

*Original Article***Asymptomatic carotid artery stenosis in patients with severe peripheral vascular diseases**

Rasoul Mirsharifi<sup>a</sup>, Faramarz Karimian<sup>a</sup>,  
Mohammad Reza Farahmand<sup>a</sup>, Ali Aminian<sup>\*a</sup>

**Abstract**

**BACKGROUND:** The prevalence of carotid artery stenosis (CAS) in the general population is not high enough to justify screening programs. This study was done to determine the prevalence of asymptomatic carotid artery stenosis (ACAS) among patients with severe peripheral vascular disease (PVD).

**METHODS:** Between March 2005 and February 2006, 54 consecutive patients with severe PVD admitted at a vascular surgery unit and underwent carotid duplex scanning in a prospective study. A questionnaire was used to collect data concerning known risk factors. Significant CAS was defined as a stenosis of 70% or greater.

**RESULTS:** The mean age was 62.5 years (51-72). Out of 54 patients, 2 (3.7%) had an occluded internal carotid artery. Significant CAS was found in 9 (16.7%) and its presence was correlated with diabetes, hypertension, hypercholesterolemia, hypertriglyceridemia, coronary artery disease, severity of symptoms, ankle-brachial index, and carotid bruit. On multivariate analysis, only hypercholesterolemia and carotid bruit seemed to have independent influence.

**CONCLUSION:** The prevalence of significant ACAS is higher among patients with severe PVD. This patient population may indicate a suitable subgroup for screening of ACAS, especially when hypercholesterolemia and carotid bruit are present.

**KEYWORDS:** Carotid artery stenosis, duplex ultrasound scanning, peripheral vascular disease, carotid endarterectomy, cerebrovascular accident.

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Optimal management of asymptomatic carotid artery stenosis (ACAS) is still a matter of debate and controversy. An important area of investigation is to identify those with significant carotid artery stenosis (CAS) who may benefit from carotid endarterectomy (CE) to reduce the risk of cerebrovascular events.<sup>1,2</sup> Today, duplex ultrasound scanning (DUS) is considered a valuable imaging modality to evaluate carotid arteries with high sensitivity and specificity and virtually non-existent hazards.<sup>3,4</sup> Screening of the general population for identification of asymptomatic patients with CAS does not seem justifi-

fied because the prevalence of significant CAS in unselected elderly people with no history of cerebrovascular accidents is reported to be 1.5%.<sup>5</sup> A recent meta-analysis reported that asymptomatic patients benefit from CE only by a narrow margin of statistical significance.<sup>6</sup> These issues imply that noninvasive identification of asymptomatic patients and the definition of population who may benefit from CE subsequent to detection of significant stenosis need further clarification.

In this study, we performed DUS on patients who were referred to a vascular surgery department. Our main objective was to pro-

<sup>a</sup> Department of Surgery, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.

\* Corresponding Author

E-mail: aliaminian@doctor.com

vide a better definition of asymptomatic patients for whom noninvasive carotid examination could be justified.

## Methods

The study was conducted in the vascular surgery unit of a referral teaching hospital. The study population was patients referred for peripheral vascular disease (PVD) between March 2005 and February 2006. Severity of presenting symptoms was classified into two types: limb-threatening and non-limb-threatening ischemia. Claudication was considered as non-limb threatening symptom. Rest pain, ulceration, and gangrene were severe limb-threatening conditions. Indications for surgical revascularization included disabling claudication (severely limiting lifestyle or work), severe ischemia (rest pain, ulceration, and gangrene) and microembolization of the toes in which no other source was identified.<sup>7</sup> Patients with ischemic neurologic symptoms or history of stroke at any time were excluded. A standard questionnaire was used to collect baseline data (age, gender, diagnosis, severity of symptoms of PVD, ankle-brachial index (ABI), type of surgery and presence of bruit) as well as known risk factors including hypertension (blood pressure  $\geq$  140/90 mmHg), hypercholesterolemia (fasting total cholesterol level  $\geq$  200 mg/dL), hypertriglyceridemia (fasting triglycerides level  $\geq$  200 mg/dL), diabetes (fasting glucose level  $\geq$  126 mg/dL), smoking, and history of coronary

artery disease (CAD) for each patient. Serum levels of total cholesterol, triglycerides and glucose were analyzed enzymatically using the commercial kits (Pars Azmon, Iran). Blood pressures were measured by mercurial sphygmomanometer in a standard situation.

All patients underwent preoperative DUS of both internal carotid arteries (ICAs) by a single radiologist. Significant stenosis was defined as a stenosis of 70% or more. Since atherosclerotic involvements of the two carotid arteries in a single patient are not considered independent phenomena and since the study unit for all our analyses were the patients, instead of reporting affections in total number of arteries, the artery with greater involvement is reported. T-test was applied for comparison of continuous data and chi-square test was used for comparison of categorical data. A significance level of 0.05 was considered for all comparisons. Data were analyzed using SPSS 11 (SPSS Inc, Chicago, Ill) for Windows.

## Results

54 consecutive patients with mean age of 62.5 years (range 51 to 72) who met the inclusion criteria were recruited during the study period. Most of the patients (78%) were men. Table 1 demonstrates diagnoses and operations of this series of patients with PVD.

Ischemic wound was the most common reason for referral. Cigarette smoking was the only risk factor that had a prevalence of more than %50 among patients (table 2).

**Table 1.** Causes of peripheral vascular diseases and performed operations in 54 patients

Diagnosis	n (%)	Operation	n (%)
Unilateral aorto-iliac disease	13 (24.1%)	Aorto-unifemoral bypass	7 (13%)
Bilateral aorto-iliac disease	5 (9.3%)	Aorto-bifemoral bypass	5 (9.3%)
Unilateral femoral disease	15 (27.8%)	Unilateral femoro-popliteal bypass	15 (27.8%)
Bilateral femoral disease	9 (16.7%)	Bilateral femoro-popliteal bypass	9 (16.7%)
Popliteal disease	6 (11.1%)	Femoro-femoral bypass	6 (11.1%)
Buerger's disease	6 (11.1%)	Axillo-femoral bypass	1 (1.9%)
Total	54 (100%)	Amputation	11 (20.4%)
		Total	54 (100%)

**Table 2.** The distribution of parameters related to significant carotid stenosis (70% or more)

	Stenosis < 70%	Stenosis ≥ 70%	p value	Total
Number	45 (83.3%)	9 (16.7%)		54 (100%)
Gender			0.38	
Male	36 (80%)	6 (66.6%)		42 (78%)
Female	9 (20%)	3 (33.3%)		12 (22%)
Severity of symptoms				
Intermittent claudication	12 (26.7%)	0 (0%)	0.001	12 (22.2%)
Rest pain	16 (35.5%)	0 (0%)		16 (29.6%)
Ischemic ulcer	16 (35.5%)	6 (66.6%)		22 (40.7%)
Gangrene	1 (2.2%)	3 (33.3%)		4 (7.4%)
Ankle-Brachial Index (ABI)				
Normal	2 (4.4%)	0 (0%)	< 0.0001	2 (3.7%)
0.7-1	34 (75.5%)	0 (0%)		34 (63%)
0.4-0.7	9 (20%)	6 (66.6%)		15 (27.8%)
<0.4	0 (0%)	3 (33.3%)		3 (5.6%)
Carotid bruit	8 (17.8%)	9 (100%)	< 0.0001	17 (31.5%)
Diabetes	8 (17.8%)	7 (77.7%)	< 0.0001	15 (27.8%)
Hypertension	13 (28.9%)	8 (88.9%)	0.001	21 (38.9%)
Hypercholesterolemia	3 (6.7%)	6 (66.6%)	0.0001	9 (16.7%)
Hypertriglyceridemia	3 (6.7%)	6 (66.6%)	< 0.0001	9 (16.7%)
Cigarette smoking	37 (82.2%)	6 (66.6%)	0.29	43 (79.6%)
Coronary artery disease	11 (24.4%)	9 (100%)	< 0.0001	20 (37%)

Table 3 summarizes the DUS findings of the left and right ICAs and the most severe involvement among the two arteries in each patient. There was no difference in significant stenosis between the two sides. Out of all 54 patients, 2 (3.7%) had an occluded ICA. 9 (16.7%) patients suffered from significant CAS.

We evaluated the association between CAS of 70% or greater and the recorded parameters using univariate analyses (table 2). Presence of hypertension, hypercholesterolemia, hypertriglyceridemia, diabetes, and history of CAD correlated with significant CAS. Severity of symptoms of PVD and ABI were also associated with significant CAS. Bruit was audible in all patients with significant CAS, but only in about 17.8% of patients with CAS less than 70% (p-value < 0.0001). In our study, age and

gender had no effect on CAS prevalence, neither had cigarette smoking.

A multivariate analysis was performed with diabetes, hypertension, hypercholesterolemia, hypertriglyceridemia, CAD, severity of symptoms, ABI, and carotid bruit in a step-wise forward logistic regression model, with CAS of 70% or more. In this model, only hypercholesterolemia (p value 0.04, odds ratio 1.1226) and carotid bruit (p value 0.038, odds ratio 1.0951) were found to have independent influence on CAS. Presence of both of these factors had sensitivity of 66.7% and specificity of 98% for estimation of significant CAS.

## Discussion

Our study shows higher prevalence of significant CAS among patients with severe PVD.

**Table 3.** Duplex findings of the left and right internal carotid arteries and the most severe involvement among the two arteries in each patient

Degree of stenosis	Right carotid	Left carotid	Patient
<b>Less than 70%</b>	<b>48 (88.9%)</b>	<b>49 (90.7%)</b>	<b>45 (83.3%)</b>
0%	24(44.4%)	25 (46.3%)	18 (33.3%)
1-29%	13 (24.1%)	14 (25.9%)	17 (31.5%)
30-69%	11 (20.4%)	10 (18.5%)	10 (18.5%)
<b>70% or more</b>	<b>6 (11.1%)</b>	<b>5 (9.3%)</b>	<b>9 (16.7%)</b>
70-99%	4 (7.4%)	5 (9.3%)	7 (13%)
100%	2 (3.7%)	0 (0%)	2 (3.7%)

This finding is also reported in other studies with similar design. Ballota et al performed DUS on 312 patients with PVD over an 18-month period. A 30% or greater CAS was detected in 189 patients, whereas 65 of the 132 asymptomatic patients had 60-99% stenosis.<sup>8</sup> House et al showed ACAS of  $\geq 50\%$  in 35% and  $\geq 70\%$  in 18% of patients with PVD. 5% had an occluded carotid vessel at first presentation.<sup>9</sup>

However, the investigation of correlation between risk factors and significant CAS has produced somewhat controversial results. Klop et al performed DUS to assess ICA disease in 416 consecutive patients with PVD. Major ICA disease, meaning  $\geq 75\%$  stenosis or occlusion, was found in about 15%. They found no correlation between the severity of the CAS and PVD. Their results showed that there was no correlation between major ICA disease and hypertension, gender, age, diabetes, hypercholesterolemia, smoking and CAD.<sup>10</sup>

Ahn et al retrospectively reviewed 78 patients of PVD with carotid DUS. Individual risk factors for atherosclerosis, including age, CAD, hypertension, diabetes, smoking, and a recent or past history of cardiac or vascular surgery did not predict the detection of high-grade CAS. However, all 11 patients with CAS  $\geq 50\%$  were 68 years of age and older, and this age range, in combination with the various risk factors, increased the incidence of significant CAS ( $\geq 50\%$ ) to as high as 45%.<sup>11</sup>

Ascher et al examined findings of carotid DUS in 307 patients aged 65 years and older referred to a vascular surgeon for problems

other than carotid disease. Their study showed that the prevalence of ACAS  $> 70\%$  was high (21%) and was associated with male gender, advanced age, diabetes and having quit smoking.<sup>12</sup>

In study of Rancic et al, 109 patients with symptomatic lower extremities atherosclerosis underwent routine carotid DUS to detect the presence of ACAS. Forty patients (36.69%) had hemodynamically significant CAS  $> 60\%$  or occlusion, and 32 patients (29%) had CAS  $> 70\%$  or occlusion. They found that significant CAS was associated with prior vascular surgery, in patients over 60 years of age, arterial hypertension, and carotid bruit. Probability that various factors influenced the prevalence of CAS was assessed by multivariate stepwise logistic regression analysis. Only carotid bruit was associated with CAS  $> 60\%$  ( $t = 0.50$ ;  $p = 0.01$ ), with sensitivity of 67% and specificity of 56%.<sup>13</sup>

Pilcher et al conducted a study on 200 patients with PVD but no previous cerebrovascular history to determine the prevalence and severity of ACAS. A total of 50 patients (25%) were found to have CAS  $> 50\%$ , with 27 (13.5%) of these having  $> 70\%$  stenosis. Bilateral CAS  $> 50\%$  was seen in 21 (10.5%) patients, of which 10 (5%) had bilateral stenosis of  $> 70\%$ . No correlation was found between the significant CAS and severity of PVD or individual atherosclerotic risk factors.<sup>14</sup>

Kurvers et al investigated whether screening for CAS and abdominal aortic aneurysm (AAA) was indicated in patients with either

manifest atherosclerotic disease or with only risk factors for atherosclerosis. The presence of CAS or AAA was determined with DUS in 2274 patients enrolled in the large prospective cohort study of patients referred to a vascular center. The prevalence of CAS  $\geq 70\%$  was low in patients with risk factors for atherosclerosis (only 1.8%-2.3%), intermediate in patients with CAD (3.1%), and highest in patients with PVD (12.5%) or AAA (8.8%). They concluded that screening for CAS should be limited to patients referred with PVD or AAA, especially those with advanced age or with low diastolic blood pressure.<sup>15</sup>

Another comprehensive study was performed in 2002 by Cina et al. They investigated 620 patients with PVD, who had no recent neurologic symptoms, by carotid DUS. An occluded ICA was found in 4.8% of patients. The prevalence of a CAS  $> 50\%$  was 33%. Age of more than 70 years ( $p = 0.007$ ), diabetes mellitus ( $p = 0.042$ ), history of stroke ( $p = 0.011$ ), and ABI of less than 0.8 ( $p = 0.0006$ ), were independently associated with CAS  $> 50\%$ . They

concluded that screening for CAS in asymptomatic patients with PVD is justifiable, but not mandatory, when two or more risk factors are present or when the ABI is low. Rates of progression to clinically significant stenosis are low and do not justify reevaluation every 6 months.<sup>16</sup>

Our finding of significant CAS in about 17% of patients with PVD is similar to other studies. Our patients were younger than most other studies and this may explain lack of correlation between age and significant CAS in this study. Univariate analysis demonstrated correlation between diabetes, hypertension, hypercholesterolemia, hypertriglyceridemia, CAD, severity of symptoms, ABI, and carotid bruit and the presence of significant CAS among our patients. Of these factors, only hypercholesterolemia and carotid bruit showed independent influence. We believe that the results of this study support the idea that patients with severe PVD may be a suitable population to screen for ACAS, especially in subgroups with hypercholesterolemia and/or carotid bruit.

### Conflict of Interests

The authors have no conflicts of interest.

### Authors' Contributions

RM and FK supervised the study and managed the patients.

MRF collected the data and prepared the draft of manuscript.

AA provided assistance for all parts of study and prepared the manuscript for publication.

All authors have read and approved the content of the manuscript.

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