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Chronic kidney disease is an independent risk factor of postoperative seizures after burr hole surgery for chronic subdural hematomas

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Abstract

Background: Postoperative seizures are serious neurological complications of chronic subdural hematomas (CSDH). The identification of risk factors of seizures after CSDH is needed to determine which patients require antiepileptic prophylaxis. *Methods:* We retrospectively collected data on patients diagnosed with CSDH from 2015 to 2018. Postoperative seizures are defined as those occurring within 30 days after surgery. Non-hemorrhagic subdural effusion and acute subdural hemorrhage after craniotomy were precluded in the study. We collected data from 221 patients who had burr hole surgery. We retrospectively recorded patient characteristics, hematoma characteristics, symptoms at admission, comorbid conditions, and other related parameters to evaluate the impact of these parameters on postoperative seizures. *Results:* Postoperative seizures occurred in 16 patients (7.24%). The univariate analysis showed that previous chronic kidney disease (31.25% vs. 5.37%, p= 0.001), age (60.44 vs. 66.54 y, p = 0.029), low Glasgow Coma Score (GCS) at admission (13.69 vs. 14.46, p = 0.015), and preoperative midline shift (9.79 vs. 8.57 mm, p = 0.021) were significantly correlated with postoperative seizures. The multivariate analysis revealed that previous chronic kidney disease (odds ratio [OR] = 27.103; 95% confidence interval [CI] = 4.887-150.296; p < 0.001), younger age (OR = 0.921; 95% CI = 0.866-0.979; p = 0.009) and preoperative midline shift (OR = 1.782; 95% CI = 1.175-2.702; p = 0.007) were independent risk factors of seizures. However, there was no significant difference in GCS at admission.
Conclusions: The independent predictors of postoperative seizures in patients with CSDH were preoperative midline shift, chronic kidney disease, and younger age. For younger patients with chronic kidney disease and preoperative midline displacement, we recommend antiepileptic preventive measures during the perioperative period.

Keywords: Chronic subdural hematoma, seizures, postoperative, burr hole, antiepileptic drugs

INTRODUCTION

Chronic subdural hematomas (CSDH) is usually caused by minor head trauma. The incidence of CSDH increases proportionally with age. Recently, the incidence of CSDH was estimated to be 58/100,000/year for patients aged 70–79 years and 127.1/100,000/year for patients aged over 80 years.[1,2] In neurosurgical practice, the optimal surgical treatments for CSDH include burr hole drainage, mini-craniotomy, and closed system drainage.[3] With better surgical results, treatment of postoperative complications, such as seizures, subdural hematoma recurrence, and hydrocephalus, has become more important. Previously, the incidence of postoperative seizures in patients with CSDH was reported to be 1%–23.4%.[4,5] Prevention of seizures is important because they negatively affect the quality of life of patients. Moreover, postoperative seizures may prolong hospital stays, leading to poorer functional outcomes and increase morbidity and mortality.[6]

In general, seizures are treated with antiseizure medications (ASMs). However, they can induce

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latent side effects, such as lack of tolerance and neurocognitive impairments[7-9], particularly in older adults who are predisposed to CSDH. Because of the lack of prospective studies, there are uncertainties in regard to drug selection, dosage, and duration of ASM administration, which has led to the debate surrounding the use of ASMs for the prevention of postoperative seizures in patients with CSDH.[10] However, there is limited research on individually assessed risk factors of seizures in patients with CSDH.

Therefore, we non-selectively and consecutively collected data from CSDH patients and analyzed the clinical characteristics, imaging features, and outcomes of early postoperative seizures in patients with CSDH. The objective of this study was to determine the independent risk factors of postoperative seizures.

METHODS

We non-selectively and consecutively collected data from CSDH patients who were treated via burr hole surgery at the Adult Neurosurgery Service Center from January 2015 to December 2018. According to the institutional guidelines and because of the retrospective nature of this observational study, approval by an ethics committee was not required. All patients who underwent burr hole surgery to clear a CSDH (> 3 weeks after injury) were included in our study. Exclusion criteria included: (1) Other types of traumatic brain injury, including epidural hematoma, brain contusion, subacute or acute subdural hematoma, intraventricular hemorrhage, intracerebral hematoma, or subarachnoid hemorrhage; (2) Hematoma recurrence; (3) Conservative treatment or open craniotomy; (4) History of epilepsy disorder or regularly taking AEDs for seizures or other clinical indications; and (5) Generalized cerebral edema.

At our institution, burr hole evacuation is considered the first-line surgical procedure option for CSDH. All patients received standard surgical treatment and followed a postoperative monitoring program. After a radiological diagnosis of CSDH, a multi-disciplinary team of neuroradiologists, neurologists, and neurosurgeons determined the indications for treatment following a discussion with the patient. As a general rule, if the thickness of the hematoma was > 1 cm and/or the patient was symptomatic, the patient was indicated for surgical hematoma removal. All patients underwent a standard operation, and all operations were performed under local anesthesia infiltration of the scalp (1% lidocaine mixed with 1:100000 adrenaline), with anesthesia provided for sedation and monitoring. The patient was placed in a supine position on a circular headrest. A 3–4 cm skin incision was made at the largest width of the hematoma, and a 1.0 cm diameter burr hole was made. After exposure and hemostasis, the dura mater was incised in a cruciform shape. A syringe with physiological saline was used to flush the hematoma cavity until the clear subdural fluid was observed to eliminate any solid blood masses, and a catheter was inserted into the subdural drainage tube for gravity drainage. The subdural drainage tube remained in place for 24 hours, and computerized tomography (CT) of the brain was performed before the drainage tube was removed to evaluate the effect of the subdural drainage.

Antiepileptic drugs are not used as routine prophylaxis for pre- or postoperatively. Medical records included admission history, discharge summary, and daily course records. Postoperative seizures are defined as those occurring within 30 days after surgery. If there were acute postoperative seizures, a standard diagnosis by EEG was required, and treatment included levetiracetam, valproic acid, or carbamazepine.

We included the potential risk factors of seizures of subdural hematoma that were reported in previous literature.[11] We included the following parameters in the analysis: age; sex; history of head trauma; symptoms at admission; GCS score at admission; pre-existing illnesses, such as hypertension, stroke, dementia, diabetes mellitus, coronary arterial disease, kidney disease, respiratory disease, hematological disease, liver disease, and malignant tumor; alcohol abuse; tobacco abuse; preoperative anticoagulation; and radiological parameters of the hematoma, such as location, maximal thickness, midline shift measurements, size, density, air trapped in postoperative CT scan, septa, and hematoma recurrence within 30 days.

Statistical analyses were performed using the classification frequency chi-square test, Wilcoxon rank-sum test, and Fisher's exact test. The student's t-test was used to analyze continuous data with a normal distribution. Statistical significance was set at 5%. All statistical analyses were performed using SPSS software version 25.0 (IBM, New York, USA)

RESULTS

Of the 258 patients with CSDH who received surgical treatment, 221 patients (37 females

and 184 males) were included according to our inclusion criteria. A total of 16 patients developed seizures after burr hole surgery, and the postoperative seizure rate was 7.24%. Table 1 summarizes the basic characteristics of the patients. The mean age of patients was 66.10± 10.763 years, and ages ranged from 18 to 85 years. At the time of admission, the mean GCS score was 14.41 points. Forty-one patients had alcohol abuse (18.55%), 79 had nicotine abuse (35.75%), and 11 had taken anticoagulant drugs (4.98%). Among them, 130 patients (58.82%) had a clear history of head trauma, whereas the other patients had no history or did not recall having a traumatic event resulting in a CSDH. The most common symptoms on admission were headache (52.49%) and lateralizing limb weakness (42.99%), followed by syncope, nausea, hypoconsciousness, speech disorder, and confusion. Seven patients (3.17%) had no symptoms, which were accidental discoveries, and 108 patients (48.87%) had at least one underlying disease. Hypertension, diabetes, and coronary artery disease were the three most frequent comorbidities in patients without seizures, whereas the most common comorbidities in those with seizures were chronic kidney disease, hypertension, and diabetes.

There were 99 cases (44.80%) with a left-sided hematoma, 64 cases (28.96%) with right-sided hematoma, and the remaining patients had bilateral CSDHs (26.24%). There were 78 patients with hypodense hematoma (35.30%), 98 patients with an isodense hematoma (44.34%), and 45 patients with mixed-density hematoma (20.36%). The mean thickness of the hematoma was 18.29 ±

Table 1: Baseline patient characteristics

Parameter	Total (%)	Seizure	No seizure	P Value
Basic characteristics				
Patient number (n)	221	16	205	
Age(years)		60.44±14.071	66.54±10.376	0.029
Female	37(16.74)	2	35	0.901
Symptoms at admission				
Headache	116(52.49)	5	111	0.077
Reduced consciousness	28(12.67)	3	25	0.712
Nausea/vomiting	33(14.93)	3	30	0.936
Lateralizing limb weakness	95(42.99)	6	89	0.645
Speech disorder	15(6.79)	2	13	0.669
Syncope	37(16.74)	2	35	0.901
Confusion	14(6.33)	2	12	0.604
None	7(3.17)	1	6	0.414
Underlying disease				
Diabetes mellitus	26(11.76)	4	22	0.192
Hypertension	51(23.08)	5	46	0.619
Coronary arterial disease	19(8.60)	2	17	0.908
Stroke	18(8.14)	3	15	0.256
Dementia	4(1.81)	1	3	0.261
Chronic Kidney Disease	16(7.24)	5	11	0.001
Respiratory disease	14(6.33)	1	13	1.000
Hematologic disease	6(2.71)	1	5	0.366
Malignant tumor	5(2.26)	1	4	0.316
Liver disease	13(5.88)	2	11	0.240
Head injury history	130(58.82)	6	124	0.072
Alcohol abuse	41(18.55)	1	40	0.327
Tobacco abuse	79(35.75)	3	76	0.141
Anticoagulation	11(4.98)	2	9	0.184
Mean GCS at admission		13.69±1.138	14.46±1.231	0.015

Table 2: Baseline hematoma and radiologic characteristic

Parameter	Total (%)	Seizure	No seizure	P Value
Hematoma localization				0.133
Left	99(44.80)	8	91	
Right	64(28.96)	7	57	
Both sides	58(26.24)	1	57	
Hematoma density				0.877
Hypodense	78(35.30)	5	73	
Isodense	98(44.34)	7	91	
Mixed dense	45(20.36)	4	41	
Hematoma thickness (mm)		19.50±2.556	18.20±2.893	0.082
Midline shift (mm ± SD) (unilateral cSDH)		9.79±1.718	8.57±1.87	0.021
Hematoma septa	13(5.88)	1	12	1.000
Postoperative course				
Trapped air in CT scan	77(34.84)	5	72	0.754
Recurrence within 30 d	5(2.26)	1	4	0.316

2.884 mm, and the mean midline shift was 8.86 ± 1.884 mm. The hematoma was septated in 13 patients (5.88%). Recurrence within 30 days of operation occurred in 2.26% of patients, and recurrence within 90 days of discharge occurred in 5.42% of patients. Table 2 shows the basic characteristics of hematomas.

The univariate analysis showed that the significant predictors of seizures were chronic kidney disease, age, mean GCS at admission, and midline shift. The multivariate analysis revealed that age (OR = 0.921; 95% CI = 0.866-0.979), chronic kidney disease (OR = 27.103, 95% CI = 4.887-150.296), and midline shift (OR = 1.782; 95% CI = 1.175-2.702) were independent predictors of seizures. Table 3 shows the results of the multivariate analysis.

Among the sixteen postoperative seizures, six cases had generalized seizures and ten focal seizures. Among generalized seizures, one case developed into generalized tonic-clonic seizures. All seizures occurred during hospitalization and within 30 days of the operation. At 12 months follow-up, all 16 patients with seizures received ASMs, nine were being treated with levetiracetam, five with valproic acid, and two with levetiracetam and carbamazepine. During the follow-up period, the patients with seizures have been completely seizure-free after ASM treatment, and one had died of pneumonia. There were no major adverse reactions related to ASM treatment.

DISCUSSION

In the present study, we evaluated the incidence and risk factors of seizures after burr hole surgery for CSDH and found that seizure rates during the 30-day follow-up was 7.24%. The incidence of seizures at our single centre was within the range of that reported in the literature, which was between 2.3% and 23.4%.[4-6,12-14] The difference in relative prevalence may be attributed to differences in surgical techniques used (such as closed-system drainage), inclusion and exclusion criteria, seizure time and recording method, follow-up time, other accompanying traumatic brain injury, ASM prevention measures, and patient selection. The pathophysiological mechanisms underlying seizures after CSDH include: (1) the effect of space-occupying lesions, such as a decrease in

Table 3: Multivariate analysis

Parameter	OR (95% CI)	P Value
Age	0.921[0.866-0.979]	0.009
Chronic kidney disease	27.103[4.887-150.296]	<0.001
Preoperative midline shift	1.782[1.175-2.702]	0.007

OR, odds ratio; CI, confidence interval.

cerebral blood flow, which may lead to instant seizures[15]; (2) various surgical operations may result in an unexpected intraoperative injury that may trigger early seizures[5]; and (3) the presence of glial hyperplasia or softening foci caused by previous cerebral cortical injury may provoke late-onset seizures.[16]

In our cohort, the analysis of demographic data, hematoma characteristics, medical history, clinical factors, and surgery factors revealed three independent predictors of postoperative seizures. Chronic kidney disease was the first independent factor; other comorbidities were not independent factors of postoperative seizures. There are undoubtedly other factors that may affect the results, whereas, in our study, the only limiting factor was that compared with the control group, patients with chronic kidney disease had significantly more seizures. Seifi *et al*. reported that major organ dysfunction was associated with status epilepticus and that patients diagnosed with SDH who have respiratory, renal, or neurological dysfunction are most likely to develop status epilepticus.[17]

Preoperative midline shift was the second independent predictor. Midline shift was higher in the seizure group than in the non-seizure group (9.79 vs. 8.57mm). It is well-established that intracranial tumors are closely related to seizures. Studies have suggested that lesions, such as large brain tumors and intracranial hematomas, reduce cerebral blood flow and cause seizures.[13] Similarly, it was recently reported that preoperative midline shift is an independent predictor of postoperative seizures, which is consistent with our findings.[18]

In our population, the multivariate analysis revealed that younger age predicted postoperative seizures and was observed in the univariate analysis. Old age was not a significant risk factor for epileptic seizures.[6,19] Other retrospective studies have demonstrated that younger people are more likely to have postoperative seizures than older people, although this difference did not reach statistical significance.[17,18,20] However, because these and our studies were both retrospective studies with patient sample sizes, only limited conclusions can be made in regard to the outcomes of this study.

One study reported that a one-point decrease in the average GCS score would increase the seizure rate by 21.6%.[6] In our study, patients who had seizures tended to have poorer GCS scores when they were admitted to hospital. The univariate analysis showed that the GCS score at admission was negatively correlated with seizures, although this was not reflected in the multivariate analysis. Chen *et al*. reported that patients with left unilateral and mixed-density CSDHs on preoperative CT had a relatively high postoperative seizure rate and recommended that preventive ASMs should be administered to these patients.[21] Our study found that neither the location nor density of subdural hematomas differed significantly between the occurrence or non-occurrence of postoperative seizures. Current literature on the propensity for seizures and the location of CSDHs report inconsistent findings.[6,14]

The evidence on the effectiveness of prevention of postoperative seizures using ASMs is controversial. Because of the lack of prospective randomized trials, it is difficult to offer formal recommendations.[10] However, a recent review indicated that some researchers oppose routine ASM prophylaxis in patients with CSDH. For example, Flores *et al*. discourage the routine use of ASMs for the prevention of postoperative seizures because of the lower incidence of seizures after burr hole surgery and the possible side effects.[20] Furthermore, Chen *et al*. and Branco *et al*. recommend the use of ASMs in high-risk patients only.[21,22] In light of our research, we also discourage the routine use of ASMs for the prevention of postoperative seizures in CSDH patients. However, our findings suggest that ASMs may be recommended for seizure prevention in patients with chronic kidney disease and a large midline shift. Large-scale, prospective, and randomized multicenter studies are required to confirm this result.

The current research has several limitations. The main limitations are that it was a retrospective single-center study and that it may have a bias of unmeasured factors. These issues may be exacerbated by the exclusion of some patients and the loss of patients to follow up. Secondly, because of the small number of patients with chronic renal disease, we did not stage the disease. This study was observational, which may not be as reliable as a prospective analysis. Moreover, we cannot deduce etiological or causal relationships between the variables and outcomes. In addition, in the univariate analysis, we observed several variables with trend significance, which was likely due to the small sample size. Furthermore, we only assessed the risk of seizures during a 30-day follow-up period. Finally, not all patients were diagnosed using EEG, and few patients had continuous EEG monitoring, which may have reduced the detection rate of seizures.

In conclusion, in this study, the seizure rate after

burr hole surgery was 7.24%. The independent predictors for seizures after burr hole surgery for CSDH were preoperative midline shift, chronic kidney disease, and young age. A prospective randomized study is needed to resolve the ongoing debate regarding the benefits of using AEDs to prevent postoperative seizures in patients with CSDH.

DISCLOSURE

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Conflict of interest: None

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