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

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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.
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 ≥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 ± 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

<table>
<thead>
<tr>
<th></th>
<th>Significant CAS group (n=16)</th>
<th>Non-significant CAS group (n=84)</th>
<th>p</th>
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<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>Mean±SD</td>
</tr>
<tr>
<td>Age (year)</td>
<td></td>
<td></td>
<td>61.9±8.2</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>12</td>
<td>75.0</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>4</td>
<td>25.0</td>
<td></td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td></td>
<td>28.6±4.4</td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td>4</td>
<td>25.0</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>8</td>
<td>50.0</td>
<td></td>
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<tr>
<td>Diabetes mellitus</td>
<td>9</td>
<td>56.2</td>
<td></td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>11</td>
<td>68.8</td>
<td></td>
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<tr>
<td>Ischemic heart disease</td>
<td>4</td>
<td>25.0</td>
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<tr>
<td>Chronic renal dysfunction</td>
<td>2</td>
<td>12.5</td>
<td></td>
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<tr>
<td>Chronic hepatic dysfunction</td>
<td>1</td>
<td>6.2</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>10</td>
<td>62.5</td>
<td></td>
</tr>
</tbody>
</table>

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 ≥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 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, Bavil 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 noninvasive 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.

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REFERENCES


