

Frequency of asymptomatic stenotic carotid artery disease in patients with lower extremity peripheral arterial disease

Yusuf Velioglu , Ahmet Yüksel 

Department of Cardiovascular Surgery, Bolu Abant İzzet Baysal University Faculty of Medicine, Bolu, Turkey

ABSTRACT

Objectives: This study aims to investigate the frequency of asymptomatic carotid artery stenosis (CAS) in patients with peripheral arterial disease (PAD) of the lower extremity.

Patients and methods: Between January 2017 and May 2018, a total of 100 patients (74 males, 26 females; mean age 60.6±9.7 years; range, 37 to 78 years) with lower extremity PAD without previous cerebrovascular event were retrospectively analyzed. All patients received carotid Duplex ultrasonography as a non-invasive screening test to detect the coexistence of CAS. Significant CAS was defined as a stenosis of ≥70% of an internal carotid artery. Data including demographic and clinical characteristics of the patients were recorded and compared between the patients with and without significant CAS.

Results: A significant CAS was present in 16 patients with PAD. Of them, 14 patients had an internal CAS of 70 to 99% and the remaining two patients had a totally occluded internal carotid artery. Bilateral significant CAS was observed in four patients. Only hyperlipidemia was found to be significantly more frequent in patients with significant CAS, compared to those without significant CAS.

Conclusion: The frequency of significant asymptomatic CAS is high in patients with PAD. We recommend routine screening for patients with lower extremity PAD for the existence of asymptomatic CAS.

Keywords: Carotid artery disease, coexistence, frequency, generalized screening, peripheral arterial disease.

Peripheral arterial disease (PAD) is a chronic progressive atherosclerotic disease, which is usually seen in advanced age, and is associated with significant cardiovascular morbidity and mortality. It may be asymptomatic, but may also occur in a wide range of symptoms including intermittent claudication, critical leg ischemia, extremity necrosis, gangrene, and even amputation. Atherosclerosis risk factors play a key role in the development and progression of PAD.^[1-3] Atherosclerosis is a long-term process which begins in childhood and progresses asymptotically during adulthood.

Cerebrovascular diseases (CVDs) are one of the most important public health problems in both developed and developing countries. They are the second most common cardiovascular pathology after coronary heart disease and are one of the leading causes of

morbidity and mortality worldwide.^[4] Atherosclerotic diseases of the carotid arteries are associated with an increased risk of CVDs which increases with the severity of carotid artery stenosis (CAS) secondary to carotid atherosclerosis.^[5-8] Carotid artery stenosis can often be easily diagnosed by carotid artery Duplex ultrasound (CADU) examination. Early identification of CAS is one of the most important precautions that may be useful in the prevention of cerebrovascular events (CVEs). The Tromsø Study investigating the prevalence and associated risk factors of CAS reported that the risk of CVE increased by 26% for each 10% increase in the degree of CAS.^[9]

There are several studies in the literature regarding the frequency of asymptomatic CAS in patients with PAD.^[10-14] However, these studies from different countries have reported different results;

Received: January 12, 2019 Accepted: January 24, 2019 Published online: March 15, 2019

Correspondence: Ahmet Yüksel, MD. Bolu Abant İzzet Baysal Üniversitesi Tıp Fakültesi Kalp ve Damar Cerrahisi Anabilim Dalı, 14030 Gököy, Bolu, Turkey.
e-mail: ahmetyuksel1982@mynet.com

Citation:

Velioglu Y, Yüksel A. Frequency of asymptomatic stenotic carotid artery disease in patients with lower extremity peripheral arterial disease. Turk J Vasc Surg 2019;28(2):73-77

consequently, the exact frequency of both diseases has not yet been clearly elucidated. In addition, due to this inconsistency, applying a routine generalized screening for CAS (e.g., with CADU) in patients with PAD has still remained a controversial issue, and there is no consensus on this issue, yet.

In this study, we aimed to investigate the frequency of asymptomatic CAS in patients with lower extremity PAD.

PATIENTS AND METHODS

This retrospective study was conducted at the Cardiovascular Surgery Department of Bolu Abant Izzet Baysal University Faculty of Medicine. Between January 2017 and May 2018, a total of 100 consecutive patients (74 males, 26 females; mean age 60.6 ± 9.7 years; range, 37 to 78 years) who were admitted to our outpatient clinic or emergency department with a diagnosis of lower extremity PAD and without previous CVE were retrospectively analyzed. Those having neurological symptoms, previous transient ischemic attack or stroke, and previous carotid artery stenting or carotid endarterectomy were excluded. A written informed consent was obtained from each patient. The study protocol was approved by the institutional Ethics Committee (Date: 27/11/2018-No. 69124690-619). The study was conducted in accordance with the principles of the Declaration of Helsinki.

After the initial clinical examination and confirmation of the PAD diagnosis, all patients received bilateral CADU as a non-invasive screening test to detect the coexistence of CAS. Data including

demographic and clinical characteristics of the patients were recorded and radiological data were obtained from the computerized medical database of our hospital. The patients were divided into two groups in terms of the existence of significant CAS according to the CADU results as Group 1 (n=16) involving patients with significant CAS and Group 2 (n=84) involving those without significant CAS. The groups were compared to analyze significant differences.

The diagnosis of lower extremity PAD was primarily established with resting ankle-brachial index (ABI) measurement. A resting ABI value less than 0.9 was considered as the main diagnostic criterion of PAD. To confirm the PAD diagnosis, all patients with a resting ABI value less than 0.9 were also evaluated radiologically with CADU scanning and/or angiographic modalities such as computed tomography (CT) angiography, magnetic resonance (MR) angiography or digital subtraction angiography (DSA). Significant CAS was defined as a stenosis of $\geq 70\%$ of an internal carotid artery (ICA).

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 20.0 software (IBM Corp., Armonk, NY, USA). The independent sample t-test was used to compare continuous variables, while the chi-square test was used to compare categorical variables. Continuous variables were expressed in mean \pm standard deviation (SD) and range (min-max) values, whereas categorical variables were expressed in number and frequency. A p value of <0.05 was considered statistically significant.

Table 1. Baseline demographic and clinical characteristics of the patients

	Significant CAS group (n=16)			Without-significant CAS group (n=84)			p
	n	%	Mean \pm SD	n	%	Mean \pm SD	
Age (year)			61.9 \pm 8.2			60.3 \pm 10.0	0.549
Gender							0.921
Male	12	75.0		62	73.8		
Female	4	25.0		22	26.2		
Body mass index (kg/m ²)			28.6 \pm 4.4			27.4 \pm 3.6	0.270
Obesity	4	25.0		16	19.0		0.585
Hypertension	8	50.0		41	48.8		0.930
Diabetes mellitus	9	56.2		35	41.7		0.281
Hyperlipidemia	11	68.8		30	35.7		0.014
Ischemic heart disease	4	25.0		19	22.6		0.836
Chronic renal dysfunction	2	12.5		9	10.7		0.834
Chronic hepatic dysfunction	1	6.2		4	4.8		0.802
Smoking	10	62.5		48	57.1		0.691

CAS: Carotid artery stenosis; SD: Standard deviation; Independent sample t-test and chi-square test were used to compare for continuous and categorical variables, respectively.

RESULTS

Of all patients, 88% had at least a single comorbid disease. The most common comorbidities were hypertension (HT) in 49 patients, diabetes mellitus (DM) in 44 patients, and hyperlipidemia (HL) in 41 patients. In total, 58% patients had a smoking habit. Baseline demographic and clinical characteristics of the patients are shown in Table 1.

According to the CADU findings, the carotid artery system had an increased intima-media thickness and/or atherosclerotic appearance in 86% of the patients. However, significant CAS was present in 16 patients with PAD. Of them, 14 patients had an internal CAS of 70 to 99% and the remaining two patients had a totally occluded ICA. Bilateral significant CAS was observed in four patients. In addition, 21 patients had an internal CAS of 50 to 69%.

Hyperlipidemia was found to be statistically significantly more frequent in the significant CAS group compared to those without. There was no statistically significant difference in the other parameters between the groups (Table 1).

DISCUSSION

The main finding of the present study is that significant CAS was found in 16% of the patients with symptomatic lower extremity PAD and additional 21 patients had ICA stenosis of 50 to 69%. Using a cut-off value of degree of significant ICA stenosis as 50%, there would be a coexistence rate of 37% in our study group. Nevertheless, the aforementioned frequency rate (16%) was not low. In the literature, there are many reports from different countries regarding the frequency of asymptomatic CAS in patients with PAD. The reported frequency rates of asymptomatic significant CAS in patients with PAD vary between 4 and 29%.^[10-18] In addition, a meta-analysis of 19 studies demonstrated that the frequency of $\geq 70\%$ asymptomatic CAS was 14% in patients with PAD.^[19] The result of our study is, therefore, consistent with these studies.

Another finding of the present study is related to the demographic characteristics of the patients. The patients with lower extremity PAD in our study should not be considered as a young adult population, although the mean age was 60.6 years. As stated by Sir William Osler, who is regarded as the pre-eminent physician of his time, "A man is only as old as his arteries"; therefore, our study population can be deemed as older

than 60.6 years old. Smoking habit was existing in more than half of the patients, as well. The majority of our patients had one or more comorbid diseases. The most common comorbidities were HT, DM, and HL. On the other hand, only HL was significantly more frequent in the patients with significant CAS than those without. Although other comorbidities were also more frequent in the significant CAS group, it did not reach statistical significance.

Many previous studies have shown an association between age, as a risk predictor, and asymptomatic significant CAS in patients with PAD.^[11,12,15,17,20,21] However, the results of these studies are inconsistent with our findings. Although the patients with significant CAS were slightly older than those without significant CAS in our study population, we found no any significant correlation between the age and significant CAS. Of note, the discrepancy in the results can be attributed to the small sample size of our study.

Furthermore, several comorbidities have been shown to be predictive factors for significant CAS in the literature. In a study involving 620 patients with PAD, Cinà et al.^[21] reported that DM was independently associated with CAS. In their study involving 546 patients with PAD, Yun et al.^[12] found that asymptomatic significant CAS was significantly more frequent in patients with coronary artery disease. In another study by Rancić et al.,^[17] HT was found to be a predictive factor for asymptomatic significant CAS in patients with PAD. In addition, Abu Arab et al.^[14] showed that both DM and HL were independent predictors for significant CAS. Mirsharifi et al.^[18] also showed the independent effect of HL on significant CAS in patients with PAD. Our results are consistent with the results of the studies performed by Abu Arab et al.^[14] and Mirsharifi et al.^[18] On the other hand, Bivil et al.^[13] and Pilcher et al.^[16] found no significant association between comorbidities and significant CAS in patients with PAD.

Although CADU is a valuable non-invasive radiological imaging method to detect carotid artery diseases, some previous studies could not prove its usefulness in the cost-effectiveness analysis of CADU screening in the general population.^[22,23] Moreover, Ahmed and Al-Khaffaf^[19] recommended targeting patients with PAD rather than the general population in routine carotid artery screening. According to the results of our study, we also suggest that the patients with PAD should be routinely screened by CADU to detect the existence of stenotic carotid artery

disease, particularly in HL patients. On the other hand, Cinà et al.^[21] concluded that the screening for asymptomatic CAS in patients with PAD was justifiable, but not obligatory.

To the best of our knowledge, there is no study investigating the frequency of asymptomatic CAS in patients with PAD in Turkey. Therefore, this is the first report from our country investigating the frequency of asymptomatic CAS in patients with lower extremity PAD.

Nonetheless, there are some limitations to this study. The main limitations are its retrospective design and relatively small sample size. Although individual risk factors except for HL were more frequent in the significant CAS group, only HL was found to be statistically significant. Small sample size might have led to an underestimation for the possible correlations between variables and significant CAS. In addition, our study group does not reflect the general population due to the single-center design and small sample size. Further large-scale and prospective studies are needed to confirm these findings.

In conclusion, the frequency of significant asymptomatic CAS is high in patients with PAD. We recommend routine screening for patients with lower extremity PAD, particularly in HL patients, for the existence of asymptomatic CAS. It should be also kept in mind that comorbidities are the subject of a multidisciplinary team involving the disciplines of cardiovascular surgery, cardiology, neurology, and radiology.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

REFERENCES

1. Yuksel A, Velioglu Y, Cayir MC, Kumtepe G, Gurbuz O. Current Status of Arterial Revascularization for the Treatment of Critical Limb Ischemia in Infrainguinal Atherosclerotic Disease. *Int J Angiol* 2018;27:132-7.
2. Gungör M. Periferik arter hastalığı olan hastalarda diyabetes mellitus varlığının koroner arter çapları üzerine etkisi. *Turk J Vasc Surg* 2017;26:29-33.
3. Senol S, Bahcivan M, Yuksel A, Es MU. Adducin and methylenetetrahydrofolate reductase gene polymorphisms in patients with peripheral arterial disease. *Acta Med Mediter* 2016;32:1773-8.
4. Levi F, Chatenoud L, Bertuccio P, Lucchini F, Negri E, La Vecchia C. Mortality from cardiovascular and cerebrovascular diseases in Europe and other areas of the world: an update. *Eur J Cardiovasc Prev Rehabil* 2009;16:333-50.
5. Barnett HJM, Taylor DW, Haynes RB, Sackett DL, Peerless SJ, Ferguson GG, et al. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. *N Engl J Med* 1991;325:445-53.
6. Deser SB, Demirağ MK, Kolbakır F. Does severe contralateral carotid artery stenosis affect the outcomes of carotid endarterectomy? *Turk Gogus Kalp Dama* 2019;27:35-42.
7. Deşer SB, Demirağ MK, Kolbakır F. Does surgical technique influence the postoperative hemodynamic disturbances and neurological outcomes in carotid endarterectomy? *Acta Chir Belg* 2019;119:78-82.
8. Beyazpınar DS, Harman A, Akozalı N, Ersoy Ö, Kayıpmaz Ç, Gültekin B, et al. Our treatment strategies of carotid artery restenoses. *Turk J Vasc Surg* 2018;27:71-7.
9. Mathiesen EB, Joakimsen O, Bonna KH. Prevalence of and risk factors associated with carotid artery stenosis: the Tromsø Study. *Cerebrovasc Dis* 2001;12:44-51.
10. House AK, Bell R, House J, Mastaglia F, Kumar A, D'Antuono M. Asymptomatic carotid artery stenosis associated with peripheral vascular disease: a prospective study. *Cardiovasc Surg* 1999;7:44-9.
11. Kurvers HA, van der Graaf Y, Blankensteijn JD, Visseren FL, Eikelboom B. Screening for asymptomatic internal carotid artery stenosis and aneurysm of the abdominal aorta: comparing the yield between patients with manifest atherosclerosis and patients with risk factors for atherosclerosis only. *J Vasc Surg* 2003;37:1226-33.
12. Yun WS, Rho YN, Park UJ, Lee KB, Kim DI, Kim YW. Prevalence of asymptomatic critical carotid artery stenosis in Korean patients with chronic atherosclerotic lower extremity ischemia: is a screening carotid duplex ultrasonography worthwhile? *J Korean Med Sci* 2010;25:1167-70.
13. Babil AS, Ghabili K, Daneshmand SE, Nemati M, Babil MS, Namdar H, et al. Prevalence of significant carotid artery stenosis in Iranian patients with peripheral arterial disease. *Vasc Health Risk Manag* 2011;7:629-32.
14. Abu Arab TM, Ramzy AA, Ghareeb M. Prevalence of Significant Carotid Artery Stenosis in Patients with Significant Atherosclerotic Peripheral Arterial Disease. *J Cardiovasc Dis Diagn* 2017;5:265.
15. Cheng SW, Wu LL, Lau H, Ting AC, Wong J. Prevalence of significant carotid stenosis in Chinese patients with peripheral and coronary artery disease. *Aust N Z J Surg* 1999;69:44-7.
16. Pilcher JM, Danaher J, Khaw KT. The prevalence of asymptomatic carotid artery disease in patients with peripheral vascular disease. *Clin Radiol* 2000;55:56-61.
17. Ramić Z, Radak D, Stojanović D. Early detection of asymptomatic carotid disease in patients with obliterative arteriosclerosis of the lower extremities. *Srp Arh Celok Lek* 2002;130:258-64.
18. Mirsharifi R, Karimian F, Farahmand MR, Aminian A. Asymptomatic carotid artery stenosis in patients with severe peripheral vascular diseases. *J Res Med Sci* 2009;14:117-22.

19. Ahmed B, Al-Khaffaf H. Prevalence of significant asymptomatic carotid artery disease in patients with peripheral vascular disease: a meta-analysis. *Eur J Vasc Endovasc Surg* 2009;37:262-71.
20. Ascher E, DePippo P, Salles-Cunha S, Marchese J, Yorkovich W. Carotid screening with duplex ultrasound in elderly asymptomatic patients referred to a vascular surgeon: is it worthwhile? *Ann Vasc Surg* 1999;13:164-8.
21. Cinà CS, Safar HA, Maggisano R, Bailey R, Clase CM. Prevalence and progression of internal carotid artery stenosis in patients with peripheral arterial occlusive disease. *J Vasc Surg* 2002;36:75-82.
22. Colgan MP, Strode GR, Sommer JD, Gibbs JL, Sumner DS. Prevalence of asymptomatic carotid disease: results of duplex scanning in 348 unselected volunteers. *J Vasc Surg* 1988;8:674-8.
23. Longstreth WT J, Shemanski L, Lefkowitz D, O'Leary DH, Polak JF, Wolfson SK Jr. Asymptomatic internal carotid artery stenosis defined by ultrasound and the risk of subsequent stroke in the elderly. The Cardiovascular Health Study. *Stroke* 1998;29:2371-6.