

Predictors of acute intracranial hemorrhage and recurrence of chronic subdural hematoma following burr hole drainage

CURRENT STATUS: ACCEPTED

BMC Neurology  BMC Series

FuMei Chen

Zhejiang University School of Medicine First Affiliated Hospital

Ke Wang

Shanghai Tenth People's Hospital

KangLi Xu

Zhejiang University School of Medicine First Affiliated Hospital

Li Wang

Zhejiang University School of Medicine Sir Run Run Shaw Hospital

TianXiang Zhan

Zhejiang University School of Medicine First Affiliated Hospital

Fei Cheng

Zhejiang University School of Medicine First Affiliated Hospital

Hao Wang

Zhejiang University School of Medicine First Affiliated Hospital

Zuo-Bing Chen

Zhejiang University School of Medicine First Affiliated Hospital

Liang Gao

Shanghai Tenth People's Hospital

Xiaofeng Yang

Zhejiang University School of Medicine First Affiliated Hospital

 zjcswk@zju.edu.cn *Corresponding Author*

ORCID: <https://orcid.org/0000-0003-0994-5118>

DOI:

10.21203/rs.2.19037/v1

SUBJECT AREAS

Neurosurgery *Neurology*

KEYWORDS

chronic subdural hematoma, acute intracranial hemorrhage, recurrence, burr hole drainage, intraoperative irrigation

Abstract

Objective

To investigate predictors of postoperative acute intracranial hemorrhage (AIH) and recurrence of chronic subdural hematoma (CSDH) after burr hole drainage.

Methods

A multicenter retrospective study of patients who underwent burr hole drainage for CSDH between January 2013 and March 2019. Univariate and multiple logistic regression analyses were performed to determine the relationship between CSDH recurrence and postoperative AIH and clinical, radiological, and surgical variables.

Results

A total of 456 CSDH patients (361 males, 95 females) were enrolled in the study. The median (IQR) age was 68 (61-77) years (range: 8-98 years). CSDH recurrence occurred in 63 patients (56 males, seven females), with a recurrence rate of 13.8%. The median time interval between initial burr hole drainage and recurrence was 37 (27-46) days (range: 12-180 days). Postoperative AIH developed in 23 patients (15 males, eight females), with an incidence of 5.0%. The median time interval between initial burr hole drainage and postoperative AIH was 4 (2-6) days (range: 1-10 days). Bilateral hematoma, hyperdense hematoma and anticoagulant drug use were independent predictors of recurrence in the multiple logistic regression analyses. Preoperative headache was an independent risk factor of postoperative AIH in the multiple logistic regression analyses, however, intraoperative irrigation reduced the incidence of postoperative AIH.

Conclusions

This study found that bilateral hematoma, hyperdense hematoma and anticoagulant drug use were independently associated with CSDH recurrence. Clinical presentation of headache was the strongest predictor of postoperative AIH, and intraoperative irrigation decreased the incidence of postoperative AIH.

Introduction

Chronic subdural hematoma (CSDH) is one of the most common types of intracranial hemorrhage;

however, its pathogenic mechanism remains unclear. The incidence of CSDH is ~ 3.4-5/100 000 per year in the general population and 60-80/100 000 per year in those aged ≥ 65 .¹⁻⁵ The treatment is often surgical evacuation, using techniques such as twist-drill craniotomy and burr hole drainage (BHD) or craniotomy. BHD is the most widely used technique, and has a satisfactory outcome, but has a CSDH recurrence rate of 4-38%.⁶⁻¹² Several studies have revealed that predictors of CSDH recurrence following surgical evacuation include age, sex, antiplatelet or anticoagulation therapy, Glasgow Coma Scale (GCS), diabetes mellitus, hypertension, bilateral hematoma, preoperative hematoma size, midline shift, hematoma density, intraoperative irrigation, type of surgery and postoperative air collection, however, these results are inconsistent.^{7,13-19} The more controversial risk factors include surgery type and intraoperative irrigation.^{9,10,20-22} Previous reports have shown a CSDH mortality rate of 1.8-32%.^{6,23}

Surgical complications, such as irritability, wound infection and acute intracranial hemorrhage (AIH), occur at a rate of 0-38%.²⁴⁻²⁶ AIH, in particular, can cause severe neurological dysfunction, leading to a poor prognosis. However, the mechanism is still unclear and there is limited information on risk factors associated with AIH following surgery for CSDH. Some previous studies have evaluated recurrence risk following CSDH surgery using only a single or few predictors, however, the majority of these were single-center retrospective studies and lacked interaction between other variables and confounding factors. It is, therefore, important to identify the clinical and perioperative risk factors associated with AIH and CSDH recurrence following BHD surgery. In this multi-center retrospective study we evaluated the clinical factors associated with postoperative AIH and CSDH recurrence, to determine an optimal perioperative management strategy for BHD with or without irrigation in CSDH patients.

Methods

We retrospectively analyzed the medical records of all patients diagnosed with CSDH at the Department of Neurosurgery, the First Affiliated Hospital, College of Medicine, Zhejiang University, Hangzhou, China between September 2015 and March 2019 (n = 321), and the Department of

Neurosurgery of Shanghai Tenth People's Hospital, Shanghai, China between January 2013 and May 2016 (n = 135). The patients were diagnosed by computed tomography (CT) or magnetic resonance imaging (MRI).

Inclusion and exclusion criteria

The inclusion criteria were as follows: all patients were diagnosed with CSDH by CT or MRI; and initially underwent BHD with or without irrigation at one of the two institutions. Exclusion criteria included: CSDH that was treated conservatively or by surgical methods other than BHD (such twist-drill craniotomy and formal craniotomy with excision of subdural membrane); any other intracranial pathologies or intracranial surgery, such as ventriculoperitoneal shunt, epidural hematoma, parenchymal hemorrhage, intraventricular hemorrhage or ischemic insult within the last 12 months; and recurrent CSDH.

Definitions

We defined postoperative recurrence of CSDH as a subsequent radiographic discharge following the primary treatment, with re-bleeding and/or increased size of the subdural hematomas on the operated side, with or without any clinical presentation. AIH was identified as a hyperdense lesion in the ventricle, brain parenchyma, subarachnoid, subdural space or epidural space, visible on CT scan during hospitalization, and accompanied by neurological deterioration. Chronic intracranial hemorrhage (CIH) in this study refers to cerebral hemorrhage other than recurrent CSDH or AIH. The hematoma was classified as hypodense [< 30 Hounsfield units (HU)], isodense (30–60 HU), hyperdense (> 60 HU), or mixed density based on the density difference of the hematoma and the brain parenchyma. Patients with bilateral CSDH of different types were attributed according to which reflected the greater bleeding tendency.

Surgical evacuation of CSDH was carried out when the following indications were observed:

1. Unilateral or bilateral CSDH with maximum thickness >10 mm and/or midline shift >7 mm;
2. CSDH of any thickness causing mass effect, midline shift, or neurological signs and symptoms, such as focal deficit, and mental status changes;

3. Progressive increase in size of CSDH as observed through a series of CT or MRI scans. In bilateral CSDH, the decision to evacuate one or both sides was generally made based on hematoma size and neurological symptoms. (i) Unilateral evacuation of bilateral CSDH: when the maximum diameter of the CSDH on the operation side was > 10 mm, when the contralateral hematoma was < 10 mm thick, and when the laterality of neurological symptoms could only be attributed to the thicker hematoma. (ii) Bilateral evacuation of bilateral CSDH: both sides received the same treatment in a single operation.

Surgical procedures and general management

In all cases, a single burr hole was made under anesthesia. Local or general anesthetic was selected depending on the patient's general status and ability to co-operate. A 4–5 cm vertical skin incision was made at the superior temporal line near the coronal suture or at the point of maximum thickness of the CSDH. A 1.5–2 cm craniotomy was performed. After opening the dura and outer membrane of the hematoma, a soft silicon tube was inserted into the subdural space through the burr hole overlying the large part of the subdural cavity, and tunneled for a minimum of 5 cm away from the scalp incision. Irrigation was not carried out in all surgeries. If carried out, irrigation was with 0.9% normal saline via the tube, until the output was clear. The drain was connected to a soft collection bag and the drainage tube was removed when there was no more drainage fluid. The patient stayed in bed until the drain was removed. If CT scan showed that subdural collections remained in the hematoma cavity after the operation, the patient was treated with urokinase, according to the surgeon's preference. CT scanning indicated if the affected brain region showed sufficient re-expansion or when the amount decreased to < 50 ml per day.

All patients had their anticoagulant or antiplatelet status optimized prior to surgery, ensuring a preoperative international normalized ratio (INR) between 0.8 and 1.2. It was managed in various ways depending on the type of anticoagulant treatment. Agents used to reverse anticoagulant or antiplatelet medications were vitamin K1, thrombocytes, blood plasma, tranexamic acid, prothrombin complex concentrate, and desmopressin analogs. Antiplatelet or anticoagulant agents were usually re-started 1 month from the day of surgery.

Following CSDH diagnosis, some patients were given atorvastatin (20 mg per night) prior to the operation. The decision to give the patient preoperative atorvastatin was made by the neurosurgeon. In general, atorvastatin was discontinued for at least 1 month after surgery or based on follow-up imaging. All patients were followed-up for at least 12 months.

Data collection

Demographic, clinical and radiographic data were collected using a standardized case report form and the information was added to a database. The following data were included: gender, age, history of anticoagulant or antiplatelet, head trauma event, GCS score on admission, medical history (e.g., hypertension, diabetes), preoperative main clinical symptoms (e.g., headache, dizziness), operation side (unilateral, unilateral evacuation of bilateral CSDH, bilateral evacuation of bilateral CSDH), hematoma density characteristics on CT (hyperdense, hypodense, mixed density, isodense), hematoma maximal thickness (preoperative hematoma thickness on the axial cut that showed the maximal diameter), midline shift, anesthesia method, intraoperative irrigation (non-irrigation versus irrigation), duration of drainage (days), urokinase injection after operation, complications (including acute intracranial bleeding, fever > 38 °C, seizure, irritability, poor wound healing and intracranial infection), time interval between initial operation and recurrence (days), time interval between initial operation and bleeding (days), and hospitalization time (days). All CT interpretations and measurements were made by a neurosurgeon and recorded after corroborating with the neuroradiologist's report.

Statistical analyses

SPSS software (version 16.0) was used for the statistical analysis.

Continuous data are expressed as the mean \pm standard deviation and categorical data are expressed as the median value (IQR). Univariable (Student t-test and the Mann-Whitney U-test), bivariable (Chi-square) and multivariable (multiple logistic regression) analyses were performed to determine which, if any, of the studied variables were associated risk factors of CSDH recurrence and AIH. The variables with $P < 0.1$ in the univariate analysis were included in the multivariate model. Statistical significance was defined as $P\text{-value} < 0.05$.

Results

Baseline clinical characteristics of patients

A total of 456 patients (361 males, 95 females) were included in the analysis. The median (IQR) age was 68 (61–77) years (range: 8–98 years). CSDH recurrence occurred in 63 (13.8%) patients, including 27 with unilateral BDH evacuation, 13 with unilateral evacuation of bilateral CSDH, and 23 with bilateral evacuation of bilateral CSDH. Complications occurred in 126 patients (27.6%), including 23 (5%) with AIH (16 patients with unilateral evacuation, five with unilateral evacuation of bilateral CSDH, and two with bilateral evacuation of bilateral CSDH). One patient died (mortality rate = 0.2%). The median (IQR) duration of hospitalization time was 13 (10–16) days (range: 3–42 days). Patient information is provided in Table 1.

Analysis of patients with recurrence

Sixty-three patients (56 males, seven females) experienced CSDH recurrence following the initial BHD. The median (IQR) age was 69 (62–78) years (range: 8–88 years). The median time interval between initial BHD and recurrence was 37 (27–46) days (range: 12–180 days).

Univariate analysis (Table 2) showed that risk factors including gender ($P = 0.041$), anticoagulant drugs ($P = 0.043$), density of hematoma ($P = 0.008$), operation side ($P < 0.001$), and atorvastatin administration ($P = 0.024$) were significantly related to CSDH recurrence. Unilateral or bilateral evacuation of bilateral CSDH were not significantly correlated with CSDH recurrence following BHD (2.9% versus 5.0%, $P = 0.928$). Although there was no significant correlation between preoperative history of intracranial surgery and recurrence ($P < 0.1$), it was included in the multivariate analysis according to our multivariate inclusion analysis criteria. Other variables that were not significantly correlated with CSDH recurrence are shown in Table 2.

In the multivariate logistic regression model, bilateral hematoma [Odds ratio (OR), 2.635; 95% confidence interval (CI), 1.493–4.651; $P = 0.001$], mixed density (OR, 0.415; 95%CI, 0.220–0.784; $P = 0.007$, hyperdense as reference) and anticoagulant drugs (OR, 4.394; 95%CI, 1.272–15.181; $P = 0.019$) were significantly associated with CSDH recurrence. Other variables not significantly associated with CSDH recurrence are detailed in Table 3.

Analysis of patients with acute intracranial hemorrhage

Twenty-three patients (15 males, eight females) experienced postoperative AIH. The mean age was

68.5 ± 11.5 years (range: 42–87 years). The median time interval between initial BHD and postoperative AIH was 4 (2–6) days (range: 1–10 days).

Univariate analysis indicated that preoperative headache (P = 0.045), preoperative hematoma thickness (P = 0.041) and intraoperative irrigation (P = 0.018) were significantly related to postoperative AIH (Table 4). Operation side (P = 0.712) was not significantly related to postoperative AIH, and there was no significant difference in the incidence of postoperative AIH between unilateral or bilateral evacuation of bilateral CSDH (1.1% versus 0.4%, P = 0.098). Other variables with P > 0.1 in the univariate analysis are shown in Table 4.

Multivariate analysis showed that preoperative headache (OR, 3.067; 95%CI, 1.188–7.915; P = 0.021) and intraoperative irrigation (OR, 0.284; 95%CI, 0.112–0.722; P = 0.008) were significantly associated with postoperative AIH. Other variables not significantly associated with postoperative AIH or CSDH recurrence are shown in Table 5.

Discussion

CSDH is one of the most commonly treated neurosurgical disorders and BHD is a universal surgical treatment.^{11,18,27} The rate of CSDH recurrence following BHD is 4–38% and the complications rate is 0–38%.^{6–12,24,26} In this study, we found the CSDH recurrence rate after BDH was 13.8% and the complication rate was 27.6%. Of the 126 patients with complications, 23 had postoperative AIH (5% incidence). Pang et al. similarly reported an incidence of postoperative AIH of 4.57%.²⁵ According to the literature, the mortality rate due to CSDH is 1.8–32%, however, in this study, only one patient died of respiratory failure, giving a lower mortality rate of 0.2%.^{6,23} Comparing our results with previous studies, our definition of postoperative recurrence of CSDH and postoperative AIH are in accordance with medical norms and logic.

CSDHs are usually unilateral, but do present as bilateral in ~ 9.2–34.9% of cases.^{5,28–30} However, not all patients with bilateral CSDH warrant evacuation of both sides at initial presentation. The major determinants of unilateral or bilateral evacuation are preoperative maximal thickness, the degree of midline shift, and lateralized clinical symptoms, followed by surgical treatment of only the largest or

the symptomatic hematoma, leaving the other hematoma non-operated.³¹ In our study, 155 patients (34%) had bilateral CSDH. Fifty-five (12.1%) had unilateral evacuation and 100 (21.9%) were evacuated bilaterally. Previous studies have shown that simultaneous bilateral decompression in bilateral CSDH reduces complications and the rate of CSDH recurrence, however, others have not corroborated this result.^{31–33} In our study, there was no significant difference between the rate of CSDH recurrence and incidence of AIH following unilateral or bilateral evacuation in bilateral CSDH. The recurrence rate in unilateral CSDH is lower than that of bilateral CSDH, making bilateral hematoma a risk factor for CSDH recurrence.^{16,19} This could be due to poor brain re-expansion in bilateral CSDH compared to unilateral CSDH, which may result in a brain parenchymal shift, tearing of the blood vessels, postoperative pneumocephalus and cerebrospinal fluid accumulation in the hematoma cavity, leading to a higher recurrence rate.^{19,34,35} Another theory is that patients with bilateral CSDH tend to have a history of brain atrophy, which leads to poor re-expansion, resulting in a higher recurrence rate.^{19,35} In our study, bilateral hematoma was found to be a risk factor for postoperative recurrence of CSDH, but was not a risk factor for postoperative AIH. Whether the brain re-expansion theory or the brain atrophy theory were correct will require time to accumulate results. In our study, the median time interval (4 days) between initial surgery and postoperative AIH was significantly lower than the median time interval (37 days) between initial surgery and postoperative recurrence.

Some studies have reported that male sex is an independent risk factor of CSDH recurrence, and that males likely have more trauma and more frequent complications than females. However, other studies have suggested that gender is not associated with CSDH recurrence.^{13,36} In our study, 298 patients had a history of trauma, including 236 males and 62 females. According to multivariate logistic regression analysis, there was no significant correlation between gender and CSDH recurrence. To date, no literature has reported the relationship between gender and postoperative AIH. We found that gender was not significantly associated with postoperative AIH.

In our study, history of intracranial surgery was not significantly associated with CSDH recurrence or

postoperative AIH. Some studies have suggested that ventriculoperitoneal shunt leads to excessive drainage, which may lead to CSDH;³⁷ however, the results are controversial. According to our results, only two patients underwent ventriculoperitoneal shunt, however, neither experienced recurrent CSDH or postoperative AIH.

The clinical presentation of CSDH varies from asymptomatic to headache, limb weakness, incontinence, etc. According to our study, preoperative headache is an independent risk factor for postoperative AIH. When CSDH presents as a clinical manifestation of headache, it indicates a higher intracranial pressure and a secondary cerebral blood flow reduction in the deep cerebral regions, causing blood vessels to spasm and increasing the risk of vascular accidents.³⁸ Thus, when blood flow in the brain changes or intracranial pressure changes significantly in a short period of time, blood vessels rupture, resulting in bleeding.

Many studies suggest that preoperative hematoma density is associated with CSDH recurrence, and hyperdense hematoma is an independent risk factor for CSDH recurrence.^{13,39} In our study, hyperdense hematoma were more prone to CSDH recurrence than mixed density (OR, 0.415; 95%CI, 0.220-0.784; P = 0.007, hyperdense as reference). The relationship between hematoma density and postoperative AIH has not been reported in the literature. In our study, hematoma density was not significantly associated with postoperative AIH. We suspect that when hyperdense hematoma are compared with the other three types of hematoma density, repeated microhemorrhages from the immature capillary network in the outer membrane take place and accumulate over time, causing CSDH recurrence.³⁹

Preoperative hematoma thickness has been reported as an independent risk factor for CSDH recurrence.⁷ It is thought that hematoma thickness has an increased tendency to recur because the subdural space is larger than a small lesion postoperatively.^{7,36} As hematoma thickness is related to many factors, such as age, midline shift and brain atrophy, it may not be a useful predictor of CSDH recurrence and postoperative AIH. However, other studies have shown no significant relationship between hematoma thickness and CSDH recurrence,^{13,40} and the relationship between hematoma

thickness and postoperative AIH has not been reported. In our study, there was no significant relationship between hematoma thickness and CSDH recurrence or postoperative AIH. Our results showed that anticoagulant drug use is an independent risk factor for CSDH recurrence. Antiplatelet drugs did not increase the CSDH recurrence rate following BHD. Similarly, a recent systematic study showed that anticoagulant drugs increased re-bleeding on the operation side of CSDH, but antiplatelet therapy did not.⁴¹ However, this result is controversial as in other studies, antiplatelets or anticoagulants were not associated with CSDH recurrence.^{16,36,42} The authors speculated that the reason for this finding may be that the patients were not adequately anticoagulated, especially in the non-recurrence group. At present, only one study has reported that anticoagulants or antiplatelet drugs do not increase the incidence of postoperative AIH.²⁵ Similar to our results, we suspect that it may be the result offset caused by insufficient sample size. Therefore, a large sample clinical trial is necessary to verify this result.

Atorvastatin is another management option, which may be used alone or in conjunction with surgery. Several studies have shown that CSDH is caused by impaired angiogenesis in the neomembrane and localized inflammation, and that atorvastatin improves angiogenesis and reduces the inflammatory response.^{43,44} A randomized control study showed that the oral administration of atorvastatin is safe and effective in treating CSDH, and promotes the resolution of hematoma.⁴⁵ A prospective study showed that atorvastatin administration may decrease the risks of CSDH recurrence.⁴⁶ However, in our study, atorvastatin did not reduce the rate of CSDH recurrence, nor did it reduce the incidence of postoperative AIH. We suspect that different research methods may lead to varying results.

In our study, intraoperative saline irrigation was based on the surgeon's preference. Some studies have shown that intraoperative saline irrigation of the hematoma cavity does not improve the incidence of postoperative AIH and CSDH recurrence.^{25,47} According to our results, intraoperative irrigation does not reduce the risk of CSDH recurrence, however, it does reduce the incidence of postoperative AIH. We speculate that BHD for CSDH without irrigation significantly reduces intracranial pressure for a short period of time. The abrupt decrease in intracranial pressure may

cause further damage to the intracranial blood vessels and lead to acute intracranial bleeding.

Conclusions

In this study, we evaluated predictors of CSDH recurrence and postoperative AIH following BHD in a multi-center retrospective study of patients with CSDH. We identified bilateral hematoma, hyperdense hematoma and anticoagulant drugs as independent risk factors for recurrence of CSDH. Preoperative headache is an independent risk factor for postoperative AIH, and intraoperative irrigation reduces the incidence of postoperative AIH. Further prospective multi-center studies will be required to evaluate these findings.

Abbreviations

CSDH: chronic subdural hematoma; AIH: acute intracranial hemorrhage; CIH: Chronic intracranial hemorrhage; BHD: burr hole drainage; CT: computed tomography; MRI: magnetic resonance imaging; GCS: Glasgow Coma Scale.

Declarations

Acknowledgment

Not applicable.

Authors' contributions

XFY, LG, ZBC, HW designed research, performed research, analyzed data. FMC, KW, KLX collected data, analyzed the data and drafted the manuscript. LW, TXZ, FC collected and analyzed the data. All authors checked and agreed on the final manuscript.

Funding

This study was supported the National Natural Science Foundation of China (No.81470052).

Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study was approved by the ethics committees of the two medical centers. The requirement for obtaining informed consent from patients was waived because the data sets were anonymous.

Consent for publication

Informed consent was waived because of the anonymous nature of the data.

Competing interests

The authors declare that they have no competing interests.

References

1. Santarius T, Hutchinson PJ. Chronic subdural haematoma: time to rationalize treatment? *Br J Neurosurg* 2004; **18**(4): 328-32.
2. Asghar M, Adhiyaman V, Greenway MW, Bhowmick BK, Bates A. Chronic subdural haematoma in the elderly--a North Wales experience. *J R Soc Med* 2002; **95**(6): 290-2.
3. Chronic subdural hematoma in elderly people: present status on Awaji Island and epidemiological prospect. 1992.
4. Karibe H, Kameyama M, Kawase M, Hirano T, Kawaguchi T, Tominaga T. [Epidemiology of chronic subdural hematomas]. *No Shinkei Geka* 2011; **39**(12): 1149-53.
5. Hsieh CT, Su IC, Hsu SK, Huang CT, Lian FJ, Chang CJ. Chronic subdural hematoma: Differences between unilateral and bilateral occurrence. *J Clin Neurosci* 2016; **34**: 252-8.
6. Koliass AG, Chari A, Santarius T, Hutchinson PJ. Chronic subdural haematoma: modern management and emerging therapies. *Nat Rev Neurol* 2014; **10**(10): 570-8.
7. Chon KH, Lee JM, Koh EJ, Choi HY. Independent predictors for recurrence of chronic subdural hematoma. *Acta Neurochir (Wien)* 2012; **154**(9): 1541-8.
8. Berghauer Pont LM, Dammers R, Schouten JW, Lingsma HF, Dirven CM. Clinical factors associated with outcome in chronic subdural hematoma: a retrospective cohort study of patients on preoperative corticosteroid therapy. *Neurosurgery* 2012; **70**(4): 873-80; discussion 80.

9. Ducruet AF, Grobelny BT, Zacharia BE, et al. The surgical management of chronic subdural hematoma. *Neurosurg Rev* 2012; **35**(2): 155-69; discussion 69.
10. Lega BC, Danish SF, Malhotra NR, Sonnad SS, Stein SC. Choosing the best operation for chronic subdural hematoma: a decision analysis. *J Neurosurg* 2010; **113**(3): 615-21.
11. Lind CR, Lind CJ, Mee EW. Reduction in the number of repeated operations for the treatment of subacute and chronic subdural hematomas by placement of subdural drains. *J Neurosurg* 2003; **99**(1): 44-6.
12. Miranda LB, Braxton E, Hobbs J, Quigley MR. Chronic subdural hematoma in the elderly: not a benign disease. *J Neurosurg* 2011; **114**(1): 72-6.
13. Fujitani S, Ishikawa O, Miura K, Takeda Y, Goto H, Maeda K. Factors predicting contralateral hematoma growth after unilateral drainage of bilateral chronic subdural hematoma. *J Neurosurg* 2017; **126**(3): 755-9.
14. Rust T, Kiemer N, Erasmus A. Chronic subdural haematomas and anticoagulation or anti-thrombotic therapy. *J Clin Neurosci* 2006; **13**(8): 823-7.
15. Tahsim-Oglou Y, Beseoglu K, Hänggi D, Stummer W, Steiger H-J. Factors predicting recurrence of chronic subdural haematoma: the influence of intraoperative irrigation and low-molecular-weight heparin thromboprophylaxis. *Acta Neurochirurgica* 2012; **154**(6): 1063-8.
16. Torihashi K, Sadamasa N, Yoshida K, Narumi O, Chin M, Yamagata S. Independent predictors for recurrence of chronic subdural hematoma: a review of 343 consecutive surgical cases. *Neurosurgery* 2008; **63**(6): 1125-9; discussion 9.
17. Song DH, Kim YS, Chun HJ, et al. The Predicting Factors for Recurrence of Chronic Subdural Hematoma Treated with Burr Hole and Drainage. *Korean Journal of Neurotrauma* 2014; **10**(2).

18. Motiei-Langroudi R, Stippler M, Shi S, et al. Factors predicting reoperation of chronic subdural hematoma following primary surgical evacuation. *J Neurosurg* 2018; **129**(5): 1143-50.
19. Han MH, Ryu JI, Kim CH, Kim JM, Cheong JH, Yi HJ. Predictive factors for recurrence and clinical outcomes in patients with chronic subdural hematoma. *J Neurosurg* 2017; **127**(5): 1117-25.
20. Mondorf Y, Abu-Owaimer M, Gaab MR, Oertel JM. Chronic subdural hematoma--craniotomy versus burr hole trepanation. *Br J Neurosurg* 2009; **23**(6): 612-6.
21. Wang W, Liu H, Yang J. Burr hole craniostomy irrigation with and without drainage during surgical treatment of chronic subdural hematoma: A retrospective study of 87 cases. *Turk Neurosurg* 2017.
22. Yuan Y, Wang QP, Cao YL, et al. Burr hole drainage and burr hole drainage with irrigation to treat chronic subdural hematoma: A systematic review and meta-analysis. *Medicine (Baltimore)* 2018; **97**(33): e11827.
23. Fetit AE, Doney AS, Hogg S, et al. A multimodal approach to cardiovascular risk stratification in patients with type 2 diabetes incorporating retinal, genomic and clinical features. *Sci Rep* 2019; **9**(1): 3591.
24. Rohde V, Graf G, Hassler W. Complications of burr-hole craniostomy and closed-system drainage for chronic subdural hematomas: a retrospective analysis of 376 patients. *Neurosurgical Review* 2002; **25**(1-2): 89-94.
25. Pang CH, Lee SE, Kim CH, et al. Acute intracranial bleeding and recurrence after burr hole craniostomy for chronic subdural hematoma. *Journal of Neurosurgery* 2015; **123**(1): 65-74.
26. Bucher B, Maldaner N, Regli L, Sarnthein J, Serra C. Standardized assessment of outcome and complications in chronic subdural hematoma: results from a large case

- series. *Acta Neurochirurgica* 2019; **161**(7): 1297-304.
27. Ramachandran R, Hegde T. Chronic subdural hematomas--causes of morbidity and mortality. *Surg Neurol* 2007; **67**(4): 367-72; discussion 72-3.
28. Park HS, Park ES, Park JB, et al. Chronic Subdural Hematomas: Comparison between Unilateral and Bilateral Involvement. *Korean J Neurotrauma* 2014; **10**(2): 55-9.
29. Huang YH, Yang KY, Lee TC, Liao CC. Bilateral chronic subdural hematoma: what is the clinical significance? *Int J Surg* 2013; **11**(7): 544-8.
30. Tsai TH, Lieu AS, Hwang SL, Huang TY, Hwang YF. A comparative study of the patients with bilateral or unilateral chronic subdural hematoma: precipitating factors and postoperative outcomes. *J Trauma* 2010; **68**(3): 571-5.
31. Motiei-Langroudi R, Thomas AJ, Ascanio L, et al. Factors Predicting the Need for Surgery of the Opposite Side After Unilateral Evacuation of Bilateral Chronic Subdural Hematomas. *Neurosurgery* 2018.
32. Andersen-Ranberg NC, Poulsen FR, Bergholt B, Hundsholt T, Fugleholm K. Bilateral chronic subdural hematoma: unilateral or bilateral drainage? *J Neurosurg* 2017; **126**(6): 1905-11.
33. Sadrolhefazi A, Bloomfield SM. Interhemispheric and bilateral chronic subdural hematoma. *Neurosurgery Clinics of North America* 2000; **11**(3): 455-63.
34. Kung WM, Hung KS, Chiu WT, et al. Quantitative assessment of impaired postevacuation brain re-expansion in bilateral chronic subdural haematoma: possible mechanism of the higher recurrence rate. *Injury* 2012; **43**(5): 598-602.
35. Shen J, Gao Y, Li Q, et al. Risk Factors Predicting Recurrence of Bilateral Chronic Subdural Hematomas after Initial Bilateral Evacuation. *World Neurosurg* 2019.
36. Bartek J, Sjøvik K, Kristiansson H, et al. Predictors of Recurrence and Complications After Chronic Subdural Hematoma Surgery: A Population-Based Study. *World*

- Neurosurgery* 2017; **106**: 609-14.
37. Ou Y, Dong J, Wu L, et al. The Clinical Characteristics, Treatment, and Outcomes of Chronic Subdural Hematoma in Young Patients. *World Neurosurg* 2019.
 38. Okuyama T, Saito K, Fukuyama K, Yamamoto K, Morimoto M, Aburano T. [Clinical study of cerebral blood flow in bilateral chronic subdural hematoma measured by 99mTc-HMPAO SPECT]. *No To Shinkei* 2000; **52**(8): 709-14.
 39. Lin CC, Lu YM, Chen TH, Wang SP, Hsiao SH, Lin MS. Quantitative assessment of post-operative recurrence of chronic subdural haematoma using mean haematoma density. *Brain Inj* 2014; **28**(8): 1082-6.
 40. Nakaguchi H, Tanishima T, Yoshimasu N. Factors in the natural history of chronic subdural hematomas that influence their postoperative recurrence. *J Neurosurg* 2001; **95**(2): 256-62.
 41. Nathan S, Goodarzi Z, Jette N, Gallagher C, Holroyd-Leduc J. Anticoagulant and antiplatelet use in seniors with chronic subdural hematoma Systematic review. *Neurology* 2017; **88**(20): 1889-93.
 42. Okano A, Oya S, Fujisawa N, et al. Analysis of risk factors for chronic subdural haematoma recurrence after burr hole surgery: optimal management of patients on antiplatelet therapy. *Br J Neurosurg* 2014; **28**(2): 204-8.
 43. Xu M, Chen P, Zhu X, Wang C, Shi X, Yu B. Effects of Atorvastatin on Conservative and Surgical Treatments of Chronic Subdural Hematoma in Patients. *World Neurosurgery* 2016; **91**: 23-8.
 44. Tang R, Shi J, Li X, et al. Effects of Atorvastatin on Surgical Treatments of Chronic Subdural Hematoma. *World Neurosurg* 2018; **117**: e425-e9.
 45. Jiang R, Zhao S, Wang R, et al. Safety and Efficacy of Atorvastatin for Chronic Subdural Hematoma in Chinese Patients. *JAMA Neurology* 2018; **75**(11).

46. Liu H, Luo Z, Liu Z, Yang J, Kan S. Atorvastatin May Attenuate Recurrence of Chronic Subdural Hematoma. *Front Neurosci* 2016; **10**: 303.
47. Almenawer SA, Farrokhyar F, Hong C, et al. Chronic subdural hematoma management: a systematic review and meta-analysis of 34,829 patients. *Ann Surg* 2014; **259**(3): 449-57.

Tables

Table 1. Clinical characteristics of patients	
Variables	No. (%)
Total patients	456
Gender	
Male	361(79.1)
Female	95(20.8)
Age, median (IQR), years	68.0(61.0-77.0)
Head trauma event	298(65.4)
Medical history	
Hypertension	175(38.4)
Diabetes	63(13.8)
Heart disease	48(10.5)
Cerebral infarction	28(6.1)
Renal failure dialysis	3(0.7)
Intracranial surgery	8(1.8)
Antiplatelet or anticoagulant use	
Antiplatelet use	32(7.0)
Anticoagulant use	15(3.3)
Preoperative clinical symptoms	
Headache	205(45.0)
Dizziness	140(30.7)
Motor weakness	257(56.4)
Nausea/vomiting	31(6.8)
Speech impairment	17(3.7)
Unsteady gait	8(1.8)
Incontinence	11(2.4)
Memory impairment	15(3.3)
GCS at admission	
15	391(85.7)
3-14	65(14.3)
Operation side	
Unilateral hematoma	301(66.0)
Bilateral hematoma	155(34.0)
Bilateral evacuated unilaterally	55(12.1)
Bilateral evacuated bilaterally	100(21.9)
Radiological characteristics	
Midline shift	
<10mm	297(65.1)
≥10mm	159(34.9)
Preoperative maximal thickness	
<20 mm	100(21.9)
≥20 mm	356(78.1)
Hematoma density	
Hyperdense	135(29.6)
Hypodense	73(16.0)
Mixed density	214(46.9)
Iso-dense	34(7.5)
Treatment	
Atorvastatin perioperatively	173(37.9)
Anesthesia	
Local	204(44.7)
General	252(55.3)
Intraoperative irrigation	
Irrigation	384(84.2)
Non-irrigation	72(15.8)
Injection urokinase after operation	12(2.6)
Duration of drainage, day	
1	63(13.8)
2	312(68.4)

≥3	81(17.8)
Outcomes and complications	
Clinical symptoms changes at discharge	
Improvement	389(85.3)
Unchanged	19(4.2)
Deterioration	48(10.5)
GCS at discharge	
Improvement	63(13.8)
Unchanged	380(83.3)
Deterioration	13(2.9)
Complications	
Fever	73(16.0)
Irritability	19(4.2)
Poor wound healing	1(0.2)
Seizure	2(0.4)
Deep vein thrombosis	1(0.2)
AIH	23(5.0)
CIH	7(1.5)
Recurrence	63(13.8)
Mortality	1(0.2)
Hospitalization time, Median (IQR), days	
	13.0(6)

GCS: Glasgow Coma Scale; AIH: acute intracranial hemorrhage;

IQR: interquartile range; CIH: chronic intracranial hemorrhage

Table 2. Univariate analysis of factors for recurrence of CSDH			
Variables	Recurrence	No recurrence	P Value
Patients	63(%)	393(%)	
Gender			0.041
Male	56(88.9)	305(77.6)	
Female	7(11.1)	88(22.4)	
Age (years)			0.642
<70	32(50.8)	212(53.9)	
≥70	31(49.2)	181(46.1)	
Head trauma event	38(60.3)	260(66.2)	0.366
Medical history			
Hypertension	27(42.9)	148(37.7)	0.431
Diabetes	11(17.5)	52(13.2)	0.367
Heart disease	10(15.9)	38(9.7)	0.136
Cerebral infarction	5(7.9)	23(5.9)	0.569
Renal failure dialysis	1(1.6)	2(0.5)	0.361
Intracranial surgery	3(4.8)	5(1.3)	0.084
Antiplatelet or anticoagulant drugs			
Antiplatelet drugs	6(9.5)	26(6.7)	0.423
Anticoagulant drugs	5(7.9)	10(2.5)	0.043
The main symptoms			
Headache	28(44.4)	177(45.0)	0.930
Dizziness	17(27.0)	123(31.3)	0.491
Motor weakness	33(52.4)	224(57.0)	0.493
Nausea/vomiting	2(3.2)	29(7.4)	0.288
Speech impairment	3(4.8)	14(3.6)	0.717
Unsteady gait	2(3.2)	6(1.5)	0.305
Incontinence	1(1.6)	10(2.5)	1
Memory decline	1(1.6)	14(3.6)	0.705
GCS at admission			0.442
15	56(88.9)	335(85.2)	
3-14	7(11.1)	58(14.8)	
Operation side			P<0.001
Unilateral hematoma	27(42.8)	274(69.7)	
Bilateral hematoma	36(57.2)	119(30.1)	
Radiological characteristics			
Midline shift			0.993
<10mm	41(65.1)	256(65.1)	
≥10mm	22(34.9)	137(34.9)	
Preoperative maximal thickness			0.211
<20 mm	10(15.9)	90(22.9)	
≥20 mm	53(84.1)	303(77.1)	
Hematoma density			0.008
Hyper-dense	30(47.6)	105(26.7)	
Hypo-dense	9(14.3)	64(16.3)	
Mixed density	21(33.3)	193(49.1)	
Iso-dense	3(4.8)	31(7.9)	
Treatment			
Atorvastatin perioperatively	32(50.8)	141(35.9)	0.024
Anesthesia			0.824
Local	29(46.0)	175(44.5)	
General	34(54.0)	218(55.5)	
Intraoperative irrigation	52(82.5)	332(84.5)	0.695
Injection urokinase after operation	3(4.8)	9(2.3)	0.222
Duration of drainage, day			0.739
1	9(14.3)	54(13.7)	
2	45(71.4)	267(68.0)	
≥3	9(14.3)	72(18.3)	
Complications			
Fever	7	66	0.253
Irritability	4	15	0.316
Poor wound healing	1	0	---
Seizure	1	1	0.257
Deep vein thrombosis	0	1	---
AIB	0	23	---
Hospitalization time, Median (IQR), days	12(5)	13(6)	0.224

GCS: Glasgow Coma Scale; AIH: acute intracranial hemorrhage; IQR: interquartile range.

Table 3. Multivariate logistic regression analysis of factors for recurrence of CSDH			
Risk factors	OR	95% CI	P value
Gender	2.205	0.927-5.245	0.074
Intracranial surgery	4.600	0.928-22.793	0.062
Operation side (Unilateral vs Bilateral)	2.635	1.493-4.651	0.001
Hematoma density			
Hyperdense	Reference	Reference	Reference
Hypodense	0.527	0.227-1.225	0.137
Mixed density	0.415	0.220-0.784	0.007
Iso-dense	0.368	0.901-2.814	0.126
Atorvastatin perioperatively	1.592	0.944-3.006	0.110
Anticoagulant drugs	4.394	1.272-15.181	0.019

OR: Odds ratio; CI: confidence interval.

Table 4. Univariate analysis of factors for postoperative AIH			
Variables	AIH	No AIH	P Value
Patients	23(%)	433(%)	
Gender			0.111
Male	15(65.2)	346(80.0)	
Female	8(34.8)	87(20.0)	
Age (years)			0.895
<70	12(52.2)	232(53.6)	
≥70	11(47.8)	201(46.4)	
Head trauma event	14(60.9)	284(65.6)	0.643
Medical history			
Hypertension	12(52.2)	163(37.6)	0.163
Diabetes	2(8.7)	61(14.1)	0.755
Heart disease	1(4.3)	47(10.9)	0.494
Cerebral infarction	1(4.3)	27(6.2)	1.00
Renal failure dialysis	0(0)	3(0.7)	—
Intracranial surgery	0(0)	8(1.8)	—
Antiplatelet or anticoagulant drugs			
Antiplatelet drugs	3(13.0)	29(6.7)	0.213
Anticoagulant drugs	1(4.3)	14(3.2)	0.546
Preoperative clinical symptoms			
Headache	15(65.2)	190(43.9)	0.045
Dizziness	0(0)	140(32.3)	—
Motor weakness	14(60.9)	243(56.1)	0.654
Nausea/vomiting	2(8.7)	29(6.7)	0.664
Speech impairment	0(0)	17(3.9)	—
Unsteady gait	1(4.3)	7(1.6)	0.341
Incontinence	0(0)	11(2.5)	—
Memory decline	0(0)	15(3.5)	—
GCS at admission			0.758
15	21(91.3)	370(85.5)	
3-14	2(8.7)	63(14.5)	
Operation side			0.712
Unilateral hematoma	16(69.6)	285(65.9)	
Bilateral hematoma	7(30.4)	148(34.1)	
Bilateral evacuated unilaterally	5(21.7)	50(11.5)	
Bilateral evacuated bilaterally	2(8.7)	98(22.6)	
Radiological characteristics			
Midline shift			0.364
<10mm	17(73.9)	280(64.7)	
≥10mm	6(26.1)	153(35.3)	
Preoperative maximal thickness			0.041
<20 mm	9(39.1)	91(21.0)	
≥20 mm	14(60.9)	342(79.0)	
Hematoma density			0.924
Hyper-dense	7(30.4)	128(29.6)	
Hypo-dense	4(17.4)	69(15.9)	
Mixed density	10(43.5)	204(47.1)	
Iso-dense	2(8.7)	32(7.4)	
Treatment			
Atorvastatin perioperatively	9(39.1)	164(37.9)	0.904
Anesthesia			0.243
Local	13(56.5)	191(44.1)	
General	10(43.5)	242(55.9)	
Intraoperative irrigation	15(65.2)	369(85.2)	0.018
Injection urokinase after operation	0(0)	12(2.8)	—
Duration of drainage, day			0.875
1	1(4.3)	62(14.3)	
2	19(82.7)	293(67.7)	
≥3	3(13.0)	78(18.0)	

Table 5. Multivariate logistic regression analysis of factors related to postoperative AIH				
Risk factors		OR	95% CI	P value
Headache		3.067	1.188-7.915	0.021
Preoperative thickness	maximal	0.537	0.216-1.335	0.181
Intraoperative irrigation		0.284	0.112-0.722	0.008

OR: Odds ratio; CI: confidence interval.

