Clinicoradiological features of recurrent ischemic stroke: healthcare for poststroke patients

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Objective: Little is known about recurrent risk profile of brain infarct (BI) in Japan. The study aimed to clarify clinicoradiological features of recurrent BI patients.

Methods: 374 consecutive BI patients (231 men and 143 women) were admitted to our department between 2007 and 2008. Recurrent BI was defined as a prior history of BI. Cardiovascular disease (CVD) risk profile, stroke mechanism subtypes and Bamford subtypes were compared between the first BI and the recurrent BI group. CVD risk factors, stroke subtypes of the first BI and preventative medication were analyzed in recurrent BI patients.

Results: Recurrent BI existed in 72 patients (40 men and 32 women). Age of the recurrent BI group was significantly older than the first BI group (P<0.01). In comparison to the first BI group, the recurrent BI group had a high frequency of hypertension (P<0.01) and CVD comorbidity (P<0.05). Recurrent rates were increased significantly in cardioembolic patients as compared to the first BI patients (P<0.05). Bamford BI subtypes did not differ between both groups. Mean recurrent interval (SD) was 3.1 (2.3) years. Approximately half the patients experienced recurrent BI less than 2 years after the first BI. Antiplatelet agents were used in 33 patients and warfarin was used in 12 patients as preventative medication. The remaining 27 patients had no prevention therapy by self-cessation. Nine warfarin users were controlled poorly. There were no significant correlations between the first and recurrent Bamford subtypes in recurrent BI patients.

Conclusions: The present study indicated that the recurrent frequency of BI was 19.3%. Causative profile of recurrent BI suggested elderly age (≥65 years), hypertension, prior history of CVD, cardioembolism, 2 years poststroke, insufficient treatment of warfarin and self-cessation of preventative medication. Thus, physicians should pay more attention to these aspects for prophylaxis of recurrent BI in poststroke patients.

Keywords: brain infarct, recurrence, cardiovascular disease risk profile, secondary prevention

Introduction

Recurrent stroke is an important cerebrovascular event affecting the life of survivors of ischemic stroke.1 The second stroke event is an important predictor of functional outcomes as well as mortality after the first stroke.2,3 Together with therapeutic development of acute brain infarcts (BI), secondary prevention of BI is always required in patients with the first BI event. Many prospective studies of recurrent stroke have been reported previously in European and North American populations.1-10 Asian prospective studies suggested clinicoradiological hallmarks of recurrent BI.11-14 The present retrospective study aimed to elucidate cardiovascular disease (CVD) risk factors and neuroradiological features of recurrent BI in Japanese BI patients. We attempted
to confirm the importance of preventative healthcare for poststroke patients.

Methods
BI patients
390 consecutive patients (241 men and 149 women) were diagnosed as BI and admitted to our department between January 2007 and December 2008. Mean age (SD) was 69.6 (12.1) years [67.6 (12.5) in men and 73.0 (10.7) years in women]. We reviewed medical and neuroradiological records. All patients had acute BI within 1 week of clinical onset. BI patients who did not undergo magnetic resonance imaging (MRI) and angiography (MRA) were excluded from the present study. The present study was approved by ethical committee of Toho University Omori Medical Center.

Brain MRI and MRA
Brain MRI and MRA were performed by a 1.5-tesla superconducting system. Axial T1-weighted imaging, T2-weighted imaging, fluid-attenuated inversion imaging and diffusion-weighted imaging (DWI) were obtained. A slice/gap thickness of MRI was 6.0/0.5 mm and the matrix size was 224 \times 256 for all sequences. The number of acquisitions was 2. MRA was applied by 3-dimensional time-of-flight technique. A slice thickness was 0.6 mm and the matrix size was 256 \times 256 on MRA. Experienced neuroradiologists reviewed brain MRI and MRA. Acute BI lesions were defined as hyperintensity signal areas on DWI and the subsequent new hyperintensity signal areas on T2-weighted imaging.

Diagnosis and preventative medication of recurrent BI
Among the patients fulfilling the MRI definition mentioned above, recurrent BI was defined as obvious prior history of BI events. The interval between the first and the second BI was assessed. Use of antiplatelet and anticoagulant agents was analyzed in recurrent BI patients. International ratio (INR) of prothrombin time was evaluated in warfarin-treated patients.

CVD risk factors
CVD risk factors were analyzed on the following 7 items:
- obesity (body mass index \( \geq 25.0 \) kg/m\(^2\));
- current smoker;
- hypertension (systolic blood pressure \( \geq 140 \) mmHg or diastolic blood pressure \( \geq 90 \) mmHg) or currently under treatment;
- diabetes mellitus [(DM) fasting blood sugar \( \geq 126 \) mg/dL or hemoglobin A\(_1c\) \( \geq 6.5\%\)] or currently under treatment;
- dyslipidemia (serum low-density lipoprotein cholesterol \( \geq 140 \) mg/dL or high-density lipoprotein cholesterol \(< 40 \) mg/dL) or currently under treatment;
- chronic or paroxysmal atrial fibrillation (AF);
- prior history of CVD.

CVD was defined as ischemic heart diseases, including myocardial infarction and angina pectoris. CVD risk profile was compared between the first and the recurrent BI group.

Neuroradiological assessment
Stroke mechanism subtype was divided into lacunar infarct (LACI), cardioembolism, atherothrombosis and other. BI topography was classified to four categories according to Bamford subtypes.\(^1\) LACI; total anterior circulation infarct (TACI); partial anterior circulation infarct (PACI); posterior circulation infarct (POCI). Frequency of stroke mechanism subtype and Bamford subtypes was compared between the first and the recurrent BI group. In recurrent BI patients, stroke mechanism subtype and Bamford subtype of the first BI were analyzed by a medical history and MRI findings.

Statistical analysis
Statistical analyses of CVD risk factors and neuroradiological data used unpaired Student’s T-test, \( \chi^2 \) test and one-way analysis of variance. All significance levels were set at 0.05.

Results
Frequency of recurrent BI
Among 390 patients, 16 patients (10 men and 6 women) excluded, as brain MRI and MRA were not undergone. Recurrent BI existed in 72 patients (40 men and 32 women). Four patients (2 men and 2 women) had 3 BI events. Frequency of recurrent BI was 19.3%, 17.3% in men and 22.4% in women. There were no significant differences of sex between the first and recurrent BI patients (Table 1).

CVD risk profile of recurrent BI patients
Frequency of CVD risk factors is listed in Table 1. Mean age (SD) of the recurrent BI group was 74.5 (9.8) years [72.0 (9.8) in men and 77.7 (9.0) in women]. The age of the first BI group was 68.4 (12.3) years [64.7 (13.3) in men and 74.7 (6.9) in women]. The age of the recurrent BI group was significantly older than that of the first BI group (\( P < 0.01 \)). The frequency of elderly patients (\( \geq 65 \) years) was increased in the recurrent BI group, in comparison with the first BI group (\( P < 0.01 \)). In comparison to the
first BI group, hypertension rates were significantly higher in the recurrent BI group \( (P < 0.01) \). Frequency of prior CVD history was significantly increased in the recurrent BI group more than the first BI group \( (P < 0.05) \). Other CVD risk factors did not differ between the first and the recurrent BI group.

### Interval and preventative medicine of recurrent BI

Mean interval (SD) between the first and the recurrent BI was 3.1 (2.3) years. Approximately half the patients (52.8%) experienced recurrent BI within 2 years from previous BI. Of 72 recurrent patients, 33 patients received antiplatelet agents: 19 patients aspirin; 11 patients cilostazol; 3 patients clopidogrel. Warfarin was used in 12 patients. The remaining 27 patients had no preventative medication by self-cessation (Table 2). Chronic AF or prior history of CVD existed in 10 antiplatelet users and 12 warfarin users. Mean INR (SD) was 1.5 (0.3) and INR was less than 1.4 in 9 warfarin users. A total of 36 patients disclosed self-cessation of antiplatelet agents or uncontrolled warfarin medication.

### Stroke mechanism and Bamford subtypes of the first and recurrent BI

There were no significant differences in stroke mechanism and Bamford subtypes between the first and the recurrent BI group (Table 3). The first BI subtypes of recurrent patients are expressed in Table 2. The most common subtype of the first BI was cardioembolism on stroke mechanism and LACI on Bamford subtype. Recurrent rates were increased significantly in cardioembolic patients as compared to the first BI patients \( (P < 0.05) \). As compared to the first BI patients, significant differences of CVD profile were not found in recurrent cardioembolic patients and LACI patients.

### Discussion

Our retrospective study indicated that the frequency of recurrent BI was 19.3%, 17.3% in men and 22.4% in women. Approximately half of recurrent BI occurred within 2 years post-BI. Recurrent BI profiles revealed elderly patients, hypertension, prior history of CVD, cardioembolism, uncontrolled preventative medication.

Predictors of recurrent stroke have been reported previously in many prospective studies.\(^1\)\(^-\)\(^1^4\) The risk of a recurrent cerebrovascular event is highest in the first month and year after a stroke and transient ischemic attack (TIA). Approximate 12% of patients have a recurrent stroke within the first year.
Other clinical predictive factors of embolic BI recurrence in cardioembolic stroke patients exhibited alcohol abuse, hypertension, valvular heart disease and AF. Hypertension and DM were shown as significant factors of recurrent LACI in 733 consecutive patients with LACI. We also compared CVD risk factors in the first and the recurrent patients with cardioembolic infarct or LACI. There were no statistical differences of CVD profile in our recurrent cardioembolism or LACI patients. Besides CVD risk factors and stroke subtype, 27 recurrent patients stopped preventative therapy by themselves in the present study. Half the recurrent BI patients received no satisfactory prophylactic medication. Thus, physicians should give strict informed consent of preventative medication to BI patients.

**Conclusion**

The present study indicated that recurrent rates of BI were not uncommon in Japanese poststroke patients. Clinical hallmarks of recurrent BI patients suggested older age, hypertension, CVD events, cardioembolic infarct, recent 2 years post-BI, uncontrolled warfarin treatment and self-cession of medication. Thus, we emphasize that physicians should pay more attention to those high-risk aspects of recurrent BI.

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**Disclosure**

The authors report no conflicts of interest in this work.

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**Table 3** Stroke mechanism and Bamford subtypes of the first and recurrent BI group

| SM subtype          | First BI group (n = 302) | Recurrent BI group (n = 72) | All patients (n = 374) |
|---------------------|-------------------------|-----------------------------|-----------------------|
| LACI                | 107 (35.5%)             | 25 (34.7%)                  | 132 (35.3%)           |
| Cardioembolism      | 66 (21.9%)              | 23 (31.9%)                  | 89 (23.8%)            |
| Atherothrombosis    | 49 (16.1%)              | 9 (12.5%)                   | 58 (15.5%)            |
| Others              | 80 (26.5%)              | 15 (20.9%)                  | 95 (25.4%)            |
| BS                  |                         |                             |                       |
| LACI                | 107 (35.5%)             | 25 (34.7%)                  | 132 (35.3%)           |
| TACI                | 27 (8.9%)               | 4 (5.6%)                    | 31 (8.3%)             |
| PACI                | 93 (30.8%)              | 23 (31.9%)                  | 116 (31.0%)           |
| POCI                | 75 (24.8%)              | 20 (27.8%)                  | 95 (25.4%)            |

Abbreviations: BI, brain infarct; BS, Bamford subtype; LACI, lacunar infarct; TACI, total anterior circulation infarct; PACI, partial anterior circulation infarct; POCI, posterior circulation infarct; SM, stroke mechanism.
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