheduled for emergency surgery were excluded from the study.

The medical records of patients who were admitted to this study were reviewed up to six months after the initial surgery. Recurrence was defined as the accumulation of a hematoma that grew to its pre-surgical size on the operated side within the first three months after intervention. The surgical intervention for recurrent CSH was determined according to characteristics of the hematoma as described above.

The patients were divided into two groups: recurrent and non-recurrent CSH. SPSS software (version 20.0, SPSS Inc., Chicago, USA) was used to analyze data. Independent sample t-test and chi-squared test were used for univariate statistical analyses. A logistic regression model was used for multivariate statistical analyses. The relationship between each predictive factor and recurrence of CSH is expressed as an odds ratio with a 95% confidence interval. A p-value <0.05 indicated statistical significance.

RESULT

A total of 291 patients with CSH were studied and included 216 men and 75 women, whose mean age and age range were 70.4 ± 11.3 and 38–90, respectively. Tables II and III show their demographics and clinical presentation. The total CSH recurrence rate was 28.8% (84 out of 291). Males showed a 31.9 % recurrence rate (69 out of 216), while females showed a 20% recurrence rate (15 out of 75). The difference was not statistically significant (p=0.256). A history of head trauma before initial surgery was reported among 234 patients (80.4%): 63 patients in the recurrence group (26.9%), and 171 patients in the non-recurrence group (73%) (p=0.392). Fifty-seven patients did not have an obvious trauma history (19.6%).

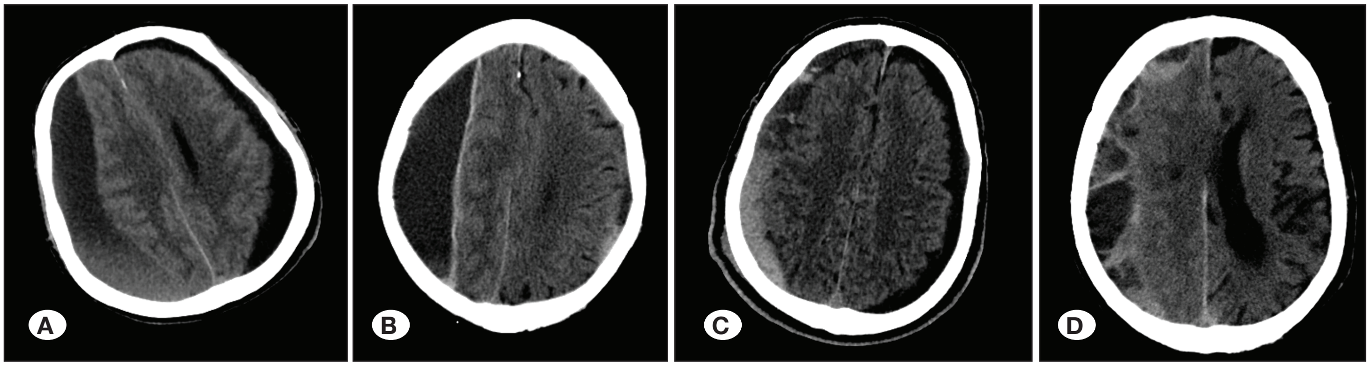

Figure 1: Computed tomography characteristics of chronic subdural hematoma. Homogeneous **(A)**, laminar **(B)**, separated **(C)**, and trabecular **(D)** architecture.

Table I: The Classification System of Patients according to Their Initial Clinical Status

Markwalder Grading Scale	
Grade 0	Neurologically normal
Grade 1	Alert and orientated: absence of mild symptoms such as headache, or mild neurologic deficit such as reflex asymmetry
Grade 2	Drowsy or disorientated, or variable neurologic deficit such as hemiparesis
Grade 3	Stuporous but responding appropriately to noxious stimuli, several focal signs such as hemiplegia
Grade 4	Comatose with absent motor responses to painful stimuli, decerebrate or decorticate posturing

Table II: Continuous Variables were Assessed Using the Student's t-test

Factors	**Non-recurrent group (n=207)**	**Recurrent group (n=84)**	**p**
Age (years)	70.4 ± 10.8	70.6 ± 12.7	0.304
Midline shift* (mm)	4.39 ± 3.5	6.33 ± 4.38	0.025
Maximum thickness of hematoma (mm)	19.82 ± 6.57	22.17 ± 9.31	0.163
Hemoglobin (g/dl)	13.9 ± 1.8	13.9 ± 2.07	0.935
WBC ($x10^3/\mu L$)	8.3 ± 2.5	8.4 ± 2.8	0.979
Platelet ($x10^3/\mu L$)	256.50 ± 82.88	222.82 ± 78.75	0.069
INR	1.29 ± 0.91	1.15 ± 0.56	0.449
Albumin (g/dl)	3.85 ± 0.47	3.64 ± 0.77	0.120

statistically significant; p<0,05, craniotomy **WOM: Without membranectomy.*

Table III: Categorical Variables were Assessed Using the Chi-Square Test

Factors	**Non-recurrent group (n=207)**	**Recurrent group (n=84)**	**p**
Markwalder Grading Scale			0.410
Grade 0	3 (1.4)	0 (0)	
Grade 1	162 (78.3)	57 (67.9)	
Grade 2	30 (14.5)	15 (17.9)	
Grade 3	12 (5.8)	9 (10.7)	
Grade 4	0 (0)	3 (3.6)	
Sex			0.313
male/female	147/60 (71/29)	69/15 (82.1/17.9)	
Diabetes Mellitus			0.491
no/yes	165/42 (79.7/20.3)	72/12 (81.4/18.6)	
Hypertension			0.243
no/yes	84/123 (40.6/59.4)	45/39 (53.6/46.4)	

Table III: Cont.

Factors	Non-recurrent group (n=207)	Recurrent group (n=84)	p
History of trauma			0.408
no/yes	36/171 (17.4/82.6)	21/63 (25.0/75.0)	
Drug use			0.101
no/anticoagulant/ antiaggregant	150/27/30 (72.5/13.0/14.5)	75/0/9 (89.3/0/10.7)	
Surgery type			
single burrhole/double burrhole/craniotomyWOM	99/27/81 (47.8/13/39.1)	24/9/51 (28.6/12.4/45.4)	0.870
Density of hematoma*			
hypo/iso/mix	48/75/84 (23.2/36.2/40.6)	18/9/57 (21.4/10.7/67.9)	0.023
Membrane layer*			0.044
homogeneous/laminar / separated/trabecular	91/50/50/16 (43.9/24.1/24.1/7.8)	8/32/42/2 (10/38/50/2)	
Side			0.910
unilateral/bilateral	138/69 (66.7/33.3)	57/27 (67.9/32.1)	
Membranectomy*			0.001
no/yes	177/30 (85.5/14.5)	42/42 (50/50)	
Ambient cistern compression*			0.001
no/yes	168/39 (81.2/18.8)	18/66 (21.4/78.6)	

Values are given as number and percentage (%).
**statistically significant; p<0.05.*

Hypertension, DM, preoperative laboratory findings, and use of antiplatelet and anticoagulant drugs were not significantly associated with CSH recurrence.

Table III describes CT findings upon admission: 66 patients with hypo-density (22.6%), 84 patients with iso-density (28.9%), 141 patients with mix-density (48.5%) (p=0.023). Basal cisterns were compressed in 105 patients (36.8%), of which 66 were in the recurrence group (p=0.001). Midline shift was 4.39 ± 3.54 mm in the non-recurrence group and 6.33 ± 4.38 mm in the recurrence group (p=0.025). CSH architecture in the recurrence group was characterized in the recurrence group as homogeneous in eight patients (10%), laminar in 32 patients (38%), separated in 42 patients (50%), and trabecular in two patients (2%). CSH recurrence was associated with hematoma layers (p=0.044).

Surgical procedures were not related to recurrence (p=0.144). Specifically, however, wide membranectomy was significantly associated with recurrence (p=0.001).

Univariate analyses showed that the recurrence of CSH was significantly associated with midline shift, mix-density hematoma, internal architecture of the hematoma, ambient cistern compression, and membranectomy. Multivariate logistic regression analyses identified separated architecture, membranectomy, and ambient cistern compression as independent risk factors for the recurrence. The results of multivariate analyses are shown in Table IV. Patients who experienced recurrence underwent the following procedures: double burr hole craniotomy (10.7%), single burr hole craniotomy (28.6%), and craniotomy (60.7%).

DISCUSSION

CSH is a common type of intracranial hemorrhage whose recurrence can be attributed to many risk factors that often conflict across studies (5,8,22). For example, Motoie et al. associated recurrence of hematoma with age and sex, contrary to our study (13). Importantly, the mean age of the population in the former study (79 years) was slightly higher than ours (70 years). Less brain atrophy in younger patients could contribute to these differences. Sex may also contribute to recurrence of CSH: Kim et al. reported that males more frequently experi-

Table IV: The Relation of Risk Factors to CSDH Recurrence was Assessed Using Logistic Regression Analysis

Factors	p	OR	95% CI
Hematoma type†	0.456		
laminar	0.268	0.343	0.052-2.274
separated	**0.003***	0.627	0.075-5.221
Hematoma density‡	0.107		
iso-density	0.659	0.640	0.088-4.644
mix-density	0.456	4.625	0.652-32.811
Membranectomy	**0.004***	7.965	1.960-32.367
Ambient cistern compression	**0.000***	27.881	6.482-119.917

Values are given as number and percentage (%).
statistically significant; p<0.05, **† reference; Homogeneous, **‡ reference;** Hypo-density, **OR:** Odds ratio, **CI:** Confidence interval.*

enced recurrence of hemorrhage. The authors attributed this finding to estrogen, which helps repair damaged vessels (6), yet estrogen levels are higher in older men than in post-menopausal women (10). Here, we assessed the medical records of 291 patients with CSH who underwent surgical intervention in our hospital and identified independent risk factors for CSH recurrence.

Some of our results agreed with previous studies. For example, we also found that history of head trauma was not related to hemorrhage recurrence (2,7). Other factors that did not predict hematoma recurrence in this study included DM, hypertension, and the use of anticoagulant and/or antiaggregant drugs. Yamamoto et al. suggested that hyperviscosity of the blood induced by hyperglycemia could play a role in decreasing recurrence rate in diabetic patients (24). Motoie et al. claimed that using antiaggregant and/or anticoagulant drugs does not increase the recurrence rate because these prevent the formation of clots in the subdural space, but further studies are required to confirm this (13). Our results also concur with Song et al., who associated preoperative midline shift with hemorrhage recurrence (20). Kim et al. suggested that preoperative midline shift diminishes adhesion between the inner and outer membrane, which increases risk of recurrence due to insufficient post-operative brain expansion (7). As a more objective indicator of brain compression, ambient cistern compression was found to be highly correlated with recurrence. To our knowledge, there is only one study that explored the relationship between ambient cistern compression and recurrence of CSH (13).

The density of hematoma indicates the amount of fresh blood clot in the hematoma cavity and shows that blood vessels are actively growing in the membrane of the CSH; a high hematoma density therefore reflects the formation of an active capillary network (9). Similarly, we linked mixed-density hematoma (hyperdense areas were present) to recurrence. The recurrence rate was associated with multiple layer hematoma featuring excessive neo-membrane structures and active blood vessel formation. Wakuta et al. showed that expansion-induced tension in mixed-density and trabecular hematomas may induce bleeding from cortical vessels (21). Yet Ohba et al. reported that the recurrence rate is not related to hematoma density (15).

Nakaguchi et al. classified CSH into four stages based on the internal architecture and density of hematomas (3,14). CSH is first classified as homogeneous or laminar but then matures into the separated type and is finally absorbed as the trabecular type (14). Experimental studies have shown that blood in the subdural space causes inflammation and increases cytokine production, which peaks during the separated stage (4). The recurrence rate is reportedly high for CSH with separated architecture, which we also found (3,17).

Surgical technique (single/double burr hole/craniotomy) was not associated with recurrence. However, the recurrence rate was significantly higher in patients who underwent membranectomy. The optimal surgical technique for CSH is unclear: post-operative mortality and morbidity rates reportedly do not differ between burr hole craniostomy and craniotomy with or without membranectomy (16). Generally, the outer membrane is highly vascularized, and exudation is prerequisite to CSH accumulation (19). Although a wide membranectomy can be performed, the residual membrane may bleed. Fenestration or partial resection of the outer membrane may prevent long-term blood accumulation (1). According to our experience, the double burr hole craniostomy method is the most reliable method if the integrity of the outer membrane was sufficiently impaired but widely membranectomy was not performed.

This study included a relatively small number of patients, whose diverse inclusion criteria may have affected our results. Differences in surgical technique, hematoma density, and follow-up times can significantly affect patient outcomes. We also did not consider pediatric cases, which could have helped reveal the connection between brain anatomical structure (cortical atrophy, ventriculomegaly, etc.) and rebleeding.

CONCLUSION

We analyzed the medical records of nearly 300 patients with CSH who underwent treatment at our hospital and determined independent risk factors for CSH recurrence. We found that double burrhole craniostomy with closed-system drainage can effectively treat CSH. Membranectomy, separated architecture, and ambient cistern compression can independently predict hemorrhage recurrence. Although hematoma classification is controversial, ambient system compression appears to be an objective and reliable indicator of CSH recurrence.

AUTHORSHIP CONTRIBUTION

Study conception and design: MEA, HHK

Data collection: MEA, HHK

Analysis and interpretation of results: MEA, HHK

Draft manuscript preparation: MEA, HHK

All authors (MEA, HHK) reviewed the results and approved the final version of the manuscript.

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