



## Chronic Subdural Hematoma in Women

Kazuko Hotta<sup>1</sup>, Takatoshi Sorimachi<sup>1</sup>, Yumie Honda<sup>1,2</sup>, Mitsunori Matsumae<sup>1</sup>

■ **OBJECTIVE:** Sex differences in various diseases recently have been recognized as an important factor in the approach to more efficient preventive and therapeutic medicine. We clarified sex differences in the clinical characteristics of chronic subdural hematoma (CSDH) by comparing men and women with CSDH, as there is a well-known male predominance in the prevalence of CSDH.

■ **METHODS:** Clinical factors and computed tomography findings were investigated retrospectively in 490 consecutive patients admitted to our hospital between 2006 and 2015 who were diagnosed with CSDH.

■ **RESULTS:** On univariate analysis, women were significantly older than men ( $P < 0.05$ ). In women, premorbid impaired activities of daily living, consciousness disturbance, acute-to-chronic subdural hematoma, and death as outcomes at discharge were significantly more frequent than in men ( $P < 0.05$ ). In contrast, women had less frequent instances of good recovery and less alcohol intake ( $P < 0.05$ ). Multivariate analysis demonstrated female sex as an independent predictor of consciousness disturbance at admission. Female sex also was identified as a predictor of death at discharge.

■ **CONCLUSIONS:** We demonstrated sex differences in the clinical characteristics of CSDH. In the future, management of patients with CSDH with regard to sex differences in disease characteristics could be expected to improve the outcomes of women, which have been worse than in men.

## INTRODUCTION

A male predominance in the prevalence of chronic subdural hematoma (CSDH) is a well-known characteristic of this disease.<sup>1-5</sup> Recently, sex differences in various diseases have been recognized as an important factor in the approach to more efficient health care, including sex-based preventive measures and therapies.<sup>6</sup> Biological and behavioral differences between the 2 sexes affect the manifestation, epidemiology, and pathophysiology of many diseases. Clarification of sex differences in clinical characteristics is considered to be a preliminary step in sex-based medicine.<sup>6</sup> CSDH is one of the most commonly encountered operative diseases in the field of neurosurgery.<sup>7</sup> Considering the apparent sex difference in the prevalence of CSDH, we hypothesized that sex differences also may exist in the clinical characteristics of the disease. To the best of our knowledge, sex differences in the characteristics of CSDH, except for the male predominance in its occurrence, have not been reported.

In the present retrospective study, we first clarified the clinical characteristics of women with CSDH using univariate analyses to compare women and men. Then, we re-evaluated major factors that appeared to have sex differences based on univariate analyses, including consciousness level at admission and outcomes, used as dependent predictors of multivariate analysis to exclude confounding factors.

## METHODS

### Patient Population

We retrospectively assessed consecutive patients diagnosed with CSDH who were admitted to our hospital between January 2006

### Key words

- Chronic subdural hematoma
- Consciousness disturbance
- Outcome
- Sex difference
- Sex

### Abbreviations and Acronyms

- ADL:** Activity of daily living
- CSDH:** Chronic subdural hematoma
- CT:** Computed tomography
- D:** Dead
- GCS:** Glasgow Coma Scale
- GOS:** Glasgow Outcome Scale
- GR:** good recovery
- MD:** Moderate disability

**OR:** Odds ratio

**SD:** Severe disability

**SDH:** Subdural hematoma

**VS:** Vegetative state

From the <sup>1</sup>Department of Neurosurgery, Tokai University, Kanagawa; and <sup>2</sup>Department of Emergency and Critical Care Medicine, Tokai University, Kanagawa, Japan

To whom correspondence should be addressed: Takatoshi Sorimachi, M.D. Ph.D.  
[E-mail: sorimachi@tokai-u.jp]

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and December 2015. Patients who underwent surgery for CSDH were included. Conservatively treated patients diagnosed with CSDH also were included. Patients 20 years old or younger were excluded, as were outpatients who were not admitted to our hospital. All patients were evaluated by neurosurgeons. The Institutional Review Board for Clinical Research at Tokai University Hospital approved all protocols for this retrospective study (IRB No.13R-069).

Clinical data were obtained through chart review. The following patient data were recorded: age and sex; premorbid activities of daily living (ADLs); laterality of the hematoma; history of trauma >3 weeks earlier; history of trauma <7 days before admission; previous diagnosis of dementia; alcohol intake almost every day before the onset of CSDH symptoms; malignancy during treatment and/or advanced malignancy, including cancers, leukemia, and myelodysplastic syndrome; hemodialysis; use of anticoagulants and/or antiplatelets; presence of acute-to-chronic SDH; level of consciousness (Glasgow Coma Scale [GCS] score) on admission or just before surgery; presence of headache and paresis; treatment, including surgical methods; and surgical complications.

To evaluate premorbid ADL, the modified Rankin Scale score before occurrence of symptoms caused by CSDHs was used. In this study, a patient with a modified Rankin Scale score of 2–5 was classified as having a premorbid impaired ADL. GCS score evaluated just before surgery was used in surgical cases, although crude measurement of the GCS score was not used. In patients treated conservatively, the GCS score as evaluated on admission was used. A GCS score of  $\leq 14$  was regarded as indicating a disturbance of consciousness. Because the GCS includes a verbal response category, the presence of aphasia lowers the GCS score. Some senile patients experiencing CSDH had pre-existing dementia. When the GCS is used as an index of the level of consciousness in patients showing low verbal response scores, a mild disturbance of consciousness cannot be differentiated from a mental disturbance or aphasia. As a result, patients, who had a previously diagnosed dementia and/or a left-sided CSDH, which possibly caused the aphasia, who demonstrated both an eye response score of 4 and a motor response score of 6, were defined as patients without consciousness disturbance to avoid the effects of dementia and aphasia on GCS scores.<sup>8</sup> We defined acute-to-chronic subdural hematoma (SDH) as acute SDH evolving to CSDH after >3 weeks.<sup>9</sup>

The following laboratory data were investigated: platelet count; activated partial thromboplastin time; prothrombin time—international ratio; glutamyl oxaloacetic transaminase; and glutamyl pyruvic transaminase. Liver dysfunction was defined as glutamyl oxaloacetic transaminase >50 IU/L and/or glutamyl pyruvic transaminase >50 IU/L. Clinical outcomes were assessed using the Glasgow Outcome Scale (GOS) score at discharge with scores classified as follows: good recovery (GR), moderate disability (MD), severe disability (SD), vegetative state (VS), and dead (D). In 55 patients who had hematomas with minimal mass effect or who were in critical general condition, conservative treatment was selected. Bed rest, administration of antifibrinolytics, and CT follow-up were used for conservative treatment. During the period of investigation, patients with CSDH were treated with burr-hole craniostomy under local anesthesia. The primary surgeon

determined whether repeated irrigation of the hematoma with normal saline and/or a closed subdural drainage system was used.

#### Image Acquisition and Imaging Analysis/Interpretation

Computed tomography (CT) was performed on either a 40-slice scanner (Brilliance; Philips, Best, the Netherlands) or a 128-slice scanner (Definition AS; Siemens, Erlangen, Germany). Noncontrast imaging of the head was acquired from the skull base to the vertex with the following parameters: 120 kVp; 360 mA; and 1 s/rotation. Axial reformats were 5 mm for noncontrast CT. The following CT findings were investigated: presence of acute-on-chronic SDH, distance of midline shift, and presence of bilateral CSDH. According to the previous study, we used the definition of acute-on-chronic SDH as follows<sup>8</sup>: 1) An acute-on-chronic SDH showed a fresh hematoma within the CSDH, occupying more than one-fifth of the subdural hematoma area on at least one CT slice; 2) a fresh hematoma in an acute-on-chronic SDH had both a greater and relatively more uniform density in comparison to the surrounding CSDH and a well-demarcated rim; 3) an acute-on-chronic SDH had no crosswise septum in a surrounding CSDH. CT images were evaluated by 2 board-certified neurosurgeons (K.H. and T.S.) with more than 10 years of experience in their specialty. For analysis, images were viewed on a PACS workstation. An identical window that best visualized subdural hematomas was applied to all studies (approximately window width/window level 100/40).

#### Statistical Analysis

Univariate analyses were performed with  $\chi^2$  analysis and the Fisher exact probability test for categorical variables and the Student t test or the Mann-Whitney U test for continuous variables. Numerical data are expressed as the mean  $\pm$  standard deviation. The following clinical factors were used in the comparison for univariate and multivariate analyses: age, sex, premorbid impaired ADL, hematoma side, history of trauma >3 weeks previously, history of trauma <7 days previously, previously diagnosed dementia, alcohol intake, malignancy, liver dysfunction, hemodialysis, use of anticoagulants and/or antiplatelets, acute-to-chronic SDH, acute-on-chronic SDH, midline shift on CT, bilateral CSDH on CT, platelet count, activated partial thromboplastin time, prothrombin time—international ratio, and outcome. Each variable was analyzed by the use of univariate analyses to identify which of the evaluated predictors were significant; variables showing significance at the <0.10 level were then included in multivariate logistic regression analysis, which was reduced by successive removal of the least significant variable from the model. All variables showing significance at the <0.10 level were retained in the final model. Analyses resulting in values of <0.05 were considered statistically significant. All statistical analyses were performed with JMP 10 software (SAS Institute, Cary, North Carolina, USA).

#### RESULTS

Between January 2006 and December 2015, we treated 490 consecutive patients diagnosed with CSDH. Of these 490 patients, 140 patients (28.6%) were women, and 350 (71.4%) were men. Mean age was  $74.0 \pm 12.6$  years (range, 21–96 years).

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