

Clinical and radiological factors predicting recurrence of chronic subdural hematoma: A retrospective cohort study

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ABSTRACT

Background: Chronic subdural hematoma (CSDH) is commonly encountered in the elderly patients and the recurrence rate is still high, therefore, identifying risk factors for CSDH recurrence is essential. The present study aimed to identify clinical and radiological factors predicting the recurrence of CSDH.

Methods: We retrospectively identified 461 patients with CSDH who underwent surgical evacuation in our department. Univariable analyses were performed at first, variables with a *P*-value of <0.05 were entered into multivariable logistic regression model. Kendall's tau-b test was used to evaluate the relationship between brain atrophy and postoperative pneumocephalus.

Results: Univariable analyses revealed that patients with the following characteristics have a higher recurrence rate, including age ≥ 80 years, antiplatelet and/or anticoagulant use, GOS=3, the volume of drainage ≥ 100 ml, midline shift ≥ 10 mm, severe brain atrophy, severe postoperative pneumocephalus. Multivariable logistic regression demonstrated that midline shift ≥ 10 mm, severe brain atrophy, severe postoperative pneumocephalus, and volume of drainage ≥ 100 ml were independent risk factors for CSDH recurrence. Kendall's tau-b test revealed that there was no correlation between brain atrophy and postoperative pneumocephalus.

Conclusions: Midline shift ≥ 10 mm, severe brain atrophy, severe postoperative pneumocephalus, and volume of drainage ≥ 100 ml were independent risk factors for CSDH recurrence, CSDH patients with these characteristics should be taken precautions of recurrence and a closely follow-up should be carried out.

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Introduction

Chronic subdural hematoma (CSDH) is one of the most frequent neurologic pathologies and tends to occur in elderly patients after minor head injury. Burr-hole craniotomy with closed-system drainage is the most commonly used technique for treating CSDH patients. Although CSDH has a favorable prognosis following

the surgical evacuation, the recurrence rate has been estimated to range from 3% to 33% [1].

Factors predicting the recurrence of CSDH have been documented in many studies, including age [2], male sex [2], antiplatelet and/or anticoagulant use [3–5], bilateral hematomas [6–9], midline shift [5,9,10], computed tomography (CT) density [3,11–15], preoperative hematoma volume [5,14,16,17], ways of subdural drainage [18], postoperative pneumocephalus [19,20], postoperative haematoma residual [4,10,12], patients with history of seizure, and diabetes mellitus [5,14]. Identifying risk factors for CSDH recurrence contributes to the postoperative management of the patients and therapeutic trials such as Dexamethasone, Atorvastatin and Goreisan [21–24].

However, there are penurious uniform parameters available to predict the recurrence of CSDH after surgery. Different definitions of these parameters may result in statistical bias. In this study, we retrospectively analyzed the data of patients with CSDH in our department and included as many parameters as possible to identify risk factors for CSDH recurrence.

Abbreviations: CI, confidence interval; CSDH, chronic subdural hematoma; CSF, cerebrospinal fluid; CT, computed tomography; GCS, Glasgow Coma Scale; GOS, Glasgow Outcome Scale; mRS, Modified Rankin Scale; NRG, non-recurrence group; OR, odds ratio; RG, recurrence group.

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Patients and methods

We retrospectively identified 461 patients with CSDH who underwent surgical evacuation in the Department of Neurosurgery, YijiShan Hospital of WanNan Medical College, China, between October 2012 and April 2018. The diagnosis was confirmed by CT scan in all patients. The exclusion criteria included (1) age less than 18 years; (2) CSDH due to a vascular cause, such as aneurysm or arteriovenous malformation; (3) Patients who underwent any other form of intracranial surgery during the last 6 months prior to CSDH intervention; and (4) patients with missing data.

Patient characteristics

The following clinical data were analyzed: sex, age, history of head trauma, antiplatelet and/or anticoagulant use, pre-existing diseases, presenting Glasgow Coma Scale (GCS) score, and Glasgow Outcome Scale (GOS) at discharge.

CT imaging evaluation

All patients received a head CT scan at admission. Postoperative CT scan was performed within 3 days after surgery. The following radiological parameters were identified: unilateral or bilateral, hematoma side, midline shift, brain atrophy, hematoma density, the maximum width of the hematoma, maximum hematoma/fluid thickness after surgery, and postoperative pneumocephalus. Brain atrophy was classified as: (1) no or mild atrophy, (2) moderate atrophy, such as dilated sulci, and (3) severe atrophy, such as widely dilated sulci and subdural space [25]. All hematomas were classified into six types according to their density on CT scan and as illustrated in Fig. 1: (1) homogeneous (including three subtypes, homogeneous hyper-dense, homogeneous iso-dense, and homogeneous hypo-dense), (2) separated, (3) gradation, (4) laminar, (5) trabecular, and (6) mixed density. The separated type containing two components of different densities, a higher density component located below a lower density component with a clear boundary lying between them. If the two components mingled without a boundary, this was called the gradation type. The laminar

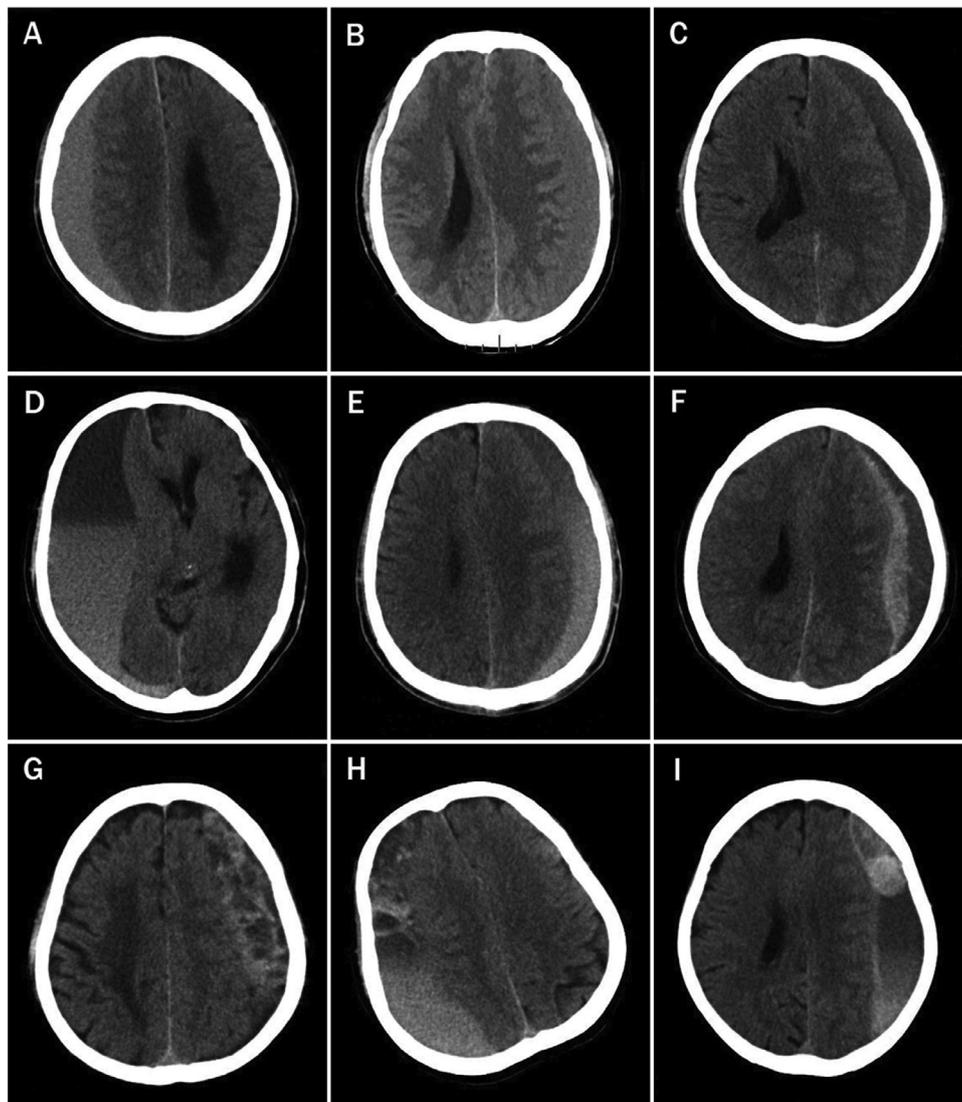


Fig. 1. CT imaging of different types of CSDH. A, homogeneous hyper-dense; B, homogeneous iso-dense; C, homogeneous hypo-dense; D, separated; E, gradation; F, laminar; G, trabecular; H, mixed density (gradation and trabecular in one CT scan simultaneously); I, mixed density (hyper-dense, gradation and laminar in one CT scan simultaneously).

type was defined as a hematoma exhibiting a high-density layer running along the inner membrane. The trabecular type was defined as a hematoma with a low-density to iso-dense components and separated by high-density septa which running between the inner and outer membrane. The mixed type was defined as a hematoma containing two or more types of density above [11]. Postoperative pneumocephalus was classified as: (1) no or mild pneumocephalus, the volume of subdural air is less than 1/3 of postoperative residual cavity, (2) moderate pneumocephalus was defined as the volume of subdural air is between 1/3 to 1/2 of postoperative residual cavity, and (3) the volume of subdural air on postoperative CT scan more than 1/2 of postoperative residual cavity was defined as severe pneumocephalus.

Surgical management

The surgical treatment and postoperative management were uniform in all patients. Briefly, a single burr hole was created at the thickest point of the hematoma under local or general anesthesia, hematoma was evacuated as much as possible. Subsequently, the hematoma cavity was irrigated with saline solution, and finally, a silicon catheter was inserted into the cavity and connected a closed drainage system. The catheter was removed within 72 h after surgery and a CT scan was performed. The volume of drainage and the ways of anesthesia were analyzed.

Followed-up and evaluation of recurrence

No recurrences occurred prior to the postoperative CT scan within 3 days and during the hospitalization. All patients were followed-up for at least 3 months after surgery. During the follow-up, a CT scan would be performed soon if the patient's neurological status deteriorated. The radiological and clinical criteria were integrated to evaluate the CSDH recurrence. The radiological criteria included an increase in the volume and a change in the density of the hematoma on the treated side in follow-up CT scan compared with the volume and density evaluated within three days after surgery. Clinical criteria included a new-onset headache, the reappearance of symptoms such as the focal neurological deficit, or a deterioration of consciousness.

Statistical analysis

All analyses were performed using SPSS (version 22.0, IBM Corp.). The statistical significance was defined as a *P* value < 0.05. All tests were 2-sided. Data were described using means (standard deviations) and numbers of patients (percentages) for continuous and categorical variables, respectively. Categorical variables were compared using the chi-square test, continuous variables were assessed using the Student's *t*-test. Variables with a *P*-value of < 0.05 in univariable analysis were entered into multivariable logistic regression model to identify the independent risk factors of CSDH

recurrence. Kendall's tau-b test was used to evaluate the relationship between brain atrophy and postoperative pneumocephalus.

Results

Of the 461 patients who met the inclusion criteria, 4 (0.8%) died prior to discharge and were excluded from the analyses (one patient died of spontaneous ventricular hemorrhage after operation, one patient died of postoperative acute epidural hemorrhage, two patients died of their accompanied disease: uremia.).

During the study period, a total of 563 surgical procedures with 475 anesthetics were performed for 457 consecutive patients. There were 311 patients with unilateral hematoma and 146 patients with bilateral hematomas, the unilateral operation of the bilateral chronic subdural hematomas (CSDHs) was observed in 40 patients, and 106 patients were operated on both sides. Among the 106 patients, 92 cases were operated on both sides simultaneously and 14 cases suffered contralateral hematoma growth and reoperation after unilateral drainage of bilateral CSDHs. Of the 457 patients, hematoma recurrence was observed in 69 patients (15.1%), including 56 males and 13 females. In the recurrence group, 48 patients were unilateral and 21 patients were bilateral, among the 21 patients, 4 patients suffered both sides recurrence and 17 patients suffered single side recurrence (Table 1).

The results of the clinical and radiological characteristics of the 457 patients were presented in Tables 2 and 3. There were 376 males (82.3%) and 81 females (17.7%), the male/female ratio is 4.64. The mean age at diagnosis was 68.8 years (ranging from 23 to 92 years), the age was significantly older in the Recurrence Group (72.8 ± 9.4) than that of the Non-recurrence Group (68.1 ± 11.8) ($P = 0.002$), following chi-square test revealed that the recurrence rate was significantly higher in the patients who older than 80 years ($P = 0.022$). 235 patients with a clear history of head trauma, the average interval between the first operation and the head trauma was 94.8 days. Univariable analyses revealed that age over 80 years, antiplatelet and/or anticoagulant use, GOS scored 3, the volume of drainage ≥ 100 ml, midline shift ≥ 10 mm, severe brain atrophy, and severe postoperative pneumocephalus were significant related to the CSDH recurrence.

A multivariable logistic regression analysis was then performed. Because of the three categories of GOS score and brain atrophy, the recurrence rate was significantly higher in GOS scored 3 than GOS scored 4 and 5, and was significantly higher in severe brain atrophy than moderate and no or mild brain atrophy, we therefore selected GOS scored 3 and severe brain atrophy enter into the model. The results demonstrated that midline shift ≥ 10 mm (OR, 3.01; 95% CI, 1.35–6.74; $P = 0.007$), severe brain atrophy (OR, 13.12; 95% CI, 4.78–36.04; $P < 0.001$), severe postoperative pneumocephalus (OR, 2.09; 95% CI, 1.08–4.01; $P = 0.028$), and volume of drainage ≥ 100 ml (OR, 2.31; 95% CI, 1.29–4.14; $P = 0.005$) were independent risk factors for the recurrence of CSDH (Table 4). A further re-analysis confirmed that these four variables were

Table 1
Surgical information of CSDH patients.

		Unilateral (N)		Bilateral (N)	
		Unilateral operation		Bilateral operation	
				Simultaneously	Contralateral hematoma growth and performed operation
RG	48	8		9 (4 both sides recurrence)	4
NRG	263	32		83	10
Total	311	40		92	14

N = Number; NRG = Non-recurrence Group; RG = Recurrence Group.

Table 2
The clinical characteristics of recurrence and no recurrence groups.

Factors	N. of patients (%)		P
	Recurrence	No recurrence	
Sex			0.926
Male	56 (15)	320 (85)	
Female	13 (16)	68 (84)	
Age			0.035
≥80 years	18 (24)	58 (76)	
<80 years	51 (13)	330 (87)	
History of head trauma			0.790
Yes	37 (16)	198 (84)	
No	32 (14)	190 (86)	
Antiplatelet and/or anticoagulant use			0.02
Yes	9 (32)	19 (68)	
No	60 (14)	369 (86)	
Hypertension			0.731
Yes	23 (14)	141 (86)	
No	46 (16)	247 (84)	
Diabetes Mellitus			0.061
Yes	10 (27)	27 (73)	
No	59 (14)	361 (86)	
Stroke history			0.676
Yes	2 (10)	19 (90)	
No	67 (15)	369 (85)	
Presenting GCS			0.423
15	64 (16)	344 (84)	
≤14	5 (8)	44 (92)	
GOS			0.002
3	8 (35)	15 (65)	
4	19 (23)	62 (77)	
5	42 (12)	311 (88)	
Anesthesia			0.897
Local	25 (15)	139 (85)	
General	44 (14)	263 (86)	
Volume of drainage			<0.001
≥100 ml	46 (22)	159 (78)	
<100 ml	27 (8)	331 (92)	

CI = Confidence Interval; OR = Odds Ratio; RG = Recurrence Group. Significant P values are in bold type.

effective predictors of CSDH recurrence (Table 5). Kendall's tau-b test revealed that no correlation between the brain atrophy and postoperative pneumocephalus ($R = 0.049$; $P = 0.202$).

Discussion

The incidence of CSDH is 8–58:100,000 per year in people who older than 65 years [1]. With the development of population aging, patients with CSDH will increase year by year and gradually become one of the major diseases that endanger the elderly. Burr-hole craniostomy remains the preferred treatment for CSDH patients, but with or without drainage is still controversial. A retrospective study of WANG W, et al. [26] revealed that the hospitalization, postoperative complications and recurrence rate did not differ between with drainage group and without drainage group. Heringer LC, et al. [27] have inferred that patients with CSDH with or without drainage after burr-hole craniostomy did not alter the rate of recurrence and complications. However, a randomised controlled trial performed by Thomas Santarius and his colleagues found a drain after burr-hole craniostomy of CSDH is associated with reduced recurrence rate and mortality [28]. Two meta-analyses concluded that postoperative drainage can reduce the complications and recurrence rate of CSDH, and recommend that the drainage should be performed routinely in the surgical procedure [29,30]. In this cohort study, closed-system drainage was performed in all patients.

Few studies have reported on the relationship between CSDH recurrence and volume of postoperative drainage. Univariable and multivariable regression analysis demonstrated that volume of

drainage ≥ 100 ml was an independent risk factor for the recurrence of CSDH. We supposed that the excessive drainage may be due to pia mater rupture during the operation, resulted in cerebrospinal fluid (CSF) accumulation in the hematoma cavity, and impelled CSDH recurrence if the CSF is not absorbed in time. To the best of our knowledge, this was the first time demonstrated that excessive drainage increased the risk of CSDH recurrence.

The recurrence rate of this study was 15.1%, different definition of CSDH recurrence may result in bias in recurrence rate. Some authors defined CSDH recurrence as a subsequent increase in hematoma volume in the surgical side and need another operation [6,8,15]. We and others defined it as an increase in the volume and a change in the density of the hematoma on the surgical side, new-onset headache, reappearance of symptoms such as the focal neurological deficit, or deterioration of consciousness [16,17,20]. To our best knowledge, some patients refuse reoperation based on economic or physical health conditions, and some recurrent hematomas may be absorbed by themselves during the follow-up. Therefore, it is not accurate to define the CSDH recurrence as reoperation or not. Additionally, different definitions of clinical and radiological parameters may result in statistical bias. As a comparison, we have reviewed the independent risk factors of the CSDH recurrence in previous studies, and listed combined with the present results in the Table 6.

In the present study, univariable analyses revealed that sex, history of head trauma, hypertension, diabetes mellitus, stroke history, presenting GCS, ways of anesthesia, unilateral or bilateral hematomas, hematoma side, hematoma density, maximum width of the hematoma, and maximum hematoma/fluid thickness after surgery were all not related to CSDH recurrence. Age over 80 years, antiplatelet and/or anticoagulant use, GOS scored 3, the volume of drainage ≥ 100 ml, midline shift ≥ 10 mm, severe brain atrophy, and severe postoperative pneumocephalus were significant related to the CSDH recurrence. However, in the case of univariable analysis, false positive results were inevitable. The following multivariable logistic regression analysis demonstrated that only midline shift ≥ 10 mm, severe brain atrophy, severe postoperative pneumocephalus, and volume of drainage ≥ 100 ml were independent risk factors of the CSDH recurrence.

Previous studies have described that the laminar, separated, homogenous hyper-dense and isodense of lesions were risk factors for CSDH recurrence [11–15]. However, we did not find the relationship between the hematoma density and the recurrence of CSDH. Additionally, the previous classification of hematoma based on CT density cannot include all patients [11], we found two or more types of density described above may appear in one CT image, which we defined as the mixed type (As shown in Fig. 1H and I). Antiplatelet and/or anticoagulant use [3–8], bilateral hematomas [6–9] and age [2,4] were thought to be risk factors of CSDH recurrence in many studies but not in our cohort. Although age was significantly older in the Recurrence Group than that of the Non-recurrence Group ($P = 0.002$), and the recurrence rate was significantly higher in the patients who older than 80 years ($P = 0.022$), it was not an independent risk factor of CSDH recurrence in multivariable logistic regression analysis.

Our study confirmed that the midline shift ≥ 10 mm, severe brain atrophy, and severe postoperative pneumocephalus were independent risk factors for CSDH recurrence, these results were similar to the other researches [9,14,15,19]. The gap between the dura and pia mater increase in both severe brain atrophy and severe postoperative pneumocephalus of CSDH, where CSF can accumulate and difficult to be absorbed for a long time, which may increase the risk of CSDH recurrence. We speculate that there may be a correlation between brain atrophy and postoperative pneumocephalus, a Kendall's tau-b test was therefore performed, but the result denied our speculation.

Table 3
The radiological characteristics of recurrence and no recurrence groups.

Factors	N. of patients (%)		P
	Recurrence	No recurrence	
Unilateral or bilateral			0.879
Unilateral	48 (15)	263 (85)	
Bilateral	21 (14)	125 (86)	
Hematoma side			0.181
Left	46 (15)	264 (85)	
Right	27 (11)	226 (89)	
Midline shift			0.008
≥10 mm	36 (21)	140 (79)	
<10 mm	12 (9)	123 (91)	
Brain atrophy			<0.001
Severe	56 (31)	127 (69)	
Moderate	13 (6)	216 (94)	
No or mild	4 (3)	147 (97)	
Hematoma density			0.419
Homogeneous			
Homogeneous hyper-dense	11 (15)	62 (85)	
Homogeneous iso-dense	16 (11)	130 (89)	
Homogeneous hypo-dense	11 (13)	71 (87)	
Separated	5 (24)	16 (76)	
Gradation	9 (15)	53 (85)	
Laminar	3 (8)	36 (92)	
Trabecular	14 (17)	69 (83)	
Mixed	4 (7)	53 (93)	
Maximum width of the hematoma			0.521
≥20 mm	49 (14)	306 (86)	
<20 mm	24 (12)	184 (88)	
Maximum hematoma/fluid thickness after surgery			0.758
≥20 mm	7 (16)	38 (84)	
<20 mm	66 (13)	452 (87)	
Postoperative pneumocephalus			<0.001
Severe	29 (24)	91 (76)	
Moderate	8 (11)	68 (89)	
No or mild	36 (10)	331 (90)	

CI = Confidence Interval; N = Number; OR = Odds Ratio.
Significant P values are in bold type.

Table 4
Multivariate logistic regression analysis of factors related to the recurrence of CSDH.

Factors	Adjusted OR	95% CI	P value
Age ≥80 years	0.68	0.33–1.40	0.29
Midline shift > 10 mm	3.01	1.35–6.74	0.007
Severe brain atrophy	13.12	4.78–36.04	<0.001
Severe postoperative pneumocephalus	2.09	1.08–4.01	0.028
Antiplatelet and/or anticoagulant use	2.62	0.98–7.01	0.055
GOS = 3	1.35	0.47–3.87	0.582
Volume of drainage ≥ 100 ml	2.31	1.29–4.14	0.005

CI = Confidence Interval; OR = Odds Ratio.
Significant P values are in bold type.

Table 5
Re-analysis of independent risk factors related to the recurrence of CSDH in multivariate logistic regression model.

Factors	Adjusted OR	95% CI	P value
Midline shift > 10 mm	2.96	1.34–6.55	0.007
Severe brain atrophy	12.93	4.86–34.37	<0.001
Severe postoperative pneumocephalus	2.32	1.23–4.38	0.009
Volume of drainage ≥100 ml	2.19	1.24–3.88	0.007

CI = Confidence Interval; OR = Odds Ratio.
Significant P values are in bold type.

Although we included as many parameters as possible in this large cohort patients to predict the recurrence of CSDH, there were lack of uniform parameters in the previous studies, such as definition of CSDH recurrence, grouping of ages, volume of drainage, qualitative or quantitative analysis of postoperative pneumocephalus, and degree of midline shift, these may lead to statistical errors. Uniform clinical and radiological parameters of CSDH should be proposed to predict the recurrence.

Dexamethasone, Atorvastatin, and Goreisan have the potential to reduce the volume of hematoma and avoid surgery [21–24]. A recent randomized double-blind controlled study demonstrated that administering of Atorvastatin reduced chronic subdural hematomas by 29 ml in 8 weeks and suggested that Atorvastatin is an effective drug for CSDH patients [23]. Berghauer Pont LM, et al. demonstrated that patients who longer use of Dexamethasone prior to surgery is associated with a lower recurrence rate

Table 6
Independent risk factors for the recurrence of CSDH in previous studies and present study.

Factors	OR	P Value	References
Age	1.04	0.0018	Motoie R, et al. [2]
Male sex	2.00	0.012	Motoie R, et al. [2]
Antiplatelet and/or anticoagulant use			
Clopidogrel	9.9	0.04	Motiei-Langroudi R, et al. [3]
Warfarin	7.9	0.03	Motiei-Langroudi R, et al. [3]
uncategorized	3.68	0.03	Leroy HA, et al. [4]
uncategorized	3.148	0.005	Chon KH, et al. [5]
	2.05	<0.01	Bartek J Jr, et al. [6]
Bilateral hematomas	1.953	0.044	Torihashi K, et al. [8]
	4.22	0.023	Schwarz F, et al. [9]
Midline shift			
Postoperative midline shift ≥5 mm	3.572	0.001	Chon KH, et al. [5]
Preoperative midline shift >10 mm	1.16	0.006	Schwarz F, et al. [9]
Postoperative midline shift >5 mm	NM	0.017	Escosa Baé M, et al. [10]
Midline shift >10 mm	3.01	0.007	Present study
Computed tomography density			
Hematoma loculation	12.3	0.003	Motiei-Langroudi R, et al. [3]
Isodense, hyperdense, laminar and separated	7.9	0.006	Stanišić M, et al (2017). [11]
	5.106	0.012	Stanišić M, et al (2013). [12]
Separated	7.585	0.026	Ohba S, et al. [13]
Multiplicity of hematoma cavities	0.03	0.0096	Yamamoto H, et al. [14]
Homogeneous hyper-dense	4.939	0.012	You W, et al. [15]
Preoperative haematoma volume			
Layering of haematoma	5.93	0.009	Huang YH, et al. [16]
Width of hematoma ≥20 mm	2.134	0.003	Chon KH, et al. [5]
Width of hematoma	1.22	0.029	Yamamoto H, et al. [14]
Postoperative haematoma residual			
Residual hematoma thickness >14 mm	3.88	0.005	Leroy HA, et al. [4]
Postoperative residual haematoma	1.009	0.022	Stanišić M, et al. [12]
Severe postoperative pneumocephalus	13.7	<0.001	Kawabata S, et al. [19]
	2.09	0.028	Present study
History of seizure	2.564	0.014	Chon KH, et al. [5]
	23.4	0.0146	Yamamoto H, et al. [14]
Diabetes mellitus	2.148	0.01	Chon KH, et al. [5]
	0.06	0.049	Yamamoto H, et al. [14]
Severe brain atrophy	13.12	<0.001	Present study
Volume of drainage ≥100 ml	2.31	0.005	Present study

CI = Confidence Interval; NM, Not mentioned; OR = Odds Ratio.

[21]. Zhang Y, et al. revealed that recurrent CSDH can be treated successfully with Dexamethasone without reoperation [22]. Goto S, et al. confirmed that Goreisan is effective in preventing recurrence of CSDH after surgery [24]. Based on these studies, identifying risk factors for CSDH recurrence contributes to postoperative management such as shorten the follow-up period and drug therapeutic trials.

There were some limitations to this study. First, this was a single-center retrospective and non-randomized study, therefore, potentially subject to sources of bias and variation was inevitable. Second, different surgeons have their own surgical procedure and irrigation ways of the hematoma cavity, which cannot be captured in the present study. Third, although a radiologist and a clinician worked together to measure the radiological parameters, the bias is still exist. At last, there is lack of long-term follow-up data.

Conclusions

The results of the present study indicated that midline shift ≥10mm, severe brain atrophy, severe postoperative pneumocephalus, and volume of drainage ≥100 ml were independent risk factors for the CSDH recurrence. CSDH patients with the characteristics above should be taken precautions of the recurrence, a closely follow-up should be carried out. There was no correlation between brain atrophy and postoperative pneumocephalus in CSDH patients. We added a new type of CT density of CSDH.

Ethics statement

The ethics committee of the Yijisha Hospital of Wannan Medical College approved this retrospective study.

Declaration of Competing Interest

The authors declare no conflict of interest.

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