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Vascular cognitive impairment in patients with late-onset seizures after an ischemic stroke

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Abstract

Background: Cognitive impairment and seizures are both common conditions in patients with cerebrovascular disease.
Purpose: The present study investigates whether the occurrence of late-onset seizures, following an ischemic stroke, contributes to vascular cognitive impairment.
Patients and methods: The mean Mini-Mental State Examination (MMSE) and the median modified Rankin (mR) scores were compared between 125 patients who developed late-onset seizures (66 with a single seizure and 59 with repeated seizures or epilepsy) following an ischemic stroke and 125 patients who did not during, at least, a 2-year follow-up.
Results: There were no differences in age, gender, etiology and degree of neurological impairment on admission for their stroke between the groups with and without seizures. Although the mean MMSE score was similar between both groups the median mR score was significantly higher in the seizure patients. Comparing the patients with a single seizure to the non-seizure ones showed the same results. On the other hand, comparison of the patients with epilepsy to the non-seizure group revealed, in addition to the higher median mR score, a significantly lower mean MMSE score in the former group.
Conclusion: Repeated seizures following an ischemic stroke promote vascular cognitive impairment.

Keywords: Vascular cognitive impairment; Late-onset seizures; Ischemic stroke; Mini-Mental State Examination; Modified Rankin scale

1. Introduction

The term "vascular cognitive impairment" (VCI) has been introduced to replace previous denominations such as multi-infarct and vascular dementia [1]. Although this term has contributed to confusion and questioned the existence of vascular dementia [2], it covers the heterogenetic contribution of cerebrovascular lesions to cognitive decline [3,4]. Cognitive defects may occur in up to 30% of stroke survivors at 3 months [5] and increase up to 42% after 5 years [6].

The overall incidence of cerebrovascular related seizures is approximately 8.9% [7]. The main predictors of late-onset seizures and epilepsy are the severity of the initial neurological impairment [7,8] and the presence of a large cortical infarct on computed tomography (CT) scan of the brain [7,9–11].

There are no specific studies available who investigate the possible harmful effect of late-onset seizures on cognition in patients after an ischemic stroke. One study, examining the role of hypoxic and ischemic disorders on the incidence of dementia after stroke, included generalized seizures as possible cause of new-onset dementia in three patients [12]. Another study on clinical features and risk factors of post-stroke dementia included seizures in a logistic regression analysis but did not mention them as an independent outcome factor [13].

The present study investigates whether late-onset seizures after an ischemic stroke contribute to VCI. No attempt will be made to subdivide VCI according to its underlying cause or to assess whether the patients were demented or not.

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2. Patients and methods

Hundred-twenty-five patients with late-onset seizures after an ischemic stroke were selected from the Ghent Stroke Register whenever the cognitive status and the degree of disability had been assessed with the Mini-Mental State Examination (MMSE) [14] and the modified Rankin scale (mR) [15] on discharge from the hospital. In a paradigm comparable to posttraumatic epilepsy an arbitrary cut point of 2 weeks after stroke onset has been recognized to distinguish between early- and late-onset seizures [16,17]. The control population consisted of 125 consecutive patients, admitted between the years 2000 and 2002 with an ischemic stroke, who did not develop subsequent seizures and from whom the MMSE and mR scores on discharge were available. Both study groups included patients with hemispheric infarcts of thrombo- and cardio-embolic origin as well as patients with lacunes and white matter changes. The average follow-up in both stroke groups was 38 months (range: 4–102 months). Patients with severe aphasia, persistent loss of consciousness and previous long-lasting mental retardation had been excluded from this study.

The average MMSE score was used as a measure of global cognitive function to compare the stroke patients with and without seizures, but was not intended to signify the presence or absence of dementia. Educational level was not taken into account, as it was not known accurately in our study population [18].

Also the numbers of patients with a MMSE score less than 17 (definite cognitive impairment), those between 17 and 24 (probable cognitive impairment) and those with a score above 24 were also compared between both study groups [19].

The mR score compared the degree of disability between the groups of stroke patients with and without seizures on discharge from the hospital.

All patients had been admitted to the Ghent University Hospital for investigation and treatment of their ischemic stroke. Patients with hemispheric as well as lacunar infarcts were included in the study, while those with transient ischemic attacks or haemorrhagic lesions on computed tomography (CT) were excluded. Patients who developed seizures were readmitted after the single or the last epileptic spell. All patients had on admission for their stroke as well as for their seizure episode a complete cardiovascular work-up, a CT scan of the brain and other neuroradiological investigations if necessary. Depending from the suspected etiology of the infarct, treatment with aspirin, aspirin and dipyridamole, ticlopidine or clopidogrel, heparin or coumarine was started after the stroke.

Sixty-six patients suffered from a single seizure and 59 had repeated ones (mean 4.1; S.D. 2.5) and developed epilepsy. The initial seizure occurred on average 17.8 (S.D. 19.8) months after stroke onset. Sixty (48.0%) patients developed simple partial seizures with or without secondary generalization, 29 (23.2%) had complex partial ones and 36 (28.8%) primary generalized tonic-clonic ones, according to the description gained from the close relatives or the care persons. Thirteen (10.4%) patients were admitted with a status epilepticus (seven simple partial with secondary generalization, five primary generalized and one complex partial status). Those patients were classified and included in the epilepsy group. An interictal electroencephalogram (EEG) was performed in 78 out of the 125 patients admitted for seizures. In the non-seizure group an EEG had been carried out in 51 of the 125 patients. EEG and neuroimaging findings will not be discussed at present. In 95 out of the 125 patients, antiepileptic drug (AED) treatment was initiated after the first seizure. Carbamazepine was the most frequently used AED (36.0%).

Age, gender, stroke type, stroke etiology and degree of neurological impairment on admission, assessed according to the NIH stroke scale criteria [20], were compared between patients with and without seizures. Vascular risk factors were not compared any more as no differences had been found in our previous analysis between the seizure and the non-seizure group [21].

Also patients with a single seizure and those with epilepsy, due to repeated seizures or status epilepticus, were mutually compared.

Statistical analysis was performed using the Fisher's Exact test for the dichotomized variables and the Mann–Whitney *U*-test for continuous variables. The mR scores are described in terms of median with interquartile range (IQR).

3. Results

Age, gender and etiology of the stroke are similar in the groups with and without subsequent seizures. Hemispheric infarcts are significantly more frequent in the seizure group, while lacunes with or without white matter changes predominate in the non-seizure patients ($P < 0.001$). The mean NIH scores at stroke onset are not statistically different ($P = 0.581$) between the seizure group (9.7, S.D. 6.6) and the non-seizure group (9.0, S.D. 5.8). The median mR score in the seizure group (median 4, IQR 3–4) is significantly higher ($P < 0.001$) than in the non-seizure group (median 3, IQR 2–4). The mean MMSE scores are not statistically different ($P = 0.222$) between the seizure (19.8, S.D. 7.7) and the non-seizure (20.9, S.D. 7.8) group (Table 1).

The frequency of patients with definite cognitive impairment, probable cognitive impairment and without impairment is similar ($P = 0.235$) between both groups (Table 2).

Comparison between the patients with a single seizure episode and those without seizures shows similar results: the mean NIH scores at stroke onset are not statistically different ($P = 0.493$) between the single seizure group (8.7, S.D. 6.6) and the non-seizure group (9.0, S.D. 5.8). The median mR score is significantly higher ($P = 0.029$) in the single seizure group (median 4, IQR 2–4) compared to the non-seizure group (median 3, IQR 2–4). The mean MMSE scores are comparable ($P = 0.860$) between the former (20.8, S.D. 8.1) and the latter (20.9, S.D. 7.8) group (Table 3).