Peripheral Artery Disease -In Slovakia We Have a Chance To Find Out More

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Abstract:

Aim: The aim of our study was to compare the referral of patients with suspected peripheral arterial disease (PAD) to the angiological department before and after the inclusion of the ankle-brachial index (ABI) measurement in the preventive examination performed by a general practitioner.
Design: Retrospective study.
Participants: 151 patients referred by general practitioners or other specialists (surgeon, diabetologist, internist, cardiologist, neurologist).
Methods: We determined the presence of atherosclerosis risk factors and measured the ABI using a Doppler ultrasound probe.
Results: We found that in the first half of 2019, 2.8 times more patients with suspected PAD were referred to the outpatient clin-

ic than in the first half of 2015. In 2015, general practitioners sent 32.5% of patients, and in 2019 it was 40.1% of patients.
Conclusion: A retrospective study shows that the inclusion of ABI measurement into the preventive examinations accelerated the detection of PAD.

The retrospective study was supported by an internal grant from the Slovak Medical University.

Biography of the first author:

MUDr. Katarina Dostálová, PhD, MPH comes from Slovakia. She is an internist, an angiologist and a general practitioner, assistant professor at Faculty of Public Health, Slovak Medical University. She completed her PhD in Public Health. As a member of the Slovak Angiological Society Committee she is responsible for cooperation with Slovak Society of General Practice. She is a member of the editorial board of several medical journals. Her professional interest focuses on prevention and community medicine, which she considers to be a promising modality of medicine in the future with the support of new technologies.

Introduction

Peripheral arterial disease (PAD) is a syndrome characterized by an imbalance between the need and the supply of oxygen and nutrients (blood perfusion) in the tissues of the lower limbs (1). Peripheral arterial disease (PAD) includes obliterative diseases of limb arteries and other arterial beds with the exception of coronary arteries (2). The most important risk factors for PAD remain smoking, diabetes mellitus (DM), arterial hypertension (AH) and dyslipoproteinemia (DLP). Less significant ones are gender, age and chronic renal failure. Their management is mainly the responsibility of angiologists and diabetologists. Smoking and diabetes mellitus show the strongest association with the occurrence and progression of PAD. PAD reduces the quality of life; it can even lead to the amputation of the affected limb (3). A characteristic symptom is claudication pain, which occurs during exertion and stops after a short rest. However, only a certain part of patients has typical symptoms (4).

Claudication pain may be absent in patients with polyneuropathy, and it is often absent in diabetics. Claudication does not occur in patients who cannot walk due to immobility caused by musculoskeletal diseases, exertional dyspnoea or other difficulties due to polymorbidity. Interestingly, up to 10-50% of patients with intermittent claudication have never consulted a medical doctor about their problems (4).

PAD of the lower limbs is characterized by narrowing and/or thickening of the arteries supplying the lower limbs, which leads to a deterioration of blood supply to the tissues and nerves, and thus to their damage.

PAD of the limb arteries occurs in about 5-10% of the population older than 60 years, while its incidence varies in individual epidemiological studies depending on the diagnostic methods used to diagnose PAD (based on anamnestic data or also using instrumental examination methods). The choice of the investigated file is also decisive.

In a German prospective study that followed the fate of 109 patients with intermittent claudication for 10 years, 62.3% of patients developed "polyvascular" disease, with 20% of patients having 3 vascular beds affected (3). Similarly, in a Slovak study of 2,207 patients who were examined by general practitioners, it was found that patients with an ankle-brachial index of less than 0.9 had a significantly higher incidence of myocardial infarction, angina pectoris and stroke (2).

In an inpatient study of 990 patients who were treated for various causes in a department of internal medicine, it was found that 6% of the patients had a history of PAD, but measurement of ankle-brachial pressure index revealed that up to 43.7% of patients had an index of less than 0.9 (4). In a German epidemiological study of 6,880 patients (average age 72.5 years) where GPs measured the ankle-brachial index (ABI) in all patients over 65 years of age, a prevalence of PAD (ABI less than 0.9) in 19.8% of men and 16.8% of women was found (5).

The measurement of ankle pressures and subsequently the calculation of the ankle-bra-

chial index (the abbreviation ABI from the English Ankle-Brachial Index is commonly used) is a basic auxiliary examination in the diagnosis of PAD. The ABI index is defined as the ratio of the blood pressure measured on the lower limb (ankle) and the blood pressure measured on the upper limb. Reduced pressure in the lower limbs occurs in ischemic disease of the lower limbs. The ABI index is thus an important risk marker of ischemic disease of the lower limbs and predicts the probability of a heart attack or stroke (6). It has been shown that ABI is an indirect indicator of atherosclerotic damage in other vascular beds (coronary, cerebral, renal) (7). It is a very simple and at the same time informative examination for the identification of patients that are at risk. The ABI value reliably confirms or excludes vascular limb disability.

Under physiological circumstances, arterial blood pressure (BP) values increase slightly towards the periphery. Any pathology in terms of narrowing or closing of the artery will be manifested by a drop in blood pressure in the periphery. We measure systolic BP on the peripheral arteries at the place of the applied cuff. It responds most sensitively to hemodynamic changes and is easily detected using a Doppler ultrasound meter.

Ankle BP is measured at a. dorsalis pedis in a supine patient. We record the BP at which the Doppler signal appears when the cuff is inflated. The value of the measured BP is from the place where the cuff is applied. If we measure on 2 or 3 arteries of the lower limb, the highest measured ankle BP is decisive. However, at some workplaces, ABI is calculated for each examined artery separately. We also measure BP on both aa. brachialis. Decisive is the higher measured systolic blood pressure (sBP). ABI for the right lower limb (RABI - right ankle-brachial index) and ABI for the left lower limb (LABI - left ankle-brachial index) are then calculated according to the formula:

$$\text{RABI} = \frac{\text{systolic pressure on the peripheral artery of the right lower limb}}{\text{higher systolic pressure in the upper limb}}$$

$$\text{LABI} = \frac{\text{systolic pressure on the peripheral artery of the left lower limb}}{\text{higher systolic pressure in the upper limb}}$$

Physiological ABI values range between 1 and 1.4 (8). Values below 0.9 are pathological. Borderline values (0.9-1) may occur after exercise, but should normalize within 30 seconds. ABI is measured at rest and 1 minute after exercise. With narrowed arteries, the pathological result becomes more pronounced after the load. If BP remains reduced by 20%, it is a diagnostic criterion for PAD (9). An absolute value of ankle BP below 50 mmHg indicates impending critical limb ischemia. The overall survival of patients with ABI<0.3 is significantly shorter than that of patients with a higher value (4). Increased ABI values ≥1.4 indicate mediocalcinosis.

An ABI value of <0.9 confirms the diagnosis of PAD and at the same time detects PAD in asymptomatic patients. A pathologically reduced ABI value confirms the vascular etiology of pain in the lower limbs, and we also use it to assess the severity of the disease. It thus gives us key information about the patient's long-term prognosis (Table no. 1).

Table 1 Diagnostic significance of ABI<0.9 (modified according to Norgren, 2007)

Confirms the diagnosis of PAD
Detects PAD in asymptomatic patients
Confirms a vascular etiology of pain in the lower limbs
Helps in assessing the severity of the disease
Helps to assess the development of the disease (progression, improvement, stabilization)
Has a high correlation with coronary and cerebrovascular disease
Key information about long-term prognosis (increased risk of cardiovascular mortality)

Ankle BP should be measured in all patients over 65 years of age, in smokers and ex-smokers, in patients with diabetes from the age of 50 (8), in patients with atherosclerosis, in those with dyslipoproteinemia, in hypertensive patients, in patients with pain in the lower limbs, an in patients with claudication or rest pain (7).

In the context of the anamnesis and clinical examination of the patient (inspection, palpation - especially of peripheral pulsations, auscultation over large arteries, and in questionable situations also the use of stress tests -e.g., according to Ratschow), the general practitioner evaluates the results of the ABI measurement (Table 2):

In 2016, ABI measurement was included in the preventive check-up performed by a general practitioner for all patients over 60 years of age and for patients over 50 years of age if they have at least one risk factor (10).

Methods

The aim of our work was an analysis focusing primarily on the risk factors of atherosclerosis in a set of patients suspected of having PAD who were referred for the first time to the Angiological Outpatient Clinic at the Academician Ladislav Dérer Hospital of the Bratislava University Hospital.

As in 2016 in the Slovak Republic the ABI measurement was included in the preventive check-up in the general practitioner's clinic for adults, we compared the characteristics of patients referred in the first half of 2015 and in the first half of 2019.

Another aim was to compare the characteristics of patients referred by general practitioners and other specialists.

Into our research sample group, we included 151 patients who were examined for the first time in the Angiological Outpatient Clinic at the Academician L. Dérer Hospital of the Bratislava University Hospital in the first half of 2015 (40 patients) and the first half of 2019 (111 patients) with a suspected diagnosis of peripheral arterial disease. Of the 151 patients, 75 were men (49.7%) and 76 were women (50.3%). Patients were referred by general practitioners or other specialists (surgeon, diabetologist, internist, cardiologist, neurologist).

We took patient's medical history, including the identification of atherosclerosis risk factors. We also drew information from medical records or we added laboratory tests. Patients underwent clinical examination. Subsequently, we measured the systolic blood pressure on the upper limbs above the brachialis artery and the systolic blood pressure on the lower limbs in the area of the ankle above the tibialis posterior artery and the dorsalis pedis artery with a BIDOP 100V3 portable doppler device. We calculated the ABI according to the standard formula (the ratio between the systolic pressure at the arm and at the ankle).

Statistical analyses were carried out using SPSS (Statistical package for social sciences) software (11). For the basic statistical analysis, we used frequency tables, and as numeric characters also mean, standard deviation, minimum, maximum and range (12). To compare the results for the investigated subsets, we used contingency tables and Fisher's exact test for nominal characters (13). For numerical characters, for comparison, we used non-parametric exact Mann-Whitney U test and Kruskal Wallis Test

Table 2 ABI interpretation and following procedure

ABI	Interpretation	Following procedure
> 1,3	Mediocalcinosis	Angiological examination Prevention according to the patient's risk profile
1,0 – 1,29	Normal values	Prevention according to the patient's risk profile
0,9 – 1,0	Borderline values	Repeat ABI, ABI after load Prevention according to the patient's risk profile
0,5 – 0,8	PAD	Angiological examination Prevention according to the patient's risk profile
< 0,5	A severe form of PAO	Early angiological examination Prevention according to the patient's risk profile

(14). The relationships between the investigated variables are significant when the corresponding p-value is: $p < 0.05$ (15). Tables and graphic presentation of the comparisons were made using the MS Excel program.

Results

The research sample group consisted of 151 patients, who were examined for the first time in the Angiological Outpatient Clinic at the Academician L. Dérer Hospital of the Bratislava University Hospital in the first half of 2015 and the first half of 2019 with a suspected diagnosis of peripheral arterial disease (Table 3). Of the 151 patients, 75 were men (49.7%) and 76 were women (50.3%). Patients were referred by general practitioners or other specialists (surgeon, diabetologist, internist, cardiologist, neurologist).

Table 3 Characteristics of the research sample group

Year of examination		2015	2019
Sex	M	12	63
		30,0%	56,8%
	F	28	48
		70,0%	43,2%
Age	mean	70,80	72,78
	median	72,00	72,00
BMI	mean	28,79	27,41
	median	28,47	26,99
RABI	mean	0,95	0,94
	median	0,95	0,93
LABI	mean	0,91	0,96
	median	0,95	0,93

In the first half of 2015, 12 men and 28 women were referred to the Angiology Outpatient Clinic. In the first half of 2019, it was 63 men and 48 women. Using Fisher's exact test, we found that the proportion of women in 2015 was statistically significantly higher (Fisher's exact test, $p = 0.004$).

We were also interested in the risk profile of the referred patients. By comparing the risk factors of patients referred in the first half of 2015 and of 2019, we found that the proportion of smokers increased statistically significantly (Fisher's exact test, $p=0.005$). The proportion of patients with hyperlipoproteinemia also increased by 15.8 percentage points, but it was not statistically significant (Fisher's exact test, $p=0.089$) (Table. 4).

We determined the body mass index (BMI) of the patients. We found that not even 27.8% of referred patients had a BMI>30 kg/m^2; 18.7% of men and 36.8% of women, which is a statistically significant difference using Fisher's exact test ($p=0.018$). Given the higher proportion of obese women, the higher proportion of female diabet-

Table 4 Risk factors present in patients referred in the first half of 2015 and 2019

Risk factors	2015 (40 patients)	2019 (111 patients)	p (Fisher's exact test)
Smoking	15 (37,5%)	70 (63,1%)	0,005
Hyperlipoproteinemia	20 (50 %)	73 (65,8%)	0,089
Diabetes mellitus	23 (57,5%)	64 (57,7%)	0,966
Arterial hypertension	38 (95,0%)	94 (84,7%)	0,104

Table 5 Risk factors in men and women

Risk factor	Men 75 (49,7%)	Women 76 (50,3%)	p (Fisher's exact test)
Smoking	51 (68,0%)	34 (44,7%)	0,005
Hyperlipoproteinemia	38 (50,7%)	50 (65,8%)	0,090
Diabetes mellitus	42 (56,0%)	45 (59,2%)	0,743
Obesity (BMI>30 kg.m^{-2})	14 (18,7%)	28 (36,8%)	0,018
Arterial hypertension	71 (95,0%)	64 (84,7%)	0,104

ics (59.2%) compared to male diabetics (56.0%) is not surprising, but using Fisher's exact test (p=0.743) this is not statistically significant.

We were also interested in the proportion of smokers between men and women. Of the referred men, 68% were smokers and 44.7% of the referred women were smokers. Using Fisher's exact test, this difference was found to be significant, p=0.005 (Table 5).

From the point of view of anamnestic data, specifically the leading clinical symptom of peripheral arterial disease - intermittent claudication, we observed only a slight increase of 2.3 percentage points over 4 years (40.0% in 2015, 42.3% in 2019), which was not statistically significant (Fisher's exact test, p=0.474) (Table 6).

From the point of view of a serious clinical finding regarding the occurrence of ulceration (which is a sign of the most serious involvement of PAD - critical limb ischemia), there was an increase of 25.6 percentage points after 4 years, which is statistically significant (in the first half of 2015 it was 5% of patients, and in the first half of 2019, it was 30.6% of patients (p=0.001, Fisher's exact test) (Table 6).

We found that in the first half of 2019, 3.5 times more patients with suspected peripheral arterial disease were referred than in the 2015. The share of general practitioners increased from 32.5 to 41.4%, (an increase of 8.9 percentage points, which is not statistically significant (Fisher's exact test, p=0.211) (table no. 7).

We were interested in the difference in the occurrence of individual risk factors between patients referred by specialists and general practitioners in individual years. Between the first half of 2015 and 2019, we did not detect statistically significant changes in smoking, hyperlipoproteinemia or arterial hypertension. However, the number of patients with diabetes mellitus increased statistically significantly (Fischer's exact test, p=0.11) (Table 8).

We were interested whether the patients who were referred used thromboprophylaxis in the form of antiplatelet or anticoagulant treatment. In the first half of 2015, 62.5% of patients had thromboprophylaxis, in the first half of 2019 it was 8.7 percentage points higher (71.2%). However, Fisher's exact test did not show that it was statistically significant (p=0.325).

Table 6 Clinical picture of the referred patients

Clinical picture	2015 40 patients	2019 111 patients	p Fisher's exact test
Claudication	16 (40,0%)	47 (42,3%)	0,797
Ulceration	2 (5,0%)	34 (30,6%)	0,001

Table 7 Patients referred by general practitioners (GPs) and by other specialists

Referring specialist	2015 40 patients	2019 111 patients
GPs	13 (32,5%)	46 (41,4%)
other specialists	27 (67,5%)	65 (58,6%)

Table 8 Risk factors of patients referred by general practitioners and specialists

Risk factor	General practitioner 59 patients	Other specialist 92 patients	Fisher's exact test p
Smoking	35 (59,3%)	50 (54,3%)	0,615
Hyperlipoproteinemia	38 (64,4%)	55 (59,8%)	0,610
Arterial hypertension	50 (84,7%)	82 (89,1%)	0,458
Diabetes mellitus	26 (44,1%)	61 (66,3%)	0,011

We found that 59.5% of patients who were referred with ulcerations (critical limb ischemia) died within three years of referral and 37.7% of referred patients without ulcerations died within 3 years of referral. The difference is statistically significant (p=0.020, Chi-square according to Pearson) (Table 9).

The odds ratio of death within 3 years of referral to an angiological outpatient clinic was 2.422 (95% confidence interval = 1.135-5.167). We can say that patients referred with ulceration have a 2.422 times higher chance of death within 3 years of being referred to an angiological outpatient clinic than patients without ulceration.

Discussion

The results of the PAOS study, which was devoted to PAD screening in the Slovak Republic, showed that of the 2,207 examined patients, 9.4% had a pathologically reduced ABI<0.9. Patients with pathologically reduced ABI had a significantly higher risk of myocardial infarction, angina pectoris and stroke. The affected were mostly men, smokers, diabetics, patients with hypertension, patients with dyslipoproteinemia and patients with lower education (7). In our retrospective study, we also confirmed the following fact: in 2015, there were 37.5% of smokers and in 2019 it was up to 63.1%. In 2015, there were 50% of patients with hyperlipoproteinemia and in 2019 it was 65.8%. In 2015, 57.8% of patients had diabetes mellitus and 57.7% in 2019. The proportion of hypertensive patients was high - in 2015, 95%, and in 2019 it was 84.7%.

Peripheral arterial disease of the limb arteries occurs in about 5-10% of the population older than 60 years, while its incidence is different in individual epidemiological studies depending on the diagnostic methods used to diagnose PAD (on the basis of anamnestic data or using instrumental examination methods). The choice of the investigated file is also decisive.

We state that in 2019, 3.5 times more patients were referred with suspected peripheral arterial disease than in 2015. The share of referring general practitioners increased from 32.5% to 41.4%, but this is not statistically significant. We assume that the higher proportion of general practitioners to referring specialists indicates a higher level of awareness among general practitioners. We assume that general practitioners also participate indirectly in the overall increase in patient referrals. Apparently, patients with ulcerations are primarily referred to surgeons, vascular surgeons, who after the initial examination of the patient consult an angiologist for the purpose of diagnostic clarification and further follow-up. This fact is also confirmed by the increased number of referred patients with ulcerations in 2019. The proportion of patients with ulcerations (which is a sign of the most serious involvement of PAD - critical limb ischemia) increased after 4 years by 25.6 percentage points, which is statistically significant (p=0.001, Fisher's exact test). In our research sample group, patients with ulcerations were sent for angiological examination by specialists other than general practitioners statistically significantly more often (p<0.001, Fisher's exact test).

We expected the mortality of patients with critical limb ischemia to be high, but we were surprised that the findings were statistically significant in a not so large cohort. We found that 59.5% of patients who were referred with ulcerations (critical limb ischemia) died, which is statistically significantly more in contrast to patients referred without ulcerations (37.7%) -(p=0.020 Chi-square according to Pearson).

Conclusion

In the 21st century, peripheral artery disease has become a global problem. Governments, NGOs as well as the private sector must address the social and economic implications and evaluate the best strategies for optimal

Table 9 Survival of patients referred with and without ulcerations

Patient condition within 3 years of referral	ulceration 37 patients	without ulceration 114 patients
alive	15 (40,5%)	71 (62,3%)
exitus	22 (59,5%)	43 (37,7%)

prevention and treatment of peripheral artery disease (16).

From a public health point of view, we can say that general practice medicine in the Slovak Republic has seen significant professional development over the last decade. One of the important milestones is also the inclusion of ABI measurement by an automatic device using the oscillometric method in the preventive examination of patients over 50 years of age with risk factors and in all patients over 60 years of age. The measurement of ABI as well as the expansion of competences by the possibility of carrying out pre-operative examinations, the expansion of competences and prescription options all broaden the experience of general practitioners, who can thus, with greater knowledge, make decisions even in the differential diagnosis of pain in the lower limbs. Based on our work, we believe that in smokers and diabetics, it is worth considering performing the ABI measurement in younger age groups.

After treatment at a specialized vascular clinic, such a patient returns to ambulatory care. The general practitioner has a great responsibility in the subsequent management of atherosclerosis risk factors (careful monitoring and treatment of arterial hypertension, hyperlipoproteinemia, diabetes mellitus, influencing the patient's weight and motivating the patient in their physical activities) (17). Whether the result of the revascularization procedure will have long-term clinical success and will result in prolongation of life and improvement of its quality depends on this. Interest in a healthy lifestyle (healthy eating, stress prevention, active participation in screening programs, common physical activities) is a good starting point for the creation of communities of patients, which have great motivational potential (18).

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