Background Factors and Clinical Symptoms of Major Depression With Silent Cerebral Infarction

Tokumi Fujikawa, MD; Shigeto Yamawaki, MD; Yoshikuni Touhouda, MD

Background and Purpose  We previously reported that major depression developing during or after the presenile period is frequently combined with silent cerebral infarction and that these patients have a high risk of stroke. Therefore, we investigated whether the background factors and clinical symptoms of patients with major depression with silent cerebral infarction (SCI+) differed from those in patients with major depression without silent cerebral infarction (SCI-) before medical treatment.

Methods  Patients with major depression with onset after 50 years of age were classified based on magnetic resonance imaging findings into the SCI+ (n=37) or SCI- (n=20) group. The diagnostic criteria for major depression were those of the American Psychiatry Association (DSM-III-R). Patients with stroke or focal neurological symptoms were excluded. The SCI+ group was subclassified according to whether the infarction area was perforating, cortical, or mixed artery. Family history of affective disorder, risk factors for stroke, and Zung’s Self-rated Depression Scale (SDS) score before medical treatment of the group were compared.

Results  The SCI+ group had a significantly lower (P<.05) frequency of family history of affective disorder but a significantly higher (P<.01) frequency of hypertension than did the SCI- group. The mean SDS score in the SCI+ group was significantly higher than that in the SCI- group (P<.01). The mean SDS score of the mixed artery infarction group was higher than that of the perforating artery infarction group (P<.05).

Conclusions  Patients with major depression with silent cerebral infarction present more marked neurological factors and more severe depressive symptoms than do those without silent cerebral infarction. Because these features were more prominent in the patients with mixed artery infarction with broad obstructions, we consider that the area of brain damage caused by cerebral infarction is positively related to the severity of depressive symptoms. (Stroke. 1994;25:798-801.)

Key Words  ● cerebral infarction ● depression ● hypertension ● magnetic resonance imaging

A symptomatic or silent cerebral infarction (SCI) is that detected by magnetic resonance imaging (MRI) or other imaging modalities in a patient who demonstrates no localized neurological symptoms or stroke. Patients with SCI, which is classified as a cerebrovascular disorder type III by the National Institute of Neurological Disorders and Stroke,1 may be at increased risk of subsequent overt stroke, and SCI may represent a prodromal stage before the development of overt stroke.

We previously studied the incidence of SCI detected by MRI in patients with presenile or senile major depression.2 Our findings suggested that organic depression related to SCI is present in approximately half of those with presenile-onset major depression and the majority of those with senile-onset major depression. Major depression with SCI may be a warning sign of cerebrovascular disease because it is associated with a high risk of subsequent symptomatic ischemic stroke. Therefore, we suspected that the background factors (heredity and risk factors for stroke) and clinical symptoms before medical treatment in patients with major depression with SCI differ from those in patients without SCI.

In this study we classified patients with major depression aged older than 50 years according to MRI findings as those with and without SCI. Differences between these groups in regard to family history of affective disorder, history of hypertension, diabetes mellitus, and hyperlipidemia; and depression scale score before medical treatment were investigated.

Subjects and Methods  The subjects were prospectively selected at their initial consultation for major depression at either the Department of Neurology and Psychiatry at Hiroshima Prefectural Hospital or the Department of Psychiatry and Neurosciences at Hiroshima University School of Medicine between April 1992 and March 1993. All patients completed Zung’s Self-rated Depression Scale (SDS)3 at the initial consultation. All patients were diagnosed with major depression according to Diagnostic and Statistical Manual of Mental Disorders, edition 3, revised (DSM-III-R) criteria,4 and all were aged older than 50 years. Patients with alcoholism, cerebral degenerative disease, dementia, or systemic disease that could induce a depressive state were excluded, as were patients who had previously been treated with psychotropic drugs, including tricyclic antidepressants. All patients underwent MRI within 3 months after the first consultation. All patients received a neurological examination on the same day as the MRI study, and those with evidence of stroke or focal neurological symptoms were ex-
The risk factors for symptomatic cerebral infarction include hypertension, diabetes mellitus, hyperlipidemia, and atrial fibrillation. Various studies have been conducted to determine whether the risk factors for SCI are the same as those for symptomatic cerebral infarction. A Dutch transient ischemic attack study\(^8\) revealed that patients with SCI have a high incidence of advanced age, hypertension, or smoking. Subsequently, in a study of brain screening subjects who had no history of cerebral disease and who were socially active and neuropsychologically normal, Kobayashi et al\(^9\) found that a history of hypertension was observed significantly more often in patients with SCI compared with those without SCI.

**Table 1. Background Factors in Patients With Major Depression With and Without Silent Cerebral Infarction**

<table>
<thead>
<tr>
<th>Factor</th>
<th>SCI(-) Group</th>
<th>All Types</th>
<th>Perforating Type</th>
<th>Cortical Type</th>
<th>Mixed Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family history of affective disorder</td>
<td>7/20 (35.0%)</td>
<td>3/37 (8.1)(^\dagger)</td>
<td>2/19 (10.5)</td>
<td>0/6 (0.0)</td>
<td>1/12 (8.3)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1/20 (5.0)</td>
<td>15/37 (40.5(^*))</td>
<td>7/19 (36.8)</td>
<td>1/6 (16.6)</td>
<td>7/12 (58.3)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1/20 (5.0)</td>
<td>1/37 (2.7)</td>
<td>1/19 (5.3)</td>
<td>0/6 (0.0)</td>
<td>0/12 (0.0)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>3/20 (15.0)</td>
<td>5/37 (13.5)</td>
<td>1/19 (5.3)</td>
<td>0/6 (0.0)</td>
<td>4/12 (33.3)</td>
</tr>
</tbody>
</table>

SCI(-) indicates patients with major depression without silent cerebral infarction (SCI); SCI(+), patients with major depression with SCI. Values in parentheses are percentages.

\(^*P<.01, \dagger P<.05\) compared with SCI(-) group.

Magnetic Resonance Imaging Findings

Magnetic resonance imaging was performed in 43 patients using a 0.5-T apparatus (Picker Co) at Hiroshima Prefectural Hospital and in 14 patients using a 1.5-T apparatus (General Electric Co) at Hiroshima University School of Medicine. \(T_1\)-weighted images (repetition time [TR], 2000 milliseconds; echo time [TE], 100 milliseconds) were obtained in the transverse plane parallel to the orbitomeatal line, and \(T_2\)-weighted images (inversion-recovery; TR, 2000 milliseconds; TE, 100 milliseconds) were obtained as coronal slices at 10-mm intervals.

Infarcts were defined as high-intensity lesions greater than 5 mm on \(T_2\)-weighted images that coincided with low-intensity lesions on \(T_1\)-weighted images. To avoid overdiagnosis of SCI, the following diagnostic criteria were adopted: lesions ranging from 5 to 20 mm were defined as small infarcts, and lesions greater than 20 mm were classified as large infarcts. Although detected lesions less than 5 mm may also be small infarcts, these were excluded from analysis because they are difficult to distinguish from état crible.\(^a\) Regarding the number of small infarcts that can be interpreted as indicating SCI, Shimada et al\(^a\) have reported that the mean number of small infarcts in hypertensive asymptomatic elderly subjects was 2.8±4.6, whereas that in normotensive elderly subjects was 1.1±1.5. Matsubayashi et al\(^a\) have studied the relation between small infarcts and cognitive function in normal elderly subjects and reported that four or more small infarcts are associated with the development of cognitive impairment. In the present study SCI was defined as the presence of four or more small infarcts in the same cerebral hemisphere or one or more large infarcts. Patients with fewer than four small infarcts and no large infarct were classified as not having SCI. Parietal hyperintensity was not assessed.

For statistical analysis, mean±SD values of parametric data were calculated, and Student's t test was used to compare groups. The \(\chi^2\) test was used for comparison of nonparametric numerical data in the two groups.
Hougaku et al\textsuperscript{10} found that in patients with SCI the rate of complications was significantly higher in those with essential hypertension; they reported a strong causative relation of hypertension to perforating artery infarction. Lechner et al\textsuperscript{11} found that the number of risk factors for cerebral infarction, such as hypertension or diabetes mellitus, was positively associated with the rate of complication after SCI. They also reported that abnormal MRI findings were recognized in all of their patients with three or more simultaneous risk factors.

In the present study of patients with major depression with onset after 50 years of age with and without SCI, hypertension was found to be more frequent in those with SCI, but no difference between the two groups was recognized in the incidence of diabetes mellitus or hyperlipidemia. Thus, we conclude that among patients with major depression, hypertension is more common in those with SCI.

The difference between the two groups in the rate of family history of affective disorder indicates that patients with major depression without SCI frequently have a family history of affective disorder but have fewer risk factors for cerebral infarction. Endogenous factors may be especially important in this group. In contrast, in patients with major depression with SCI, neurological factors may be more important. A subgroup of patients with depression of presenile or senile onset may manifest a sequence of events, ie, hypertension as a risk factor that causes either perforating artery infarction or mixed artery infarction and eventually leads to major depression. Post\textsuperscript{12} and Murphy\textsuperscript{13} described a group of patients with senile depression with poor long-term prognosis. Mendlewicz\textsuperscript{14} reported that as the age at the onset of depression increases, the incidence of hereditary involvement decreases. We therefore suspect that when SCI is present in patients with presenile and senile major depression, the role of neurological factors is increased while that of heredity is decreased, and that such patients have poor long-term prognosis because of cerebrovascular impairment.

### Clinical Symptoms of Major Depression With Silent Cerebral Infarction

Robinson et al\textsuperscript{15-18} reported that the severity of poststroke depression was significantly increased in patients with left anterior lesions. In a comparative study of poststroke depression and endogenous depression using the Present State Examination (PSE), Lipsey et al\textsuperscript{19} found that the symptomatic profiles of the two types of depression were similar, and there was no difference between the two groups in Hamilton depression scores. However, patients with poststroke depression showed significantly lower PSE scores. In the present study the SDS score of the patients with major depression with SCI was significantly higher than that of those without SCI. In a recent study of the relation between subjective symptoms and MRI findings in 124 normal adults, Kobayashi et al\textsuperscript{20} found that the incidence of SCI and the SDS score in subjects who showed forgetfulness with decreased motivation and concentration were significantly higher than those in subjects who did not. Of our patients with major depression with SCI, those with mixed artery infarction showed significantly higher SDS scores than did those with perforating artery infarction. These results indicate that depression is more severe in patients with mixed artery infarction, and we consider this finding to be due to the larger area of brain damage caused by cerebral infarction.

### Acknowledgments

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### References


#### Table 2. Zung's Self-rated Depression Scale Score in Patients With Major Depression With and Without Silent Cerebral Infarction

<table>
<thead>
<tr>
<th>Type</th>
<th>SCI(-) Group (n=20)</th>
<th>All Types (n=37)</th>
<th>Perforating Type (n=19)</th>
<th>Cortical Type (n=6)</th>
<th>Mixed Type (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>61.4±5.8</td>
<td>67.5±7.9*</td>
<td>70.0±7.5</td>
<td>63.8±11.0</td>
<td>65.5±4.7</td>
</tr>
<tr>
<td>SDS score</td>
<td>52.6±9.1</td>
<td>58.6±7.0*</td>
<td>56.4±6.3</td>
<td>59.3±7.3</td>
<td>62.3±6.2†</td>
</tr>
</tbody>
</table>

SCI(-) indicates patients with major depression without silent cerebral infarction (SCI); SCI(+), patients with major depression with SCI; and SDS, Zung's Self-rated Depression Scale. Values are mean±SD.

*P<.01 compared with SCI(-) group.
†P<.05 compared with perforating type.


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