Prevalence of Extracranial Carotid and Vertebral Artery Disease in Chinese Patients with Coronary Artery Disease

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Abstract

Background and Purpose Chinese have been reported to have an extremely low prevalence of carotid and vertebral artery disease in comparison with Caucasians. Previous studies, however, have been limited to general hospital stroke admission or post-mortem series and were prone to selection bias. Extracranial cerebrovascular disease (ECCVD) is associated with coronary artery disease (CAD) in Caucasians. Data associating ECCVD with CAD in Chinese patients are not available.

Methods We studied 153 consecutive Chinese patients with angiographically documented CAD. Duplex ultrasonography was performed to identify any underlying extracranial carotid and vertebral artery disease. Patient demographics, vascular risk factors, history of myocardial infarction, transient ischemic attack (TIA) or stroke, concomitant peripheral vascular disease (PVD), degree of left ventricular dysfunction, extent and severity of CAD were also noted and analyzed.

Results Significant (≥50%) stenosis of one or more of the extracranial cerebral arteries was found in 32 patients (21%). The internal and external carotid arteries were involved in 17/153 (11%) and 19/153 (12%) of the patients respectively. The vertebral artery was involved in 9/153 (6%) while the common carotid artery was involved in 3/153 (2%) of the patients. Diabetes mellitus, hypertension, a history of TIA or stroke, and PVD were significantly associated with the presence of ECCVD.

Conclusions Significant ECCVD is not uncommon in Chinese patients with CAD and the prevalence is comparable to that reported in Caucasian population. Patients with a history of diabetes, hypertension, TIA, stroke, and PVD are more likely to have concomitant ECCVD.

Key Words

• carotid artery disease • cerebral arteries • Chinese • coronary artery disease • vertebral artery

Atherothrombosis of the large cerebral arteries is an important cause of cerebrovascular disease and accounts for 30-60% of all ischemic strokes[1,2]. The distribution and severity of atherosclerotic cerebrovascular disease has been reported to vary among patients of different ethnic origin[3-9]. Previous studies reported that Chinese stroke patients had more intracranial small vessel disease than Caucasians whereas extracranial disease was extremely rare. However, these reports had been limited by relatively small study sample size[8,10] or lack of detailed clinical and laboratory (e.g. duplex ultrasonography or cerebral arteriography) evaluation for extracranial disease[9]. Another major limitation of any general hospital stroke presentation or autopsy series in developing countries is selection bias. These include factors relating to the popularity of alternative therapy, difference in economic power and threshold of hospital presentation between the male and female sex[11,12], and difference in rates of presentation to, and admission by, a private versus public hospital. Thus, in Hong Kong, patients with hemorrhagic strokes are more likely to present to and be admitted by a hospital whereas those with minor strokes or transient ischemic attacks (TIA's) are more likely to seek treatment from Chinese herbalists or acupuncturists or are refused admission by an overcrowded public hospital. In fact, patients with TIA's are often excluded from previous series[8,9,11,12]. These patients may have significant extracranial cerebrovascular disease with large artery to small artery embolization as a cause of their TIA or minor stroke.

Coronary artery disease (CAD) has been associated with extracranial cerebrovascular disease (ECCVD) in Caucasian series. In patients with CAD, significant ECCVD has been reported to be present in 12-28%[13-18]. There have been no similar studies on Chinese patients with CAD. The objectives of this study are therefore, to 1) determine the prevalence, distribution and severity of ECCVD in Chinese patients with CAD, and 2) identify those clinical variables which are associated with ECCVD.

Subjects and Methods

153 consecutive patients presenting to our center for diagnostic cardiac catheterization and who had angiographically proven CAD were included in this study. A detailed history and physical examination were performed by either one of two physicians (WHC and DSWH). Data collected included age, sex, history of cigarette smoking, diabetes mellitus, hypertension,

hypercholesterolemia (defined as pre-treatment fasting total cholesterol level ≥5.4mmol/L), TIA, stroke and peripheral vascular disease (PVD). The overall patient characteristics are summarized in Table I.

All patients underwent coronary angiography and left ventriculography by the trans-femoral route. Biplane technique was used and each coronary artery was studied by at least two different projections. CAD was defined as ≥50% luminal diameter stenosis of one or more of the major epicardial coronary arteries. The extent and severity of CAD, as well as the left ventricular systolic function were noted. Ultrasonographic assessment of the extracranial carotid and vertebral arteries was performed in every patient. An Accuson duplex ultrasound system (128XP/10) with a 5MHz scanning probe was used. The duplex examination was carried out by a single ultrasonographer. The results were interpreted independently by two different readers. Peak systolic velocities of ≥1.25m/s and ≥1.4m/s were used to define the presence of a lesion in the carotid arteries of ≥50% stenosis and ≥80% stenosis respectively[19]. A focal velocity increase of >0.4m/s in peak systole accompanied by disturbed flow in the adjacent (downstream) portion of the vessel was used to define the presence of a vertebral artery lesion of ≥50% stenosis[20,21].

Statistical analysis was performed using the chi-square test. A p value of <0.05 was considered statistically significant.

Results

Significant (≥50%) stenosis of ≥1 extracranial cerebral arteries was found in 32 (21%) patients (Table II). The lesions were located in the common carotid artery in 3/153 patients (2%), internal carotid artery in 17/153 patients (11%), external carotid artery in 19/153 patients (12%) and vertebral artery in 9/153 patients (6%). Bilateral internal carotid artery stenosis was found in 3 patients (2%). Nine (6%) patients had ≥80% stenosis in one or both of the internal carotid arteries. The characteristics of patients with and without ECCVD are shown in Table I. Diabetes mellitus, hypertension, a history of TIA, stroke, and PVD were significantly associated with the presence of ECCVD.

Discussion

Many published series have reported on the differences in ECCVD between Whites and Orientals[3-9]. Angiographic study in Japanese stroke patients showed that extracranial internal carotid artery lesions were less frequent and milder in Japanese than in Americans while intracranial disease was more common in Japanese[4]. Studies on Chinese patients with TIA or ischemic stroke have reported a 9-30% prevalence of extracranial carotid disease as opposed to 30-60% in Caucasian patients[3,7,10,22]. Autopsy series on Hong Kong Chinese revealed extracranial carotid artery stenosis of ≥50% in 18% and total occlusion in 2% of the cases[8]. This is much lower than the corresponding figures of 40% and 8-11% reported in two Caucasian series[23,24]. Small sample size and selection bias are major limitations of these studies. In addition, hemorrhagic strokes are often over-represented in hospital-based series since patients often present with more severe symptoms such as headache, vomiting and loss of consciousness[25]. This is all the more important in developing countries since patients with milder or transient symptoms tend to be turned away by overcrowded public hospitals or seek alternative treatment from herbalists and acupuncturists.

In our study, instead of performing another stroke or autopsy series, we took a different approach to address the impression that ECCVD is rare among Chinese. It has been well reported that ECCVD is associated with CAD. In 4 Caucasian studies[13-16] on the prevalence of carotid artery disease among patients with CAD, significant (defined as ≥50%) internal carotid artery stenosis was found in 12-28% of the patients. When a definition of ≥80% was used, the prevalence of internal carotid artery stenosis was reported to range from 6 to 9%[17,18]. In our study, we found a prevalence of 11% and 6% when ≥50% and ≥80% was used to define significant internal carotid artery stenosis respectively. Thus, the prevalence of significant internal carotid artery stenosis in our cohort is comparable to those reported in Caucasian series and significant ECCVD is definitely not rare amongst Chinese. This is in accord with two recent studies on patients of Asian origin which suggest a rising prevalence of ECCVD in Japanese and Taiwan Chinese stroke victims[26,27]. Thus, severe extracranial internal carotid artery stenosis was found to be five times more prevalent in a recent cohort (1989 to 1993) compared to an earlier cohort (1963 to 1965) of Japanese ischemic stroke patients[26]. In a recent

study on Taiwan patients with cortical infarcts, ipsilateral internal carotid artery stenosis of ≥50% was found to be present in 32% of the cases[27]. This compares with two Caucasian studies that found 37% of the patients with cortical infarcts[28] and 41% of the patients with non-lacunar infarctions[29] had ipsilateral internal carotid artery stenosis of ≥50%. Increased affluence and westernization of lifestyles in our region could partly explain the rising prevalence of ECCVD in Chinese and Japanese[26]. Another explanation is increased diagnosis and detection as a result of lower threshold of presentation to and admission by hospitals in these countries as a result of improved public education and increased health spending. Availability and improved treatment for ECCVD in these countries over the last two decades may have also played a part. All these factors could explain the rising prevalence of atherosclerotic disease in the extracranial cerebral arteries in Chinese. Among patients with CAD in our series, diabetes, hypertension, TIA / stroke, and PVD were identified as predictors of concomitant ECCVD. This is also in accord with two other studies which found TIA / stroke, and PVD to be significantly associated with severe carotid stenosis[17,18].

Limitations

Duplex scanning is an accurate non-invasive method for identifying significant carotid artery disease. A sensitivity of up to 95% and a specificity of up to 90% have been reported[30-33]. In our vascular laboratory, a peak systolic velocity of ≥1.25m/s as a cutpoint in identifying carotid artery stenosis of ≥50% is associated with a sensitivity of 90% and a specificity of 95%. A peak systolic velocity of ≥1.4m/s as a cutpoint in identifying carotid artery stenosis of ≥80% is associated with a sensitivity of 95% and a specificity of 95%. These figures were based on an analysis of 80 consecutive cases where each patient had undergone both angiogram and duplex scan in our centre.

Although the role of ultrasound in the assessment of vertebral artery disease is less well defined and the accuracy of duplex scanning in identifying vertebral artery disease is lower than that of carotid artery disease, sensitivity of 73-76% and specificity of 94-97% have been reported in two large series[21,34]. In any case, the relatively poor sensitivity of duplex scanning in identifying significant vertebral artery disease could have only underestimated the true

prevalence of ECCVD, further emphasizing that ECCVD in Chinese is not as rare as previously thought.

This study only addressed the prevalence of ECCVD among Chinese patients with CAD and not the prevalence in the general population or stroke population. Relatively few statistics are available on the prevalence of CAD in Chinese. Although the prevalence of CAD among Hong Kong Chinese has been reported to be lower than that of white populations[35], one autopsy series found the incidence of atherosclerosis among Hong Kong Chinese to be comparable with that in Western populations[36]. Local cardiologists have also noted an increasing demand for coronary care units, coronary angiography, angioplasty and surgery. For example, the demand for coronary angioplasty in Hong Kong (500 procedures per million population per year) is comparable to many European countries[37]. Nevertheless, many patients who suffer stroke or TIA do not have concomitant CAD. Significant racial difference in the prevalence of ECCVD among stroke patients may still exist. Thus, caution should be exercised in generalizing these results to the general population.

In conclusion, in contrast to previous reports, we find that significant extracranial atherosclerotic cerebral arterial disease is not uncommon in Chinese patients with coronary artery disease. The prevalence of 21% is comparable to those reported for Caucasian populations. This is in accord with two recent studies[26,27] on patients of Asian origin which suggested a rising prevalence of ECCVD in Japanese and Taiwan Chinese stroke victims. Among patients with coronary artery disease, clinical variables such as diabetes, hypertension, TIA, stroke, and PVD were predictive of concomitant extracranial cerebrovascular disease. These findings are also in accord with those reported in Caucasian series.

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Table I. Patient Characteristics

	Overall (n = 153)		Without ECCVD (n = 121)		With ECCVD (n = 32)		
	N	(%)	N	(%)	N	(%)	
Age (66 ± 8 y)			mean = 65 y		mean = 68 y		
Sex: M	88	(58)	70	(58)	18	(56)	p = ns
F	65	(42)	51	(42)	14	(44)	
Smoking history	82	(54)	63	(52)	19	(59)	p = ns
Diabetes mellitus	42	(27)	26	(21)	16	(50)	p = 0.001
Hypertension	99	(65)	73	(60)	26	(81)	p = 0.03
Hypercholesterolemia	113	(74)	91	(75)	22	(69)	p = ns
History of MI	41	(27)	33	(27)	8	(25)	p = ns
Extent of CAD							
One vessel	50	(33)	42	(35)	7	(22)	
Two vessel	51	(33)	38	(31)	13	(41)	p = ns
Three vessel	52	(34)	39	(33)	12	(37)	
Normal LV function	112	(73)	90	(74)	22	(69)	p = ns
TIA or stroke	13	(8)	6	(5)	7	(22)	p = 0.02
PVD	10	(7)	3	(2)	7	(22)	p <0.0001

MI, myocardial infarction; CAD, coronary artery disease; LV, left ventricle; TIA, transient ischemic attack; and PVD, peripheral vascular disease.

ns = not statistically significant

Table II. Distribution of Extracranial Cerebrovascular Disease

Artery Involved	Number of Patients	%
Vertebral artery	9	6
Common carotid artery	3	2
External carotid artery	19	12
Internal carotid artery	17*	11
Degree of internal carotid artery stenosis:		
50 - 79%	8†	5
80 - 99%	5‡	3
100%	4δ	3

* bilateral disease in 3 patients;

† one patient had bilateral disease;

‡ one patient had contralateral carotid occlusion;

δ one patient had bilateral carotid occlusion.