Clinical Investigation of Refractory Chronic Subdural Hematoma: A Comparison of Clinical Factors Between Single and Repeated Recurrences

Hiroaki Matsumoto, Hiroaki Hanayama, Takashi Okada, Yasuo Sakurai, Hiroaki Minami, Atsushi Masuda, Shogo Tominaga, Katsuya Miyaji, Ikuya Yamaura, Yasuhisa Yoshida, Kozo Yoshida

■ BACKGROUND: **Chronic subdural hematoma (CSDH) is sometimes refractory, and this is troublesome for neurosurgeons. Although many studies have reported risk factors or treatments in efforts to prevent recurrence, those have focused on single recurrence, and few cumulative data are available to analyze refractory CSDH.**

■ METHODS: **We defined refractory CSDH as ≥2 recurrences, then analyzed and compared clinical factors between patients with single recurrence and those with refractory CSDH in a cohort study, to clarify whether patients with refractory CSDH experience different or more risk factors than patients with single recurrence, and whether burr-hole irrigation with closed-system drainage reduces refractory CSDH.**

■ RESULTS: **Seventy-five patients had at least 1 recurrence, with single recurrence in 62 patients and ≥2 recurrences in 13 patients. In comparing clinical characteristics, patients with refractory CSDH were significantly younger ($P = 0.04$) and showed shorter interval to first recurrence ($P < 0.001$). Organized CSDH was also significantly associated with refractory CSDH ($P = 0.02$). Multivariate logistic regression analysis identified first recurrence interval <1 month (odds ratio, 6.66, $P < 0.001$) and age <71 years (odds ratio, 4.16, $P < 0.001$) as independent risk factors for refractory CSDH. On the other hand, burr-hole irrigation with closed-system drainage did not reduce refractory CSDH.**

■ CONCLUSIONS: **When patients with risk factors for refractory CSDH experience recurrence, alternative surgical procedures may be considered as the second surgery, because burr-hole irrigation with closed-system drainage did not reduce refractory CSDH in our study.**

INTRODUCTION

Chronic subdural hematoma (CSDH) is one of the most common diseases seen by neurosurgeons and is usually associated with good recovery after treatment with burr-hole irrigation and drainage under local anesthesia.[1-7] Despite this situation, approximately 5%–33% of patients experience recurrence and require reoperation.[1-5] Although recurrence usually involves only a single episode, repeated recurrences (i.e., refractory CSDH) sometimes occur. Refractory CSDH is often challenging for both neurosurgeons and patients, because of the need for repeat surgeries and the associated risks, complications, and costs. To prevent refractory CSDH, knowing the risk factors and performing effective treatments is important for patients with these risk factors when the first recurrence occurs.

Many studies have reported risk factors associated with recurrence of CSDH or treatments for reduction of recurrence. Risk factors for recurrence are split into 3 groups: patient-related, radiologic, and surgical.[8] Patient-related risk factors include older age, male sex, brain atrophy, hepatic dysfunction, cardiac disease, malignant neoplasm, diabetes mellitus, use of anticoagulant or antiplatelet drugs, hemodialysis, blood coagulopathy

Key words
- Chronic subdural hematoma
- Craniotomy
- Endovascular treatment
- Kampo medicine
- Middle meningeal artery
- Recurrence
- Refractory chronic subdural hematoma

Abbreviations and Acronyms
AMA: Accessory meningeal artery
CSDH: Chronic subdural hematoma
CSF: Cerebrospinal fluid
CT: Computed tomography
MMA: Middle meningeal artery
RCT: Randomized controlled trial

Department of Neurosurgery, Cerebrovascular Research Institute, Eishokai Yoshida Hospital, Kobe, Japan

To whom correspondence should be addressed: Hiroaki Matsumoto, M.D., Ph. D. [E-mail: hiroaki-matsu@umin.ac.jp]

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disorder, chronic alcoholism, or conditions associated with cerebrospinal fluid (CSF) shunt placement.[3,5,8-18] Radiologic risk factors include bilateral hematomas, mixed-density or high-density hematoma on computed tomography (CT), or larger hematoma volume.[8,11,16-21] Surgical risk factors include lack of closed-system drainage.[8] In addition, specific hematoma subtype such as septated or organized CSDH is often associated with recurrence.[16,22,23] On the other hand, artificial CSF as an intraoperative irrigation solution or adjunctive therapies such as steroid, angiotensin-converting enzyme inhibitor, tranexamic acid, atorvastatin, and Kampo medicine have often been used for preventing recurrence.[24-31]

Although many risk factors and treatments have been reported, as described earlier, these factors have been inconsistent and contraversial.[17] Moreover, the focus has been on single recurrence, and few cumulative data have been collected to analyze refractory CSDH. We therefore hypothesized that refractory CSDH might be a different type of CSDH or that patients with refractory CSDH might show different or significantly more risk factors than do patients with single recurrence of CSDH.

The present cohort study analyzed patients with recurrence of CSDH and examined whether patients with refractory CSDH show different or significantly more risk factors than patients with single recurrence, and whether effective treatments for reduction of refractory CSDH exist.

METHODS

This study was approved by the institutional review board of our hospital. The prospectively maintained database of our hospital was searched for patients with CSDH between January 2010 and December 2015. Medical records, radiographic studies, operative reports, and clinical follow-up evaluations were reviewed retrospectively. Patient informed consent was obtained before surgery.

Definition of CSDH Recurrence and Refractory CSDH

We defined CSDH recurrence as ipsilateral hematoma that developed on follow-up CT and caused neurologic deficits within 3 months after the last operation. Using this criterion, we then defined patients with refractory CSDH as those individuals presenting with recurrence on 2 or more occasions.

Surgical Procedure

We performed burr-hole irrigation with or without closed-system drainage for initial and secondary operations. Saline or artificial CSF was used as irrigation solution. The selection of irrigation solution and the judgment of whether to use closed-system drainage were up to the attending neurosurgeon.

In cases of refractory CSDH, we performed not only repetitive burr irrigation but also alternative surgical procedures such as endovascular embolization of the middle meningeal artery (MMA) or craniotomy for hematoma removal and membranectomy. Craniotomy was performed when organized CSDH was suspected.

Postoperative Management

In all cases, early ambulation was prescribed. When closed-system drainage was placed, the drain was removed within 2 days. Patients without complications were generally discharged within 10 days. Although antiplatelet or anticoagulant agents were discontinued before surgery in all cases, they were usually restarted 1 week after the last surgery. Some patients received an adjunctive drug for prevention of recurrence such as Kampo medicine after the first recurrence.

After discharge, patients received regular follow-up CT in our ambulatory practice every month during the first 3 months after the last operation. When follow-up CT showed disappearance of the hematoma, we considered CSDH to have been cured and ceased follow-up. If a residual hematoma lasted longer than 3 months in the absence of neurologic deficits, we planned on continuing follow-up. However, no patients showed any such condition. When recurrence was identified, patients underwent further operation and follow-up until cure was achieved.

Patient Population

We surgically treated 563 patients (360 men, 203 women) for primary CSDH at our institution between January 2010 and December 2015. All patients were able to receive follow-up in our ambulatory practice. Subsequently, 75 of the 563 patients (13.3%) experienced recurrence of CSDH. These 75 patients were analyzed.

CT Findings and Definition of Organized Hematoma

We performed CT in all cases at initial diagnosis. We investigated the laterality of hematoma such as bilateral or unilateral hematoma and classified hematomas under 5 types (high-density, isodensity, low-density, mixed-density, and niveau formation) based on CT findings (**Figure 1A–E**). Moreover, we focused on whether the hematoma was organized. We diagnosed organized hematoma based on operative findings, because diagnosis from CT findings was difficult (**Figure 1F**).[32,33] When the hematoma was too hard to wash out with vigorous and sufficient irrigation, we selected craniotomy as third surgery. We then diagnosed organized hematoma if organized hematoma was identified.

Outcome Measures

We assessed the 3-month recurrence rate after the second surgery. All 75 patients were able to be assessed. Patients with recurrence after the second surgery were considered to have refractory CSDH.

Primary Evaluation Items and Study Design

Clinical factors were obtained from medical records, including age, sex, interval to first recurrence (interval between first and second operations), outcomes after the second surgery, and use of adjunctive therapies for prevention of recurrence (such as Kampo medicine). Underlying diseases that have been reported as a risk factor for recurrence (such as hypertension, diabetes mellitus, malignant neoplasm, cerebral vascular disease, liver disease, renal disease, coagulopathy, dementia, and heart disease), use of anticoagulants or antiplatelet drugs and drinking history were obtained from patient/guardian self-reporting and questionnaire. CT findings were obtained from radiographic studies and assessed by the attending neurosurgeon. Surgical procedure at first recurrence (second surgery) and hematoma subtype such as organized hematoma were obtained from operative reports. The obtained information was summarized using the checklist shown in **Figure 2**. All items except drinking history were obtained.