

Asymptomatic carotid stenosis, arterial hypertension and cognitive impairment: A longitudinal population-based epidemiological study

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Abstract

The aim of this epidemiological study is to estimate the significance of asymptomatic carotid stenosis (ACS \geq 50%) and arterial hypertension (AH) for cognitive impairment (CI) in a population without signs and symptoms of stroke or TIA. Methods: A total of 500 volunteers, aged 50-79 years, were enrolled and followed-up for cognitive performance. CI has been defined as a score between 24 and 27 of MMSE. Additional neuropsychological tests have also been conducted. Results: CI in persons without any degree of ACS has been detected at only 13.85% (27/195). In comparison to the whole group investigated ($p<0.012$), as well as to the subgroup without ACS, CI has significantly increased in participants with ACS $<$ 50% (22.3% - 61/273, $p<0.01$) and especially with ACS \geq 50% (40.6% - 13/32, $p<0.001$). Significant differences in the prevalence of CI have also been found between the two subgroups with ACS $<$ 50% or ACS \geq 50% ($p<0.05$). Logistic regression analysis has been conducted between the group with ACS \geq 50% and an age and sex adjusted control group. It has revealed no relation between CI and ACS \geq 50%. However, multiple logistic regression analysis has shown that the combination of ACS \geq 50% and systolic AH (SAH) attributes to CI (OR=10.7; 95%CI: 3.36-34.14; $p=0.0001$). CI has been presented as a decline in attention, verbal fluency and verbal working memory at the end of the study. Conclusion: This pattern of CI, which is specific for a cerebral small vessel disease in long lasting AH, has supported the thesis that SAH and ACS \geq 50%, not only ACS \geq 50%, are attributable for CI.

To investigate potential associations between carotid artery stenosis and cognitive impairment among patients with acute ischemic stroke and to provide important clinical implications. We measured the degree of carotid artery stenosis and recorded the Mini-Mental State Examination score (MMSE) at admission in 3116 acute ischemic stroke patients. The association between carotid stenosis and cognitive impairment assessed by MMSE was tested using multivariate regression analysis. Other clinical variables of interest were also studied. After adjusting for

age, gender, education level, marriage, alcohol use, tobacco use, physical activity, hypertension, diabetes, hypercholesterolemia, atrial fibrillation, myocardial infarction and NIHSS (National Institutes of Health Stroke Scale) score, we found that participants with high-grade stenosis of the carotid artery had a higher likelihood of cognitive impairment compared to those without carotid artery stenosis (OR = 1.49, 95%CI: 1.05–2.11, $p<0.001$). Left common carotid artery stenosis was associated with cognitive impairment in the univariate analysis, although this effect did not persist after adjustment for the NIHSS score. Cognitive impairment was associated with high-grade stenosis of the right carotid artery. The present cohort was obtained from the Study on Oxidative Stress in Patients with Acute Ischemic Stroke (SOS-Stroke), a prospective, multi-center registry. The SOS-Stroke study consisted of consecutively selected patients ($n = 4164$) with acute ischemic stroke. Patients (age range, 18 to 96 years) who had suffered a stroke and were admitted to one of the 43 designated hospitals in China within 7 days were included in this study from January to October 2014. The inclusion criteria for SOS-Stroke were as follows: (1) patient age over 18 years; (2) neurologist-diagnosed acute ischemic stroke that was confirmed with computed tomography (CT) or magnetic resonance imaging (MRI); (3) time from initial stroke to diagnosis less than two weeks; and (4) patient-provided informed consent.

The exclusion criteria were as follows: (1) bleeding or other pathological brain diseases, such as vascular malformations, tumors, abscesses, multiple sclerosis or other common non-ischemic cerebral diseases revealed via head CT and/or MRI; (2) transient ischemic attack (TIA); and (3) iatrogenic stroke due to angioplasty or surgical operation. We excluded 417 participants who had incomplete MMSE data and 631 participants who had incomplete carotid stenosis data. Finally, only 3,116 participants (2,031 men, 1,085 women) remained for analysis. The study was sponsored by the Stroke Screening and Prevention Engineering Office of the National Health and Family Planning Commission and was approved by the Ethics Committee of Beijing Tiantan

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Hospital, Xuanwu Hospital Capital Medical University and Peking Union Medical College Hospital, in compliance with the Declaration of Helsinki. All patients provided written informed consent prior to participation. Atherosclerosis of the carotid bifurcation with plaque formation causes asymptomatic carotid artery stenosis (ACAS), which may also be associated with cerebral hypoperfusion. Cerebral hypoperfusion adversely affects multiple aspects of mobility and cognition. This study tests the hypothesis that community-dwelling older adults with a 50% or greater diameter-reducing ACAS will have mobility and cognitive impairments that heighten their risk for falls. Cerebrovascular risk factors (eg, hypertension, coronary artery disease) and stroke can lead to vascular cognitive impairment. The Asymptomatic Carotid Stenosis and Cognitive Function study evaluated the isolated impact of asymptomatic carotid stenosis (no prior ipsilateral or

contralateral stroke or transient ischemic attack) on cognitive function. Cerebrovascular hemodynamic and carotid plaque characteristics were analyzed to elucidate potential mechanisms affecting cognition. The study is limited by small numbers and the absence of brain imaging, but provides some evidence for an association between severe carotid stenosis and neuropsychological impairment. The presence of clinically 'silent' cerebrovascular disease affecting frontal lobe function may be missed in routine clinical practice. Our findings suggest that patients with asymptomatic bilateral severe internal carotid artery stenosis may be at risk of developing cognitive impairment. The evaluation of the hemodynamic status, besides providing insights about the possible mechanism behind the cognitive dysfunction present in carotid atherosclerotic disease, may be of help for the individuation of subjects deserving earlier and more aggressive treatments.