CLINICAL INVESTIGATIONS

Comparison of Ankle-Brachial Index in Patients With and Without Atrial Fibrillation

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Key words: *ankle-brachial index; atrial fibrillation; peripheral arterial disease; cardiovascular disease.*

Summary. *The aim of this study was to compare the ankle-brachial index between patients with atrial fibrillation (AF) and those without atrial fibrillation.*

Material and Methods. A total of 286 patients admitted to the Departments of Neurology or Cardiology, Kaunas Clinical Hospital, during 2008–2010 and referred for a consultation with an internist and/or a cardiologist were included in this study. All patients had at least one prevalent cardiovascular disorder and were screened for diagnosis of permanent AF based on medical records and electrocardiogram and evaluated for the ankle-brachial index (ABI). Peripheral artery disease (PAD) was defined as an ABI of <0.9 assessed by using a 5-MHz Doppler ultrasound device.

Results. The patients with permanent AF had a significantly lower ABI compared with the patients without AF (P<0.001). Binary regression analysis revealed that permanent AF was associated with PAD (OR, 2.5; 95% 1.5–4.2). The likelihood of having an ABI of <0.9 increased with each additional risk factor: AF (OR, 2.2; 95% CI, 1.3–3.8), stroke (OR, 2.3; 95% CI, 1.3–4.2), age of >69 years (OR, 2.4; 95% CI, 1.3–4.7), and myocardial infarction (OR, 2.4; 95% CI, 1.1–5.5). Nearly one-fourth (24.5%) of all patients with an ABI of <0.9 did not report any PAD-specific symptoms.

Conclusions. The patients with cardiovascular disorders and permanent atrial fibrillation were found to have a significantly lower mean ankle-brachial index and higher prevalence of peripheral artery disease compared with cardiovascular patients without atrial fibrillation. The patients who were found to have a lower ankle-brachial index and permanent atrial fibrillation were older and often had several cardiovascular diseases (angina pectoris, stroke, myocardial infarction, or hypertension).

Introduction

Early diagnosis of peripheral artery disease (PAD) is important in preventing further cardiovascular complications. The ankle-brachial index (ABI) is a simple and reliable tool for diagnosing PAD. It is simple enough to be performed in any physician's office, especially if a patient reports limb symptoms. Normal ABI values generally range from 0.91 to 1.3, and the value of 0.9 or less is considered as an evidence of PAD (1). Many studies have underscored the importance of using ABI values as independent predictors of cardiovascular events, such as stroke, myocardial infarction, heart failure, lower extremity amputation, and mortality (2, 3). Atrial fibrillation (AF) in patients with symptomatic PAD is associated with worse cardiovascular outcomes. It

has been reported that all-cause mortality and cardiovascular mortality rates are substantially higher in patients with AF than those without AF (7.7% and 5.6% vs. 2.5% and 1.6%, respectively; *P*<0.001) (4). The incidence of PAD increases with age. Usually it is asymptomatic and thus frequently undiagnosed (1, 5). The aim of this study was to study associations between ABI and atrial fibrillation in patients with various cardiovascular disorders, referred to Kaunas Clinical Hospital.

Material and Methods

Patients admitted to the Departments of Neurology or Cardiology, Kaunas Clinical Hospital, and referred for a consultation with an internist and/or a cardiologist were enrolled into this study. A total of 286 patients (136 men and 150 women) treated for stroke (58%), hypertension (15%), and angina pectoris (27%) were examined between 2008 and 2010. Most of them had a medical history of two or

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more cardiovascular diseases, and clinical data were gathered using medical records and patients' interview. The patients were divided into two groups: with and without AF. The diagnosis of permanent atrial fibrillation was based on ECGs and medical records using the ACC (American College of Cardiology)/AHA (American Heart Association)/ESC (European Society of Cardiology) definitions (6). Hypertension was defined as a blood pressure higher than 140/90 mm Hg documented in medical records. The diagnosis of diabetes mellitus was based on medical records and/ or current use of medications to treat diabetes mellitus. Normal left ventricular ejection fraction (LVEF) was defined as ⩾50% measured by two-dimensional echocardiography.

All patients were asked specific questions and assessed regarding the following symptoms: intermittent claudication, pain at rest, muscle cramps, fatigue, decreased hair growth on legs, changes in skin color or temperature of the feet, and muscular atrophy (7). All the patients were examined in the supine position after 10 minutes of rest. Systolic blood pressures were measured at the level of the brachial artery of each arm and both the posterior tibial and dorsalis pedis arteries of each ankle by using a 5-MHz Doppler ultrasound device (Elite model No. 100, Nicolet Vascular Inc., USA).

The right and the left ankle and brachial ABI values were calculated as a mean of 3 consecutive measurements at each site. The ABI for each lower extremity was calculated by dividing the systolic blood pressure in the posterior tibial and dorsalis pedis arteries by the highest brachial artery pressure. The lowest ABI value was used in the analysis (1, 8).

Statistical analysis was carried out using the Statistical Package for Social Sciences (SPSS), version 13.0. The following clinical parameters were included in the analysis: age, body mass index, history of hypertension, coronary artery disease (CAD), stroke, diabetes mellitus, smoking status (current smokers, ex-smokers, and nonsmokers), blood pressure, and LVEF. Continuous data are expressed as mean and standard deviation. The samples of continuous variables were checked for normality using the Kolmogorov-Smirnov test. Associations were assessed by the Student t test and ANOVA for normally distributed continuous variables; the Mann-Whitney and Kruskal-Wallis tests were employed for nonnormally distributed data. Associations between categorical variables were tested by the chi-square test. Binary regression analysis was used to test relationships between variables. The adjustments were performed for the following parameters: age (⩽69; >69 years), AF, stroke, hypertension, myocardial infarction, angina pectoris, and diabetes. The Spearman correlation was used when testing continuous variables. Differences were considered statistically significant if P was less than 0.05.

Results

Of the 286 patients with cardiovascular diseases (mean age, 74.8 years; range, 50–104 years), 109 had a diagnosis of permanent atrial fibrillation. Both the groups (without and with AF) were matched for mean body mass index (P=0.9), blood pressure (P=0.8), and proportions of patients with hypertension (P=0.5) and diabetes (P=0.4). There were significant differences between the two groups regarding age (patients with atrial fibrillation were older, P<0.001), gender (more female patients in the atrial fibrillation group, P=0.004), proportion of patients with a history of angina pectoris or stroke (more patients in the atrial fibrillation group; P<0.001 and P<0.01, respectively), and history of myocardial infarction (P<0.02) (Table 1). The percentage of current smokers and ex-smokers taken together was lower in the patients with AF than those without AF, but the difference was not significant (P=0.1).

Of the 286 patients, 116 (40.8%) had an ABI of <0.9: 31.3% in the group without AF and 56.5% in the group with AF (P<0.01) (Table 1).

The patients with permanent AF had a significantly lower ABI compared with the patients without AF (P<0.001). Consistent with this finding in the overall study population, significant differences was also seen comparing the subgroups of patients with various cardiovascular disorders and diabetes (Table 2).

Permanent AF was found to be associated with PAD (ABI <0.9) (OR, 2.5; 95% CI, 2.5–7.1) irrespective of gender (OR, 2.5; 95% CI, 2.5–7.1) and dependent on age (OR, 2.7; 95% CI, 1.4–5.1) especially in patients older than 69 years. Receiver operating characteristic (ROC) curve analysis identified an age of 69 years to be the optimal cut point to minimize false-positive and false-negative errors. The specificity of the test was 0.734. Binary regression analysis revealed that the likelihood of having an ABI of <0.9 increased with each additional risk factor: AF (OR, 2.2; 95% CI, 1.3–3.8), stroke (OR, 2.3; 95% CI, 1.3–4.2), age of more than 69 years (OR, 2.4; 95% CI, 1.3–4.7), and myocardial infarction (OR, 2.4; 95% CI, 1.1–5.5) (P<0.05 for all analyses). Nearly one-fourth (24.5%) of all patients with an ABI of <0.9 did not report any PAD-specific symptoms. Of the 116 patients with an ABI of <0.9, only 4 (3.4%) had a previously diagnosed PAD based on their medical records. Our study showed that the likelihood of having a lower ABI (<0.9) was more than 4 times greater if a patient had

Table 1. Demographic and Clinical Characteristics of Patients in the Groups With and Without Atrial Fibrillation

Characteristic	Group		P
	Without AF (n=177)	With AF (n=109)	
Age, mean (SD), years	72.7 (10.6)	78.2 (8.1)	<0.001*
Aged more than 69 years, %	63.0	85.3	<0.001
BMI, mean (SD), kg/m^2	27.2 (3.8)	27.1 (5.0)	0.9*
Men/women, %	54.2/45.8	36.7/63.3	0.004
Systolic blood pressure, mean (SD), mm Hg	159.1 (25.6)	159.8 (25.8)	0.8*
Diastolic blood pressure, mean (SD), mm Hg	89.5 (12.8)	91.0 (16.2)	0.4*
ABI, %			χ^2=19.9; df=2; P<0.001
<0.9	31.3	56.5	<0.001
0.9–1.3	54.0	38.9	0.01
>1.3	14.8	4.6	0.008
Hypertension (systolic >140 mm Hg /diastolic >90 mm Hg), %	81.4	78.0	0.5
Angina pectoris, %	68.4	91.7	<0.001
Myocardial infarction, %	9.8	2.4	0.02
Stroke, %	61.6	76.1	0.01
Diabetes, %	22.6	18.5	0.4
Smoking, %			χ^2=4.4; df=2; P=0.1
Nonsmoker	71.2	78.0	
Current smoker	16.9	8.3	
Ex-smoker	11.9	13.8	

ABI, ankle-brachial index; AF, atrial fibrillation; χ^2, chi-square statistics; df, degree of freedom.
*Student-Mann-Whitney test for two independent samples.

Table 2. Comparison of Ankle-Branchial Index in Patients With or Without Atrial Fibrillation Within Subgroups

Subgroup	Ankle-Branchial Index		P
	Without AF	With AF	
All patients	1.0 (0.29) (n=177)	0.87 (0.34) (n=109)	0.001
Hypertension >40 mm Hg	1.0 (0.3) (n=156)	0.86 (0.31) (n=103)	<0.001
Angina pectoris	0.98 (0.32) (n=121)	0.87 (0.33) (n=99)	0.01
Stroke	0.95 (0.31) (n=109)	0.83 (0.31) (n=82)	0.009
Diabetes	0.95 (0.32) (n=40)	0.66 (0.32) (n=20)	0.001

Values are mean (standard deviation). AF, atrial fibrillation.

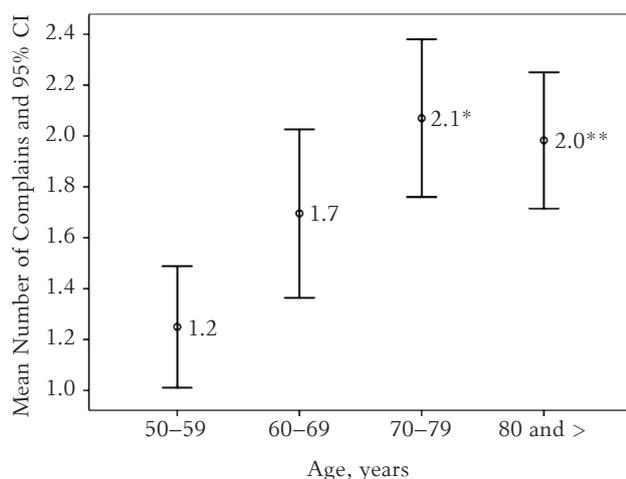*Fig.* The mean number of patients' complaints by different age groups
F=3.6; df=3; P=0.02; χ^2=10.3; df=3; P=0.02;
*P<0.05, vs. 50–59-year age group;
**P<0.01, vs. 50–59-year age group.

at least one symptom (OR, 4.2; 95% CI, 2.5–7.1). Fig. shows the mean number of patients' complains by different age groups.

In the subgroup of patients with available LVEF data (n=34), a significant positive correlation between ABI and LVEF was established: lower ABI was associated with lower LVEF (r=0.433: P=0.027).

Discussion

PAD of the lower limbs is a manifestation of systemic atherosclerosis (1), increasing the likelihood of cardiovascular diseases. The incident atherothrombotic event in one of the vascular regions (i.e., peripheral) could predict a vascular disorder in another region (i.e., cerebral) (9). The prevalence of PAD is reported to be 3%–10% in the general population, and it increases with age reaching up to 15%–20% in the population aged more than 70 years (10). Up to 50% of PAD patients are asymptomatic (11–13). According to the data of the

REACH (Reduction of Atherothrombosis for Continued Health) Registry, more than 16% of patients with various cardiovascular disorders had symptomatic PAD. One in five of them developed myocardial infarction or stroke ultimately leading to hospitalization or death from cardiovascular complications within a year. The REACH Registry has demonstrated that AF in patients with symptomatic PAD is an independent predictor of worse cardiovascular outcomes, suggesting the importance of PAD assessment and diagnosis in AF patients (2). In older patients (mean age, 80 years) with PAD, the prevalence of cardiovascular diseases was found to be 68% and that of ischemic stroke 42% (14). Similarly to the REACH Registry, the patients with AF, examined in our study, were older and had more cardiovascular disorders. PAD was diagnosed in 40.8% of the overall study population having cardiovascular conditions with a significantly greater percentage of patients being in the group with AF (56.5% vs. 31.3%, $P<0.001$). Analyzing the patients based on the presence of AF, ABI was significantly lower in the patients with cardiovascular diseases and AF compared with those who did not have AF ($P=0.001$). The same was true for the subgroups of patients with various cardiovascular risk factors. Clinical studies analyzing the relation between LVEF and ABI have reported an age-independent association between the reduced ABI and LVEF ($P<0.001$) (15, 16). Our data support this based on the analysis of a subgroup of patients with available LVEF data, showing a significant positive correlation between LVEF and ABI.

It is noteworthy that of the 116 patients with an ABI of <0.9 in our study, only 4 had previously diagnosed PAD. Moreover, none of these patients, except those 4, had undergone ABI measurements in the past. Routine ABI measurements were shown to be predictive of future cardiovascular events. Specifically, the prognosis of cardiovascular outcomes is worse in PAD patients with AF than those without AF (17). Our study suggests that cardiovascular patients with AF are at higher risk of having low ABI and PAD compared with those without AF. The odds of having PAD appeared to be even greater in symptomatic patients. As the ABI is reported to be an independent predictor of future cardiovascular events, timely ABI assessment and relevant therapy may have an impact on preventing further cardiovascular events (18, 19).

There are some limitations to the study that need to be mentioned. The patients were selected without using a randomization. The patient samples, especially in subgroups, were relatively small. These results apply only to a white population.

Conclusions

The patients with cardiovascular disorders and permanent atrial fibrillation were found to have a significantly lower mean ankle-brachial index and higher prevalence of peripheral artery disease compared with cardiovascular patients without atrial fibrillation. The patients who were found to have a lower ankle-brachial index and permanent atrial fibrillation were older and often had several cardiovascular diseases (angina pectoris, stroke, myocardial infarction, or hypertension).

Statement of Conflict of Interest
The authors state no conflict of interest.

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