## **ARTICLE IN PRESS**

## Clinical Characteristics and Outcomes of Intracerebral Hemorrhage in Very Elderly

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Background: Intracerebral hemorrhage (ICH) incidences increase with age. Patients of advanced age may have limitations during acute care and recovery. We investigated baseline characteristics, hematoma features, and outcomes of very elderly ICH patients (≥80 years old) and compared them with those of younger ICH patients (<80 years old). Methods: We studied 377 patients (122 women;  $69 \pm 11$  years old) admitted within 24 hours of ICH onset. Outcome measures included hematoma volumes, National Institutes of Health Stroke Scale scores on admission, and vital and functional prognoses at 30 days. Results: After adjustments for sex, very elderly patients had a higher subcortical hematoma prevalence (odds ratio [OR], 2.62; 95% confidence interval [CI], 1.39-4.86]. On multivariate analyses, very elderly patients had larger hematoma volumes (OR, 1.33; 95% CI, 1.01-1.75, per 10-mL increase). After adjustments for risk factors and comorbidities, modified Rankin scale scores of 0-2 in very elderly patients occurred less often (OR, .34; 95% CI, .14-.82), and those with scores of 5-6 occurred more often (OR, 3.01; 95% CI, 1.09-8.54). Conclusions: Hematomas were relatively large and often found in the subcortex in very elderly ICH patients. Outcomes of very elderly ICH patients were relatively poor. Key Words: Intracerebral hemorrhage—elderly—outcomes—cerebral amyloid angiopathy.

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#### Introduction

The incidence of intracerebral hemorrhage (ICH) increases with advancing age, and one study reported no decrease in community-based ICH incidence. The number of individuals older than 80 years of age has been rising during the last decade in most countries, including the

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United States and countries in Europe.<sup>2,3</sup> A previous study reported data for ICH patients of 85 years and older and found unfavorable outcomes compared with outcomes for younger counterparts.<sup>4</sup> However, quantitative clinical data on admission severity, hematoma volume, and National Institutes of Health Stroke Scale (NIHSS) scores or outcomes represented by modified Rankin scale (mRS) scores of isolated very elderly ICH patients have not been reported. Therefore, we formed a single-center registry of acute ICH inpatients. In the initial report, we found that low admission serum calcium levels were associated with larger hematoma volumes and higher NIHSS scores.<sup>5</sup> In the present study, we investigated the clinical findings and outcomes of very elderly patients with acute ICH.

#### **Materials and Methods**

**Patients** 

We used our prospectively collected database of stroke inpatients to retrospectively study consecutive patients Y. INOUE ET AL.

with nontraumatic ICH identified by noncontrast computed tomography who had been admitted to our department within 24 hours of ICH onset from January 2004 through June 2009. Fifty-one patients with ICH associated with vascular malformations, aneurysms, tumors, and impaired coagulation (e.g., disseminated intravascular coagulation syndrome) and those with primary intraventricular hemorrhage were excluded from the study. The ethics committee of the National Cerebral and Cardiovascular Center approved this study.

In the present study, we defined patients 80 years and older as very elderly and those younger than 80 years as younger. Baseline clinical and demographic information included sex, age, history of ischemic stroke or prior ICH, ischemic heart disease, premorbid mRS score, liver dysfunction (history of acute hepatitis, chronic hepatitis, or cirrhosis), hypertension, diabetes mellitus, dyslipidemia, history of alcohol or tobacco use, and prestroke use of anticoagulants, antiplatelet agents, antihypertensive agents, or statins. The body mass index and blood pressure levels on admission were also documented. Blood tests were performed at the time of hospital arrival, before any crystalloid infusion therapy. The estimated glomerular filtration rate was calculated by using a revised equation for the Japanese population.<sup>6</sup> A similar treatment protocol was applied to patients with both groups.

#### Methods

Initial CT was performed immediately after the arrival of patients to the hospital, and follow-up CT was performed routinely within 24 hours after the arrival. Hematoma location and the presence of intraventricular bleeding were recorded on the initial CT scan. Hematoma volumes were measured by using the ABC/2 method. Intraventricular bleeding was not included in volume calculations. Hematoma growth was defined as an increase in hematoma size of >33% or >12.5 mL between the 2 CT scans. Two trained stroke specialists who were blinded to the clinical status of the patients reviewed and evaluated all CT scans.

#### Outcomes

Acute outcome measures assessed included the NIHSS score on admission, initial hematoma volume, and hematoma growth evaluated by stroke experts. Chronic outcome measures, evaluated principally at 30 days, consisted of independence, which corresponded to mRS scores of 0-2; bedridden state or death, which corresponded to mRS scores of 5-6; and death.

#### Statistical Analysis

Baseline demographics and clinical characteristics were compared via the  $\chi^2$  test for percentages and the Kruskal–

Wallis rank-sum test for medians. Continuous variables are reported as medians (interquartile range [IQR]) unless stated otherwise. Fisher's exact test was used to compare dichotomous variables, and the Wilcoxon rank-sum test was used for continuous and ordinal variables. Differences in the acute and chronic outcomes of very elderly patients and their younger counterparts were evaluated. Hematoma volumes and NIHSS scores on admission were log-transformed to approximate normality.

Multivariate logistic regression analyses for hematoma growth and 30-day outcomes were performed by adjusting for sex and variables that were automatically selected in a backward stepwise selection method. A backward selection procedure was performed for each outcome by using P > .10 of the likelihood ratio test for exclusion. The odds ratios (ORs) with 95% confidence intervals (CIs) for the very elderly ICH group were obtained, with the younger ICH group serving as the reference. Shift analysis of mRS scores was performed by using ordinal logistic regression, and differences in mRS scores were obtained. Statistical significance was set at P < .05. Statistical analysis was performed with the JMP 9.0 statistical software (SAS Institute Inc., Cary, NC).

#### Results

A total of 377 patients (122 women,  $69 \pm 11$  years old) who had had primary ICH were admitted to our department within 24 hours of ICH onset. Of these patients, 67 (17.8%) were placed in the very elderly ICH group, and 310 (82.2%) were placed in the younger ICH group. The median initial hematoma volume was 10 mL (IQR, 4-25 mL), and the median initial NIHSS score was 12 (IQR, 6-18). The hematomas occurred mainly in the thalamoganglionic region (in 254 patients, 67.4%).

Table 1 shows baseline clinical characteristics, and Table 2 shows physiological data, ICH features, and blood test data on admission for the patients. Women were twice as common in the very elderly ICH group than in the younger group (53.7% versus 27.7%, P < .001). In the very elderly group compared with the younger group, after adjustment for sex, history of ischemic stroke (P = .007), prestroke disability (P = .044), and lobar location of the hematoma (P = .003) were more common; history of diabetes mellitus (P = .029), alcohol consumption (P = .034), and smoking habit (P = .005) were less common; levels of high-sensitivity C-reactive protein (P = .023) and D-dimer (P = .044) were higher; and values of body mass index (P < .001), diastolic blood pressure (P = .022), albumin (P < .001), total cholesterol (P = .037), triglycerides (P < .001), alanine aminotransferase (P < .001), hemoglobin (P < .001), and estimated glomerular filtration rate (P = .005) were lower.

Table 3 shows the initial outcomes. The median hematoma volume was 15 mL in the very elderly group and 10 mL in the younger group. The median NIHSS score

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