Frontal Infarcts and Anxiety in Stroke

Wai Kwong Tang, MD; Yangkun Chen, PhD; Jinyan Lu, MPhil; Huajun Liang, MPhil; Winnie Chiu Wing Chu, MD; Vincent Chung Tong Mok, MD; Gabor Sandor Ungvari, MD; Ka Sing Wong, MD

Background and Purpose—This study examined the association between poststroke anxiety symptoms (PSA) and frontal lobe infarcts.

Methods—A cohort of 693 patients was recruited. PSA was defined as an anxiety subscale of the Hospital Anxiety and Depression Scale score of 8 or above. The presence and location of infarcts were evaluated with MRI.

Results—Compared with the non-PSA group, PSA patients were more likely to have right frontal acute infarcts. Right frontal infarcts remained independent predictors of PSA in the multivariate analysis, with an odds ratio of 4.44 (P=0.002).

Conclusions—The results suggest that right frontal acute infarcts may play a role in the development of PSA. (Stroke. 2012;43:1426-1428.)

Key Words: anxiety ■ acute stroke ■ ischemia ■ frontal lobe ■ infarcts

The prevalence of poststroke anxiety (PSA) ranges from 3–28%.1 The neuroanatomical model of PSA remains unclear. Some studies have suggested that PSA is related to right-side lesions2 and cortical lesions.3 The common methodological problems of these studies include small sample size, the use of computerized tomography (CT) instead of MRI scans, and lack of detailed assessment of lesion locations.3,4

In patients with traumatic brain injury, postinjury anxiety disorder has been significantly associated with lesions of the frontal lobe.5 We could not locate any reports on the association between frontal infarcts and PSA. Hence, the aim of this study was to determine the relationship between frontal infarcts and PSA in acute ischemic stroke survivors.

Methods

A total of 4457 patients with first-ever or recurrent acute ischemic stroke were admitted to the Acute Stroke Unit at the Prince of Wales Hospital between October 2004 and October 2009. Of the 4457 patients, 2251 received MRI scans. All scanned patients were screened for the inclusion and exclusion criteria shown in the Figure. The study protocol was approved by the Clinical Research Ethics Committee of the Chinese University of Hong Kong. All participants signed a consent form at 3 months after stroke.

A research nurse collected the demographic and clinical data and assessed stroke severity, using the National Institute of Health Stroke Scale (NIHSS) within 2 days of admission; these data were stored in a stroke registry. A research assistant assessed all subjects’ handedness and administered the Mini-Mental State Examination (MMSE) and the 15-item Geriatric Depression Scale (GDS)6 3 months after the onset of the index stroke. GDS scores were treated as continuous variables.

Three months after the onset of the index stroke, the participants attended a research clinic where a research assistant who was blinded to the subjects’ radiological data administered the anxiety subscale of the Hospital Anxiety and Depression Scale (HADSA).7 PSA was defined as the presence of clinically significant anxiety symptoms indicated by a HADSA score of 8 or above.8

MRI was performed with a 1.5-T system within 7 days of admission. A neurologist (Y.K.C.) who was blinded to the PSA status of the participants assessed all of the MRIs. Details of the MRI examination have been described elsewhere.9

The demographic and clinical variables and radiological characteristics of the PSA subjects (PSA group) were compared with those without PSA (non-PSA group). Associative regression models were subsequently constructed. Risk factors with a value of P<0.05 were then analyzed by multivariate logistic regression analysis using a forward stepwise selection strategy. Correlations between the characteristics of the frontal lobe infarcts were examined by Spearman ρ. If the correlations between these characteristics were ≥0.50, then only 1 of them would be entered into the regression model to avoid collinearity. The level of significance was set at 0.05.

Results

A total of 693 patients met the entry criteria and formed the study sample (Figure). Patients who were excluded from the study were more likely to be female (49.6% versus 39.0%; P<0.001) and had a higher mean age (70.3±11.0 years; P<0.001) and NIHSS score (7.8±8.3 versus 4.2±3.3; P<0.001).

The demographic and MRI characteristics and stroke-related data are shown in Table 1. The proportion of patients with right frontal acute infarcts was significantly higher in the PSA group. The PSA group also had a higher number and volume of right frontal infarcts. The correlations between the frontal infarct variable ranged from 0.651–0.999 (P<0.001), and only the presence of right frontal acute infarcts was selected in the
Table 1. Demographic Characteristics, Psychosocial Risk Factors, Stroke Severity, and Radiological Characteristics by PSA Status

<table>
<thead>
<tr>
<th></th>
<th>PSA (n=42)</th>
<th>Non-PSA (n=651)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>62.8±9.4</td>
<td>65.8±11.1</td>
<td>0.088</td>
</tr>
<tr>
<td>Female sex</td>
<td>26 (61.9%)</td>
<td>244 (37.5%)</td>
<td>0.002†</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>9 (21.4%)</td>
<td>29 (19.2%)</td>
<td>0.405†</td>
</tr>
<tr>
<td>NIHSS total score</td>
<td>4.4±2.7</td>
<td>4.2±3.4</td>
<td>0.386‡</td>
</tr>
<tr>
<td>GDS score</td>
<td>9.7±3.7</td>
<td>4.6±3.4</td>
<td>&lt;0.001‡</td>
</tr>
<tr>
<td>Handedness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>38 (90.5%)</td>
<td>592 (90.9%)</td>
<td>0.920†</td>
</tr>
<tr>
<td>Left</td>
<td>1 (2.4%)</td>
<td>21 (3.2%)</td>
<td></td>
</tr>
<tr>
<td>Missing data</td>
<td>3 (7.1%)</td>
<td>38 (5.9%)</td>
<td></td>
</tr>
<tr>
<td>No. of acute infarcts</td>
<td>1.6±2.2</td>
<td>1.3±1.9</td>
<td>0.336‡</td>
</tr>
<tr>
<td>Volume of acute infarcts</td>
<td>4.5±8.5</td>
<td>3.1±9.2</td>
<td>0.106‡</td>
</tr>
<tr>
<td>Presence of acute infarcts in</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frontal</td>
<td>9 (21.4%)</td>
<td>56 (8.6%)</td>
<td>0.012§</td>
</tr>
<tr>
<td>Right frontal</td>
<td>9 (21.4%)</td>
<td>41 (6.3%)</td>
<td>0.002§</td>
</tr>
<tr>
<td>Left frontal</td>
<td>0 (0.0%)</td>
<td>15 (2.3%)</td>
<td>1.000§</td>
</tr>
<tr>
<td>Temporal</td>
<td>2 (4.7%)</td>
<td>27 (4.1%)</td>
<td>0.693§</td>
</tr>
<tr>
<td>Parietal</td>
<td>0 (0.0%)</td>
<td>46 (7.1%)</td>
<td>0.103§</td>
</tr>
<tr>
<td>Occipital</td>
<td>3 (7.1%)</td>
<td>12 (2.0%)</td>
<td>0.067§</td>
</tr>
<tr>
<td>No. of acute frontal infarcts</td>
<td>0.4±1.1</td>
<td>0.1±0.4</td>
<td>0.005§</td>
</tr>
<tr>
<td>Volume of acute frontal infarcts, mL</td>
<td>1.1±4.0</td>
<td>0.3±2.4</td>
<td>0.010§</td>
</tr>
<tr>
<td>No. of acute right frontal infarcts</td>
<td>0.4±1.1</td>
<td>0.1±0.4</td>
<td>&lt;0.001‡</td>
</tr>
<tr>
<td>Volume of acute right frontal infarcts, mL</td>
<td>1.0±4.0</td>
<td>0.3±2.4</td>
<td>&lt;0.001‡</td>
</tr>
</tbody>
</table>

PSA indicates poststroke anxiety; NIHSS, National Institute of Health Stroke Scale; GDS, Geriatric Depression Scale.

*Student t test.
†χ² test.
‡Mann-Whitney U test.
§Fisher exact test.
regression models. The following 4 variables were entered in regression model A: age, sex, GDS score, and the presence of right frontal acute infarcts; 78.6% of the PSA group had a GDS score >7. The presence of right frontal acute infarcts was a significant independent imaging predictor of PSA, with an odds ratio of 3.87 (Table 2). The regression model (model B) was repeated for the right-handed patients; the presence of right frontal acute infarcts remained a significant predictor (odds ratio=4.44).

**Discussion**

To the best of our knowledge, this is the first report of an association between frontal infarcts and risk of PSA. The main strength of the study is the large sample size and the detailed MRI data. The results suggest that right frontal infarcts are associated with an increased risk of anxiety in patients with well-established ischemic stroke.

No previous study has examined the role of frontal infarcts in PSA in detail. There is evidence supporting the role of the right frontal lobe in anxiety disorders in nonstroke cohorts. Right frontal lobe abnormalities have been documented by neuroimaging studies. Voxel-based morphometry studies have identified reduced gray matter volume in the right orbito-frontal cortex and right inferior frontal gyrus in patients with panic disorder.10

The main limitation of this study is that the assessment of PSA was made only once, at the 3-month follow-up. Patients who could not give consent because of dementia or aphasia-associated left-side infarcts were also excluded. This selection bias may limit the generalizability of the findings. Furthermore, PSA was defined by the HADSA, and, although high HADSA scores indicated clinically significant anxiety symptoms, a formal diagnosis should have ideally been made by using a standardized psychiatric interview. Most PSA patients may also have depression; thus, the location of lesions may be different from patients with PSA only.11

In conclusion, the results indicate that right frontal infarcts are associated with a higher risk of PSA and may contribute to its pathogenesis.

**Disclosures**

None.

**References**

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