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Letter to the Editor

Is vascular cognitive impairment more common in Asia?

Ethnicity does have an impact on the prevalence of disease (Chang et al., 1993; Jorm, 1990; Larson and Imai, 1996; Hendrie, 1998; Yeo et al., 1996). Compared to studies on Caucasians, much less has been done on Asians and researchers aspire to better understand the prevalence of vascular cognitive impairment (VCI) in Asia, and how to reduce the risk of VCI. This is a pressing issue as the society burden is high, especially with the ageing population, and with more than half of the world population living in Asia (Haub and Kaneda, 2014).

VCI is defined as cognitive impairment associated with cerebrovascular diseases. The spectrum of VCI is wide, including frank stroke, or any subclinical cerebrovascular diseases, with clinical severity ranging from mild cognitive impairment that does not meet criteria for dementia to vascular dementia (VaD), and also poststroke dementia and multi-infarct dementia, or even Alzheimer's dementia (AD) with concurrent cerebrovascular diseases (Gorelick et al., 2011; O'Brien and Thomas, 2015). By investigating VCI in light of this spectrum of disorders, the burden of VCI is likely to be enormous, considering the large population in Asia. This editorial aims to explore whether VCI is more common in Asia. A better understanding of how the disease affects Asia will raise the awareness for better management and allocation of resources, and even attract clinical trials on VCI to be focused on the Asian population.

There is no study that directly compares the race prevalence of VCI. Previous studies focused on the prevalence of VCI measured in each individual country. However, the Delphi Consensus Study showed the worldwide estimate for the absolute number of cases of dementia in general. By 2020, there will be at least 16.6 million people in Asia (including Southeast Asia and South Asia) affected with dementia; while there will be 11.1 million Caucasians (from Western Europe, Eastern Europe, and North America) affected with dementia. The study evaluated contributions of dementia to be mainly AD and VaD (Rizzi et al., 2014). VaD is the most common type of dementia, followed by AD, in Japan while the reverse patterns were found in Britain and North America (Jorm, 1991). One important note though is the existence of AD cases do not entirely rule out mixed dementia cases or the strong vascular contribution (e.g. WMH and lacunes) in dementia (Capizzano et al., 2004; Heyman et al., 1998; Snowdon et al., 1997). Not all studies have neuroradiological confirmation, and hence, subclinical vascular lesions may not have been detected (Zhang et al., 2005), which could have underestimated the vascular contribution to the dementia spectrum. Indeed, pathological studies showed that coexisting pathology of VaD and AD is highly common and account for most dementia cases (Toledo et al., 2013; Liu et al., 2015).

A population-based study found that the prevalence of confluent white matter hyperintensities (WMH), a common pathological substrate for VCI, was greater in Chinese (38.5%) than in White Australians (28.4%; Mok et al., 2014). Interestingly, Chinese ethnicity was found to be independently associated with confluent WMH even after adjusting for age and vascular risk factors (Mok et al., 2014). While the percentage of patients suffering from VaD may be large, those who have not yet illustrated dementia symptoms (VCI without dementia) can be even larger. In a Singaporean longitudinal study, 4% were demented while those "VCI without dementia" were ten times more frequent (40%; Tham et al., 2002). While VaD and "VCI without dementia" are all sub-categories under VCI, it is made apparent that the society burden and impact of VCI is large, especially in the densely populated Asian countries.

An equally important contributor to dementia in Asia is poststroke dementia. It was made apparent that the prevalence of stroke is higher in some Asian countries compared to the West. There was good evidence for higher overall stroke incidence, as well as intracerebral haemorrhage, in Chinese compared to the white populations (Tsai et al., 2013). Another study demonstrated that there was a rise in stroke incidence in most Asian countries with an earlier age of onset compared with the United States and Italy (Mehndiratta et al., 2014). In addition, strong associations between systolic blood pressure and both ischaemic and haemorrhagic strokes were found in Asians, similar to the Australasian cohort (Collaboration APCS, 2003). Other than the traditional risk factors, the non-traditional risk factors such as waterpipe use, desi ghee, chewable tobacco, and infectious cause of stroke in developing South Asian countries are understudied (Wasay et al., 2014). With the risk of dementia found in about one-third of patients after stroke (Tatemichi et al., 1994), post stroke cognitive impairment and dementia increased the burden of VCI in Asia. The frequency of post stroke cognitive impairment varies but remained high, ranging from 18% in Hong Kong (Tang et al., 2006) to 44% in Singapore (Tham et al., 2002). Further, poststroke dementia poses long-term impact after the stroke incidence (Mok et al., 2017). The STroke Registry Investigating cognitive Decline, the largest hospital-based study in Hong Kong examining stroke patients in a longitudinal setting, found that an additional 4.4% of these cognitively intact subjects developed delayed-onset poststroke dementia three years after the stroke incidence, even after excluding patients who developed dementia 3–6 months (Mok et al., 2016).

Current treatment options available for VCI include acetylcholinesterase inhibitors and NMDA receptor antagonist memantine. These treatment options are safe and provide modest cognitive benefits, however, results showed inconsistent functional measures. Other therapies include calcium channel blockers, aspirin, and vitamin supplements but these have less evidence to support the benefits on cognition (Ritter and Pillai, 2015).

Several clinical trials were performed to reduce the progression of WMH, which is one of the important risk factors of small vessel disease (SVD). Examples were the Regression of Cerebral Artery Stenosis (ROCAS) study which used statin (Mok et al., 2009), the B vitamins in patients with recent transient ischaemic attack or stroke in the VITAmins TO Prevent Stroke (VITATOPS) substudy which used B vitamins (folic acid, vitamin B6 and B12; Cavalieri et al., 2012), and another study that used mixed tocotrienols, one class of vitamin E compound (Gopalan et al., 2014). These therapies have shown effectiveness in reducing the progression of cerebral WMH, and which the effects were found especially in patients with severe WMH at

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baseline in the ROCAS and VITATOPS studies. As the prevalence of SVD, one most leading cause of VCI, is higher in Chinese than White Caucasians (Mok et al., 2014), drug therapy targeting SVD could be considered for the treatment of VCI in Asia.

It is understood that there are discrepancies in studies of disease prevalence. There is evidence suggesting the prevalences of AD and VaD in Asia were not more common but rather comparable with Caucasians (Zhang et al., 2005). Variations in results could be partially explained by methodological differences between studies. Prevalence of VaD differed in various studies due to different diagnostic criteria used. For example, the NINDS-AIREN criteria are more conservative than the DSM-IV or California ADDTC criteria (Lopez et al., 2005). DSM-IV and NINDS-AIREN criteria focus on the presence of abrupt onset of cognitive deficits, in the context of focal neurologic signs and symptoms following a clinically suspected stroke while the ADDTC criteria do not require the presence of focal neurologic signs and symptoms but focused on a clear relationship between stroke and dementia onset instead. Further, while neuroimaging is an important tool for accurate clinical diagnosis of VaD, the NINDS-AIREN criteria only had average neuroimaging agreement when attempting to operationalize the neuroimaging component of the criteria. Due to the methodological differences, NINDS-AIREN criteria was more conservative such that the diagnostic classification for probable VaD was 9%, compared to 13% in DSM-IV and 12% in California ADDTC criteria (Lopez et al., 2005). Thus, the different criteria used would have impacted the reported prevalence of VaD.

Nevertheless, with rapid urbanization and the ageing population, dementia and stroke made the largest contribution to disability in low- and middle-income Asian countries, with median population-attributable prevalence fractions of 25.1%, and 11.4% respectively (Sousa et al., 2009). Although the prevalence of VCI in various studies may vary due to different assessment criteria, the prevalence of stroke and certain risk factors, which lead to poststroke dementia, is higher in Asia than the United States, Australasian and Europe (Jorm, 1991; Tsai et al., 2013; Mehndiratta et al., 2014; Collaboration APCS, 2003; Wasay et al., 2014). Further, the lack of access to healthcare in some Asian countries could have also contributed to the high rate of vascular cognitive impairment following vascular events (OECD/WHO, 2014). Altogether, evidence suggested that VCI is more common in Asia. Improving accessibility of health care and socioeconomic factors will also reduce the risk of vascular risk factors, and hence reduce the risk of VCI in Asia (Rizzi et al., 2014). Research and epidemiological studies towards the understanding of the VCI burden and intervention, including raising awareness, early detection, better health care, and promotion of healthy lifestyle should be of utmost importance.

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Conflict of interest

There is no conflict of interest to declare.

Authors' contribution

Bonnie Y.K. Lam did the literature review and drafted the manuscript. Vincent C.T. Mok provided advice on the review topic and edited the manuscript.

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