

# High Incidence of Dementia Conversion than Stroke Recurrence in Poststroke Patients of Late Elder Society

Yumiko Nakano, MD,\* Kentaro Deguchi, MD, PhD,\* Toru Yamashita, MD, PhD,\*  
 Ryuta Morihara, MD,\* Kosuke Matsuzono, MD,\* Yuko Kawahara, MD,\*  
 Kota Sato, MD, PhD,\* Syoichiro Kono, MD, PhD,\* Nozomi Hishikawa, MD, PhD,\*  
 Yasuyuki Ohta, MD, PhD,\* Yasuto Higashi, MD,† Yoshiki Takao, MD, PhD,‡  
 and Koji Abe, MD, PhD\*

*Background:* This study investigated the incidence of current poststroke dementia (PSD), the annual conversion ratio into PSD, and the risk factors for conversion. *Methods:* In a 4.8-year follow-up period, 112 poststroke patients (ischemic stroke and intracerebral hemorrhage) were retrospectively investigated in cognitive examinations. They were categorized into 3 subgroups: converters into PSD, nonconverters who maintained their normal cognitive functions, and reverters who recovered to the normal mentality range. The clinical and demographic characteristics of these 3 subgroups were analyzed. *Results:* Among all 112 poststroke patients (61.6% male, 73.6 ± 10.4 years old), 16.1% had PSD. During the follow-up period, a part of the normal baseline mentality group (83.9% of 112 original patients) newly developed PSD (subdivided into converters) with an annual conversion rate of 7.6%. The reversion rate from the baseline PSD group was 11.3%. There were significant differences in age ( $P < .05$ ), baseline mini-mental state examination scores ( $P < .05$ ), body mass index ( $P < .05$ ), and periventricular and deep white matter hyperintensity grades ( $P < .05$  and  $P = .01$ , respectively) between converters and nonconverters. The annual rate of stroke recurrence was only 2.2% in all stroke subtypes. *Conclusions:* In comparison with stroke recurrence (2.2%), 7.6% of the annual PSD conversion rate was very high. Therefore, prevention of direct conversion into PSD without stroke recurrence may be another important aspect of poststroke clinics, especially in late elder society. **Key Words:** Poststroke dementia—stroke recurrence—vascular risk factors—secondary prevention—late elder society.

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Although stroke is a major health problem around the world, the global age-standardized mortality rates of stroke decreased significantly from 1990 to 2010.<sup>1</sup> Accu-

mulative evidence of secondary prevention of stroke suggests that the rates of stroke recurrence also decreased with advances in medical treatments.<sup>2-5</sup> On the other

From the Department of Neurology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama; †Department of Neurology, Himeji Central Hospital, Himeji; and ‡Department of Neurology, Kurashiki Heisei Hospital, Kurashiki, Japan.

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Address correspondence to Koji Abe, Department of Neurology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, 2-5-1 Shikata-cho, Kita-ku, Okayama 700-8558, Japan. E-mail: [yumikonakano@okayama-u.ac.jp](mailto:yumikonakano@okayama-u.ac.jp).

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hand, the World Health Organization indicated a rapid increase in the incidence of dementia patients (35.6 million) in a world that is rapidly aging.<sup>6</sup> In Japan, dementia is the second most frequent reason why elderly people need a nursing service (Comprehensive Survey of Living Conditions of Japan, Statistics and Information Department, Minister's Secretariat, Ministry of Health, Labour and Welfare 2013).

Because of a reduction in stroke-induced mortality and the progression of aging societies, the prevalence of dementia in poststroke patients is also rapidly increasing. Previous reports showed that the prevalence of poststroke dementia (PSD) ranged widely from 7.4% to 41.3%.<sup>7,8</sup> Although cognition improved in 50% of poststroke elderly at 15 months after stroke, a substantial proportion of those patients subsequently progressed to delayed dementia.<sup>9</sup> Thus, the conversion into dementia in poststroke patients has become a considerable problem in poststroke management, especially in late elder society.

In the present study, therefore, we investigated the incidence of current PSD among poststroke patients, examined the annual conversion ratio into PSD from baseline cognitive normal patients, and compared the risk factors for conversion or reversion.

## Methods

### *Subjects and Study Design*

This is a retrospective clinical cohort study performed in the Stroke Outpatient Clinic of Okayama University and affiliated hospitals from January 2009 to September 2014 (4.8 years). We analyzed 112 patients who were actively attending the clinic with diagnosis of ischemic stroke (IS,  $n = 107$ ) or intracerebral hemorrhage (ICH,  $n = 5$ ). The IS subtypes were atherothrombotic infarction (AT,  $n = 43$ ), lacunar infarction (LI,  $n = 41$ ), cardiogenic embolism (CE,  $n = 17$ ), or other determined etiology (other,  $n = 6$ ) according to the Trial of Org 10172 in the Acute Stroke Treatment stroke subtype classification system.<sup>10</sup> The patients with dementia were diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) or the International Classification of Diseases and Related Health Problems, 10th Revision (ICD-10).

These 112 patients were evaluated with mini-mental state examination (MMSE), Hasegawa dementia rating scale-revised (HDS-R), and frontal assessment battery (FAB) for cognitive functions, geriatric depression scale (GDS) and apathy scale (AS) for affective functions of depression and apathy, respectively. The mean interval between the onset of first-ever stroke and the initial evaluation was 4.6 years. They were first divided into 2 groups, that is, normal mentality and PSD depending on their baseline MMSE (PSD:  $MMSE \leq 23$ ; normal:  $MMSE \geq 24$ ). After the first examination, the same examinations were performed again during the above-

mentioned follow-up period (4.8 years). At that time, the normal baseline mentality group ( $MMSE \geq 24$ ) was further divided into 2 subgroups, that is, converters into new PSD with more than a 4-point decrease in MMSE and nonconverters who maintained their normal cognitive functions 1 year later. The baseline PSD patients ( $MMSE \leq 23$ ) were also followed for 1 year, some of whom recovered to the normal range mentality ( $MMSE \geq 24$ ) with more than a 3-points increase in MMSE, and these were named reverters. Stroke recurrence was also followed in the 112 poststroke patients.

Clinical demographic data such as age, gender, medical history, educational history, body mass index (BMI), and vascular risk factors (systolic blood pressure, antihypertensive medication, dyslipidemia [DL], diabetes mellitus [DM], cigarette smoking, history of cardiovascular disease, and atrial fibrillation) were also analyzed.

Endothelial function was assessed by pulse wave analysis with peripheral arterial tonometry, using Endo-PAT 2000 (CCI Corporation, Tokyo, Japan), a validated noninvasive method. This machine calculated the reactive hyperemia index (RHI), a measure of nitric oxide-mediated endothelial vasodilation, and the augmentation index (AI), a measure of arterial stiffness. Decreased RHI ( $<1.67$ ) and increased AI ( $>10\%$ ) suggested vascular endothelial dysfunctions.<sup>11</sup>

A magnetic resonance imaging (MRI) examination was performed for 110 patients. Two patients were excluded as they had an implanted pacemaker. The severity of periventricular hyperintensity (PVH) or deep white matter hyperintensity (DWMH) on T2-weighted image and fluid-attenuated inversion recovery imaging was rated according to the Fazekas scale (PVH: grade 0, no white matter change; grade I, caps or lining; grade II, bands; and grade III, irregular extension into the deep white matter; and DWMH: grade 0, no white matter change; grade I, punctuate; grade II, early confluence; and grade III, confluent).<sup>12</sup> Dot-like, low-intensity spots on a T2\*-weighted gradient recalled echo sequence (T2\*) with diameters less than 5 mm were defined as cerebral microbleeds (MBs),<sup>13</sup> and the number of MBs was calculated in the aforementioned 110 patients. These were subgrouped into 2 categories: 0-4 MBs and 5 or more MBs.

### *Statistical Analysis*

Statistical analysis was conducted with SPSS (version 22.0.0.0; IBM, Armonk, NY). To investigate the risk factors for conversion into PSD, comparisons between 3 sets of 2 subgroups (reverters versus nonconverters, converters versus nonconverters, or reverters versus converters) in each variable were conducted with a Mann-Whitney test and Fisher exact test. A *P* value of less than .05 was considered significant.

The Ethical Committee of Okayama University approved this study, and this study obtained exempted

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