Adverse Influence of Pre-Stroke Dementia on Short-Term Functional Outcomes in Patients with Acute Ischemic Stroke: The Fukuoka Stroke Registry

Yoshinobu Wakisaka a,b  Ryu Matsuo c  Jun Hata b,d  Junya Kuroda a
Takanari Kitazono a,b  Masahiro Kamouchi b,c  Tetsuro Ago a  on behalf of the Fukuoka Stroke Registry Investigators

a Department of Medicine and Clinical Science, b Center for Cohort Studies, c Department of Health Care Administration and Management, and d Department of Epidemiology and Public Health, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan

Key Words
Acute ischemic stroke · Acute stroke outcome · Dementia

Abstract
Background: Dementia and stroke are major causes of disability in the elderly. However, the association between pre-stroke dementia and functional outcome after stroke remains unresolved. We aimed to determine this association in patients with acute ischemic stroke. Methods: Among patients registered in the Fukuoka Stroke Registry from June 2007 to May 2015, 4,237 patients with ischemic stroke within 24 h of onset, who were functionally independent before the onset, were enrolled in this study. Pre-stroke dementia was defined as any type of dementia that was present prior to the index stroke. Primary and secondary study outcomes were poor functional outcome (modified Rankin Scale 3–6) at 3 months after the stroke onset and neurological deterioration (≥2-point increases on the National Institutes of Health Stroke Scale score during hospitalization), respectively. For propensity score (PS)-matched cohort study to control confounding variables for pre-stroke dementia, 318 pairs of patients with and without pre-stroke dementia were also selected on the basis of 1:1 matching. Multivariable logistic regression models and conditional logistic regression analysis were used to quantify associations between pre-stroke dementia and study outcomes. Results: Of all 4,237 participants, 347 (8.2%) had pre-stroke dementia. The frequencies of neurological deterioration and poor functional outcome were significantly higher in patients with pre-stroke dementia than in those without pre-stroke dementia (neurological deterioration, 16.1 vs. 7.1%, \( p \) < 0.01; poor functional outcome, 63.7 vs. 27.1%, \( p \) < 0.01). Multivariable analysis showed that pre-stroke dementia was significantly associated with neurological deterioration (OR 1.67; 95% CI 1.14–2.41; \( p \) < 0.01) and poor functional outcome (OR 2.91; 95% CI 2.17–3.91; \( p \) < 0.01). In the PS-matched cohort study, the same trends were observed between the pre-stroke dementia and neurological deterioration (OR 2.60; 95% CI 1.17–5.78; \( p \) < 0.01) and between the dementia and poor functional outcome (OR 3.62; 95% CI 1.89–6.95; \( p \) < 0.01). Conclusions: Pre-stroke dementia was significantly associated with higher risks for poor functional outcome at 3 months after stroke onset as well as for neurological deterioration during hospitalization in patients with acute ischemic stroke.
Introduction

Dementia and stroke are major causes of functional disability in the elderly [1], causing increased impact and burden on caregivers as well as on the society [2–4]. Because the prevalence of dementia is expanding rapidly worldwide [5] and also because dementia is a known risk factor for stroke [6, 7], an increase in the number of acute stroke patients with preexisting dementia is expected [8]. However, no established guidelines exist for the management and treatment for acute stroke patients with dementia, probably owing to conflicting results in existing literatures about the association between pre-stroke dementia and functional outcome after stroke. Several studies have reported worse functional outcomes in stroke patients with pre-stroke dementia than in those without pre-stroke dementia [8–11]. In contrast, some studies showed no significant association between pre-stroke dementia and functional outcome after ischemic stroke [12, 13], suggesting that differences that exist in functional outcome after stroke between patients with and without pre-stroke dementia are driven by differences in clinical conditions including age, stroke severity, premorbid dependency, and comorbid disorders rather than by pre-stroke dementia itself. However, these studies were limited by a small sample size [9–12], the fact that this was based on a single center [9–11], lack of adjustment for confounding factors by multivariable analysis [9–12], and inclusion of patients with premorbid functional disability [8, 9, 13], which may all have contributed to the conflicting results.

Therefore, this study aimed to determine the association between pre-stroke dementia and functional outcome in acute ischemic stroke patients without premorbid neurological dysfunction by using the Fukuoka Stroke Registry (FSR) database, which is a multicenter, hospital-based database of patients with acute stroke in Japan.

Methods

Fukuoka Stroke Registry

The FSR was approved by the Institutional Review Board of the Ethics Committees of the participating centers (Appendix). The study objectives, study design, risks, and benefits were explained in detail to each patient or surrogate family members on admission, and written informed consent was obtained. This study was performed in accordance with the Declaration of Helsinki and its subsequent amendments. Details of the study design have been previously described [14–18].

Study Participants

From June 2007 to May 2015, 10,610 stroke patients were consecutively registered in the FSR database, 1,634 (15.4%) of whom had pre-stroke dementia. We excluded patients with non-ischemic stroke, those lacking information on modified Rankin Scale (mRS) at 3 months after stroke onset, those with pre-stroke dependency (mRS ≥ 2), and those who were admitted 24 h after stroke onset. The total number of patients with acute ischemic stroke included in the study was 4,237 (all participants). To further adjust for differences in baseline characteristics, we calculated the propensity score (PS) of each patient and selected 318 PS-matched pairs of patients with and without pre-stroke dementia (PS-matched cohort; Fig. 1).

Definition of Stroke

Stroke was defined as sudden onset of nonconvulsive and focal neurological deficits persisting for more than 24 h. Ischemic stroke was identified and classified into the following 4 subtypes as was reported previously: cardioembolism, large-artery atherosclerosis, small-vessel occlusion, or others (ischemic stroke of other determined or undetermined etiology) [14–18]. Non-cardioembolic infarction was defined as either stroke subtype as large-artery atherosclerosis, small-vessel occlusion, or other [14–18].

Diagnosis of Pre-Stroke Dementia

Pre-stroke dementia was defined as any type of dementia that was present prior to the index stroke. Assessment of cognitive and functional status prior to stroke onset was based on clinical interviews and on a knowledgeable informant. The presence of chronic and slow progressive decline in memory and additional cognitive abilities was required to diagnose pre-stroke dementia. Also required was a confirmed diagnosis of dementia according to medical records, or a confirmation that cognitive deficits caused significant impairment in social or occupational functioning and represented a significant decline from a previous level of functioning according to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition Text Revision Criteria [8, 13, 19].

Clinical Assessment

Baseline characteristics were assessed on admission, and blood samples were collected within 24 h of admission. Hypertension, dyslipidemia, diabetes mellitus, ischemic heart disease, chronic kidney disease, antihypertensive therapy, antidiabetic therapy, anti-thrombotic therapy, in-hospital rehabilitation, and infectious complications were defined, and atrial fibrillation was diagnosed, as previously reported (online suppl. methods; for all online suppl. material, see www.karger.com/doi/10.1159/000453625) [14–18]. Severe stroke was defined as National Institutes of Health Stroke Scale (NIHSS) score ≥ 8 on admission [18]. Acute revascularization was defined as either endovascular thrombectomy or thrombolytic therapy with the intravenous or intra-arterial administration of thrombolytic agents in the hyperacute phase of the stroke. Infectious complications were defined as any infectious diseases such as pneumonia, urinary tract infection, and sepsis during hospitalization.

Study Outcomes

The primary outcome was poor functional outcome at 3 months after stroke onset, defined as dependency or death (mRS ≥ 3) [15]. The secondary outcome was neurological deterioration (≥ 2-point
increases on the NIHSS during hospitalization) [15, 18]. The mRS at 3 months after stroke onset was evaluated by trained and certi-
fied research nurses, and neurological severity during hospitaliza-
tion was assessed by trained stroke neurologists using the NIHSS,
as reported previously[15].

**PS Matching**

For the PS-matched cohort study, the probability of affecting
pre-stroke dementia was calculated for the patients with and with-
out pre-stroke dementia among all participants using a logistic re-
gression model. The clinical variables of interest used to generate
PS were age, gender, dyslipidemia, atrial fibrillation, ischemic
heart disease, chronic kidney disease, history of previous stroke,
pre-stroke antihypertensive therapy, pre-stroke antithrombotic
therapy, low-density lipoprotein (LDL) cholesterol, casual blood
glucose, systolic blood pressure (BP), body mass index, cardioem-
bolic infarction, NIHSS on admission, infectious complications,
and in-hospital rehabilitation. After PS generation, patients with
and without pre-stroke dementia underwent 1:1 nearest-neighbor
(greedy-type) matching of the standard deviation of the logit of the
PS with a caliper within 0.25 standard deviations [16, 17]. Match-
ing was performed without replacement, and unpaired partici-
pants not meeting the matching criteria were excluded. Each
PS-derived matched pair was assigned a unique pair identifier
(ID). In total, 318 matched-pair IDs were selected. Calculation of
PS and 1:1 matching were performed using STATA 14 (StataCorp
LP, College Station, TX, USA).

**Statistical Analysis**

Baseline characteristics were compared using the χ² test or a
logistic regression for categorical variables, and the unpaired Student
t test or Wilcoxon rank sum test were used for continuous or scor-
ing variables, as appropriate. For all participants, logistic regres-
sion analyses were used to estimate multivariable-adjusted ORs
and 95% CIs for the study outcomes. Multivariable models were
adjusted for potential confounding factors, which were selected by
considering clinical relevance to neurological deterioration and
functional outcome as well as previous findings. Interactions be-
 tween pre-stroke dementia and baseline variables for the study
outcomes were tested by adding an interaction term to the relevant
multivariable logistic model. In the PS-matched model, ORs for
study outcomes were calculated after matching using conditional
logistic regression analysis. Statistical analyses were performed us-
ing JMP software version 11 (SAS Institute, Cary, NC, USA). Prob-
ability values <0.05 were considered statistically significant.

**Results**

**Baseline Characteristics of All Participants**

Of the 4,237 eligible patients, 347 (8.2%) had pre-
stroke dementia (Fig. 1). Admission rate within 24 h after
the onset of index stroke was not different between pa-
 tients with and without pre-stroke dementia among the
ischemic stroke patients without pre-stroke dependency
(67.1 vs. 65.4%, p = 0.42; Fig. 1). Patients with pre-stroke
dementia were older than those without pre-stroke de-
mentia. Female gender, atrial fibrillation, chronic kidney
disease, cardioembolic infarction, and infectious complica-
tions were more prevalent, and dyslipidemia was less
prevalent in patients with pre-stroke dementia than in
those without pre-stroke dementia. Patients with pre-
stroke dementia showed lower levels of LDL cholesterol,
casual blood glucose, systolic BP, and body mass index
than those without pre-stroke dementia. Pre-stroke anti-
hypertensive and antithrombotic therapies as well as in-

**Fig. 1. Flowchart of patient selection.** Of the 10,610 patients with-
in 7 days of stroke onset registered in the FSR, 1,634 (15.4%) had
pre-stroke dementia. After excluding non-eligible patients, 347
(8.2%) patients with pre-stroke dementia were included as study
participants. Among 6,469 patients without pre-stroke dependency,
347 of 517 patients with pre-stroke dementia (67.1%) and 3,890
of 5,952 patients without pre-stroke dementia (65.4%) were
admitted within 24 h after the onset of index stroke. PSD, pre-stroke
dementia, mRS, modified Rankin Scale; PS, propensity score.
hospital rehabilitation were more frequently administered, while in-hospital statin therapy was less frequently administered in patients with pre-stroke dementia than in those without pre-stroke dementia (Table 1).

**Pre-Stroke Dementia and Clinical Outcomes in All Participants**

Baseline NIHSS was higher (Table 1), and severe stroke on admission was more prevalent in patients with pre-stroke dementia (39.5%) than in those without pre-stroke dementia (23.6%, $p < 0.01$). Neurological deterioration was also more frequently developed in patients with pre-stroke dementia than in those without pre-stroke dementia (Table 2). In addition, patients with pre-stroke dementia showed higher mRS at 3 months after stroke onset than those without pre-stroke dementia (median [interquartile range] 3 [2–4] vs. 1 [0–3], $p < 0.01$), resulting in a higher prevalence of poor functional outcome in patients with pre-stroke dementia (63.7%) than in those without pre-stroke dementia (27.1%, $p < 0.01$; Table 2; online suppl. Fig. IA). Age- and gender-adjusted, and multivariable-adjusted models showed that pre-stroke dementia...  

**Table 1. Clinical characteristics of all participants**

<table>
<thead>
<tr>
<th></th>
<th>Pre-stroke dementia</th>
<th>Standardized difference</th>
<th>$p$ value</th>
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<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td>81.5±7.4 (yes : $n = 347$)</td>
<td>70.0±12.2 (no : $n = 3,890$)</td>
<td>1.14</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>158 (45.5)</td>
<td>1,374 (35.3)</td>
<td>0.21</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>285 (82.1)</td>
<td>3,074 (79.0)</td>
<td>0.08</td>
</tr>
<tr>
<td><strong>Diabetes mellitus</strong></td>
<td>90 (25.9)</td>
<td>1,161 (29.9)</td>
<td>0.09</td>
</tr>
<tr>
<td><strong>Dyslipidemia</strong></td>
<td>144 (41.5)</td>
<td>2,008 (51.6)</td>
<td>0.20</td>
</tr>
<tr>
<td><strong>Atrial fibrillation</strong></td>
<td>138 (39.8)</td>
<td>1,040 (26.7)</td>
<td>0.28</td>
</tr>
<tr>
<td><strong>Ischemic heart disease</strong></td>
<td>64 (18.4)</td>
<td>569 (14.6)</td>
<td>0.10</td>
</tr>
<tr>
<td><strong>Chronic kidney disease</strong></td>
<td>167 (48.1)</td>
<td>1,263 (32.5)</td>
<td>0.33</td>
</tr>
<tr>
<td><strong>Previous stroke</strong></td>
<td>71 (20.5)</td>
<td>548 (14.1)</td>
<td>0.17</td>
</tr>
</tbody>
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Pre-stroke medication

<table>
<thead>
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<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antihypertensive</strong></td>
<td>228 (65.7)</td>
<td>2,165 (55.7)</td>
<td>0.21</td>
</tr>
<tr>
<td><strong>Antithrombotic</strong></td>
<td>145 (41.8)</td>
<td>1,239 (31.8)</td>
<td>0.53</td>
</tr>
<tr>
<td><strong>Antidiabetic</strong></td>
<td>50 (14.4)</td>
<td>704 (18.1)</td>
<td>0.10</td>
</tr>
<tr>
<td><strong>Statin</strong></td>
<td>64 (18.4)</td>
<td>711 (18.3)</td>
<td>0.003</td>
</tr>
<tr>
<td><strong>LDL-cholesterol, mmol/L</strong></td>
<td>2.82±0.81</td>
<td>2.96±0.90</td>
<td>0.16</td>
</tr>
<tr>
<td><strong>HDL-cholesterol, mmol/L</strong></td>
<td>1.36±0.38</td>
<td>1.37±0.39</td>
<td>0.03</td>
</tr>
<tr>
<td><strong>Casual blood glucose, mmol/L</strong></td>
<td>7.50±2.98</td>
<td>7.94±3.37</td>
<td>0.14</td>
</tr>
<tr>
<td><strong>HbA1c, %</strong></td>
<td>6.17±1.16</td>
<td>6.31±1.33</td>
<td>0.11</td>
</tr>
<tr>
<td><strong>Systolic BP, mm Hg</strong></td>
<td>158.2±28.5</td>
<td>161.7±29.6</td>
<td>0.12</td>
</tr>
<tr>
<td><strong>Body mass index, kg/m²</strong></td>
<td>21.9±3.3</td>
<td>23.2±3.6</td>
<td>0.38</td>
</tr>
<tr>
<td><strong>Cardioembolic infarction</strong></td>
<td>126 (36.3)</td>
<td>1,014 (26.1)</td>
<td>0.22</td>
</tr>
<tr>
<td><strong>NIHSS on admission</strong></td>
<td>5 (3–11)</td>
<td>3 (2–7)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>NIHSS on admission</strong></td>
<td>7.94±6.86</td>
<td>5.78±6.25</td>
<td>0.33</td>
</tr>
<tr>
<td><strong>Acute revascularization</strong></td>
<td>57 (16.4)</td>
<td>579 (14.9)</td>
<td>0.04</td>
</tr>
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In-hospital medication

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td><strong>Antihypertensive</strong></td>
<td>214 (61.7)</td>
<td>2,206 (56.7)</td>
<td>0.10</td>
</tr>
<tr>
<td><strong>Antithrombotic</strong></td>
<td>341 (98.3)</td>
<td>3,828 (98.4)</td>
<td>0.008</td>
</tr>
<tr>
<td><strong>Antidiabetic</strong></td>
<td>80 (23.1)</td>
<td>1,015 (26.1)</td>
<td>0.07</td>
</tr>
<tr>
<td><strong>Statin</strong></td>
<td>129 (37.2)</td>
<td>1,687 (43.4)</td>
<td>0.13</td>
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In-hospital rehabilitation

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<thead>
<tr>
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<th>Standardized difference</th>
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</tr>
</thead>
<tbody>
<tr>
<td><strong>Infectious complications</strong></td>
<td>339 (97.7)</td>
<td>3,543 (91.1)</td>
<td>0.29</td>
</tr>
<tr>
<td><strong>Length of hospitalization, days</strong></td>
<td>16±8.5</td>
<td>16±8.5</td>
<td>0.001</td>
</tr>
</tbody>
</table>

LDL, low-density lipoprotein; HDL, high-density lipoprotein; HbA1c, hemoglobin A1c; BP, blood pressure. Physical and laboratory data were evaluated on admission. Acute revascularization included thrombolytic therapy and endovascular thrombectomy. Values are expressed as mean ± SD, median (interquartile range), or number of patients (%).
dementia was significantly associated with poor functional outcome as well as with neurological deterioration (Table 2). Sensitivity analysis of the subpopulation without acute revascularization in the hyperacute phase of stroke (n = 3,601) also showed the same trend for primary and secondary outcomes (Table 2). We further evaluated the interactions between pre-stroke dementia and 6 baseline variables (age, gender, stroke subtype, history of previous stroke, baseline stroke severity, and infectious complication) for clinical outcomes. Interactions were found between pre-stroke dementia and stroke subtype and between the dementia and baseline stroke severity for neurological deterioration: among patients with non-cardioembolic infarction and those without severe stroke on admission, patients with pre-stroke dementia had a higher probability for developing neurological deterioration than those without the dementia, whereas no significant association was found in patients with cardioembolic infarction and in those with severe stroke (online suppl. Fig. II). No interactions were found between pre-stroke dementia and the baseline variables for poor functional outcome (online suppl. Fig. III).

To control confounding variables for pre-stroke dementia, we conducted a PS-matched cohort study. The mean standardized difference in covariates decreased from 0.21 (range 0.001–1.14) to 0.03 (range 0.00–0.08) after PS matching (Table 1; online suppl. Table I). Baseline covariates were statistically indistinguishable between patients with and without pre-stroke dementia in the PS-matched participants (online suppl. Table I). Because NIHSS on admission was also matched in this model, no significant difference was found in the prevalence of severe stroke on admission between patients with and without pre-stroke dementia (38.4 vs. 32.4%, p = 0.11).

However, patients with pre-stroke dementia more frequently developed neurological deterioration than those without pre-stroke dementia (17.2% vs. 6.8%, p < 0.01), resulting in higher mRS at 3 months after stroke onset than those without pre-stroke dementia (10.4% vs. 4.2%, p < 0.01). The prevalence of neurological deterioration was also significantly higher among patients with pre-stroke dementia (15.1% vs. 10.4%, p = 0.07).

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Discussion

In this study, we found that pre-stroke dementia in ischemic stroke patients was significantly associated with poor functional outcome at 3 months after stroke onset as well as with neurological deterioration during the acute phase of stroke. Our results suggest that pre-stroke dementia is an independent factor associated with the prognosis of acute ischemic stroke.

Previous studies have suggested that patients with pre-stroke dementia showed unfavorable clinical outcomes after ischemic stroke for various reasons. These reasons included patients belonging to an older age, having suffered from severe stroke, being treated less aggressively for index stroke as well as for comorbid vascular risk factors, and being more prone to developing infectious complications during the acute phase of stroke than those without pre-stroke dementia [13, 20]. These speculations, however, are not applicable to our results because we found that pre-stroke dementia was significantly and independently associated with poor functional outcome even after adjusting for possible confounding factors including these variables in the overall analysis as well as in the PS-matched cohort study. Saposnik et al. [13] previously evaluated the effect of pre-stroke dementia on functional outcome by PS-matched analysis, but no significant association was found between pre-stroke dementia and disability including mortality (mRS 3–6) at discharge. The discrepancy between this previous study and that of our own can be derived from differences in mortality rates in the PS-matched participants. Higher mortality rates of more than 20% in patients with and without pre-stroke dementia in this previous study, compared to the rates around 5–6% in both patient groups in our study (online suppl. Fig. IB), could diminish the difference in prevalence of poor functional outcome between patients with and without pre-stroke dementia because the previous study also found that patients with pre-stroke dementia had a significantly higher risk for disability (mRS 3–5) at the time of discharge than those without pre-stroke dementia when only considered patients discharged alive [13]. We were also aware that neuropsychiatric symptoms, which develop frequently during the acute stage of stroke in stroke patients especially with dementia, could be a determinant for stroke outcomes [21]. However, most previous studies and ours did not evaluate the symptoms in study participants [8–13]. Further studies are required to confirm the association between pre-stroke dementia and stroke outcomes.

Although the precise mechanisms underlying the association between pre-stroke dementia and functional outcome after ischemic stroke were not elucidated in this study, dementia-related impairment of cerebrovascular hemodynamics offers a plausible explanation. Patients with dementia, especially due to Alzheimer disease (AD) or vascular dementia (VD), show decreased cerebral blood flow, reduced number of cerebral capillaries, and diminished cerebrovascular reactivity compared with those without dementia [22–24]. Impairment of these cerebrovascular hemodynamics is known to be significant determinants of neurological deterioration and poor functional outcome after ischemic stroke [25–29]. Initial neurological severity is also a known determinant of functional outcome after ischemic stroke [30]. In this study, however, pre-stroke dementia was associated with poor functional outcome irrespective of initial neurological severity, in spite of patients with pre-stroke dementia showing more severe initial neurological symptoms than those without pre-stroke dementia. This was, in part, due to the increased probability of developing neurological deterioration in the acute phase of stroke in patients with pre-stroke dementia, especially those without severe neurological symptoms on admission, than in those without pre-stroke dementia. Collectively, it seems reasonable to consider that impairment in cerebrovascular hemodynamics prior to the index stroke in patients with dementia leads to neurological deterioration and results in poor functional outcome after ischemic stroke.

Our study had several strengths. We enrolled a large number of consecutive ischemic stroke patients from multiple stroke centers. The characteristics of patients were relatively homogeneous in that no enrolled patients had pre-stroke functional dependency and all were admitted within 24 h of onset. The number of study participants was larger than that of most previous studies, and possible confounding factors were adjusted for in multivariable analysis and mitigated in a PS-matched model.

There were also several limitations to this study. First, there is a possibility of selection bias because the study only included inpatients hospitalized in FSR-participating hospitals. Second, because the definition of pre-stroke dementia in our study did not follow quantitative neuropsychological assessments and because we have no data on the severity of cognitive dysfunction, it is possible that patients with mild dementia were not appropriately identified. This is a common limitation for diagnosing a pre-stroke dementia in acute stroke pa-
tients in daily clinical settings because it is difficult to apply comprehensive neuropsychological test batteries to patients who are physically and neurologically impaired [31]. In addition, it seems that patients with severe dementia were excluded from our study because we only included patients without premorbid functional disability and because there is good association between the severity of functional disability and severity of cognitive decline [4]. Despite the difficulty in diagnosing pre-stroke dementia with accuracy, it is interesting to note that the prevalence of pre-stroke dementia among whole subjects registered in the FSR database (15.4%; Fig. 1), was almost similar to that previously found in hospital-based studies (12.0–16.3%) [32]. Third, our study has limited information regarding dementia subtype. Most of our study subjects with pre-stroke dementia would be categorized as AD, VD, or a mixed type of AD and VD, because these are major common forms of dementia in Japan [33].

We can conclude that pre-stroke dementia was significantly and independently associated with poor functional outcome as well as with neurological deterioration after the onset of acute ischemic stroke. This association was after adjusting confounding factors including conventional pre- and post-stroke management. Our results suggested that novel therapeutic approaches are necessary to establish and improve clinical outcomes of acute ischemic stroke patients with pre-stroke dementia.

Acknowledgments

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Disclosure Statement

The authors have read the journal’s policy and state the following competing interests: T. Kitazono received honoraria and grants from Mitsubishi Tanabe Pharma Corporation, Kyowa Hakko Kirin Co., Ltd., and Daiichi Sankyo Company, Ltd. The authors confirm that this does not alter their adherence to Cerebrovascular Disease policies on sharing data and materials. Data are available upon request to the FSR data access committee.

Appendix

FSR Investigators

The participating hospitals in the FSR included the Kyushu University Hospital, National Hospital Organization Kyushu Medical Center, National Hospital Organization Fukuoka Higashi Medical Center, Fukuoka Red Cross Hospital, St. Mary’s Hospital, Steel Memorial Yawata Hospital, and Japan Labour Health and Welfare Organization Kyushu Rosai Hospital.

The Steering Committee included Takao Ishitsuka, MD (Fukuoka Mirai Hospital), Setsuro Ibayashi, MD (Seia Rehabilitation Hospital), Kenji Kusuda, MD (Seia Rehabilitation Hospital), Kenichiro Fujii, MD (Japan Seafarers Relief Association Moji Ekisaikai Hospital), Tetsushiko Nagao, MD (Midrino Clinic), Yasushi Okada, MD (National Hospital Organization Kyushu Medical Center), Masa-hiro Yasaka, MD (National Hospital Organization Kyushu Medical Center), Hiroaki Ooboshi, MD (Fukuoka Dental Collage Medical and Dental Hospital), T. Kitazono, MD (Kyushu University), Katsumi Irie, MD (Hakujyuji Hospital), Tsuyoshi Omoe, MD (Imazu Red Cross Hospital), Kazunori Toyoda, MD (National Cerebral and Cardiovascular Center), Hiroshi Nakane, MD (National Hospital Organization Fukuoka-Higashi Medical Center), M. Kamouchi, MD (Kyushu University), Hiroshi Sugimori, MD (Saga-Ken Medical Centre Koseikkan), Shuji Arakawa, MD (Steel Memorial Yawata Hospital), Kenji Fukuda, MD (St. Mary’s Hospital), T. Ago, MD (Kyushu University), Iiro Kitayama, MD (Fukuoka Red Cross Hospital), Shigeru Fujimoto, MD (Ichi Medical University), Shoji Arihiro, MD (Japan Labor Health and Welfare Organization Kyushu Rosai Hospital), J. Kuroda, MD (Kyushu University), Y. Wakisaka, MD (Kyushu University), Yoshihisa Fukushima, MD (St. Mary’s Hospital), R. Matsuo, MD (Kyushu University).

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Pre-Stroke Dementia and Stroke Outcome