Duplex screening for carotid artery stenosis in patients with peripheral arterial disease in Assiut University Hospital

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Introduction
Carotid atherosclerosis is one of the several etiological factors for stroke and is considered an important health problem with a high burden of disease in the western world and in developing countries.

Aim
This study is aimed at investigating the prevalence of asymptomatic carotid artery stenosis (ACAS) in patients with peripheral arterial disease (PAD) and identifying the predictive factors of ACAS in patients with PAD.

Patients and methods
Between September 2016 and August 2017, 750 patients with PAD (Fontaine IIb–IV) underwent percutaneous transluminal angioplasty in the Department of Vascular Surgery. Patients aged less than 50 years old and those who had a previous cerebrovascular event or carotid artery intervention were excluded (n = 105). The remaining 645 patients underwent preoperative screening for ACAS using carotid duplex ultrasonography examination. The degree of internal carotid artery (ICA) stenosis was determined by the criteria of Society of Radiologists in Ultrasound Consensus Conference.

Results
We found that 302 (46.8%) patients had patent carotid arteries without any evidence of atherosclerotic plaque, whereas 343 (53.2%) patients had ACAS. The prevalence of significant ICA stenosis (≥70% stenosis) was 2.8%. ICA occlusion was detected in 0.6%. Univariate analysis revealed that age older than 65 years (P = 0.013), male sex (P = 0.022), hypertension (P < 0.001), and ischemic heart disease (P = 0.016) are predictive factors of critical carotid artery stenosis, which is defined as peak systolic velocity more than 230 cm/s with diameter reduction of at least 50%.

Discussion and conclusion
Patients with chronic lower extremity PAD with either ischemic rest pain or tissue loss (nonhealing ulcers or gangrene), which is defined as critical limb ischemia, and patients with disabling claudication who need revascularization, particularly, males older than 65 years, who have a concomitant hypertension and ischemic heart disease, can be good candidates for carotid screening with carotid duplex ultrasonography.

Keywords:
carotid stenosis, duplex ultrasonography, peripheral arterial diseases

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Introduction

Carotid atherosclerosis is one of several etiological factors of stroke and is considered an important health problem with a high burden of disease in the western world and in developing countries. Of all stroke cases, an estimated 88% are ischemic in nature [1,2]. Less than 20% of the ischemic strokes are caused by atheroma in the carotid bifurcation [3]. It is, therefore, important to identify and manage carotid atherosclerosis with the aim of stroke prevention [4].

In December 2010, the Center for Disease Control and Prevention announced stroke as the fourth leading cause of death in the USA (down from its third place ranking, which it held for decades) [5].

The Asymptomatic Carotid Atherosclerosis Study showed that carotid endarterectomy (CE) reduces stroke risk in symptom-free patients with 60% or greater internal carotid artery (ICA) stenosis. This will surely lead to the performance of an increased number of screening duplex examinations [6]. However, a generalized screening in patients with peripheral arterial disease (PAD) is controversial, and its cost-effectiveness remains to be demonstrated.

In this study, we attempted to investigate the prevalence of asymptomatic carotid artery stenosis (ACAS) in patients with chronic lower extremity ischemia who underwent revascularization procedures in Assiut University Hospital and to identify predictive factors of ACAS.

Patients and methods

Between September 2016 and August 2017, a prospective study was carried out on all patients scheduled for revascularization of chronic atherosclerotic lower extremity ischemia (Fontaine II–IV, n = 750) admitted at the Department of Vascular Surgery, Assiut University Hospital, Egypt. Patients younger than 50 years old and those with history of cerebrovascular symptoms or previous carotid surgery (n = 105) were excluded from the preoperative carotid screening. The remaining 645 patients underwent preoperative carotid screening with carotid duplex ultrasonography (CDUS) examination and were enrolled in this study. Medical records and findings of carotid CDUS examinations were prospectively reviewed. Informed consent was explained and obtained from each patient.

Risk – benefit assessment

No expected risk on patients as dealing with patient will be limited to collection of serum samples. Confidentiality (dealing with data and data dissemination should be confidential).

The clinical data obtained from chart review, the name of the patient will not be mentioned. Dealing with data and data dissemination will be confidential. Statement describing the research procedure to be given to the participants. will be taken from participants before being included in the study.

Informed consent

Will be taken from participants before being included in the study.

Other ethical concerns

The research should be conducted only by scientifically qualified and trained personnel.

Duplex scan was performed by two vascular surgeons (H.B.E.B. and M.I.A.). Duplex imaging included examination of the common, internal, and external carotid arteries and the vertebral arteries on both sides. Through gray-scale imaging and spectral Doppler waveform analysis, diameter of common carotid artery, external carotid artery, and ICA was estimated. The peak systolic velocity and end diastolic velocity were measured in the most stenotic part of common carotid artery, external carotid artery, and ICA (Figs. 1 and 2).

Degree of ICA stenosis was defined by the criteria of Society of Radiologists in Ultrasound Consensus Conference[7] (Table 1). ICA stenosis of at least 70% was regarded as critical stenosis. When both carotid arteries were diseased, the more stenotic site was used for statistical analysis.

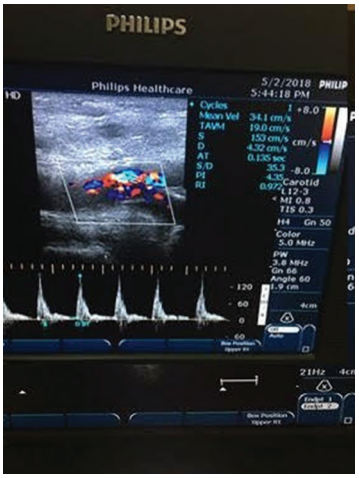
Statistical analysis

Date entry and data analysis were done using statistical package for social science, version 19 (IBM Corp. Released 2010. IBM SPSS Statistics for Windows, Version 19.0. Armonk, NY, USA). Data were presented as mean and SE. χ^2 and Fisher's exact tests were used

Figure 1

Duplex showing how to measure the diameter of common carotid artery (CCA).

Figure 2



Duplex showing high peak systolic velocity of common carotid artery equal to 153 cm/s that correlates with carotid artery stenosis 50–69%.

Table 1 Classification of degree of internal carotid artery stenosis according to Society of Radiologists in Ultrasound[7]

Degree of stenosis, %	Primary parameters		Secondary parameters	
	ICA PSV, cm/sec	Plaque estimate, %*	ICA/CCA PSV ratio	ICA EDV, cm/sec
Normal	<125	None	<2.0	<40
<50	<125	<50	<2.0	<40
50-69	125-230	≥50	2.0-4.0	40-100
≥70 but less than near occlusion	>230	≥50	>4.0	>100
Near occlusion	High, low, or undetectable	Visible	Variable	Variable
Total occlusion	Undetectable	Visible, no detectable lumen	Not applicable	Not applicable

*Plaque estimate (diameter reduction) with gray-scale and color Doppler ultrasound. CCA, common carotid artery; EDV, end diastolic velocity; ICA, internal carotid artery; PSV, peak systolic velocity.

Table 2 Patients' demographics and comorbidities

	n=645 [*n* (%)]
Age (years)	
<65	354 (54.9)
≥65	291 (45.1)
Mean±SD (range)	63.77±8.26 (50-92)
Sex	
Male	458 (71)
Female	187 (29)
Comorbidities	
Diabetes mellitus	152 (23.6)
Hypertension	183 (28.4)
Ischemic heart disease	219 (34.0)
Smoking	190 (29.5)
Hypercholesterolemia	32 (5.0)

to compare qualitative variables. Mann–Whitney test was used to compare quantitative variables in case of nonparametric data. *P* value less than 0.05 was considered statistically significant.

To identify risk factors of an asymptomatic critical ICA stenosis in patients with PAD, univariate analysis was conducted using patient demographics (age and sex), comorbidities (smoking, hypertension, diabetes mellitus, ischemic heart disease, and hypercholesterolemia), severity (claudication vs. rest pain vs. gangrene), and level of PAD (infrainguinal vs. aortoiliac vs. combined arterial occlusion).

Results

Between September 2016 and August 2017, a prospective study was carried out on all patients scheduled for revascularization of chronic atherosclerotic lower extremity ischemia (Fontaine II–IV, *n* = 750) admitted at the Department of Vascular Surgery, Assiut University Hospital, Egypt. Overall, 105 patients were excluded and did not fulfill the inclusion criteria of our study, so the remaining 645 patients underwent preoperative carotid screening with CDUS examination and were enrolled in this study (Fig. 3).

Patient demographics and clinical data are demonstrated in Table 2. Mean age of the patients was 63.77 (50–92) years. Overall, 71% were males and 29% were females.

Infrainguinal and aortoiliac arterial diseases were found in 41.4 and 23.7% of the patients, respectively, whereas 34.9% of the patients had combined lesions. Indication for treatment was claudication pain (25.9%), rest pain (37.2%), and atrophic changes/gangrene (36.9%) owing to atherosclerotic PAD (Table 3).

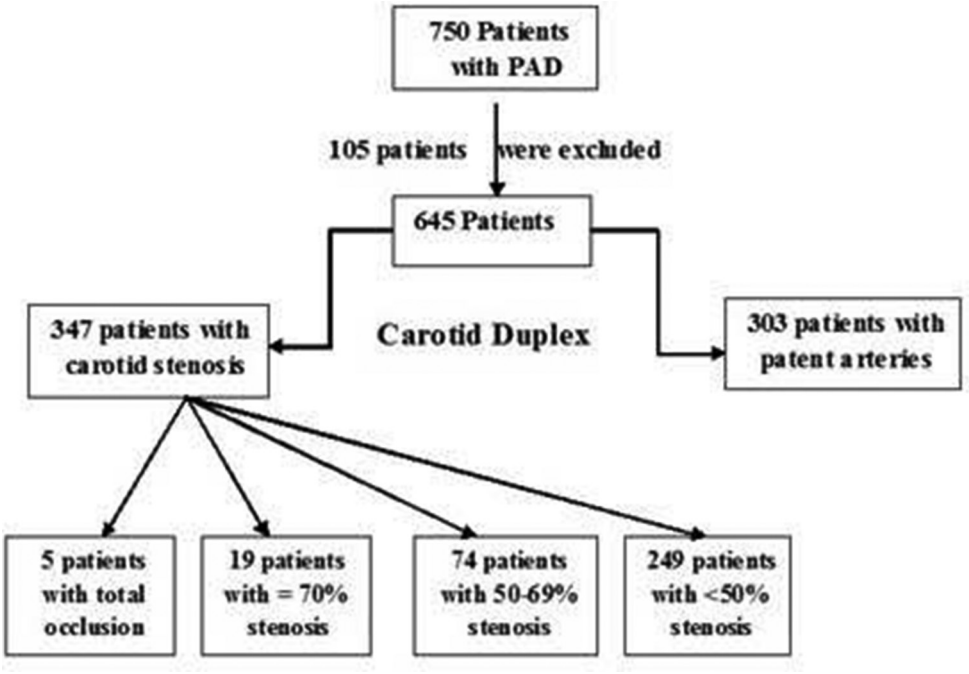
In this study, 302 (46.8%) patients had patent carotid arteries without evidence of atherosclerotic plaque. Carotid artery stenosis less than 50% was found in 38.4% (*n* = 248) of the patients. Carotid artery stenosis of 50–69% and of at least 70% was found in 11.3 and 2.8%, respectively. Total ICA occlusion was presented in four (0.6%) patients (Table 4).

The univariate analysis showed that critical ICA stenosis or occlusion was more common in older patients (>65 years old, $P = 0.013$), male sex ($P = 0.022$), hypertension ($P < 0.001$), ischemic heart disease ($P = 0.016$), infrainguinal occlusive disease ($P = 0.015$), and Fontaine grade IV severity ($P = 0.044$). Prevalence of smoking, diabetes mellitus, and hypercholesterolemia showed no statistical difference between patients with a critical stenosis and those without any carotid stenosis (Table 5).

Discussion

Cerebral ischemia is one of the disastrous perioperative complications of cardiovascular surgery (such as CE, carotid artery stenting, coronary artery bypass graft, or mitral valve replacement) and transbrachial approach of iliac angioplasty and transradial approach of cardiac catheterization. Patients who have critical carotid stenosis are vulnerable to hypotension that can occur during or after carotid artery stent placement owing to the stretching of the carotid sinus baroreceptors by the balloon and the stent or during CE owing to cross-clamping and surgical manipulation of the carotid sinus. The episode of hypotension during

Figure 3



Patient population and study algorithm. PAD, peripheral artery disease.

Table 3 Levels and grades of peripheral artery disease in our study

	n=645 [*n* (%)]
Peripheral artery disease	
Aortoiliac	153 (23.7)
Infrainguinal	267 (41.4)
Combined	225 (34.9)
Fontaine grade	
Grade II (claudication pain)	167 (25.9)
Grade III (rest pain)	240 (37.2)
Grade IV (gangrene)	238 (36.9)

Table 4 Degree of internal carotid artery stenosis

Results	*n*=645 [*n* (%)]
Patent arteries	302 (46.8)
<50%	248 (38.4)
50-69%	73 (11.3)
≥70%	18 (2.8)
Total occlusion	4 (0.6)

operation may cause cerebral ischemic infarction in these patients. There is also a hidden risk of cerebral embolism during the placement of central venous catheter before surgery [8].

Although CDUS is the best noninvasive modality for screening of ACAS, previous studies failed to prove the benefit of screening CDUS in general population on a cost–benefit analysis [1]. A preoperative screening carotid duplex provides important information about the presence of carotid artery stenosis. Carotid duplex can help surgeons identify patients at higher risk of stroke to offer them an opportunity for more intensive management of their carotid disease.

Table 5 Relation between demographic and clinical data and critical carotid stenosis (≥70%) and total internal carotid artery occlusion

	Presence of carotid stenosis [*n* (%)]		*P*
	Normal (*n*=302)	ACAS ≥70% and occlusion (*n*=22)	
Age (years)			
<65	178 (58.9)	7 (31.8)	0.013*
≥65	124 (41.1)	15 (68.2)	
Sex			
Male	204 (67.5)	20 (90.9)	0.022*
Female	98 (32.5)	2 (9.1)	
Risk factors			
Diabetes mellitus	72 (23.8)	2 (9)	0.112
Hypertension	84 (27.8)	15 (68.2)	0.000*
Ischemic heart disease	90 (29.8)	12 (54.5)	0.016*
Smoking	98 (32.5)	3 (13.6)	0.066
Hypercholesterolemia	12 (4.0)	2 (9)	0.254
PAD			
Aortoilliac	71 (23.6)	6 (27.3)	0.015*
Infrainguinal	130 (43.0)	15 (68.2)	
Combined	101 (33.4)	1 (4.5)	
Fontaine grade			
Grade II	85 (28.1)	1 (4.5)	0.044*
Grade III	119 (39.4)	10 (45.5)	
Grade IV	98 (32.5)	11 (50)	

Grade II: claudication pain, grade III: rest pain and grade IV: atrophic skin changes and gangrene. ACAS, asymptomatic carotid artery stenosis; PAD, peripheral artery disease. *ACAS was more common in patients older than 65 years old

New guidelines on the management of patients with carotid artery disease were released in January 2011 by the American College of Cardiology Foundation/American Heart Association Task Force

on Practice Guidelines [9]. Specific to screening, the task force recommended against screening of asymptomatic patients without significant risk factors for atherosclerosis or physical signs of carotid disease [9].

However, screening for carotid stenosis 'may be considered among individuals with at least two major risk factors for atherosclerosis or with a diagnosis of other cardiovascular disease such as coronary artery disease or PAD' [10]. This study suggests that it may be possible to identify patients with a higher prevalence of carotid stenosis who may benefit from screening and possible treatment of their carotid disease with CE or carotid artery stenting.

A meta-analysis of 19 studies showed a high prevalence of ACAS at 30–99% in patients with PAD [11]. The authors suggested targeting patients with PAD rather than a healthy population for routine screening. In this study, <50, 50–69, and ≥70% ACAS was seen in 248 (38.4%) patients, 73 (11.3%), and 18 (2.8%) patients, respectively, whereas total ICA occlusion was seen in four (0.6%) patients.

Our prevalence rates of carotid stenoses are in line with those reported by Ahn *et al.* [12], who screened 78 patients with PAD without recent neurologic symptoms using carotid duplex. In their study, the prevalence rates of 50–75 and >75% ACAS were 9 and 4%, respectively. In another study, carotid duplex examination of 1196 patients with vascular disease showed prevalence rates of ACAS of 11 and 2.8% for 50–79 and >80% stenosis, respectively [13].

In terms of demographic data, our results showed that critical carotid stenosis was more common in male patients (90.9%, $P = 0.022$) and in patients aged more than 65 years old (68.2%, $P = 0.013$). These results are in accordance with Cina *et al.* [14], who reported the age of more than 70 years was associated with more than 50% ACAS ($P = 0.007$). Ascher *et al.*[15] showed a high (21%) prevalence of more than 70% ACAS which was also associated with male sex and advanced age.

In terms of risk factors, our results showed that critical carotid stenosis and total ICA occlusion were more common in patients with hypertension (68.2%, $P < 0.0001$). This is in accordance with findings reported by Rancic *et al.*[16] who also found that significant ACAS was associated with hypertension ($P < 0.05$). Our results also showed that 50–69 and >70% ACAS was significantly more common in patients with ischemic heart disease. This is in agreement with O'Leary *et al.*[17] and Qureshi *et al.* [18], who reported a direct relation between the coronary artery disease and the presence of ACAS ($P < 0.001$). Other atherosclerotic risk factors, such as smoking, diabetes mellitus, and hypercholesterolemia were not found to be associated with the presence of ACAS in this study.

Lower limb revascularization was used in this study for the treatment of disabling claudications or limb salvage. In terms of the severity and level of arterial occlusion, our study showed that critical carotid stenosis was more common in patients with atrophic changes/gangrene (50%, $P = 0.044$) and infrainguinal artery occlusion (68.2%, $P = 0.015$). This is in accordance with the rates reported by Yun *et al.* [8], who also found that ACAS was more common (58.6%) in atrophic skin changes/gangrene owing to atherosclerotic PAD and 87.2% of patients with ACAS presented with infrainguinal arterial disease.

The major limitation of the present study is exclusion of patients with PAD who received only medical treatment for their limb ischemia as carotid screening was not routinely performed for those patients. Another limitation is not measuring the ankle brachial index, which could have added more information on the relation between carotid artery stenosis and the severity of PAD.

Conclusion

Our results showed that the prevalence rates of ACAS in patients with chronic atherosclerotic lower extremity ischemia are as high in the Egypt as in the western countries. ACAS was more common in patients older than 65 years old, males, and those with a concomitant hypertension or ischemic heart disease. Therefore, preoperative carotid duplex examination in those particular patients is a useful screening tool to diagnose asymptomatic carotid artery disease and to quantify the degree of carotid artery stenosis.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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