Original Article

Concomitant Coronary Artery Disease Among Asian Ischaemic Stroke Patients

Deidre Anne De Silva,[1] *MBBS, MRCP, FAMS*, Fung Peng Woon,[2] *BSc, MSc*, Kyaw Thu Moe,[2] *MBBS, PhD*, Christopher LH Chen,[3] *BMBCh, MRCP, FRCP*, Hui Meng Chang,[1] *MBBS, MRCP, FAMS*, Meng Cheong Wong,[1] *MBBS, MRCP, FRCP*

Abstract

Introduction: Coronary artery disease (CAD) is the leading cause of death following ischaemic stroke. We aimed to study the prevalence and associations of concomitant CAD among ischaemic stroke patients in Singapore. Materials and Methods: We prospectively studied 2686 consecutive Asian ischaemic stroke patients. Results: CAD was prevalent among 24% of the study patients. Older age, hypertension, diabetes, hyperlipidaemia, atrial fibrillation, large stroke and South Asian ethnicity were independently associated with CAD. Conclusions: The variables found to be associated with CAD are known atherosclerotic risk factors (older age, hypertension, diabetes, hyperlipidaemia) or associations of cardioembolic stroke (atrial fibrillation, large stroke). The over-representation of South Asians with concomitant CAD is consistent with the high burden of CAD in this ethnic group.

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Introduction

Coronary artery disease (CAD) is the leading cause of mortality following ischaemic stroke.[1,2] The annual risk for myocardial infarction following ischaemic stroke is approximately 2.2%.[3]

Concomitant CAD among ischaemic stroke patients has been studied in the West, with a prevalence of 34% in France and 56% in the United States (US).[4,5] There is a paucity of data on concomitant CAD among Asian stroke patients. A multicentre study found that CAD was prevalent among 17.9% of Asian ischaemic stroke patients and was an independent risk factor for early death.[6] We studied Asian ischaemic stroke patients in Singapore, investigating the prevalence and associations of concomitant CAD.

Singapore, a city-nation in Southeast Asia, has a population of 4 million with an ethnic distribution of 76% Chinese, 14% Malays, 8% South Asians and 2% other ethnicities. The Singapore public ambulance service sends acute stroke patients to hospital emergency departments according to geographical location. At the Singapore General Hospital (SGH), a 1400-bed tertiary teaching hospital, all acute ischaemic stroke patients are admitted to the neurology department.

Materials and Methods

In this observational study, we prospectively collated data of consecutive acute ischaemic stroke patients admitted to the SGH neurology department for 3 years in 2001, 2002 and 2003. We noted demographics and previous medical history. All patients had an electrocardiogram. Other cardiac investigations were done at the managing neurologist's discretion.

Acute ischaemic stroke was diagnosed by a neurologist based on clinical presentation and brain imaging and was defined as symptom onset within 7 days. A patient was considered to have concomitant CAD if there was prior diagnosis by a doctor or evidence on electrocardiography, echocardiography, stress testing or cardiac catheterisation. Hypertension was defined as prior diagnosis by a doctor, current use of anti-hypertensive medication or by the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure VI criteria.[7] Diabetes was defined as prior diagnosis by a doctor, current treatment with oral hypoglycaemic agents/ insulin or by the World Health Organization criteria.[8] Hyperlipidaemia was defined as prior diagnosis by a doctor, current lipid-lowering drug treatment or by the National Cholesterol Education Program

[1] Singapore General Hospital campus, Singapore
[2] National Heart Centre, Singapore
[3] National University of Singapore
Address for Correspondence: Dr Deidre Anne De Silva, 15 Saraca Road, Singapore 807361. Email: deidre.a.de.silva@sgh.com.sg

Expert Panel guidelines.[9] A patient was considered a smoker if there was a history of smoking in the past 3 years. The Oxfordshire Community Stroke Project classification was used to categorise stroke subtypes.[10] Large stroke was defined as total or partial anterior circulation infarction. Carotid duplex studies were performed, using European Carotid Surgery Trial method for measurement of carotid stenosis.[11] Extracranial carotid artery stenosis of <30% was defined as mild, 30-69% as moderate and 70-99% as severe.

Statistical analysis was performed with the SPSS software version 9.0. Chi-square test was employed for categorical variables and Student's *t*-test for continuous variables. Multivariate analysis using binary regression was performed to identify independent associations of CAD.

Results

We studied 2686 consecutive ischaemic stroke patients. The median age was 67 years and 56% were male. The ethnic distribution was 83% Chinese, 10% Malays, 6% South Asians and 1% other Asian ethnicities. Among these patients, 78% had hypertension, 44% diabetes, 40% hyperlipidaemia, 26% were smokers, 10% had atrial fibrillation, 20% large stroke and 6% severe extracranial stenosis.

The prevalence of concomitant CAD was 24% in the study population; 23% among Chinese, 23% among Malays and 39% among South Asians. Table 1 shows associations of concomitant CAD and Table 2 lists the odds ratios of risk factors for concomitant CAD. The significant associations of concomitant CAD were age, South Asian ethnicity, hypertension, diabetes, hyperlipidaemia, non-smokers, atrial fibrillation, large stroke and severe extracranial carotid stenosis. The order of categorical variables predicting CAD (from highest to lowest odds ratios) was atrial fibrillation, hypertension, South Asian ethnicity, hyperlipidaemia, diabetes, large stroke, severe extracranial disease and non-smokers.

Table 3 shows the results of multivariate analysis for concomitant CAD associations using age, ethnicity, hypertension, diabetes, hyperlipidaemia, smoking, atrial fibrillation, large stroke and extracranial carotid disease as variables. Older age, South Asian ethnicity, hypertension, diabetes, hyperlipidaemia, atrial fibrillation and large stroke were independently associated with concomitant CAD among ischaemic stroke patients.

Table 1. Associations of Concomitant Coronary Artery Disease (CAD) among Acute Ischemic Stroke Patients

	CAD n = 652	No CAD n = 2034	*P* value
Median age (y)	69	66	<0.001
Male	368 (56%)	1127 (55%)	0.644
Female	284 (44%)	907 (45%)	
Chinese	514 (79%)	1703 (84%)	<0.001
Malay	64 (10%)	210 (10%)	
South Asian	63 (10%)	99 (5%)	
Other ethnicities	11 (1%)	22 (1%)	
Hypertension	571 (88%)	1510 (74%)	<0.001
Diabetes	364 (56%)	828 (41%)	<0.001
Hyperlipidaemia	341 (52%)	721 (35%)	<0.001
Smoking	143 (22%)	567 (28%)	0.003
Atrial fibrillation	136 (21%)	135 (7%)	<0.001
Large stroke	183 (28%)	360 (18%)	<0.001
Severe extracranial carotid disease	42 (9%)	89 (6%)	0.015

Numbers shown with percentages in brackets

Table 2. Odds Ratios for Categorical Variables Predicting for Concomitant Coronary Artery Disease

	Odds ratio (confidence interval)
Atrial fibrillation	3.71 (2.87 to 4.80)
Hypertension	2.45 (1.90 to 3.15)
South Asian ethnicity	2.09 (1.50 to 2.91)
Hyperlipidaemia	2.00 (1.67 to 2.39)
Diabetes	1.84 (1.54 to 2.20)
Large stroke	1.81 (1.48 to 2.23)
Severe extracranial disease	1.50 (1.03 to 2.20)
Non-smokers	1.38 (1.12 to 1.70)
Male	1.04 (0.87 to 1.25)

Table 3. Multivariate Regression Analysis for Concomitant Coronary Artery Disease using Age, Ethnicity, Hypertension, Diabetes, Hyperlipidaemia, Smoking, Atrial Fibrillation, Large Stroke and Extracranial Carotid Disease as Variables

	Hazards ratio	*P* value
Older age	1.029	<0.001
South Asian ethnicity	4.837	<0.001
Hypertension	1.568	0.005
Diabetes	1.703	<0.001
Hyperlipidaemia	1.897	<0.001
Non-smokers	1.220	0.524
Atrial fibrillation	3.394	<0.001
Large stroke	1.513	0.004
Severe extracranial carotid disease	1.216	0.312

Conclusions

Concomitant CAD among Asian ischaemic stroke patients was common, prevalent among 24% in this study. Although this CAD prevalence is similar to the 17.9% found in another Asian study,[6] it is lower compared to reports from France (34%) and the US (56%).[4,5] Possible reasons for this difference include younger age in our study (67 years) compared to studies done in France (69 years) and the US (80 years),[4,5] differences in the methods used to investigate CAD and genetic differences between ethnicities.

The prevalence of CAD among South Asian ischaemic stroke patients was even higher at 39% in this study. The over-representation of South Asians among patients with CAD was independent of age and other risk factors. This is in keeping with the known high burden of CAD among South Asians,[12-14] which may be attributed to differences in conventional, novel and yet undiscovered risk factors.[15-17] Our previous studies have shown a high prevalence of diabetes, metabolic syndrome and reduced levels of high-density lipoprotein cholesterol among South Asian ischaemic stroke patients.[16,17] The SHARE study found that South Asians had higher concentrations of fibrinogen, homocysteine, lipoprotein [a] and plasminogen activator inhibitor-1.[15] Other risk factors including genetic ones may still be undiscovered.

The associations of older age, hypertension, diabetes and hyperlipidaemia with concomitant CAD are expected as they are known atherosclerotic risk factors. Large stroke is predominantly due to large artery cerebrovascular disease and cardioembolic stroke. CAD is a source of embolism in 25% of cardioembolic strokes.[18] CAD has been previously shown to be more common among patients with large artery cerebrovascular disease compared to other stroke subtypes.[19] These reasons explain the association between concomitant CAD and large strokes. The prevalence of atrial fibrillation among patients with concomitant CAD in this study (21%) is similar to that reported in the literature (30%).[20] The independent association found between atrial fibrillation and concomitant CAD among ischaemic stroke patients also concurs with the published literature.[20] The association of non-smokers with concomitant CAD is due to the older age of non-smokers compared to smokers (67 vs 63 years). The lack of an independent association of smoking with concomitant CAD in multivariate analysis using age as a variable confirms this.

Identification of CAD among ischaemic stroke patients is important as the risk of cardiac events is higher among stroke patients with concomitant CAD.[21] Optimisation of CAD management may improve survival as CAD is the leading cause of death following stroke.[1-4] Medical treatment and revascularisation procedures improve prognosis beyond risk factor reduction for CAD patients.[22-24]

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