



Optimal perioperative management of antithrombotic agents in patients with chronic subdural hematoma



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ABSTRACT

Objective: The use of antithrombotic agents such as anticoagulants and antiplatelet agents is widespread, and the opportunities to treat patients with chronic subdural hematoma (CSDH) under antithrombotic therapy are growing. However, whether antithrombotic therapy contributes to postoperative complications and recurrences of CSDH and how these agents should be managed in the surgical treatment of CSDH remains unclear.

Methods: We retrospectively analyzed 150 consecutive patients with CSDH who underwent neurosurgical interventions at Kyushu Rosai Hospital from 2011 to 2015 and followed them for more than 3 months.

Results: Of the 150 study patients, 44 received antithrombotic therapy. All anticoagulants and 76% of the antiplatelet agents were discontinued before surgical treatment of CSDH and resumed within 1 week except in 4 patients whose treatment was terminated and 7 patients who developed postoperative complications or underwent reoperations before resumption of these agents. Postoperative hemorrhagic complications associated with surgical treatment of CSDH occurred in 8 patients (5.3%), and there was no significant difference in the incidence of these complications between patients with and without antithrombotic therapy (6.8% vs. 4.7%, respectively; $p=0.90$). Postoperative thromboembolic complications occurred in 5 patients (5.4%), including 4 patients with antithrombotic therapy; these complications developed before resumption of antithrombotic agents in 2 patients. There was a significant difference in the incidence of postoperative thromboembolic complications between patients with and without antithrombotic therapy (9.1% vs. 0.9%, respectively; $p=0.04$). There were no significant differences in the incidence of radiographic deterioration or reoperation of ipsilateral or contralateral hematomas between patients with and without antithrombotic therapy after surgical treatment of unilateral CSDH.

Conclusion: A history of antithrombotic therapy was significantly correlated with the incidence of postoperative thromboembolic complications in patients with CSDH. Antithrombotic agents should be resumed as soon as possible when no hemorrhagic complication is confirmed after neurosurgical intervention for CSDH.

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1. Introduction

Chronic subdural hematoma (CSDH) is a common form of intracranial hemorrhage, and recurrences and complications are well-documented in affected patients. No consensus has been reached regarding whether antithrombotic therapy is a predictive factor associated with postoperative complications and recurrence in patients with CSDH [1–14]. This may be a result of different

Abbreviations: PT, prothrombin time; INR, international normalized ratio.

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antithrombotic agent management regimens such as alternative courses of continuation or termination and different timing of cessation and resumption of antithrombotic agents. Thus, how to best use these drugs to manage patients with CSDH who undergo neurosurgical intervention remains controversial.

The aim of this study was to determine the optimal perioperative management regimen of antithrombotic agents in patients with CSDH by analyzing the associations between antithrombotic therapy and postoperative complications, recurrence, and outcomes of contralateral CSDH.

2. Patients and methods

Patients with CSDH treated at Kyushu Rosai Hospital from 2011 to 2015 were retrospectively analyzed. In all patients, CSDH was confirmed by computed tomography (CT) or magnetic resonance imaging. All patients underwent neurosurgical intervention within 1 day of confirmation of symptomatic CSDH; interventions included trepanation and irrigation of the hematoma with artificial cerebrospinal fluid under local anesthesia. After the irrigation, a closed drainage system with a silicone tube was inserted into the hematoma cavity and directed toward the frontal pole. Postoperative CT scans were scheduled within 24 h and 1, 4, 8, and 12 weeks later. Follow-up was discontinued when a residual hematoma was no longer evident on CT scans.

The following patient data were collected and analyzed: age, sex, location of the hematoma, underlying disease, antithrombotic therapy, perioperative management using antithrombotic agents, postoperative complications, radiographic deterioration, and reoperation. We defined a hemorrhagic complication as an intracranial fresh bleed with a focal blood clot including acute subdural hematoma (ASDH), intracerebral hematoma, or subarachnoid hemorrhage. We defined a thromboembolic complication as a cerebral infarction, transient ischemic attack, myocardial infarction, deep venous thrombosis, or other type of peripheral arterial or venous thrombosis. Radiographic deterioration of CSDH was defined as an increase in the hematoma volume or CT attenuation value without a focal blood clot on CT within 3 months after the neurosurgical intervention. When neurological symptoms developed in addition to radiographic deterioration, reoperation was performed.

Statistical analyses were performed with ystat2000 software (Igakutoshosyuppannsya, Tokyo, Japan). Statistical significance was set at 0.05 using Student's *t*-test and the chi-square test.

3. Results

3.1. Patient characteristics

During the study period, 150 consecutive patients with CSDH, including 106 men and 44 women aged 30 to 102 years (mean, 77 years), were admitted to Kyushu Rosai Hospital and underwent neurosurgical intervention. The patients' characteristics are shown in Table 1. Forty-four (29%) of the 150 patients were taking antithrombotic agents. The mean age of patients taking antithrombotic agents was significantly higher than that of patients not taking antithrombotic agents (80 vs. 75 years, respectively; $p=0.01$), while the proportion of women taking antithrombotic agents was not significantly distributed (32% vs. 28%; $p=0.67$). Forty-nine hematomas (33%) were located in the left hemisphere, 57 (38%) were located in the right hemisphere, and 44 (29%) were bilateral. Of the 44 patients with bilateral hematomas, unilateral surgery was performed in 24 because the contralateral hematoma was small and asymptomatic. The most common risk factor for CSDH among all patients was preceding head trauma (65%), followed by preceding cranial surgery

(4%), previous shunt surgery (4%), and intracranial hypotension (4%); 23% of patients had an unknown etiology. There were no significant differences in the distribution of hematomas or risk factors for the development of CSDH between patients with and without antithrombotic therapy ($p=0.57$ and 0.56 , respectively). The patients had various underlying diseases including atrial fibrillation, cardiac disease, cerebrovascular disease, diabetes mellitus, hypertension, hyperlipidemia, chronic renal failure, and chronic liver dysfunction. The prevalence rates of atrial fibrillation, cardiac disease, cerebrovascular disease, hypertension, and hyperlipidemia were significantly higher among the patients taking antithrombotic agents.

3.2. Antithrombotic therapy and perioperative management

The perioperative management regimens using antithrombotic agents, including anticoagulants and antiplatelet agents, are shown in Fig. 1. Among the 44 patients taking antithrombotic agents, an anticoagulant agent such as warfarin or a direct oral anticoagulant (DOAC) was taken alone in 17 (39%) patients and in combination with an antiplatelet agent in 5 (11%) patients. A DOAC was taken in only 1 patient during the study period. The overall mean prothrombin time–international normalized ratio (PT-INR) at presentation among patients taking warfarin was 2.29 ± 0.83 . All 22 patients with CSDH taking anticoagulant agents discontinued taking these drugs, and vitamin K2 and prothrombin complex concentrate were intravenously administered before surgery if the PT-INR upon admission was >1.5 , representing 17 patients taking warfarin. Of these 22 patients, 16 resumed their anticoagulant agents within 1 week. Three patients terminated their anticoagulant agents, and the other 3 patients were excluded because of complications or reoperations before resumption of these agents.

Antiplatelet agents, including aspirin, clopidogrel, ticlopidine, or cilostazol, were taken by 22 (50%) patients in addition to the above-mentioned 5 (11%) patients who were taking them in combination with an anticoagulant agent. Of these 27 patients taking antiplatelet agents, 20 (74%) discontinued taking these drugs without a platelet transfusion, while 7 (26%) continued the drugs without cessation even during the perioperative period. Of the 20 patients who ceased taking antiplatelet agents, 15 resumed them within 1 week. One patient stopped taking the antiplatelet agents, and the other 4 were excluded because of complications or reoperations before resumption of these agents.

3.3. Postoperative complications

Among all 150 patients undergoing neurosurgical interventions for CSDH, postoperative complications occurred in 14 (9.3%) (Table 2). Postoperative hemorrhagic complications developed in 8 patients (5.3%) after surgical treatment of CSDH, and all of these complications were ASDH as verified by CT scans (Figs. 2 and 3). Of these 8 patients, 3 had a history of antithrombotic therapy; however, there was no significant difference in the incidence of postoperative hemorrhagic complications between patients with and without antithrombotic therapy (6.8% vs. 4.7%, respectively; $p=0.90$). Postoperative thromboembolic complications including cerebral infarction (Fig. 4) and myocardial infarction developed in 5 patients (3.3%) after surgical treatment of CSDH. Four of these 5 patients had a history of antithrombotic therapy, and there was a significant difference in the incidence of postoperative thromboembolic complications between patients with and without antithrombotic therapy (9.1% vs. 0.9%, respectively; $p=0.04$). Only one patient died of multiple organ failure; the mortality rate in the entire study population was 0.7%.

The characteristics of the patients with postoperative ASDH are listed in Table 3. In these 8 patients, 3 ASDHs occurred among

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