Incidence of Silent Cerebral Infarction in Patients With Major Depression

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

Background and Purpose: There have been few studies of the incidence of silent cerebral infarction detected by magnetic resonance imaging in patients with presenile or senile major depression.

Methods: We examined silent cerebral infarction in patients with presenile and senile major depression who were diagnosed at Hiroshima Prefectural Hospital. The diagnostic criteria of the American Psychiatric Association (DSM-III-R) were used. Patients with stroke or focal neurological symptoms were excluded.

Results: Silent cerebral infarction was observed in 51.4% of the patients with presenile-onset presenile depression, and the incidence was significantly higher than in patients with juvenile-onset presenile depression (P<0.01). Among the patients with senile major depression, silent cerebral infarction was observed in 65.9% of those with presenile-onset depression and in 93.7% of those with senile-onset depression.

Conclusions: Our findings suggest that half of presenile-onset major depression and the majority of senile-onset major depression might be organic depression related to silent cerebral infarction. Because major depression occurring for the first time during or after the presenile period may be related to silent cerebral infarction, it is important to keep this possibility in mind when treating such patients. (Stroke. 1993;24:1631-1634.)

KEY WORDS • cerebral infarction • depression • lacunar infarction • magnetic resonance imaging

In recent years, various asymptomatic cerebrovascular lesions have been discovered by magnetic resonance imaging (MRI). When cerebral infarction detected by MRI or other imaging modalities has no associated clinical symptoms, it is referred to as asymptomatic or silent cerebral infarction (SCI), and such infarcts fit into class III of the cerebrovascular disorders classification published by the National Institute of Neurological Disorders and Stroke. However, whether asymptomatic cerebral infarction is truly asymptomatic remains unclear. Although localizing neurological symptoms are not observed in these patients, the possibility of subjective or psychiatric symptoms related to the infarct needs to be considered. Because the term “asymptomatic” may be incorrect, such infarcts have more often been designated as SCI in recent years.

Sørensen et al studied the prognosis of patients with reversible ischemic attacks (ie, cerebral ischemia that recovers completely within 3 days). They reported a significant decrease in the quality of life and working capacity of patients after a single reversible ischemic attack, even though overt neurological symptoms such as paralysis did not occur. The psychological diagnosis and treatment of these patients may be important, because the disturbance of mental and social functioning may occur in such cases.

Depression is a very common disease in the psychiatric field. The prevalence of a depressive state according to Zung’s self-rating depression scale is 14.7% to 44% in the elderly population, and the prevalence of major depression according to the diagnostic criteria of the American Psychiatric Association (Diagnostic and Statistical Manual of Mental Disorders, edition 3, revised [DSM-III-R]) is 0.1% to 3.7%. In this study, we used MRI to examine the incidence of SCI in patients with presenile and senile major depression.

Subjects and Methods

The subjects were patients aged older than 50 years with major depression who were diagnosed at the Department of Neurology and Psychiatry of Hiroshima Prefectural Hospital from January 1988 to October 1992. All patients underwent MRI within 3 months after a diagnosis of major depression, which was made according to DSM-III-R criteria. All patients and their family members underwent detailed questioning about previous episodes of mood disorder. All patients received a neurological examination on the same day as the MRI study, and patients with evidence of stroke or focal neurological symptoms were excluded from the study. Informed consent was obtained from all the subjects according to institutional guidelines. Patients with alcoholism, cerebral degenerative disease or dementia, systemic disease that could induce a depressive
state, or a diagnosis of schizophrenia or atypical psychosis were also excluded.

The patients were divided into the following groups, and the incidence of SCI on MRI was compared among them: (1) JP group (juvenile-onset presenile depression); patients who developed major depression at younger than 50 years of age and were aged 50 to 65 years at the time of MRI; (2) PP group (presenile-onset presenile depression); patients who developed major depression after 50 years of age and were aged 50 to 65 years at the time of MRI; (3) PS group (presenile-onset senile depression); patients who developed major depression from 50 to 65 years of age and were older than 65 years at the time of MRI; and (4) SS group (senile-onset senile depression); patients who developed major depression after 65 years of age. Two patients who developed major depression before 50 years of age and who were older than 65 years at the time of MRI were excluded from this study.

Magnetic resonance imaging was performed using a 0.5-T apparatus (Picker Co.). T1-weighted images (repetition time [TR], 2000 milliseconds; echo time [TE], 100 milliseconds) were obtained in the transverse plane parallel to the orbitomeatal line, and T2-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 in size on T1-weighted images that coincided with low-intensity lesions on T1-weighted images. To avoid the overdiagnosis of SCI, the following strict diagnostic criteria were adopted. Lesions ranging from 5 mm to 20 mm in size were defined as lacunar infarcts, and lesions greater than 20 mm in size were classified as large infarcts. Lacunar infarction was also suspected to be present when lesions smaller than 5 mm were detected, but these were excluded from analysis because they were difficult to distinguish from état crible. Patients with four or more lacunar infarcts in a cerebral hemisphere or with one or more large infarcts were defined as having SCI. We did not assess periventricular hyperintensity to avoid the overdiagnosis of cerebral infarction.

For statistical analysis, mean±SD values of parametric data were calculated, and Student’s t test was used for comparing groups. The χ² test was used for comparing nonparametric numerical data between groups.

**Results**

A total of 205 patients (70 men and 135 women) were studied, and their mean age was 63.8±7.7 years. There were 31 patients in the JP group, 70 in the PP group, 41 in the PS group, and 63 in the SS group.

**Silent Cerebral Infarction in Presenile Major Depression**

Thirty-one patients (12 men and 19 women) in the JP group and 70 patients (25 men and 45 women) in the PP group were assessed. Their mean ages were 56.7±3.6 and 58.2±3.6 years, respectively, and there was no significant difference in the sex or age distribution of both groups. SCI was observed in 7 of the 31 JP patients (22.6%) and in 36 of the 70 PP patients (51.4%) (P<.01) (Table 1).

<table>
<thead>
<tr>
<th>Group</th>
<th>n (M/F)</th>
<th>Age, y</th>
<th>No. With SCI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>JP</td>
<td>31 (12/19)</td>
<td>56.7±3.6</td>
<td>7/31 (22.6)</td>
</tr>
<tr>
<td>PP</td>
<td>70 (25/45)</td>
<td>58.2±3.6</td>
<td>36/70 (51.4)*</td>
</tr>
</tbody>
</table>

M indicates male; F, female; SCI, silent cerebral infarction; JP, juvenile-onset presenile depression; and PP, presenile-onset presenile depression. *P<.01 by χ² test.

**Silent Cerebral Infarction in Senile Major Depression**

Forty-one patients (11 men and 30 women) in the PS group and 63 patients (22 men and 41 women) in the SS group were assessed. Their mean ages were 67.6±2.4 and 72.8±5.3 years, respectively (P<.01), but no significant difference in sex distribution was observed between the two groups. SCI was noted in 27 of the 41 PS patients (65.9%) and in 59 of the 63 SS patients (93.7%) (P<.01) (Table 2).

Silent cerebral infarction was found in 129 patients overall, including 105 with lacunar infarcts and 24 with large infarcts. There was no significant difference in the relative frequency of lacunar infarcts versus large infarcts in the JP, PP, PS, and SS groups.

**Discussion**

In recent years, apparently asymptomatic lesions in the deep white matter have been frequently discovered by MRI, and the relation between such lesions and psychosis has attracted attention.

In 1988, Krishnan et al⁹ reported that detection of deep white matter lesions by MRI was more common in patients with senile depression than in control subjects of the same age. Subsequently, Coffey et al¹⁰ compared the MRI findings in patients with depression aged older than 60 years and a control group matched for age and sex. They reported moderate or more severe periventricular hyperintensity in 57%, lesions in the thalamus and basal ganglia in 40%, and moderate or more severe deep white matter lesions in 46% of the patients with major depression, and found that these rates were significantly higher than in the control group. However, the age of onset of depression was not assessed in their study.

Subsequently, Figiel et al¹¹ compared 19 patients with late-onset depression (onset after the age of 60 years) and nine patients with early-onset depression and reported basal ganglia lesions in 60% and 11%, respectively, while no difference was observed with respect to deep white matter lesions. However, Brown et al¹² demonstrated deep white matter lesions in 30% of

<table>
<thead>
<tr>
<th>Group</th>
<th>n (M/F)</th>
<th>Age, y</th>
<th>No. With SCI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PS</td>
<td>41 (11/30)</td>
<td>67.6±2.4</td>
<td>27/41 (65.9)</td>
</tr>
<tr>
<td>SS</td>
<td>63 (22/41)</td>
<td>72.8±5.3*</td>
<td>59/63 (93.7)*</td>
</tr>
</tbody>
</table>

M indicates male; F, female; SCI, silent cerebral infarction; PS, presenile-onset senile depression; and SS, senile-onset senile depression. *P<.01 by Student’s t test. †P<.01 by χ² test.
Risk factors (Hypertension, DM, etc.)

Silent cerebral infarction

 Stroke

Neurological symptoms (Paralysis, etc.)

Age

[Psychiatric symptoms] Major depression (Pre-stroke depression) Major depression (Post-stroke depression) Dementia

Schematic illustrates possible relation between cerebral infarction and psychiatric symptoms. DM indicates diabetes mellitus.

patients with major depression aged older than 45 years using MRI and noted that such lesions were more common in patients with major depression than in schizophrenic patients or control subjects of the same age group.

However, thus far standard criteria for the detection of infarcts on MRI have not been determined. Lesions showing a low intensity on T1-weighted images and a high intensity on T2-weighted images include both état criblé and cerebral infarction. Braffmann et al.\textsuperscript{13} and Heier et al.\textsuperscript{14} have reported that état criblé lesions are less than 5 mm in size; in contrast, cerebral infarcts were diagnosed as lesions greater than 5 mm in size in this study. Regarding the number of lacunes that can be interpreted as significant, Shimada et al.\textsuperscript{15} have reported that hypertensive healthy elderly individuals have 2.8±4.6 lacunes, whereas normotensive individuals have 1.1±1.5 lacunes. In this study, the presence of four or more lacunar infarcts per hemisphere was defined as indicating SCI to avoid overdiagnosis. Thus, the diagnostic criteria for SCI were stricter than in previous studies. This study also differed from previous ones in the following respects: (1) patients with a history of cerebrovascular disease and neurological findings were excluded, (2) patients with état criblé were excluded, and (3) the subjects were stratified by the onset of depression.

Kobayashi et al.\textsuperscript{16} have reported that SCI was found in 17% of healthy individuals in their 50s and 21% of those in their 60s. In our study, SCI was observed in more than half of the patients with presenile-onset major depression and in the majority of patients with senile-onset major depression. In addition, SCI was significantly more common in our depressive patients than in the healthy subjects assessed by Kobayashi et al.\textsuperscript{16} Therefore, it may be suggested that approximately half of presenile-onset major depression and most of senile-onset major depression is actually organic depression related to SCI.

Kase et al.\textsuperscript{17} and Chodosh et al.\textsuperscript{18} reported computed tomographic evidence of prior asymptomatic cerebral infarction in 10% to 11% of patients presenting with an initial stroke. Thus, there may be an increased risk of eventual overt stroke in patients with SCI, and SCI may represent a prodromal stage before the development of full-blown stroke.

It is well known that depression can occur after a stroke, and several reports have been published on the rate of depression after stroke and on the relation between infarct site and depressive state.\textsuperscript{19,20} Disturbance of mental and social functioning in patients with SCI has long been noted,\textsuperscript{2} and the present study showed that major depression is often associated with SCI (Figure). Therefore, the possibility that the illness represents a warning sign of cerebrovascular disease should always be kept in mind in patients with presenile or senile major depression. Major depression associated with SCI could be tentatively designated as prestroke depression because it is associated with a higher risk of future symptomatic ischemic stroke. Institution of treatment such as antiplatelet therapy for such prestroke depression may be important for the prevention of further cerebrovascular impairment.

Acknowledgment

The authors are grateful to Dr Shotai Kobayashi, the Third Department of Internal Medicine, Shimane Medical University, for reviewing the manuscript and making constructive comments.
References


Incidence of silent cerebral infarction in patients with major depression.

T Fujikawa, S Yamawaki and Y Touhouda

Stroke. 1993;24:1631-1634
doi: 10.1161/01.STR.24.11.1631

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/24/11/1631

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org/subscriptions/