Original Research Article

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Prevalence of cerebro-vascular disease in patients of peripheral arterial occlusive disease

Sandeep Mahapatra^{1*}, Pinjala Ramakrishna¹, G. V. Praveen Kumar²

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*Correspondence:

Dr. Sandeep Mahapatra,

E-mail: sanusandeep@gmail.com

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ABSTRACT

Background: Peripheral arterial occlusive disease (PAOD) is a surrogate marker of systemic atherosclerosis which also predicts the risk of cerebro-vascular disease (CVD).

Methods: We have conducted a prospective study in 100 symptomatic PAOD patients between 18 to 65 years of age for detection of CVD over a period of two years. Segmental blood pressure and pulse volume recording, Duplex ultrasound blood flow of the peripheral arterial system and carotid arteries were done along with evaluation for risk factors of atherosclerosis i.e., hypertension, diabetes mellitus, hyperlipidemia, smoking history.

Results: Mean age 51.83±13.17 with history of smoking (68%), followed by diabetes (57%), dyslipidemia (29%) and hypertension in (23%) of patients.78% of the patients had PAOD in lower limbs. Overall, 30% of the patients had carotid artery stenosis, out of which 17% had less than 50% stenosis of the carotid artery and 13% had greater than 50% stenosis of the carotid artery. 30.8% of patients with lower limb disease and 60% of the patients with aorto-iliac disease had carotid artery disease.

Conclusions: This association of PAOD with CVD is significant, indicating regular screening in patients of athererosclerotic PAOD .This is further increased with age, and the presence of hypertension and smoking. We could not establish any association with diabetes, dyslipidemia in the prevalence of CVD in our subset of patients with PAOD.

Keywords: CVD, Carotid artery, Duplex scan, PAOD

INTRODUCTION

Atherosclerosis is considered to be a systemic disease. Patients with symptomatic atherosclerotic disease at one location are likely to have atherosclerotic lesions in other vascular beds. Epidemiological and clinical studies have shown the association of coronary (CHD) or cerebrovascular disease (CVD) with a profound risk of cardiovascular and cerebro-vascular events and mortality. The pre-clinical stages of Peripheral arterial occlusive disease (PAOD), represented by a border line decrease of anklebrachial index (ABI), too have a strong predictive value. 3,4

Easy accessibility enables us to use peripheral arteries as surrogate markers of cerebro-vascular and systemic atherosclerosis. Moreover, detection of PAOD is a simple and reliable diagnostic (band risk assessment) tool that also predicts carotid atherosclerosis.

Carotid atherosclerosis is associated with a risk of stroke that increases with severity of stenosis. Two major trials on carotid atherosclerosis and endarterectomy, namely, the North American symptomatic carotid endarterectomy trial (NASCET) and the European carotid surgery trial have clearly demonstrated the benefits of surgery for patients with symptoms of high-grade carotid artery

¹Department of Vascular Surgery, Nizam's Institute of Medical Science, Hyderabad, India

²Department of Vascular Surgery, Krishna Institute of Medical Science, Hyderabad, India

stenosis.⁶ Another major trial of symptom-free patients, the asymptomatic carotid Atherosclerosis study (ACAS) reported the benefits from carotid endarterectomy in patients with greater than 60% carotid stenosis, further stressing the role for screening for CVD.^{7,8}

Because peripheral vascular disease is associated with high probability of carotid atherosclerosis, screening for carotid artery disease with duplex ultrasonography has been advocated in patients with PAOD to identify patients at risk of stroke.⁹

The concept linking carotid artery stenosis with noninvasive screening by Doppler ultrasonography has picked up carotid artery lesion in up to 33% of patients with peripheral atherosclerosis.¹⁰

METHODS

We have conducted a prospective study in Department of Vascular surgery in patients of symptomatic PAOD for detection of CVD over a period of two years. All the patients between 18 to 65 years with symptomatic peripheral arterial occlusive disease were included in the study.

Patients with a history of carotid endarterectomy or any other operations for cerebrovascular disease were excluded from the study. The aims and objectives of the study were to study the prevalence of asymptomatic and symptomatic carotid artery stenosis in patients with symptomatic lower extremity atherosclerosis, to study the prevalence of additional risk factors in patients with PVD with CVD.

A standardized workup of all cases was done using SBP/PVR (segmental blood pressure and pulse volume recording), duplex ultrasound blood flow of the peripheral arterial system and carotid arteries.

Patients were evaluated for risk factors of atherosclerosis i.e., hypertension, diabetes mellitus, hyperlipidemia, smoking history and alcohol consumption, coronary history, previous coronary or vascular surgery history and family history. Data was analyzed using two-way contingency table and chi square test, and multivariate, stepwise logistic regression analysis.

RESULTS

A total of 100 patients were taken in the prospective clinical study to assess the prevalence of carotid artery stenosis in patients with PAOD. 79% of the patients were males and 21% of the patients were females. Mean age was found to be 51.83±13.17. 33.3% of the patients were in the age group of 51-60 years and 19.1% of the patients were above the age of 70 years. The most common atherosclerotic risk factor prevalent among patients was smoking (68%), followed by diabetes (57%),

dyslipidemia (29%) and hypertension in (23%) of patients.78% of the patients had PAOD involving the lower limbs, 12% had disease involving the upper limbs, 10% of the patients had disease involving the aorta and iliac vessels, 61% of the patients presented with claudication, 25% of the patients presented with critical ischemia (rest pain and/or gangrene).

Table 1: Ankle brachial index in patients of PAOD.

ABI	Number of patients (n = 100)	Percentage
Normal >0.9	2	2.0
PVD (0.4 to 0.9)	61	61.0
Critical ischemia (0.4)	25	25.0
Upper limb ischemia	12	12.0

Table 2: Co-morbid conditions in patients of PAOD.

Co-morbid conditions	Number of patients $(n = 100)$	Percentage
Diabeties	57	57.0
Hypertension	23	23.0
Smoking	68	68.0
Dyslipidemia	29	29.0

Table 3: Screening results of PAOD patients for carotid stenosis.

Number of patients (n = 100)	Percentage
70	70.0
17	17.0
13	13.0
	patients (n = 100) 70

Prevalence of carotid artery stenosis

30% of the patients had carotid artery stenosis, out of which 17% had less than 50% stenosis of the carotid artery and 13%had greater than 50% stenosis of the carotid artery. 30.8% of patients with lower limb disease had carotid artery disease. 60% of the patients with aortoiliac disease (including AAA) had carotid artery disease.

57 patients with PAOD had diabetes, out of which 19.3% of the patients had less than 50% carotid stenosis, and 15, 8%had greater than 50% carotid stenosis. 23 patients with PVOD were found to be hypertensive, out of which 52.1% of the patients were found to have carotid artery stenosis., out of which 21.6% of the patients had greater than 50% carotid artery stenosis. 63 patients in the study were smokers, out of which 35.3% of the patients were found to have carotid artery stenosis. 29 patients had dyslipidemia, out of which 27.6% of the patients had carotid artery stenosis.

Table 4: Association of clinical features and co-morbid conditions with carotid stenosis.

¥7*-1-1	Total number	Carotid stenosis			D 1
Variables	of patients	Nil $(n = 70)$	<50.0% stenosis (n = 17)	>50.0% stenosis (n = 13)	P value
Age in years					
<52 years	47	41 (87.2%)	2 (4.3%)	4 (8.5%)	0.001**
>52 years	53	29 (54.7%)	15 (28.3%)	9 (17%)	
Gender					
Male	79	55 (69.6%)	15 (19%)	9 (11.4%)	0.439
Female	21	15 (71.4%)	2 (9.5%)	4 (19%)	
Diabetes	57	37 (64.9%)	11 (19.3%)	9 (15.8%)	0.428
Hypertension	23	11 (47.8%)	7 (30.4%)	5 (21.7%)	0.037*
Smoking	68	44 (64.7%)	14 (20.6%)	10 (14.7%)	0.044*
Dyslipidemia	29	21 (72.4%)	6 (20.7%)	2 (6.9%)	0.445
ABI					
Normal >0.9	2	1 (50%)	1 (50%)	0 (0%)	
PVD (0.4 to 0.9)	61	42 (68.9%)	11 (18%)	8 (13.1%)	0.707
Critical ischemia (<0.4)	25	15 (60%)	5 (20%)	5 (20%)	0.707

DISCUSSION

Peripheral arterial occlusive disease (PAOD) presents as a clinical spectrum comprising of asymptomatic disease, claudication or critical ischemia. The causes of lower limb peripheral vascular disease include atherosclerosis, complication of diabetes mellitus, buerger's disease, peripheral emboli, fibrodysplasia and primary arterial anatomical occlusion.

Intermittent claudication or functional ischemia, of the lower extremities is the most common manifestation of PAOD. Limb-threatening ischemia occurs when there is tissue loss, such as ulceration or gangrene or ischemic rest pain. Other causes of limb-threatening ischemia may include continual progression of chronic atherosclerosis or acute processes such as plaque rupture with thrombosis, or embolization.

Atherosclerosis

Atherosclerosis is a degenerative disease of the arteries characterized by accumulation of cells, matrix fibers, lipids and tissue debris in the intima, which results in narrowing and obstruction of blood flow or ulceration, embolization and thrombosis. Atherosclerosis is a generalized disorder of the arterial tree and epidemiological strokes have identified a number of clinical risk factors associated with the development on complications of plaques. ¹² Cigarette smoking, elevated serum lipid levels, hypertension, obesity, diabetes mellitus, physical inactivity, emotional stress and genetic predisposition are identified as the important risk factors for PAOD.

Some of these factors appear to be more closely associated with atherosclerosis in some arterial beds than

others. For example, serum levels of cholesterol and low density lipoproteins are strongly related to coronary heart disease but only moderately related to cerebrovascular disease or peripheral vascular disease. Cerebrovascular disease is closely related to hypertension, but cigarette smoking is associated to peripheral occlusive vascular disease (PAOD).¹³

Tobacco abuse

Tobacco use is perhaps the single most important risk factor associated with increased progression of atherosclerosis as well as increased risk of amputation 14. Result from a longitudinal study of 5209 men and women in Framingham, Massachusetts, suggested that smoking correlated more closely with the developed of intermittent claudication than did any other risk factor 15

Diabetes

Patients with diabetes have two-to fourfold increase in the risk of developing intermittent claudication compared with non-diabetic patients. In the Framingham study, which has a 16-year follow-up, the age adjusted risk of developing intermittent claudication in persons with diabetes compared with controls was increased by fivefold in men and threefold in women. In

Hypertension

Hypertension is associated with the development of atherosclerosis, particularly in the coronary and cerebral circulations, as well as with a two-to threefold increased risk of claudication.¹⁸ Guidelines such as the sixth report of the joint National Committee on the Prevention, Declaration, Evaluation and Treatment of High Blood Pressure include peripheral arterial disease as a marker of

cardiovascular disease 19 and called for maintenance of blood pressure level less than 130/85 mmHg in these patients.

Dyslipidemia

Scandinavian Simvastatin survival study (4 "S" Study) the reduction in cholesterol level by simvastatin was associated with a 38% reduction in the risk of new or worsening symptoms of intermittent claudication in a subgroup analysis.²⁰

Local factors

In addition to the differences in systemic risk factors variations, local hemodynamic and arterial wall properties appear to exert major selective effects on plaque formation. ²¹ Certain regions of each vascular bed are especially prone to plaque formation whereas others are spared. ²² For example the coronary arteries, carotid bifurcation, infrarenal abdominal aorta and iliofemorial arteries are particularly susceptible to plaque formation, but the thoracic aorta and the common carotid, distal internal carotid, renal, mesenteric and upper extremity arteries are particularly resistant. Although plaques may occur in straight vessels away from branch points, they are usually located at the bifurcation or bends where variations in hemodynamic conditions are especially likely to occur. ²³

The predilection of the carotid bifurcation for atherosclerosis plaque has been extensively studied and appears to be related to be arterial geometry, Velocity profile and wall shear stress. The proximal common carotid artery and the distal internal carotid artery are relatively spared. The internal carotid sinus has across sectional area twice that of the immediate distal internal carotid segment. This configuration in combination with the branching angle results in a large area of flow separation and low and oscillating shear stress along the outer wall of the sinus and a region of laminar flow and high unidirectional shear stress along the inner wall of the sinus.²⁴

Atherosclerosis plaque in human are found throughout the length of the aorta but are rarely clinically significant in the thoracic segment. In contrast, the infrarenal abdomen aorta is particularly prone to be development of clinically significant lesions, with the formation of obstructive plaques, ulcerations, thrombi and aneurysmal degeneration. The differences in susceptibility between the abdominal portions of the aorta may be related to differences, aortic wall micro architecture, aortic wall vasavasorum blood supply and blood flow patterns and shear stress.²⁵

Cigarette smoking and diabetes mellitus are the risk factors most closely associated factors most closely associated with atherosclerosis disease of the lower extremities. ²⁶ Of all the arteries of the lower extremity the

superficial femoral artery is the most common site of multiple stenotic lesions, and the profunda femoris tends to be spared.Greater susceptibility to plaque formation because of mechanical trauma caused by the closely associated adductor magnus tendon has been proposed to explain the selective localization of occlusive disease in this area.²⁷

Ankle brachial index (ABI)

ABI provides useful information about lower extremity perfusion as a supplement to physical examination. This test can be performed bedside with a handheld Doppler and a manual blood pressure cuff. Because ankle systolic pressure varies from central aortic pressure it is convenient to normalize these values by dividing the ankle pressure by brachial blood pressure. ^{28,29} This ratio normally averages about 1.1 when well testing subject is in supine position. Because the ABI is stable from one examination to the next in the same individual it is an effective means to following the course of the disease over a period of time. A consistent decrease indicates advancing disease or a failure of arterial reconstruction. ³⁰ A spontaneous rise in the ABI is usually attributable to the development of collateral circulation. ³¹

Irrespective if the PAOD disease is symptomatic or asymptomatic decreased ABI represents on increased risk for cerebro-vascular incidents. ARIC study showed inverse linear trend between ABI and ischaemia stroke incidence.³² The lowest ABI group (0.80) had a risk ratio of 5.68 from CVD and it was shown that there also exists an interrelationship between ABI and preclinical carotid atherosclerosis" Intima media thickness (IMT). Individuals with decreased ABI (0.9) had significantly greater carotid IMI and were twice as likely to have preclinical plaques as those with normal ABI.

Determination of ABI improves identification of subjects or high risk of cardiovascular including cerebro vascular events, especially in asymptomatic patients. Since asymptomatic PAOD patients are at very high risk for an ischemia event and they deserve special interventive effort and are likely to experience the greatest profit of risk reduction procedures.

Pulse volume recording

It is a form of air plethysmograph was developed by Raines and Darling at Massoch Usetts General hospital who called their special instruments as the Pulse volume recorder (PVR).³³ The normal segmental volume pulse is characterized by a step upstroke, a sharp systolic peak and down slope that bows towards the baseline with a dicrotic wave approximately in the middle of the down slope.³⁴ The contour provides qualitative information about the arterial blood flow, closely corresponding to the direct intra-arterial pressure waveform recording at that level.

Duplex ultrasound scan

Duplex ultrasound scanning is an integral part of vascular surgery practice. Carotid duplex scan continues to be the standard initial evaluation of patients with extra cranial cerebrovascular disease, and many surgeons use duplex as the only preoperative examination before carotid end arterectomy (CEA) (74). The initial diagnostic criteria developed by investigators at the University of Washington are still being used by many laboratories.³⁵

Table 5: University of Washington updated internal carotid stenosis grading criteria based on European method of angiographic stenosis measurement.

Normal	PSV <125cm/sec. No visibility plaque, smooth arterial wals boundary layer separation in bulb
1-15	PSV < 125 cms/Sec minimal spectral broadening
16-49	PSV < 125 cms/Sec marked spectral broadening throughout cardiac cycle, no systolic window
50-79	PSV> = 125 cm/sec EDV<140 cm/sec Marked spectral broadening
80-99	EDV> = 140 cm/sec Poststenotic turbulence
Occlusion	No internal carotid flow signal; flow to zero in common carotid artery

Carotid duplex interpretation

The carotid duplex study reports angle corrected velocity data, including peak systolic velocity (PSV) and end diastolic velocity (EDV) within the tightest portion of an ICA stenosis or representative values if there is no stenosis. PSV in the CCA is also reported in most protocols because several stenosis grading scales employ the ratio of PSV in the ICA to PSV in the CCA to determine stenosis category. A description of plaque characteristics is included, and careful note is made of unusual anatomy. In 2003 a multi-specialty consensus panel composed of radiologists, neurologists, vascular surgeons, interventional radiologists, and vascular internists tried to resolve this issue by creating a unified reporting standard for carotid duplex 36 Velocity threshold chosen for a 50% stenosis was an ICA PSV equal to a greater than 125 cm/sec with visible plaque in the bifurcation. Recommended velocity threshold for an ICA stenosis greater than 70% was a PSV greater than 230 cm/sec, with visible plaque and luminal narrowing on marked by color. Doppler showing an extremely narrow lumen and total occlusion by no detectable lumen on gray - scale ultrasound scans and no flow on color, power, or spectral Doppler scans. The panel recommended use of ICA/CCA PSV ratio and ICA EDV in situations in which it appears that ICA PSV may not represent the extent or stenosis.³⁶

The prevalence of carotid artery stenosis was 30% in our study population and greater than 50% stenosis was as high as 13%. The prevalence of carotid artery disease was independently associated with age, hypertension and smoking. They were found to be no significant association with diabetes, and dyslipidemia. These observations may be used to increase the chances of detecting carotid artery stenosis (CAS) in patients with PAOD without known cerebro- vascular disease.

The results of other study showed prevalence of carotid artery stenosis from 14% to 28%, in patients who had PAD.³⁷ The wide range of prevalence of carotid artery stenosois reported can be explained by different definition and methods used by investigators to define the study population and the degree of carotid stenosis. The duplex scan criteria used for grading carotid stenosis are especially different.

Hypertension has been independently associated with carotid artery stenosis.Other investigators found indicators such as age, carotid bruit, and severe PAD, to be associated with CAS. Klop et al reported that none of the risk factors they investigated (age, gender, history of hypertension, cardiac disease, diabetes mellitus, hypercholesterolemia, smoking and severe PAD in 416 patients who had PAD or abdominal aortic aneurysm had significantly association with CAS. 38 Unfortunately, in these studies, risk factor assessment was based on questionnaires rather than direct measurement. Some investigators recommend that all patients who have PAD should undergoing duplex scanning of the carotid arteries, because screening to patients with characteristics associated with CAS would exclude too many patients with stenosis. Ahn et al concluded that routine carotid screening in patients older than 68 years with PAD.

Clinical consequences of detecting an asymptomatic carotid stenosis is still limited. Investigators of the asymptomatic carotid atherosclerosis study (ACAS) reported a benefit of carotid endarterectomy in asymptomatic patients who had an ICAS that is greater than 60%. To prevent widespread screening, the charecrerisics we found associated with carotid artery stenosis, i.e., age, hypertension and smoking, may be used in screening programmes to increase the likelihood of the presence of carotid artery stenosis, in patients who have PAOD. According to SMART study 39 age, low body weight and low diastolic blood pressure, may be used in screening for the presence of ICAS, in patients who had PAD.

CONCLUSION

The prevalence of carotid artery stenosis in patients of peripheral arterial occlusive disease was found to be 30% and 13% in patients who had greater than 50% carotid artery stenosis. This association increases with age, and the presence of hypertension and smoking. We could not establish any association with diabetes, dyslipidemia in

the prevalence of CAS in our subset of patients with PAOD.

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