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Prevalence of Asymptomatic Coronary Artery Disease in Ischemic Stroke Patients

The PRECORIS Study

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Background—Coronary artery disease (CAD) is a significant cause of morbidity and mortality in stroke patients. Some patients with asymptomatic CAD might benefit from specific prevention, but the prevalence of asymptomatic CAD is not well known. We assessed the prevalence of ≥50% asymptomatic CAD in patients with ischemic stroke or transient ischemic attack and whether the prevalence is related to traditional vascular risk factors and cervicocephalic atherosclerosis.

Methods and Results—From January 2006 to February 2009, consecutive patients between 45 and 75 years of age with nondisabling, noncardioembolic ischemic stroke or transient ischemic attack and no prior history of CAD were enrolled in the study. All patients had a 64-section computed tomography coronary angiography and a detailed cervicocephalic arterial workup. Risk factors were assessed individually and through the Framingham Risk Score. Among 300 patients included in the study, 274 had computed tomography coronary angiography. The prevalence of ≥50% asymptomatic CAD was 18% (95% confidence interval [CI], 14 to 23; n=50). Asymptomatic CAD was independently associated with traditional risk factors assessed individually and through the Framingham Risk Score (odds ratio [OR], 2.6; 95% CI, 1.0 to 7.6 for a 10-year risk of coronary heart disease of 10% to 19%; and OR, 7.3; 95% CI, 2.8 to 19.1 for a 10 year-risk of coronary heart disease ≥20%), the presence of at least 1 ≥50% cervicocephalic artery stenosis (OR, 4.0; 95% CI, 1.4 to 11.2), excessive alcohol consumption (OR, 3.1; 95% CI 1.3 to 7.3), and ankle brachial index <0.9 (OR, 2.2; 95% CI, 0.9 to 5.2). The prevalence of ≥50% asymptomatic CAD was also related to the extent of cervicocephalic atherosclerosis.

Conclusions—About one fifth of patients with nondisabling, noncardioembolic ischemic stroke or transient ischemic attack have ≥50% asymptomatic CAD. In addition to vascular risk factors, the presence of ≥50% cervicocephalic artery stenosis is strongly related to ≥50% asymptomatic CAD. **(*Circulation*. 2010;121:1623-1629.)**

Key Words: coronary disease ■ stroke ■ tomography, x-ray computed ■ transient ischemic attack

Coronary artery disease (CAD) is usually considered a significant cause of morbidity and mortality in patients who had a stroke or a transient ischemic attack (TIA).[1] Although recurrent strokes occur more commonly than cardiac events over the long term after stroke, cardiac events still account for a greater proportionate mortality.[2,3] To improve the prevention of CAD in stroke patients, it could be relevant to identify patients with asymptomatic coronary artery stenosis who might benefit from specific additional therapeutic measures to prevent a first coronary event. The American Heart Association/American Stroke Association statement recommends an individual risk assessment based notably on Framingham Risk Score (FRS) and on the presence of significant carotid disease to identify stroke patients who should be considered for noninvasive testing for CAD.[1] However, the validity of such an approach has never been tested. In addition, classic noninvasive tests detecting silent ischemia have relatively low sensitivities and specificities for the diagnosis of significant coronary lesions.[4] The most recent 64-section computed tomography (CT) has a sensitivity of >85% and a specificity of >95% to detect coronary lesions leading to >50% stenosis, with conventional angiography used as the reference standard.[5] We therefore assessed the prevalence of ≥50% asymptomatic CAD, detected with 64-section CT, in patients with ischemic stroke or TIA and whether the prevalence is related to traditional vascular risk factors and cervicocephalic atherosclerosis.

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Clinical Perspective on p 1629

Methods

Study Population

The study was conducted in consecutive patients admitted to our stroke unit from January 2006 to February 2009. Patients were referred to our stroke unit by emergency departments from hospitals located in the south part of Paris and its suburbs and by general practitioners and emergency ambulance services in the same area. Patients were eligible if they were 45 to 75 years of age; had had an ischemic stroke (confirmed by brain imaging) regardless of the duration of symptoms[6] or a probable TIA according to the National Institute of Neurological Disorders and Stroke criteria[7] resulting from large-artery atherosclerosis, small-vessel disease, or an undetermined cause according to the Trial of Org 10172 in Acute Stroke Treatment classification[8]; and had no prior history of CAD. Patients with disabling stroke (modified Rankin scale score ≥3 on a scale of 0 to 5, with higher scores indicating more severe disability), cardioembolic stroke, contraindications to multislice CT (MSCT) coronary angiography, or life expectancy of <3 years were not eligible. The study was approved by the local ethics committee, and all patients provided informed consent.

Among the 368 eligible patients, 58 refused to participate, and 10 could not be enrolled because of participation in another study (Figure 1). Of the 300 included patients, 21 patients eventually refused to undergo MSCT coronary angiography, 3 could not have MSCT coronary angiography because of a subsequent medical event (acute coronary syndrome, brain hemorrhage, and complicated arm fracture), and 2 patients had MSCT coronary angiography that could not be interpreted. The remaining 274 patients were included in the analysis. During the study period, 74 patients 45 to 75 years of age with nondisabling stroke or TIA and no prior history of coronary disease were admitted to our stroke unit but were not eligible because they had had a cardioembolic stroke (atrial fibrillation in 55 patients, prosthetic valve in 5, cardiac tumor in 3, infective endocarditis in 2, and patent foramen ovale with atrial septal aneurysm in patients <60 years of age in 9).

Demographic data, previously known vascular risk factors, and cardiovascular medical history were collected prospectively by an investigator during a face-to-face interview using a specific case report form. Lipid profile was measured at admission, with a median time from stroke or TIA onset of 48 hours. At inclusion, systolic and diastolic blood pressures were measured after a 10-minute rest period in the supine position. Pressure was measured 3 times, and the mean of the last 2 measurements was calculated. The median time from stroke or TIA onset to inclusion blood pressure measurement was 8 days. Ankle brachial index (ABI) was determined by averaging the dorsalis and posterior tibial arterial pressures in each leg.[9] The lowest value was retained. All patients had brain magnetic resonance imaging with spin-echo diffusion-weighted imaging (n=271, 99%) or CT scan, a standardized causal workup that included standard blood tests, 12-lead ECG, prolonged 3-lead cardiac monitoring, arterial investigations, and echocardiography (transthoracic in all and transesophageal in 264 patients, 96%). Imaging of cervical and intracranial arteries consisted of cervical and transcranial Doppler ultrasound in all patients and 3-dimensional time-of-flight magnetic resonance angiography of the circle of Willis in 271 patients (99%), cervical gadolinium-enhanced magnetic resonance angiography in 263 patients (96%), 64-section CT angiography in 12 patients (4%), and conventional angiography in 8 patients (3%). CT angiography and conventional angiography were done in case of contraindication to magnetic resonance angiography or discrepancies between Doppler ultrasound and magnetic resonance angiography. Cervicocephalic atherosclerosis was assessed with a standardized method. An investigator blinded to clinical data and results of the MSCT coronary angiography reviewed all available arterial investigations and assessed each arterial segment for the presence of cervicocephalic atherosclerosis. The severity of atherosclerosis was assessed from the degree of stenosis. Cervical carotid artery stenosis was measured

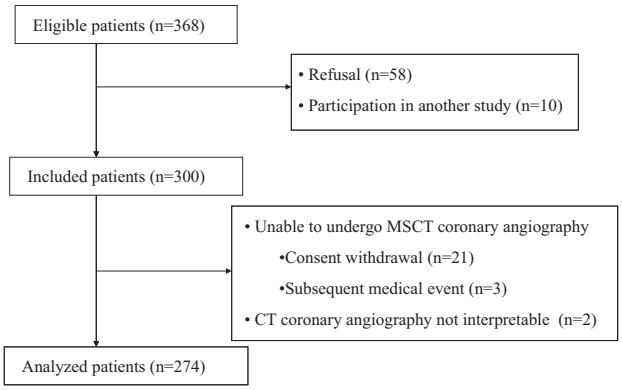

Figure 1. Flow chart.

according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method,[10] which is based on measurement of the minimum residual lumen at the point of maximum stenosis and the diameter of the normal internal carotid artery beyond the carotid bulb at a point where the walls of the artery are parallel. For other cervicocephalic arteries, we used the percent stenosis, with the estimate of the normal arterial diameter at the point of maximum stenosis taken as the closest measurable section of nondiseased artery (ie, analogous to the NASCET method of measurement of carotid stenosis).[11] Each arterial segment was then classified as normal, <50% stenosis, or ≥50% stenosis. The presence of atherosclerosis was defined by at least 1 stenosis in at least one of the following arterial segments: common carotid artery, carotid bifurcation, cervical internal carotid artery, intracranial internal carotid artery, segments of the vertebral artery (ostium, prevertebral, transversarial, atlas loop, intracranial), segments of the basilar artery (proximal, middle, distal), proximal segment of the posterior cerebral artery, or proximal segment of the middle cerebral artery. The presence of at least 2 noncontiguous stenoses in at least 2 different arterial segments and the severity of those stenoses were used to assess the extent of cervicocephalic atherosclerosis.

MSCT Coronary Angiography

We performed 64-section CT examinations of coronary arteries (LightSpeed VCT, GE Healthcare, Waukesha, Wis) using a technique that we reported elsewhere.[12] In that study conducted in patients at high risk for CAD,[12] MSCT coronary angiography had a sensitivity of 100% and a specificity of 89% (compared with conventional coronary angiography) for detecting patients with ≥50% CAD. All MSCT coronary angiographies were reviewed by a single experienced radiologist blinded to clinical data. Each coronary artery was examined using the same artery segmentation as conventional coronary angiography.[13] Only arterial segments that were visually estimated to be ≥1.5 mm in diameter were analyzed. Image quality of each segment was rated as excellent (no motion artifacts or minor artifacts and clear delineation of the coronary artery segment), fair (moderate artifacts without vessel wall discontinuity or severe artifacts with a vessel wall discontinuity but maintained visualization of the arterial lumen), or poor (noninterpretable coronary artery segments). Coronary arteries were analyzed with 3-dimensional volume-rendered, 3-dimensional maximum-intensity projection, and axial row data. Coronary artery stenosis was graded on the basis of curved reformatted and cross-sectional images. The degree of stenosis was quantified on orthogonal views with an automatic vessel analysis tool.[14] The degree of stenosis was measured only if the visually observed degree of stenosis was ≥30%. The percentage of stenosis was evaluated as a diameter percentage. Patients were categorized as no CAD (no plaque), <50% CAD (at least 1 lesion <50% and no stenosis ≥50%), and ≥50% CAD (at least 1 stenosis ≥50%).

Statistical Analysis

We assumed that the prevalence of ≥50% asymptomatic CAD would be ≈25%. This assumption was based on the results of the

only study that assessed the prevalence of coronary artery stenosis using conventional coronary angiography.[15] In that study, which involved patients scheduled for endarterectomy, the prevalence of coronary artery stenosis was 40%.[15] However, because our patients were not selected on the basis of carotid stenosis, we expected that the prevalence of ≥50% asymptomatic CAD would be lower in our population. We calculated that a sample size of 288 patients was needed to provide a precision of 5% around a prevalence of 25%. We included 300 patients to account for technique failures and consent withdrawals. We calculated the prevalence of CAD with 95% confidence intervals (CIs). FRS[16] was calculated for each patient, and standard cutoffs (<10%, 10% to 19%, and ≥20% 10-year risk of coronary heart disease [CHD]) were used.[17] The relationships between ≥50% CAD and patient characteristics were assessed by calculation of crude and adjusted odds ratios (ORs) through logistic regression models. Variables with values of $P<0.10$ in univariate analyses were entered into multivariate logistic models.[18] We also performed a backward stepwise logistic regression analysis with all variables tested in univariate analysis, with a value of $P<0.10$ used as the cutoff for retention in the model.

Results

Characteristics of the 274 patients are shown in Table 1. Mean age was 62.5 years (SD, 8.0 years), and 192 patients (70%) were male. Two hundred thirty-five patients (86%) had ischemic stroke, and 39 (14%) had TIA. Carotid territory was involved in 180 patients (66%); vertebrobasilar territory, in 94 (34%). No statistical difference was found between the 274 included patients who had MSCT (n=274) and the 79 patients who refused to participate (n=58) or eventually refused to undergo MSCT (n=21) with respect to gender, age, history of hypertension, history of diabetes, values of low-density lipoprotein (LDL) cholesterol, and presence of at least 1 ≥50% cervicocephalic stenosis (data not shown). The median time from ischemic stroke or TIA onset to MSCT coronary angiography was 68 days (interquartile range, 35 to 132 days). The quality of MSCT coronary angiography was rated as excellent for all segments in 234 patients (86%) and as fair for all segments in 19 patients (7%). In 16 patients, quality was excellent except for 1 to 6 segments, which were rated as fair in 14 and as not interpretable in 2 patients. In 5 patients, quality was fair except for 1 to 5 segments, which were not interpretable.

The prevalence of ≥50% asymptomatic CAD was 18% (95% CI, 14 to 23; n=50 patients). Among patients with ≥50% asymptomatic CAD, 26 (52%) had single-vessel disease, 13 (26%) had 2-vessel disease, 8 had (16%) 3-vessel disease, 1 had left main trunk disease only, and 2 had left main trunk disease with single- (n=1) or 2-vessel (n=1) disease. Eighty-three patients (30%) had <50% asymptomatic CAD, and 141 (52%) had no CAD.

Compared with patients with no CAD or <50% CAD, those with ≥50% asymptomatic CAD were significantly more likely to be male (OR, 8.5; 95% CI, 2.6 to 28.3), >60 years of age (OR, 2.0; 95% CI, 1.0 to 3.9), current or past smokers (OR, 3.5; 95% CI, 1.6 to 7.7), and heavy alcohol drinkers (OR, 3.3; 95% CI, 1.5 to 7.3; Table 1). They were also more likely to have a history of symptomatic peripheral artery disease (OR, 6.4; 95% CI, 1.4 to 29.6), ABI <0.9 (OR, 2.9; 95% CI, 1.4 to 6.3), blood pressure ≥140/90 mm Hg at inclusion (OR, 2.2; 95% CI, 1.2 to 4.1), and LDL cholesterol ≥130 mg/dL at inclusion (OR, 4.2; 95% CI, 1.5 to 11.3).

Table 1. Risk Factors for ≥50% Asymptomatic CAD (Univariate Analysis)

Characteristics of the Patients	n (%)*	Prevalence of ≥50% Asymptomatic CAD		
		n (%)†	Crude OR (95% CI)	*P*
Male	192 (70)	47 (24)	8.5 (2.6–28.3)	<0.0001
Age >60 y	162 (59)	36 (22)	2.0 (1.0–3.9)	0.043
Hypertension‡	122 (45)	21 (17)	0.9 (0.5–1.6)	0.691
Blood pressure ≥140/90 mm Hg	116 (42)	26 (25)	2.2 (1.2–4.1)	0.014
Dyslipidemia‡	65 (24)	15 (23)	1.5 (0.8–3.0)	0.250
LDL cholesterol, mg/dL				
<100	57 (21)	5 (9)	1	0.0003¶
100–129	98 (36)	11 (11)	1.3 (0.4–4.0)	
≥130	119 (43)	34 (29)	4.2 (1.5–11.3)	
HDL cholesterol, mg/dL				
≥60	63 (23)	9 (14)	1	0.153
35–59	102 (37)	15 (15)	1.0 (0.4–2.5)	
<35	109 (40)	26 (24)	1.9 (0.8–4.3)	
Diabetes mellitus‡	35 (13)	8 (23)	1.4 (0.6–3.3)	0.451
Alcohol consumption§				
Rare or none	171 (62)	21 (12)	1	0.0008¶
Moderate	59 (22)	15 (25)	2.4 (1.2–5.1)	
Excessive	44 (16)	14 (32)	3.3 (1.5–7.3)	
Smoking (active or past)	177 (65)	42 (24)	3.5 (1.6–7.7)	0.002
FRS-predicted 10-y CHD risk, %				
<10	109 (40)	7 (6)	1	<0.0001¶
10–19	102 (37)	18 (18)	3.1 (1.2–7.8)	
≥20	63 (23)	25 (40)	9.6 (3.8–24.0)	
Body mass index, kg/m^2				
<25	112 (41)	17 (15)	1	0.482
≥25 and <30	112 (41)	24 (21)	1.5 (0.3–3.0)	
≥30	50 (18)	9 (18)	1.2 (0.5–3.0)	
ABI <0.9	37 (14)	13 (35)	2.9 (1.4–6.3)	0.006
Ischemic stroke (vs TIA)	235 (86)	43 (18)	1.0 (0.4–2.5)	0.958
Carotid (vs vertebrobasilar territory)	180 (66)	31 (17)	0.8 (0.4–1.6)	0.543
Symptomatic peripheral artery disease	7 (3)	4 (57)	6.4 (1.4–29.6)	0.017
Past history of stroke	21 (8)	3 (14)	0.7 (0.2–2.6)	0.626
Family history of stroke	44 (16)	9 (20)	1.2 (0.5–2.7)	0.679
Family history of CAD	52 (19)	7 (13)	0.6 (0.3–1.5)	0.324

HDL indicates high-density lipoprotein.
*Percentage of the total population (n=274) in each category.
†Percentage of asymptomatic ≥50% CAD in each category.
‡Known and treated before ischemic stroke or TIA.
§Moderate alcohol consumption: at least 10 but ≤20 g/d for women and ≤30 g/d in men; rare consumption: <10 g/d.
¶*P* for trend.

There was a nonsignificant association between ≥50% asymptomatic CAD and diabetes mellitus (OR, 1.4; 95% CI, 0.6 to 3.3), history of dyslipidemia (OR, 1.5; 95% CI, 0.8 to 3.0), and high-density lipoprotein cholesterol <35 mg/dL

Table 2. Relationship Between Severity of Cervicocephalic Stenosis and Extent of Cervicocephalic Atherosclerosis and ≥50% Asymptomatic CAD (Univariate Analysis)

Characteristics of the Patients	n (%)	Prevalence of ≥50% Asymptomatic CAD		
		n (%)†	Crude OR (95% CI)	P‡
Severity of cervicocephalic stenosis				
No atherosclerosis	89 (32)	6 (7)	1	<0.0001
At least 1 <50% stenosis	109 (40)	19 (17)	2.9 (2.6–7.7)	
At least 1 ≥50% stenosis	76 (28)	25 (33)	6.8 (2.6–17.7)	
Extent of cervicocephalic atherosclerosis				
No atherosclerosis	89 (32)	6 (7)	1	<0.0001
1 <50% stenosis	39 (14)	4 (10)	1.6 (0.4–6.0)	
≥2 <50% stenosis	70 (26)	15 (21)	3.8 (1.4–10.3)	
1 ≥50% stenosis	53 (20)	15 (28)	5.5 (2.0–15.2)	
≥2 ≥50% stenosis	23 (8)	10 (43)	10.6 (3.3–34.2)	

*Percentage of the total population in each category.
†Percentage of asymptomatic ≥50% CAD in each category.
‡*P* for trend.

(OR, 1.9; 95% CI, 0.8 to 4.3). The prevalence of ≥50% asymptomatic CAD increased gradually with FRS levels (*P* for trend <0.0001; Table 1). The predictive value of FRS was not modified after further adjustment for delay from stroke onset to blood pressure measurement (data not shown). Asymptomatic ≥50% CAD was unrelated to family history of stroke or CAD, arterial territory of stroke or TIA, and whether the patient had ischemic stroke or TIA.

Table 2 shows that the prevalence of ≥50% CAD increased with the presence and degree of stenosis of cervicocephalic atherosclerosis from 7% in patients with no cervicocephalic atherosclerosis to 17% in those with <50% cervicocephalic stenosis and rose to 33% in those with at least 1 ≥50% cervicocephalic stenosis (*P* for trend <0.0001). Asymptomatic ≥50% CAD was also related to the extent of cervicocephalic atherosclerosis, ranging from 10% in patients with 1 <50% cervicocephalic stenosis to 43% in patients with at least 2 ≥50% cervicocephalic stenoses (Table 2).

Figure 2 shows that the prevalence of ≥50% asymptomatic CAD increased with the severity of cervicocephalic artery stenosis in each FRS stratum, from 2% in patients with FRS-predicted 10-year risk of CHD <10% and no cervicocephalic atherosclerosis to 50% in those with FRS-predicted 10-year risk ≥20% and ≥50% cervicocephalic stenosis. Patients with ≥50% cervicocephalic stenosis, ≥20% FRS-predicted 10-year risk of CHD, or both accounted for 41% (113 of 274) of the total population. The prevalence of ≥50% asymptomatic CAD in these patients was 33% (37 of 113), accounting for 74% (37 of 50) of patients with ≥50% asymptomatic CAD. In these patients, the prevalence of 3-vessel disease or left main trunk disease was 9% (10 of 113), accounting for 91% (10 of 11) of patients with 3-vessel disease or left main trunk disease.

Multivariate analyses are shown in Table 3. In model 1 (using individual risk factors), male gender, age >60 years, LDL cholesterol ≥130 mg/dL, and presence of at least 1 ≥50% cervicocephalic stenosis were significantly associated with ≥50% asymptomatic CAD. There was a nonsignificant association between ≥50% asymptomatic CAD and smoking, blood pressure ≥140/90 mm Hg, and excessive alcohol consumption. In model 2 (using FRS), FRS, excessive alcohol consumption, and the presence of at least 1 ≥50% cervicocephalic stenosis were significantly associated with ≥50% asymptomatic CAD. In both models, the association between ABI <0.9 and ≥50% asymptomatic CAD did not reach statistical significance. Stepwise logistic regression analyses using all variables tested in the univariate analysis provided the same set of independent predictors of ≥50% asymptomatic CAD as the logistic regression analyses shown in Table 3 (data not shown).

Table 4 shows that the prevalence of ≥50% asymptomatic CAD also increased with the extent of cervicocephalic atherosclerosis in patients with <50% and in those with ≥50% cervicocephalic atherosclerosis. Adjusted ORs for other variables were similar to those presented in Table 3 (data not shown).

Discussion

This study shows that 18% of patients between 45 and 75 years of age with nondisabling, noncardioembolic ischemic

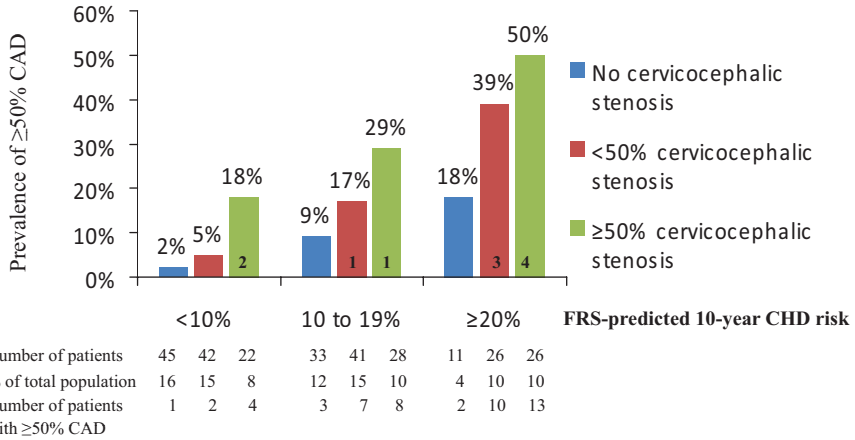

Figure 2. Prevalence of ≥50% asymptomatic CAD according to severity of cervicocephalic stenosis and FRS-predicted 10-year CHD risk strata. Numbers in bold within bars are the numbers of patients with 3-vessel disease or left main trunk disease.

Table 3. Risk Factors for ≥50% CAD (Multivariate Analysis)*

	Adjusted OR (95% CI)	
	Model 1 (Using Individual Risk Factors)	Model 2 (Using FRS)
Male gender	7.7 (2.0–29.5)	
Age >60 y	2.6 (1.2–5.6)	
Blood pressure ≥140/90 mm Hg	1.9 (0.9–4.0)	
LDL cholesterol, mg/dL		
<100	1	
100–129	1.9 (0.6–6.5)	
≥130	5.3 (1.7–16.4)	
Alcohol consumption		
Rare or none	1	1
Moderate	1.1 (0.5–2.7)	1.7 (0.7–3.8)
Excessive	1.8 (0.7–4.6)	3.1 (1.3–7.3)
Smoking (active or past)	2.1 (0.8–5.1)	
FRS-predicted 10-y risk of CHD, %		
<10		1
10–19		2.6 (1.0–7.6)
≤20		7.3 (2.8–19.1)
ABI <0.9	2.2 (0.9–5.5)	2.2 (0.9–5.2)
Severity of cervicocephalic stenosis		
No atherosclerosis	1	1
<50% stenosis	2.3 (0.8–6.7)	2.3 (0.8–6.4)
≥50% stenosis	3.7 (1.3–10.9)	4.0 (1.4–11.2)

*Variables with $P<0.10$ in univariate analyses were entered into these logistic models.

stroke or TIA have ≥50% asymptomatic CAD. In addition to traditional vascular risk factors, the severity of cervicocephalic artery stenosis and extent of cervicocephalic atherosclerosis were strongly associated with ≥50% asymptomatic CAD.

Table 4. Relationship Between Extent of Cervicocephalic Atherosclerosis and ≥50% Asymptomatic CAD*

	Adjusted OR (95% CI)	
	Model 1 (Using Individual Risk Factors)	Model 2 (Using FRS)
Cervicocephalic atherosclerosis†		
No atherosclerosis	1	1
1 <50% stenosis	1.3 (0.3–5.3)	1.3 (0.3–5.3)
≥2 <50% stenosis	3.0 (1.0–9.2)	2.9 (1.0–8.5)
1 ≥50% stenosis	3.2 (1.0–10.2)	3.6 (1.2–10.8)
≥2 ≥50% stenosis	5.3 (1.4–20.4)	5.3 (1.4–19.5)

*Variables with $P<0.10$ in univariate analyses were entered into these logistic models.

†Cervicocephalic atherosclerosis is a single variable with 5 classes, and the models take into account other variables shown in Table 3 (male gender, age, blood pressure, LDL cholesterol, alcohol consumption, smoking, and ABI for model 1; alcohol consumption, 10-year risk of CHD according to the FRS, and ABI for model 2).

Most previous studies that assessed the prevalence of asymptomatic CAD in patients with cerebrovascular disease looked for silent myocardial ischemia through exercise ECG tests or stress imaging techniques.[19] However, these noninvasive techniques have a low sensitivity compared with coronary angiography.[4] In addition, the studies either were small or enrolled highly selected populations.[19] Only 1 study used coronary angiography to detect asymptomatic CAD in stroke/TIA patients.[15] In that study involving 506 patients scheduled for carotid endarterectomy, including 288 patients with no previously known CAD, 40% had at least 1 coronary artery lesion ≥70%. In a study using 8-section CT coronary angiography, the prevalence of ≥50% asymptomatic CAD was 38% in 104 Japanese stroke patients.[20] Finally, an autopsy study reported a prevalence of ≥50% coronary artery stenosis of 29% among 188 patients with fatal ischemic stroke and no history of symptomatic CAD.[21]

An American Heart Association/American Stroke Association statement has recommended that stroke/TIA patients with an FRS-predicted 10-year CHD risk ≥20% should be considered for noninvasive testing for asymptomatic CAD.[1] Our finding that traditional risk factors for coronary events taken either individually or through the FRS are strongly associated with ≥50% asymptomatic CAD supports this recommendation. However, because our patients were investigated for asymptomatic CAD early after stroke/TIA, it remains unknown whether the impact of conventional risk factors is similar in patients who are investigated several years after their event and whose risk factors are controlled. Several cohort studies have shown that ABI is an accurate and reliable marker for generalized atherosclerosis and that people with a low ABI have an increased risk of vascular events, including coronary events.[22–24] Our finding that the prevalence of ≥50% asymptomatic CAD was higher in patients with low ABI is in agreement with those data.

In addition to those well-known risk factors for CAD, our study shows that the severity of cervicocephalic stenosis and extent of cervicocephalic atherosclerosis are strong and independent predictors of ≥50% asymptomatic CAD. Few studies previously assessed the relationships between cervicocephalic atherosclerosis and CAD. Old autopsy studies of persons who died of any cause showed an association between the extent and severity of atherosclerotic lesions in cervicocephalic and coronary arteries.[25,26] A similar association was found in a recent autopsy study of patients who died of stroke.[21] However, the results of this study cannot be generalized to all stroke patients, particularly because cardioembolic strokes were overrepresented. In a few cross-sectional studies, asymptomatic CAD (detected by noninvasive cardiac tests) was more common in patients with stroke attributable to atherosclerosis than in those with other stroke subtypes.[27–29] However, those studies either were small[29] or enrolled selected populations.[27,28] In patients with suspected CAD scheduled for conventional coronary angiography, CAD was found to be more common in those with carotid artery disease.[30,31] Finally, cohort studies have shown that asymptomatic carotid stenosis is an independent risk factor

for myocardial infarction[32] and that patients with bilateral carotid atherosclerosis are more likely to have previous myocardial infarction and to die as a consequence of myocardial infarction.[33] Our results, taken together with those previous findings, therefore support the need for a thorough assessment of cervical and intracranial atherosclerosis to identify stroke/TIA patients with a high risk of asymptomatic CAD.

Our study, however, has potential limitations. First, this study was a single-center study, and the generalizability of our results may be questionable. However, patients were referred to our stroke unit by emergency departments from general hospitals located in our geographic area, general practitioners, and emergency ambulance services without selection criteria. Second, inclusion of only patients 45 to 75 years of age could have affected the prevalence of asymptomatic CAD, considering the strong relation between age and CAD. However, we aimed at including patients in whom specific CAD preventive strategies such as revascularization could be contemplated. Moreover, it is unlikely that the relative effects observed in our population would be different in older patients. Third, our results do not apply to patients with cardioembolic stroke. The decision not to include these patients was driven mainly by the fact that artifacts on CT scan can be problematic in patients with atrial fibrillation.

Although all patients with stroke/TIA require risk factor modification, conventional risk factors and the FRS are able to identify those with more advanced asymptomatic CAD. When these conventional risk factors are combined with the severity of cervicocephalic atherosclerosis, about three quarters of patients with ≥50% asymptomatic CAD and 90% of those with 3-vessel disease or left main trunk disease could be identified in a subset of patients, accounting for 40% of this stroke population.

This study demonstrates the systemic nature of atherosclerosis in that significant disease in 1 territory is related to asymptomatic disease in another organ (the heart), especially with elevations of the common risk factors for atherosclerosis. This study cannot address the value of screening for asymptomatic CAD, particularly because TIA and stroke are considered "coronary risk equivalents" and warrant intensive atherosclerosis risk factor modification. Unless tested in further studies, screening stroke patients for asymptomatic CAD is not recommended, and the need for coronary revascularization should be addressed by standard algorithms as suggested by national guidelines.[34]

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Disclosures

None.

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CLINICAL PERSPECTIVE

Coronary artery disease (CAD) is a significant cause of morbidity and mortality in stroke patients. Using 64-section CT coronary angiography, we assessed the prevalence of ≥50% asymptomatic CAD in 274 consecutive patients with ischemic stroke or transient ischemic attack and whether asymptomatic CAD is related to traditional risk factors and cervicocephalic atherosclerosis. The prevalence of ≥50% asymptomatic CAD was 18% (95% confidence interval, 14 to 23). Asymptomatic CAD was independently associated with traditional risk factors assessed individually and through the Framingham Risk Score, the presence of at least 1 ≥50% cervicocephalic artery stenosis, excessive alcohol consumption, and ankle brachial index <0.9. The prevalence of ≥50% asymptomatic CAD was also related to the extent of cervicocephalic atherosclerosis. The majority of patients (75%) with ≥50% asymptomatic CAD and 90% of those with 3-vessel disease or left main trunk disease had either a 10-year-risk of coronary heart disease ≥20% according to the Framingham Risk Score or at least 1 ≥50% cervicocephalic artery stenosis. This subset of stroke patients accounted for 40% of the study population. This study cannot address the value of screening for asymptomatic CAD. The decision to screen for asymptomatic CAD stroke patients and the need for coronary revascularization should be addressed by standard algorithms as suggested by national guidelines.