Prevalence, risk factors and consequences of cerebral small vessel diseases - data from three Asian countries

SUPPLEMENTARY FILE ON STUDIES METHODS:

Epidemiology of Dementia In Singapore study (EDIS):
The EDIS study draws subjects from the on-going population-based community-dwelling study of Chinese, Malays and Indians cohorts aged 40-80 years who participated in the Singapore Epidemiology of Eye Disease (SEED; n=10,033), which comprises the Singapore Chinese Eye Study (SCES; n=3,353), Singapore Malay Eye Study (SiMES; n=3,280) and Singapore Indian Eye Study (SINDI; n=3,400). As part of the SEED study, participants are randomly selected from the community, and are invited to Singapore Eye Research Institute for interview and clinical assessments, as described previously. Briefly, SiMES, SINDI and SCES were designed to study the prevalence and risk factors for chronic eye diseases. At this stage, as part of the first phase of the EDIS study, SEED participants who are above 60 years old (44% of the total population) undergo cognitive screening using the 10 point Abbreviated Mental Test (AMT) and a self-report of progressive forgetfulness (PF) (yes/no), both of which have been previously validated in Singapore. Screen positives are defined as AMT ≤ 6, among those with up to 6 years of formal education, or ≤ 8 among those with more than 6 years of formal education; or if the caregiver confirms progressive forgetfulness. Thus, the inclusion criteria of the study included: 1) Screen positives on AMT or PFQ, 2) written informed consent given by participants or legally acceptable representative. Exclusion criteria of the study included participant/legally acceptable representative who were not willing to provide written consent.

Subsequently, these screen-positive subjects are invited to participate in the second phase of the EDIS study, which is conducted at the Centre for Life Sciences, National University of Singapore (NUS). Information on participants is collected by means of a questionnaire, physical examination, 3 Tesla imaging and cognitive testing in NUS.

Risk Index for Subclinical brain lesions in Hong Kong study (RISK):

RISK drew functionally independent participants by advertisement of the study in local community centers and word-of-mouth in the local community network using stratified sampling. Inclusion criteria were 1) age≥65; 2)
functional independence as defined by a score of 20 on the 20-point Barthel Index and <2 on the Lawton’s Instrumental of Daily Living Scale (IADL); 3) Cantonese-speaking, 4) sufficient sensorimotor and language competency for cognitive testing; and 5) written informed consent given. Exclusion criteria were 1) history of clinical stroke or transient ischemic attack ascertained by medical records on the Clinical Management System of the Hospital Authority, which is the public healthcare provider in Hong Kong that covers ≥90% local inpatient service; 2) history of neurological or psychiatric conditions affecting cognitive functions; and 3) dementia determined by medical history; 4) evidence of brain tumors, large cerebral infarcts (i.e. infarcts ≥20mm in diameter) or hydrocephalus on MRI. Subjects fulfilling the inclusion criteria were then invited to the neurology research facilities at the Prince of Wales Hospital. Clinical data was first collected in one visit. MRI brain was then performed only after collection of clinical data has been completed. Information from participants was collected using questionnaire, clinical examination, 3 Tesla brain imaging and cognitive testing.

**Oligomeric Beta Amyloid detection by Multimer detection system in Alzheimer’s disease (OBAMA):**

OBAMA study in Korea recruited cognitively healthy subjects, from Chung-Ang University Hospital. Cognitively normal subjects met the following inclusion criteria: 1) age between 60 to 80 years, and satisfaction of normal aging criteria, 2) scores on the MMSE of at least 1.0 standard deviation below the mean for their age and education-matched norm, 3) ≥6 years of education, 4) short form Geriatric Depression Score ≤7. Individuals were excluded if they had 1) significant or unstable medical problems, 2) psychiatric problems, 3) a cardiac pacemaker, and/or 4) a history of substance abuse or dependence within the past 10 years.