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Prevalence and Prognosis of Coexistent Asymptomatic Intracranial Stenosis

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Abstract

Background and Purpose—There are limited data on the prevalence and prognosis of asymptomatic intracranial stenosis (AIS).

Methods—Baseline cerebral angiograms and MR angiograms were used to determine AIS (50% to 99%) coexistent to symptomatic intracranial stenosis for patients enrolled in the Warfarin-Aspirin Symptomatic Intracranial Disease study.

Results—Coexisting AIS were detected in 18.9% (n=14/74) of patients undergoing 4-vessel cerebral angiography and 27.3% (n=65/238) of patients undergoing MR angiogram. During a mean follow-up period of 1.8 years, no ischemic strokes were attributable to an AIS on cerebral angiography and 5 ischemic strokes (5.9%, 95% CI: 2.1% to 12.3%) occurred in the AIS territory on MR angiogram (risk at 1 year=3.5%, 95% CI: 0.8% to 9.0%).

Conclusions—Whereas the prevalence of coexisting AIS (50% to 99%) in patients with symptomatic stenosis is high, the risk of stroke from these asymptomatic stenoses is low.

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Keywords

atherosclerosis; diabetes; intracranial disease; intracranial stenosis; prognosis; risk factors; stroke

Intracranial atherosclerosis is an important cause of stroke, especially in blacks, Hispanics and Asians.^{1,2} Based on the Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) trial, the ischemic stroke rate in the territory of a symptomatic intracranial stenosis (50% to 99%) at one year was 11% (warfarin) and 12% (aspirin).³ Corresponding data on asymptomatic intracranial atherosclerosis (AIS) are limited. Ischemic stroke rates have only been reported in asymptomatic middle cerebral artery disease, ranging from 0 to 1.4% per year,^{4,5} but these studies have been limited by inclusion of all degrees of stenosis including occlusion and no angiographic verification.

Collaboration between the WASID and the Stroke Outcomes and Neuroimaging of Intracranial Atherosclerosis (SONIA)⁶ trials provided a unique opportunity to determine the prevalence and prognosis of AIS in patients with known symptomatic intracranial stenosis.

Methods

Design

All patients enrolled in the WASID trial for whom baseline central angiogram readings or MR angiograms (MRAs) were available were evaluated in this post hoc analysis.³

Prevalence

Separate estimates of coexistent AIS (50% to 99%) were made from central readings for 4-vessel cerebral angiograms (CA) and MRA studies. We excluded patients with 2- and 3-vessel CA in the prevalence analysis to avoid misclassifying patients with partial imaging studies. Patients with 1-vessel angiograms were excluded because of the presence of the symptomatic intracranial stenosis within this territory. By definition, patients with “flow gaps” on MRA were considered to have a 50% to 99% stenosis. Asymptomatic stenoses were considered tandem if 2 ipsilateral stenoses were present outside of the territory of the symptomatic intracranial artery.

Risk Factors

Comparisons of baseline characteristics were made between patients with and without coexistent AIS (50% to 99%) as determined from either a 4-vessel CA or an MRA.

Prognosis

Among patients identified as having coexistent AIS (50% to 99%), the risk of stroke in that territory was assessed with separate estimates for coexistent AIS identified by CA (2-, 3- or 4-vessel) and MRA.

Statistical Analysis

Prevalence estimates and the risk of stroke in the territory of the coexistent AIS were calculated as percentages with 95% CIs determined using exact binomial methods. Comparisons of baseline characteristics were made between patients with and without coexistent AIS using the independent groups *t* test (for means) and the χ^2 test (for percentages). A 2-tailed probability value ≤ 0.05 was considered statistically significant.

Results

Prevalence

Baseline 4-vessel CA were available for 74 patients. Of these, 18.9% (n=14/74, 95% CI: 10.8% to 29.7%) had a coexisting AIS (50% to 99%). A total of 17 coexisting AIS were found among 14 patients, including 7 (41%) vertebral artery, 5 (29%) intracranial internal carotid artery, 3 (18%) basilar artery and 2 (12%) middle cerebral artery. Two patients had tandem asymptomatic stenoses.

Baseline MRA studies were available in 238 patients. Of these, 27.3% (n=65/238, 95% CI: 21.8% to 33.4%) had a coexisting AIS (50% to 99%). A total of 85 coexisting AIS was found among 65 patients, including 35 (41%) intracranial internal carotid artery, 26 (31%) middle cerebral artery, 18 (21%) basilar artery and 6 (7%) vertebral artery. Eight patients had tandem asymptomatic stenoses.

Risk Factors

Patients with coexistent AIS were older (66.2 versus 62.6 years, $P=0.024$) and more likely to have diabetes (48.6% versus 32.1%, $P=0.013$) and a higher mean systolic blood pressure at enrollment (144.7 versus 139.4 mm Hg, $P=0.028$) than their counterparts without coexistent AIS (Table).

Prognosis

Based on CA, 35 patients (14 with 4-vessel, 9 with 3-vessel and 12 with 2-vessel) had 40 coexistent AIS. Nine (22.5%) of these stenoses were considered severe (70% to 99%). No ischemic strokes were attributable to any of these coexisting asymptomatic stenoses over the mean follow-up period of 1.8 years. Based on MRA, 5 ischemic strokes occurred in the coexisting AIS territory among 85 stenoses, a risk of 5.9% (95% CI: 2.1% to 12.3%) over the follow-up period (risk at 1 year =3.5%, 95% CI: 0.8% to 9.0%). Four of these 5 ischemic strokes occurred in the territory of tandem asymptomatic intracranial stenoses (risk of stroke in tandem AIS=50%, 95% CI: 15.4% to 84.6%).

Discussion

We found that the prevalence of coexistent AIS (50% to 99%) in our cohort of patients with another symptomatic stenosis was high when using CA (18.9%) or MRA (27.3%). The higher prevalence detected by MRA versus CA is probably explained by data from the SONIA analysis which found that a flow gap or measured stenosis of 50% to 99% on MRA had a positive predictive value of 59% in detecting intracranial stenosis of 50% to 99% by CA.⁶ Therefore, the prevalence of true AIS in our MRA cohort is probably closer to 16.1% ($0.59 \times 27.3\%$), similar to our patients with CA evidence of asymptomatic stenosis. This prevalence of AIS is high and is likely due to the manifested atherosclerosis in our cohort that had another known symptomatic intracranial stenosis.

Diabetes and systolic blood pressure at enrollment were the only statistically significant, modifiable risk factors for coexistent AIS detected by CA or MRA. This supports previous results which have found diabetes to be an independent risk factor for AIS.¹

We found that the risk of stroke in the territory of a coexistent AIS is low based on CA (0%) or MRA (5.9%). We do not know whether the strokes in the coexistent AIS territory based on MRA occurred in true-positive or false-positive stenoses, but the low risk based on CA provides the strongest evidence for the relatively benign prognosis of AIS. However, we observed a subgroup of individuals with tandem asymptomatic stenoses who appeared to be

at high risk of stroke in the territory. Given the small number of patients with tandem AIS, further studies will be needed to clarify their risk of stroke.

Limitations of our study include that post hoc analyses were performed in patients with coexistent symptomatic intracranial disease. Also, all patients received antithrombotic or anticoagulant therapy and management of vascular risk factors in a clinical trial. Therefore, these data cannot be directly extrapolated to a community-based asymptomatic population.

Interventional techniques such as intracranial angioplasty and stenting are emerging as alternative treatments to medical therapy in symptomatic patients with intracranial stenosis. Based on data from 2 phase 1 multicenter studies, the 30 day risk of stroke or death after intracranial stenting in symptomatic patients was 4.5% to 6.6%.^{7,8} Given the low risk of stroke in the territory of an AIS in this and other studies^{4,5} and the inherent periprocedural risk of intracranial angioplasty or stenting, interventional procedures for the treatment of AIS do not appear to be warranted.

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Table

Comparison of WASID Patient Groups With and Without Coexistent AIS 50% to 99% Based on 4-Vessel Cerebral Angiography or MRA

	Presence of AIS (n=72)	Absence of AIS (n=194)	P Value
Age, y	66.2±11.4	62.6±11.4	0.024
Gender (Male)	47 (65.3%)	113 (58.2%)	0.298
Race			
Black	26 (36.1%)	72 (37.1%)	
White	36 (50.0%)	103 (53.9%)	0.632
Other	10 (13.9%)	19 (9.8%)	
Hypertension (Yes)	65 (90.3%)	166 (86.1%)	0.356
Diabetes (Yes)	35 (48.6%)	62 (32.1%)	0.013
Lipid Disorder (Yes)	53 (74.6%)	130 (69.2%)	0.386
Blood Pressure, mm Hg			
Systolic	144.7±20.2	139.4±16.3	0.028
Diastolic	77.2±11.2	76.7±10.7	0.748
Hemoglobin A1C, %	8.2±2.5	7.9±2.5	0.594
Laboratory lipids, mg/dl			
HDL	43.4±11.8	44.1±12.5	0.716
LDL	125.9±40.0	123.2±38.0	0.641
Smoking			
Never	35 (48.6%)	68 (35.0%)	
Previously	25 (34.7%)	82 (42.3%)	0.126
Currently	12 (16.7%)	44 (22.7%)	
Coronary artery disease (Yes)	25 (35.7%)	50 (26.6%)	0.152
Ischemic stroke (Yes)	21 (29.6%)	36 (19.0%)	0.064

Values in the table are mean±SD or No. (%).