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Research Article

Risk factors for incident dementia after stroke and transient ischemic attack

Jie Yang[a,b], Adrian Wong[c,d], Zhaolu Wang[a], Wenyan Liu[a], Lisa Au[a], Yunyun Xiong[e], Winnie W. C. Chu[f], Eric Y. L. Leung[g], Sirong Chen[g], Christine Lau[a], Anne Y. Y. Chan[a], Alexander Y. L. Lau[a], Florence Fan[a], Vincent Ip[a], Yannie Soo[a], Thomas Leung[a], Chi L. Ho[g], Lawrence K. S. Wong[a], Vincent C. T. Mok[a,*]

[a]*Department of Medicine and Therapeutics, The Chinese University of Hong Kong, Shatin, Hong Kong SAR, China*
[b]*Key Laboratory of Neurogenetics and Channelopathies of Guangdong Province and Ministry of Education of China, Institute of Neuroscience and the Second Affiliated Hospital of Guangzhou Medical University, Guangzhou, China*
[c]*Department of Psychological Studies, d Center for Psychosocial Health and Aging,The Hong Kong Institute of Education, Tai-po, Hong Kong SAR, China*
[d]*Center for Psychosocial Health and Aging, The Hong Kong Institute of Education, Hong Kong SAR, China*
[e]*Department of Neurology, Jinling Hospital, Nanjing University School of Medicine, Nanjing, China*
[f]*Department of Imaging and Interventional Radiology, The Chinese University of Hong Kong, Shatin, Hong Kong SAR, China*
[g]*Department of Nuclear Medicine, Hong Kong Sanatorium and Hospital, Hong Kong SAR, China*

Abstract

Background: We hypothesized that chronic brain changes are important substrates for incident dementia after stroke and transient ischemic attack (TIA).

Methods: We compared clinical and imaging features between patients with consecutive stroke/TIA with (n = 88) and without (n = 925) incident dementia at 3 to 6 months after a stroke/TIA. Pittsburg compound B (PiB) positron emission tomography was performed in 50 patients, including those with (n = 37) and without (n = 13) incident dementia.

Results: Age, history of diabetes mellitus, severity of white matter changes (WMCs), and medial temporal lobe atrophy (MTLA) were associated with incident dementia. Alzheimer's disease (AD)–like PiB retention was found in 29.7% and 7.7% ($P = .032$) of patients with and without incident dementia, respectively.

Conclusions: Chronic brain changes including WMCs, MTLA, and AD pathology are associated with incident dementia after stroke/TIA. Interventions targeting these chronic brain changes may reduce burden of vascular cognitive impairment.

Keywords: Poststroke dementia; Vascular cognitive impairment; Brain atrophy; PiB-PET; Transient ischemic attack

1. Introduction

Recent studies have recognized increasingly the contributions of vascular disease to Alzheimer's disease (AD) and dementia [1]. However, mechanisms explaining vascular cognitive impairment (VCI) are complex. The complexity stems from the heterogeneity of cerebrovascular diseases and the potential interactions between cerebrovascular and neurodegenerative diseases (e.g., AD) [1,2]. Dementia in the context of stroke and transient ischemic attack (TIA) is a prototype of VCI and provides a good clinical context for the study of VCI mechanisms. Although previous studies of dementia in stroke are numerous, data collection for many studies was biased toward certain aspects (e.g., stroke features) and neglected the others (e.g., brain atrophy) [3]. Furthermore, the sample size of most studies was, in general, small [4]. Moreover, although many

J. Yang and A. Wong are co-first authors, with equal contribution to the manuscript.

*Corresponding author. Tel.: +852-2632-2195; Fax: +852-2637-3856.
E-mail address: vctmok@cuhk.edu.hk

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suggested that concurrent AD pathology is common in dementia after stroke [1,4], support from functional imaging (e.g., amyloid positron emission tomography [PET]) is lacking. The exact contribution of concurrent AD pathology in patients with stroke/TIA with early incident dementia is as yet undetermined, because detection of concurrent AD pathology based on structural imaging only (computed tomography [CT] or magnetic resonance imaging [MRI]) is often impossible in the context of stroke. The National Institute of Neurological Disorders and Stroke–Canadian Stroke Network has proposed standards for data collection for future research in VCI, and use of amyloid PET was recommended to investigate the interaction between AD pathology and cerebrovascular disease [5].

Burden of VCI is particularly immense in developing countries (e.g., in China), where stroke incidence is high [6]. To study VCI mechanisms in a Chinese population, we set up a registry to investigate the mechanisms of cognitive decline in Chinese survivors of stroke/TIA. To capture the complexity of VCI, we collected extensive clinical, neurovascular, and neuroimaging data. We hypothesized that apart from basic demographic factors (e.g., age) and stroke-related features (e.g., number of infarcts), chronic brain changes such as brain atrophy, white matter changes (WMCs), and concurrent AD pathology are important determinants for incident dementia after stroke/TIA.

2. Methods

2.1. Participants

We conducted a cross-sectional cohort study. Participants were patients in the ongoing Stroke Registry Investigating Cognitive Decline (STRIDE) study, which aims to recruit more than 1000 patients with consecutive stroke (ischemic and hemorrhagic)/TIA and monitor them for as long as 5 years. The objective of the STRIDE study was to investigate the mechanisms of early and delayed cognitive decline after stroke/TIA. Potential participants of the STRIDE study were consecutive patients admitted to the acute stroke unit of a university-affiliated hospital because of stroke/TIA. We defined ischemic stroke according to clinical evidence of cerebral ischemic injury based on symptoms persisting 24 hours or more, and other etiologies excluded [7]. We defined TIA based on transient neurological deficits (less than 24 hours) and the absence of infarcts/hemorrhage evident on neuroimaging. Other inclusion criteria were Chinese ethnicity, fluency in Cantonese, ability to participate in cognitive assessments, and provision of signed informed consent. Exclusion criteria for this study included severe language impairment precluding cognitive assessment, presence of terminal illness, clinically significant psychiatric comorbidity, or known history of dementia before the index stroke. Severe language impairment was defined as a score of 3 points (i.e., mute) in the language score of the National Institute of Health Stroke Scale (NIHSS). The Joint Chinese University of Hong Kong–New Territories East Cluster ethics committee approved this study. During 2009 and 2010, 2078 patients with stroke/TIA were admitted to the acute stroke unit, and 1013 patients (48.7%) were recruited into the STRIDE study. Fig. 1 depicts STRIDE study recruitment. Overall, patients excluded (n = 927) and patients who refused to participate (n = 138) in this study were older (age, 73.6 ± 12.8 years [excluded] vs. 69.2 ± 11.7 years [included], $P < .001$), female (50.7% vs. 44.3%, $P = .003$), and had more severe stroke (NIHSS score, 11.0 ± 10.7 points vs. 4.7 ± 5.1 points; $P < .001$) compared with included participants (Fig. 1).

2.2. Medical history

We collected data on basic demographic and vascular risk factors during subject's hospitalization for the index event. We labeled patients as having hypertension if they had a history of hypertension or were using antihypertensive medication. Diabetes mellitus (DM) was defined as a fasting serum glucose level of 7.0 mmol/L or more, a postprandial serum glucose level of 11.1 mmol/L or more, or the use of oral hypoglycemic agents/insulin. Hyperlipidemia was defined as a total cholesterol level of 5.2 mmol/L or more, a low-density lipoprotein cholesterol level of 2.6 mmol/L or more, a triglyceride level of 1.70 mmol/L or more, or the use of lipid-lowering drugs. Ischemic heart disease was defined as a history of myocardial infarction or angina pectoris. Atrial fibrillation was diagnosed on the results of at least one electrocardiogram obtained before or during hospitalization. Smoking/alcohol intake was dichotomized as ever

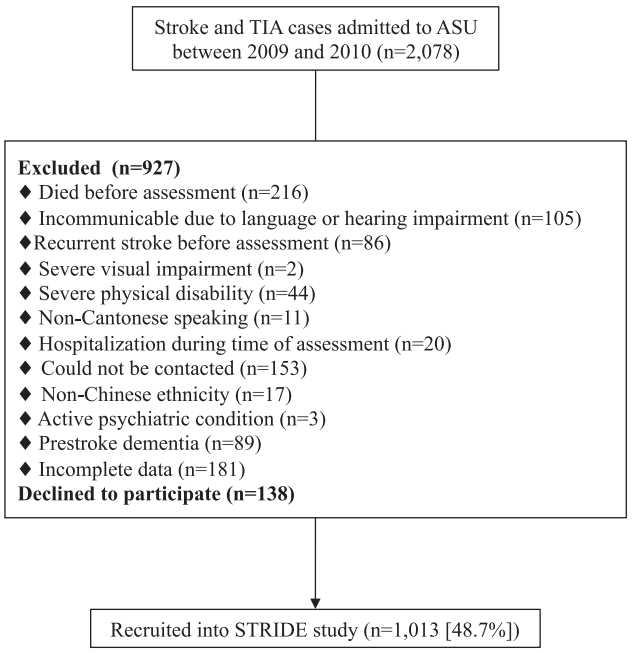

Fig. 1. Stroke Registry Investigating Cognitive Decline (STRIDE) study recruitment. TIA, transient ischemic attack; ASU, acute stroke unit.