Headache at Stroke Onset in 2196 Patients With Ischemic Stroke or Transient Ischemic Attack

Susanne Tentschert, MD; Romana Wimmer, MD; Stefan Greisenegger, MD; Wilfried Lang, MD; Wolfgang Lalouschek, MD

Background and Purpose—Headache is a common symptom in acute ischemic and hemorrhagic stroke, but many aspects of its association with other clinical factors are controversial.

Methods—We analyzed characteristics of headache symptoms at stroke onset and associations between headache at stroke onset and at several clinical parameters in 2196 patients experiencing ischemic stroke or transient ischemic attack within a multicenter hospital-based stroke registry.

Results—Five hundred eighty-eight (27%) patients experienced headache at stroke onset. In a multivariate analysis, headache at stroke onset was positively associated with female sex, history of migraine, younger age, cerebellar stroke (but not with other brain stem locations), and blood pressure values on admission <120 mm Hg systolic and <70 mm Hg diastolic. It showed no significant association with stroke severity measured by the modified Rankin Scale at days 5 to 7 after the event, presumed etiology, or time of day.

Conclusions—Our results, derived from a large number of systematically documented patients with acute ischemic cerebrovascular events, show no association of headache with stroke etiology or outcome. Our results indicate that the previously described association of headache with vertebrobasilar stroke is mainly because of its association with cerebellar stroke. We could confirm previously described associations of headache at stroke onset with younger age and a history of migraine, implicating a careful evaluation of young patients with a focal neurological deficit and a history of migraine to avoid misclassification as “complicated migraine.” (Stroke. 2005;36:e1-e3.)

Key Words: headache ■ stroke, ischemic ■ stroke onset

Headache is a common symptom in acute ischemic and hemorrhagic stroke, but many aspects of its association with clinical parameters have been controversial in previous studies. The reported frequency of stroke-related headache ranges from 7% to 65%.1–4 Previous studies provide differing results as to whether lateralized headache is related to the side of the lesion, whether headache frequency is different in anterior versus posterior lesion localization, whether it is more common in women than in men or whether headache in stroke is related to several factors, such as blood pressure (BP), history of hypertension, or history of migraine.5–8

This study sought to investigate headache characteristics and associations with clinical factors in acute ischemic stroke in a large cohort of systematically documented patients.

Materials and Methods

This study was nested in a prospective hospital-based stroke registry of patients admitted to 8 neurological departments in Vienna, Austria (Vienna Stroke Registry), serving a community of 1.9 million.9,10 The study has been approved by the local ethic committees and started in October 1998. All patients with transient ischemic attack (TIA)/stroke who were admitted to 1 of the participating centers between October 1998 and December 2001 were prospectively documented, on the basis of informed consent, with respect to clinical and neurological parameters (National Institutes of Health Stroke Scale, Scandinavian Stroke Scale, modified Rankin Scale, and Barthel Index), results of technical investigations, and presumed etiology (large vessel disease: ipsilateral carotid stenosis ≥70%, presumable local thrombosis of a large intracranial vessel, or arterioarterial embolism from aortic plaques/thrombi; small vessel disease: clinical lacunar syndrome and no lesion or subcortical lesion <1 cm in diameter and no identified source of embolism; cardioembolic: high-risk source of embolism; no determined etiology). Risk factors and medical history with special reference to myocardial infarction, peripheral artery disease, diabetes mellitus, hypertension, current smoking, and a history of migraine were assessed by a structured personal interview applied by a specially trained physician.

Patients were also asked about the presence and localization of headache at symptom onset and to describe the quality of headache according to predefined categories: dull, pressing, stabbing, burning, pulsatile, or circular.

For this cohort study, data of all patients with acute ischemic stroke or TIA whose available clinical data had been entered into the database at the time of analysis were investigated. At that time 3621 patients had been admitted because of suspected ischemic or hemorrhagic stroke. In 680 patients, the final diagnosis was nonvascular...
and 281 patients experienced intracerebral hemorrhage. From the remaining 2661 patients, those in whom no detailed information about presumed etiology, exact lesion localization, or headache at stroke onset could be obtained were also excluded (n=465). Thus 2196 patients were available for the present analysis.

**Statistical Methods**

Statistical analyses were carried out using SPSS 10.0. Univariate comparisons of continuous variables were performed with the unpaired t test or with the Mann–Whitney U test, as appropriate. Binary and categorical data were analyzed using $\chi^2$ statistics. P values of <0.05 were considered significant. To assess the relation between headache at stroke onset and >1 clinical variable simultaneously, multivariate logistic regression was applied. All variables which were at least weakly associated with headache at stroke onset were included ($P<0.2$ in univariate analyses). The Cox and Snell $R^2$ was used to assess the variability explained by each model. The Hosmer–Lemeshow test was used to assess the model fit.

**Results**

The median age of our population was 66 years (interquartile range [IQR], 56 to 75) in men and 73 years (IQR, 60 to 79) in women. Of 2196 (44% female) patients with acute ischemic stroke (22% TIA, 18% minor stroke, and 60% major stroke), 588 (27%) experienced headache at stroke onset. Headache was bilateral in the majority of the patients (n=363; 61%). One hundred and five patients (18%) experienced left-sided and 129 (21%) from right-sided headache. In those patients with hemispheric stroke and unilateral headache, headache was significantly more often on the side of the lesion (65% ipsilateral, 35% contralateral; $P<0.001$). In patients with vertebrobasilar stroke (brain stem and/or cerebellum), headache was bilateral in 57%. In those patients with vertebrobasilar stroke and unilateral headache, it was on the left side in 53% and on the right side in 47%. Pain was described as dull in 35%, as pressing in 31%, and as stabbing in 20%. Seldom was headache characterized as burning (4%), pulsatile (8%), or circular (2%). In a first step, we analyzed univariate associations between several clinical variables and headache at stroke onset (Table 1). Patients who reported headache at stroke onset were significantly younger, more often female, and more often experienced migraine in the past as well as from diabetes. The prevalence of headache was highest in the youngest age group and fell with increasing age (<40 years, 53%; 40 to 49 years, 32%; 50 to 59 years, 29%; 60 to 69 years, 27%; 70 to 79 years, 24%; 80+ years, 20%; $P<0.001$). Median BP values on admission (which were available in 1994 [91%] of the patients) seemed similar between patients with and without headache (systolic BP 160 mm Hg [140 to 180 mm Hg] versus 160 mm Hg [140 to 180 mm Hg]; diastolic BP 90 mm Hg [80 to 100 mm Hg] versus 87 mm Hg [80 to 100 mm Hg]). However, the difference was significant ($P=0.001$ for systolic and 0.043 for diastolic BP) because of an overrepresentation of headache in patients with a low (ie, <120/70 mm Hg; n=87) BP, of whom 36% had headache compared with 26% of those with higher BP values. There was no association between headache at stroke onset and presumed etiology of the event or stroke severity measured by the modified Rankin Scale at 1 week after the event (Table 2). There was also no relationship between the time of day of stroke onset and headache (data not shown). Lesion localization was significantly associated with the probability of headache at stroke onset univariately (Table 3).

Multivariate analysis (Table 4) showed that patients with a positive history of migraine had a 1.7-fold risk (95% CI, 1.3 to 2.2) to develop headache at stroke onset compared with patients with a negative history of migraine. Female patients were also more likely to develop headache at stroke onset (odds ratio [OR], 1.3; 95% CI, 1.1 to 1.6) than male patients. Regarding age, patients <40 years had a 4.2-fold odds (95% CI, 2.6 to 6.8) to experience headache at stroke onset compared with patients aged 80 years and older. The probability to develop headache decreased steadily with increasing age. Compared with lesion localization in the left hemisphere (the reference category), lesion localization in the cerebellar territory was associated with...

**Table 1. Clinical Characteristics of Patients With or Without Headache at Stroke Onset (n=2196)**

<table>
<thead>
<tr>
<th></th>
<th>Headache (n=588)</th>
<th>No Headache (n=1608)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, %, female/male</td>
<td>49/51</td>
<td>43/57</td>
<td>0.006</td>
</tr>
<tr>
<td>Age, median (IQR)</td>
<td>65 (53–76)</td>
<td>70 (59–78)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>62</td>
<td>65</td>
<td>0.204</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>21</td>
<td>26</td>
<td>0.024</td>
</tr>
<tr>
<td>Current cigarette smoking, %</td>
<td>29</td>
<td>26</td>
<td>0.159</td>
</tr>
<tr>
<td>History of migraine, %</td>
<td>22</td>
<td>13</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Table 2. Headache at Stroke Onset in Relation to Stroke Etiology and Severity**

<table>
<thead>
<tr>
<th></th>
<th>Headache (n=588)</th>
<th>No Headache (n=1608)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Etiology, %, n=2196</td>
<td></td>
<td></td>
<td>0.859</td>
</tr>
<tr>
<td>Large vessel</td>
<td>15</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Cardioembolic</td>
<td>23</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Small vessel</td>
<td>21</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Other determined</td>
<td>1.5</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td>Undetermined</td>
<td>40</td>
<td>39</td>
<td></td>
</tr>
</tbody>
</table>

**Table 3. Association Between Headache at Stroke Onset and Lesion Localization (n=2196)**

<table>
<thead>
<tr>
<th></th>
<th>Left Hemisphere</th>
<th>Right Hemisphere</th>
<th>Both Hemispheres</th>
<th>Brainstem</th>
<th>Cerebellum</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>77% (734)</td>
<td>71% (633)</td>
<td>64% (9)</td>
<td>73% (211)</td>
<td>21% (45)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Yes</td>
<td>23% (223)</td>
<td>29% (255)</td>
<td>36% (5)</td>
<td>27% (79)</td>
<td>26% (55)</td>
<td></td>
</tr>
</tbody>
</table>
Discussion

The results of our study, obtained in a large cohort of systematically documented patients, confirm previous investigations which found an association of headache at stroke onset with younger age and/or a history of migraine.1,4,6,8 We also found that women had a higher probability of headache at stroke onset than men. Several previous studies reported a higher frequency of headache in patients with an event in the vertebrobasilar territory. Principally, our results confirm these findings. However, a distinction between brain stem and cerebellar territory events seems to be important. Headache was particularly frequent in patients with cerebellar events, whereas the frequency of headache in patients with brain stem events was not higher than in the other patient groups. Our results indicate that the association of headache with vertebrobasilar stroke found in previous studies1,5,6,8 (which did not distinguish between brain stem and cerebellar territories) may have been mainly because of its association with cerebellar stroke. Only 1 study with 182 patients mentioned a higher probability of headache in cerebellar and posterior cerebral artery stroke.4 Possible pathophysiological mechanisms of this association have previously been discussed.4,8 We also found a higher prevalence of headache in patients with a right-hemispheric lesion than in patients with a left-hemispheric lesion. Because patients in whom explicit information about headache at stroke onset could not be obtained (eg, because of aphasia) were excluded from our analysis, it seems unlikely that this difference was only due to a bias because of language disturbances in patients with a left-hemispheric lesion. However, possible pathophysiological mechanisms underlying such a difference between right- and left-hemispheric lesions remain to be elucidated.

Stroke severity and vascular risk factors, such as hypertension or current cigarette smoking and also time of day, did not show a significant association to headache at stroke onset in our study, which is partly in contrast to previous studies.1,4,5,6 The association between low systolic and diastolic BP values on admission (<120 mm Hg systolic and <70 mm Hg diastolic) and headache at stroke onset found in our study had not been investigated so far. The association with diabetes did not remain significant after multivariate adjustment. Interestingly, stroke etiology was not related to headache at stroke onset.

The majority of former studies1–7 referred to markedly smaller patient numbers compared with our analysis; only 1 study8 also included a comparable number of patients, but ischemic and hemorrhagic stroke were not differentiated. For the current analysis, we were able to resort to a great number of prospectively documented patients experiencing ischemic cerebrovascular events only.

In conclusion, we could confirm previously described associations of headache at stroke onset with younger age and a history of migraine. Therefore, in clinical practice, young patients with a focal neurological deficit and a history of migraine should be evaluated carefully to avoid misclassification as “complicated migraine.” Our results also indicate that the previously described association of headache with vertebrobasilar stroke is mainly because of its association with cerebellar stroke.

References

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